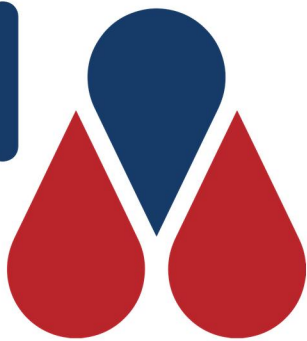




Blood 2026



Auckland, New Zealand
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Abstract Book

The combined Conference of the:



Contents

Oral and Invited presentations

Ordered by session

SOCIETY	SESSION	PAGE
NURSES	Symposium · Patient-centered care and free communications	2
NURSES	Symposium · Transplant and cellular therapies	5
ANZSBT	Presidential Symposium	9
HSANZ	Free Communications 1 · Acute leukaemia and MDS	21
HSANZ	Free Communications 2 · Myeloma	30
HSANZ	Free Communications 3 · CLL / basic science lymphoid malignancy	39
HSANZ	Free Communications 4 · CML and classical MPN	49
NURSES	Free Communications · Myeloma	57
THANZ	Free Communications 1 · Perspectives in thrombosis and haemostasis	60
HSANZ	Presidential Symposium	68
THANZ	Presidential Symposium	77
HSANZ	Free Communications 5 · Stem cell transplantation	85
NURSES	Symposium · Thrombosis and haemostasis	95
NURSES	Symposium · Abstracts and invited speaker	96
ANZSBT	Free Communications 2 · Science	104
HSANZ	Free Communications 6 · Aggressive lymphoma	110
HSANZ	Free Communications 7 · Advancing patient outcomes more than the latest treatment	122
NURSES	Symposium · Transfusion-related nursing	129
THANZ	Free Communications 2 · Small but mighty: Platelets	133
HSANZ	Free Communications 10 · Navigating inborn errors to autoimmunity	141
HSANZ	Free Communications 8 · Albert Baiki Memorial Medal	146
HSANZ	Free Communications 9 · Low-grade lymphoma	155
NURSES	Free Communications · Leukaemia and lymphoma	164
HSANZ	Free Communications 11 · Pre-clinical cell biology and novel diagnostic approaches	167
NURSES	Symposium	175

Posters

Ordered by society and theme

SOCIETY	THEME	PAGE
ANZSBT		
	Clinical	179
	General	205
	Haemovigilance/Patient Blood Management	239
	Quality Improvement	258
	Scientific	278
HSANZ		
	Acute leukaemia	294
	BMT	355
	CLL	388
	CML	403
	Lymphoma	408
	MDS	471
	MPD	485
	Myeloma	493
	Non-malignant	544
	Supportive care	589
NURSING	All posters	611
THANZ	All posters	628

Equity-Driven Support Service Innovation: Improving Access to Blood Cancer NZ Services for Māori and Pacific Whānau

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Aim:

Inequitable access to supportive care services contributes to disparities for Māori and Pacific peoples affected by blood cancer in Aotearoa New Zealand. This study evaluates an equity-focused national model designed to improve access to, and utilisation of, Blood Cancer New Zealand support services among priority populations.

Method:

A national service redesign was implemented, including strengthened referral pathways, targeted regional expansion, and culturally responsive models of care. Key approaches included dedicated Māori and Pacific support groups, partnerships with Māori health providers and Pacific community networks, and collaboration with kaiawhina and clinical teams to support engagement with BCNZ services. Tailored health literacy resources, rural outreach, and access to financial and psychosocial support were also introduced to address barriers to utilisation.

Results:

Overall service utilisation increased by 6% (n=1,801 referrals), with BCNZ reaching 58% of all diagnosed patients and whānau. Māori and Pacific referrals doubled from 8% to 16% year-on-year, equating to a combined reach of 64%. Pacific utilisation reached 83%, while Māori utilisation reached 55%, demonstrating substantial gains alongside ongoing inequities in access.

Conclusion:

Equity-focused service design can significantly improve utilisation of supportive care services among underserved populations. Case studies will demonstrate how culturally responsive and community-connected approaches enabled engagement with high-needs whānau in practice. Sustained and targeted investment is required to address remaining inequities for Māori and embed equitable access across supportive cancer care services.

Implementation of a regional shared care clinic for early post-acute CAR T-cell therapy toxicity management: A nurse-led and patient centred model of care.

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Aim:

To implement and evaluate an outpatient nurse-led clinic for Chimeric Antigen Receptor T-cell therapy (CAR-T) early post-acute patient follow-up at University Hospital Geelong (UHG), a regional health service in Victoria, Australia.

Method:

The CARER-T study (HREC/BH/2026/533904) will prospectively evaluate patients referred for standard of care CAR-T for appropriateness for early transfer back to UHG for outpatient CAR-T toxicity management. This will occur through collaboration between the referring haematologists at UHG and Peter MacCallum Cancer Centre. Disease indications currently include Large B-cell Lymphoma (LBCL), B-cell Acute Lymphoblastic Leukaemia and Mantle Cell Lymphoma, and the commercially approved CAR T-cell products Axicabtagene Ciloleucel, Tisagenlecleucel, Brexucabtagene Autoleucel. Cohort allocation will incorporate risk assessment for cytokine release syndrome (CRS) and immune effector cell-associated neurotoxicity (ICANS), using variables including disease burden, CAR-T product, consideration of co-morbidities, and clinical stability following CAR-T. Cohort framework (Table 1) has been developed from recent evidence identifying that patients treated with CAR-T for LBCL, most have resolution of CRS and ICANS within two weeks, and once resolved these toxicities are unlikely to reoccur after three consecutive days.^{1,2} To ensure patient safety and support stepwise development of clinician competency at UHG, a graduated approach to regional transfer will be implemented. Progression through cohorts will occur once target recruitment to initial cohorts is achieved and evaluation of toxicities, management and response has been reviewed. Patients who are not appropriate for Cohort 2 or 3 may be allocated to earlier cohorts at any time throughout the study.

Table 1: Cohort allocation for post CAR T-cell therapy toxicity management

	Day of transfer to UHG following CAR-T Infusion	N
Cohort 1	Day +14 or 3 days following CRS and ICANS resolution, whichever occurs later.	3-6
Cohort 2	Day +7 to +13	3-6
Cohort 3	Day 0-1	3-6

Results:

Currently enrolling, preliminary data will report transfer activity and early safety including toxicity monitoring and interventions.

Conclusion:

By embedding a regional CAR-T early shared care model, this project will enhance the workforce expertise at UHG, reduce unnecessary dislocation for patients and carers, allow

for continuity of care, mitigate psychosocial burdens associated with relocation and deliver high-quality cancer care closer to home. Together these outcomes directly support the Australian Cancer Plan objectives for equitable cancer care.

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ReFRESHing autologous stem cell transplantation - The Christchurch transplant programme's experience using fresh stem cells for myeloma patients

Ms Jenny Roberts

Aim:

Autologous stem cell transplantation (ASCT) remains standard of care for eligible patients with multiple myeloma. While cryopreservation of peripheral blood stem cells is routine, infusion of fresh, non-cryopreserved products offers streamlined pathways for patients, alongside logistical and cost advantages.

Method:

Since January 2025, our centre has implemented the use of fresh autologous stem cells for myeloma patients. Neutrophil and platelet engraftment times, infusion-associated adverse events, blood product transfusion requirements, and resource utilisation were compared with historical controls extracted from our in-house transplant and New Zealand Blood Service (NZBS) databases.

A systematic literature review was undertaken to examine practice patterns at other centres and to quantify the frequency of fresh cell infusion utilization in multiple myeloma.

Results:

As of May 2026, fresh stem cells have been successfully infused in approximately 60 patients. Median time to neutrophil and platelet engraftment was comparable to or faster than that observed with historical cryopreserved controls. Infusion-associated side effects were minimal. Patient-reported outcomes indicated favourable experiences, including reduced wait time for treatment, minimal infusion-related adverse effects, and a streamlined treatment trajectory.

The findings are consistent with those found at other centres using fresh cell infusions for myeloma patients.

Conclusion:

In this single centre experience, fresh autologous stem cell transplant represents a safe and streamlined approach to patient care.

Additional benefits include reduced storage requirements and associated costs.

Ongoing data collection will include progression-free survival (PFS) and overall survival (OS) for comparative analysis with historical cohorts.

Building a skilled and confident CAR-T Nursing workforce: Assessing the impact of nurse-led CAR-T education.

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Aim:

To evaluate the impact of a nurse-led CAR-T education day on participants' knowledge and confidence in caring for patients receiving CAR-T Cell therapy.

Methods:

A multidisciplinary curriculum was developed to cover CAR-T mechanisms of action; leukapheresis and cell processing; clinical signs and management of toxicities; clinical trials; and medication management. A pre- and post-education survey assessed self-reported knowledge and confidence. Knowledge was measured using a 5-point Likert scale (1='Very poor understanding' to 5='Very good understanding') while confidence rated on a 10-point scale (0='Not at all confident' to 10= 'Extremely confident'). Independent samples t-tests compared pre- and post- education scores, with a statistical significance set at 0.05.

Results:

Nine CAR-T education days were conducted between March 2023 to November 2025, involving 255 participants. Pre-education surveys were completed by 239 participants, and post-education surveys by 218 participants. Attendees included registered nurses (47.1%), clinical trial coordinators (21%), nurse managers (9.2%), clinical nurse specialists (6.2%), clinical nurse consultants (5%), nurse educators (2.5%), ICU liaison nurses (2.5%), scientists (1.5%), and others unspecified health professionals (5%).

Significant improvements in self-reported knowledge were observed across all domains, including CAR-T Cell mechanisms of action (median 3.04 to 4.49); patient eligibility criteria, workup, and apheresis (median 2.54 to 4.30); role of the cellular therapies unit (median 2.64 to 4.32); daily nursing care (median 3.17 to 4.53); CRS assessment and management (median 3.32 to 4.57); ICANS assessment and management (median 3.24 to 4.58); CAR-T medications (median 2.77 to 4.44); Discharge patient education (median 2.73 to 4.39); and Outpatient nursing care (median 2.66 to 4.36) (all $p < 0.001$). Confidence in caring for patients receiving CAR-T therapy improved significantly (median 5.20 to 8.18, $p < 0.001$).

Conclusion:

A structured, nurse-led CAR-T education program significantly improves nursing knowledge and confidence, directly supporting safe and effective CAR-T patient care.

Criteria based approach to management of grade three Immune Cell Associated Neurotoxicity Syndrome (ICANS), a single centre experience

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Aim:

Chimeric antigen receptor (CAR) T-cell therapy is standard of care (SOC) therapy for relapsed/refractory (R/R) B-cell malignancies in Australia. Toxicity with Cytokine Release Syndrome (CRS) or Immune Cell Associated Neurotoxicity Syndrome (ICANS) often require care in intensive care unit (ICU). An analysis of our database identified half of patients admitted to ICU did not require intervention, with grade 3 ICANS the most common indication for admission. We amended our internal toxicity management policy, to provide a criteria-based approach for ICU admission for G3 ICANS, rather than a mandatory admission criterion.

Method:

A retrospective analysis of a prospectively collected database for patients treated with CD19 CAR T-cell therapy products was conducted. All patients infused between 15/04/2019 and 31/12/2025 at the Peter MacCallum Cancer Centre and Royal Melbourne Hospital. Descriptive statistics were used to summarise ICU resource utilisation.

Results:

Of 308 infusions, 19% required ICU admission. Grade ≥ 3 ICANS was the most common indication with 67% admissions, followed by 24% for grade ≥ 3 CRS. Of all patients admitted to ICU, 56% did not require ICU intervention. Following policy implementation, 50% (n=3) of patients with G3 ICANS have been managed safely on our inpatient haematology ward.

Conclusion:

Our ICU data analysis indicated a potential indication for change in mandatory admission for G3 ICANS. Small numbers currently indicate patient and safe safety, while ensuring appropriate resource utilisation. Ongoing data and analysis will be provided, including our clinical deterioration policy and new toxicity management protocol.

Phase I development of a core outcome set for immunoglobulin replacement therapy in haematological malignancies for use in both clinical research and routine clinical data collection

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Aim:

Core outcome sets (COS) are agreed-upon outcomes used to improve inter-study comparability and data reporting. The NHMRC-funded OPTIMAL Centre of Research Excellence are developing a COS for immunoglobulin (Ig) clinical research and routine data collection to improve the evidence for Ig use for infection prophylaxis in blood cancers. The present study reports phase I, which aims to identify all possible outcomes that could be included in a COS and identify any barriers to the collection of routine clinical data.

Method:

COS development uses the COMET¹ methodology. Phase I comprises a descriptive qualitative study using online semi-structured interviews to data saturation to understand the perspectives of various stakeholders, including exploring potential implementation barriers to routine data collection. Interviews were transcribed and analysed using a hybrid reflexive thematic and content analysis approach. Identified outcomes were triangulated with included studies from a Cochrane review² assessing the evidence for Ig use for infection prophylaxis in blood cancers.

Results:

Ten people were interviewed: 4 patients, 4 clinicians and 2 lab staff. Identified outcomes were classified using the Outcomes Measurement Framework and broadly included; mortality and infection; outcomes related to symptoms, function and quality of life; and outcomes related to feasibility, resource use, and adherence. No outcomes related to pain, mental health or psychosocial needs were identified. The barriers to collecting Ig data in routine clinical practice were identified as resourcing, data ownership, privacy, and reporting. Patient participants felt they could self-report infection data, whilst clinicians were most concerned about resourcing for data collection.

Conclusion:

Phase I of the COS development is complete and has identified possible outcomes that could be included in the COS. Phase II will involve a Delphi process followed by a stakeholder meeting to reach consensus on the final COS and to develop definitions and measures, as needed.

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Lessons learned from using artificial intelligence to detect transfusion-associated circulatory overload from unstructured data in electronic medical records: A single-hospital pilot study

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Aim:

Detection of serious adverse transfusion reactions, such as transfusion-associated circulatory overload (TACO) reactions relies on clinician recognition and reporting to institutional haemovigilance committees. The reported incidence of TACO varies from 1.1-2.7% of transfused patients, a likely underestimation. There is scant work with artificial intelligence (AI) as a tool to detect transfusion-related adverse events using unstructured data within electronic medical records.

Method:

We used CogStack, a natural language processing tool that utilises unstructured data, to identify admissions with possible TACO reactions, prior to 7 December 2024 from a single hospital. Using keywords relating to fluid status, oxygenation, comorbidities and medications, transfused patients were classified as having a TACO reaction, no TACO reaction, or 'TACO could not be ruled out'. These cases were loaded into a clinical review tool for clinician validation, and this was used to label more data and retrain models, improving performance iteratively.

Results:

The model initially predicted 20,783 TACO reactions were present in 51,015 patient admissions (40.7%). Over two model iterations, a clinician reviewed a total of 299 admissions which were enriched for predicted TACO events, of which the clinician identified 12 TACO cases (4% of reviewed cases) and could not rule out TACO in a further 31 admissions (10.4% of reviewed cases). CogStack identified all TACO cases and 21 out of 31 cases where TACO could not be ruled out (68%). The accuracy of the model was 0.39, sensitivity was 0.78, specificity was 0.32 and the negative predictive value was 0.89.

Conclusion:

Use of CogStack tools to identify TACO from unstructured data show suboptimal sensitivity and specificity. This was likely due to the low incidence of TACO reactions and ambiguity of information from medical records. A successful iteration of this model could aid haemovigilance committees in screening for transfusion adverse reactions rather than relying only on clinician reporting.

Perioperative haemostatic changes in neonates undergoing cardiopulmonary bypass: insights from the BABies Study

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¹Murdoch Children's Research Institute, Parkville, Australia, ²The University of Melbourne, Parkville, Australia, ³The Royal Children's Hospital, Parkville, Australia, ⁴Walter and Eliza Hall Institute, Parkville, Australia, ⁵Institute for Clinical and Translational Research, Johns Hopkins All Children's Hospital, St. Petersburg, USA, ⁶Johns Hopkins University, , USA

Aim:

To compare perioperative proteomic profiles in neonates undergoing cardiopulmonary bypass with and without clinically significant intraoperative post-CPB bleeding across defined perioperative timepoints.

Method:

Neonates (0-1 month) undergoing cardiac surgery at the Royal Children's Hospital (RCH) were enrolled after obtaining informed consent from parents/guardians. This study was approved by the RCH Human Research Ethics Committee. Citrated plasma samples were collected from an indwelling arterial line at baseline (pre-CPB), pre-protamine (post-CPB), post-protamine and approximately 12 hours post-surgery and then stored at - 80°C. Data-independent acquisition mass spectrometry (DIA-MS) analysis was conducted on neat plasma samples from 12 patients who had intraoperative post-CPB bleeding and 12 who did not. Patients were defined as bleeders if they received prothrombin complex concentrate or recombinant factor VIIa, or were in the top quintile of both platelet and cryoprecipitate transfusions between the end of CPB and leaving the operating room. Differential expression and global longitudinal analyses were performed to examine differences in the proteomes between bleeders and non-bleeders.

Results:

Differential expression analysis determined the abundance of 30 to 62 proteins across time points were significantly different between bleeders and non-bleeders.

Global longitudinal analysis identified 12 proteins with significant temporal variation across the peri-operative period (Figure 1).

These proteins demonstrated differential trajectories between bleeders and non-bleeders, consistent with altered dynamic haemostatic responses.

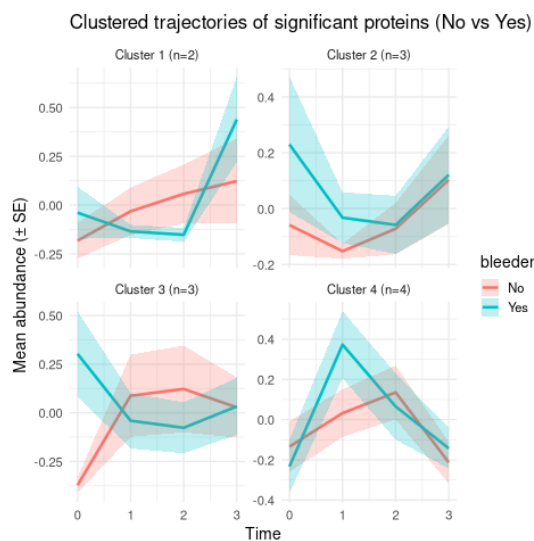


Figure 1. Clustered trajectories of significant proteins in bleeders and non-bleeders across the perioperative time points. (0 = baseline, 1 = pre-protamine, 2 = post-protamine, 3 = morning after surgery).

Conclusion:

Perioperative proteomic profiling identifies dynamic, trajectory-based differences in haemostatic pathways between bleeders and non-bleeders, advancing understanding of the biological processes underpinning bleeding following cardiopulmonary bypass in neonates.

These findings provide a foundation for biomarker-driven risk stratification and the development of targeted, time-specific interventions to improve bleeding management in this high-risk population.

Culturally safe blood donation and transfusion from an Aboriginal and/or Torres Strait Islander perspective

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Background:

Aboriginal and/or Torres Strait Islander peoples are underrepresented in blood donation and may face barriers to engaging with transfusion services (Hawkins & Gillett, 2015; Perry, 2025). The limited incorporation of Culturally Safe, informed approaches to donation and transfusion practices may contribute to ongoing inequities in healthcare experiences and outcomes.

Aim:

To explore Aboriginal and/or Torres Strait Islander peoples' perspectives on blood donation and transfusion and identify considerations for Culturally Safe practice.

Methods:

This qualitative study was grounded in Indigenous Knowledges methodology (Rigney, 1999). Individual yarning was undertaken with Aboriginal and/or Torres Strait Islander participants (n=12). Data were analysed thematically, privileging Indigenous ways of knowing, being, and doing across both data generation and interpretation (Rigney, 1999).

Results:

Participants described complex and relational understandings of blood donation and transfusion. Donation was often framed as an act of care, reciprocity, and community contribution. However, concerns were raised regarding the movement of blood, its connection to identity, and trust in healthcare systems. Historical public health messaging shaped perceptions of safety. Participants emphasised the importance of Culturally Safe care, including clear communication, trust-building, and recognition of Indigenous identities. Preferences for culturally respectful processes and donor identity were also highlighted, with some expressing comfort in receiving blood from an Aboriginal donor if available via an Aboriginal Blood Bank.

Conclusion:

Culturally Safe approaches to blood donation and transfusion require embedding Aboriginal and/or Torres Strait Islander perspectives into policy and practice. Strengths-based, relational approaches that prioritise trust, transparency, and cultural respect are essential to improving engagement and care experiences. The expressed desire for an Aboriginal Blood Bank further highlights the importance of identity, sovereignty, and cultural connection within blood donation and transfusion systems for Aboriginal and/or Torres Strait Islander peoples.

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Aseptic meningitis with immunoglobulin therapies in New Zealand

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Background:

The New Zealand Blood Service (NZBS) manages a national haemovigilance programme that captures adverse events related to transfusion, fractionated plasma products, and blood donation. Reported adverse events are reviewed and analysed to identify potential safety signals and to inform the clinical community of emerging concerns.

Aim:

To examine reports of aseptic meningitis associated with immunoglobulin (Ig) therapies received by NZBS between 2005 and 2025.

Method:

Adverse event reports from New Zealand hospitals are submitted to NZBS and recorded into the haemovigilance reporting system. All fractionated product reports are reviewed, and serious reports are evaluated by Transfusion Medicine Specialists to determine event type, severity, and imputability. Fractionated product reports are forwarded to the manufacturer in a de-identified format. Finalised data are then extracted, cleaned, and analysed using descriptive statistics.

Results:

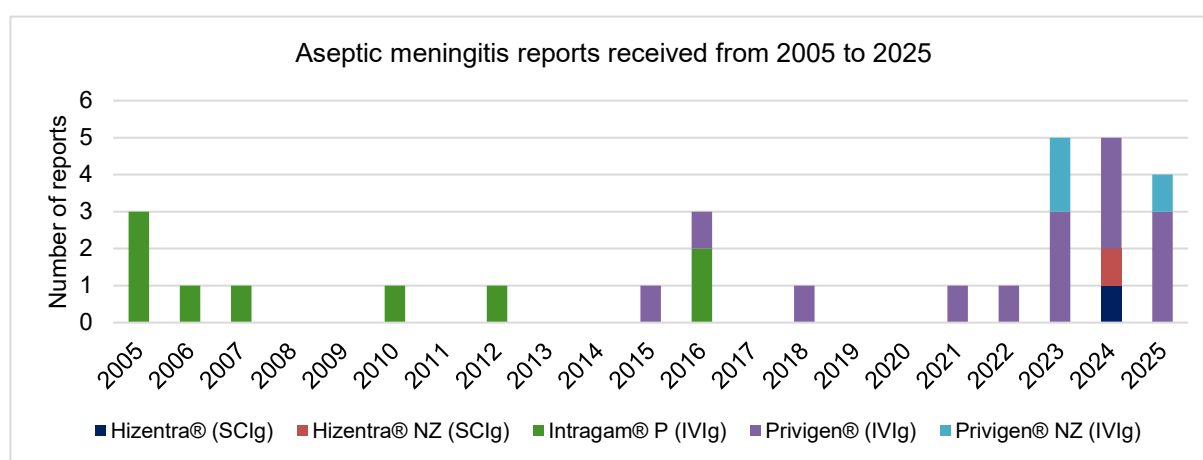


Figure 1. Aseptic meningitis with immunoglobulins - 2005 to 2025

In earlier years, Intragam® P was the primary intravenous immunoglobulin (IVIg) nationally. Seven reports of aseptic meningitis related to Intragam® P were received between 2005-2014 (Figure 1). Privigen® was introduced in NZ in 2015, with Privigen® NZ following in mid-2023. From 2023 onwards, Privigen® and Privigen® NZ became the dominant Ig products nationally. An increase in reports of aseptic meningitis was observed between 2023-2025. This increase may reflect changes in product availability and increased pharmacovigilance awareness and reporting. Although international literature describes cases of IVIg-associated aseptic meningitis,^{1,2} the NZBS dataset also includes reports linked to subcutaneous (SC) Ig. Notably, SCIg-associated aseptic meningitis is less frequently reported in the literature, and some anecdotal evidence supports switching from IVIg to SCIg following such events.

Summary / Conclusions:

Since 2023, NZBS has observed an increase in reports of aseptic meningitis associated with Ig therapies. The underlying reasons for this trend remain unclear and further investigation is required. The NZBS haemovigilance programme will continue to monitor these reports and identify practice points to mitigate the risk (and recurrence) of aseptic meningitis.

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Multiplex prime editing enables safe, drug-controllable and immunosuppression-resistant T-cell therapies in vivo

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Aim:

To develop a multiplex prime-editing platform that corrects pathogenic variants in primary patient T-cells and installs resistance mutations to commonly used immunosuppressants, converting standard drugs into tools for *in vivo* selection.

Method:

Primary T-cells from healthy donors and patients with *HAVCR2*-driven subcutaneous panniculitis-like T-cell lymphoma (SPTCL) were prime edited using optimized pegRNAs. Editing efficiency was quantified by targeted sequencing. Off-target effects were evaluated using CIRCLE-seq, transcriptional profiling, immunophenotyping, and TCR sequencing. Drug-resistance variants were introduced into the targets of tacrolimus (*FKBP1A*), methotrexate (*DHRF*) and mycophenolate (*IMPDH2*). Functional validation was performed *in vitro* and in NSG xenografts models under immunosuppression. The platform was extended to CD19 CAR and CMV-specific virus-specific T-cells (VSTs).

Results:

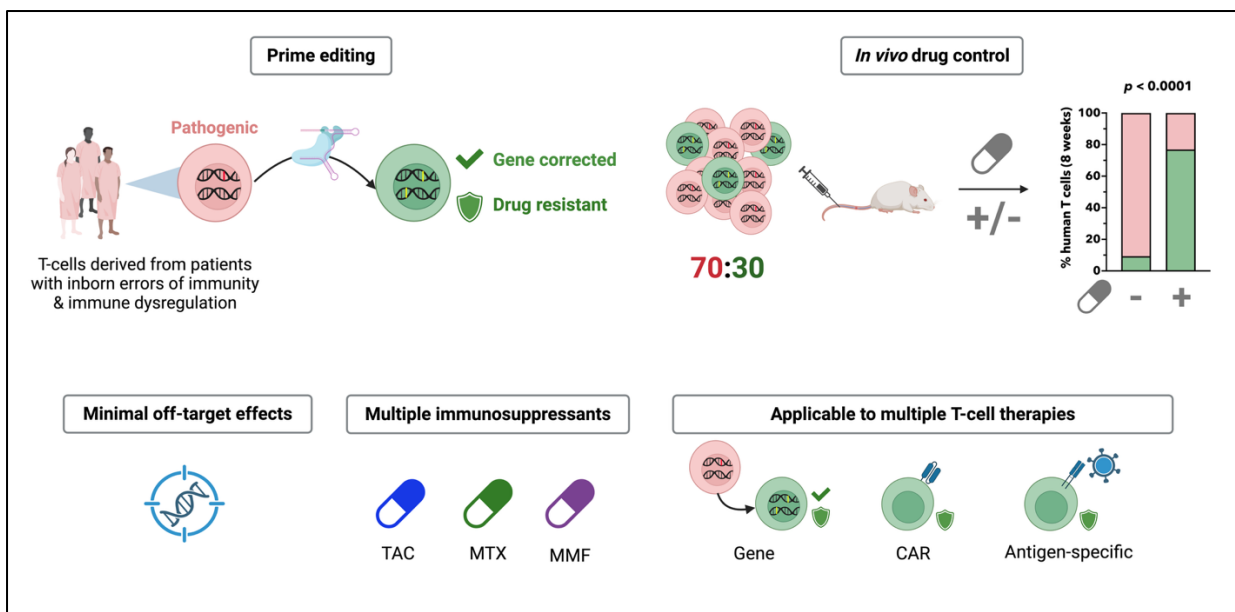
Prime editing corrected multiple disease loci with minimal indels (mean 1.8%), and approximately 30-fold higher edit-to-indel ratios compared to Cas9/HDR. In SPTCL patient T-cells (n=3), optimized editing corrected 18.7–35.8% (mean 29.8%) of *HAVCR2* alleles and restored TIM-3 surface expression.

Drug-resistance variants conferred resistance to tacrolimus, methotrexate, or mycophenolate while preserving sensitivity to alternative agents, providing an intrinsic safety mechanism. *FKBP1A*-edited T-cells maintained proliferation and IFN- γ production under tacrolimus exposure. Editing of *HAVCR2* and *FKBP1A* enabled robust *in vivo* enrichment. Corrected *HAVCR2* alleles increased from approximately 10% at infusion to 76.8% in tacrolimus-treated mice, with no enrichment in vehicle-treated controls. Conversely, sensitivity of *FKBP1A*-edited cells to cyclosporin *in vivo* was comparable to unedited cells, confirming bidirectional drug control.

Tacrolimus-resistant CD19 CAR and CMV-specific T-cells exhibited preserved effector function under immunosuppression, demonstrating broad applicability of the platform.

Conclusion:

Prime editing enables precise correction of pathogenic variants and programmable resistance to widely used immunosuppressants without detectable off-target effects. This approach transforms standard immunosuppressants into clinically familiar tools for *in vivo* selection and control of therapeutic T-cells, supporting translation toward first-in-human clinical evaluation.



Outcomes of patients with relapsed/refractory FLT3mut+ acute myeloid leukemia who resumed gilteritinib therapy after HSCT: Post hoc analysis from the ADMIRAL and COMMODORE trials

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Aim:

This pooled analysis of ADMIRAL (NCT02421939) and COMMODORE (NCT03182244) evaluated overall survival (OS) in 2 subgroups of patients with relapsed/refractory (R/R) *FMS*-like tyrosine kinase 3-mutated (*FLT3*^{mut+}) acute myeloid leukemia (AML): (1) patients who did vs did not receive allogeneic hematopoietic stem cell transplantation (HSCT) during the study period independent of prior treatment; (2) gilteritinib-treated patients who received HSCT during the study period, were relapse-free at day 60 post-HSCT and resumed gilteritinib vs those who did not resume gilteritinib.

Method:

All randomized patients were pooled and summarized by HSCT status. Gilteritinib-treated patients were allowed to resume gilteritinib post-HSCT if specific criteria were met.

Results:

Of 647 total patients, 125 (19.3%) received HSCT during the study period. Of these, 95 (76.0%) were gilteritinib-treated; 58 (61.1%) resumed gilteritinib post-HSCT. Median (95%

CI) follow-up for OS was 42.0 (37.1–46.1) and 37.1 (35.4–38.4) months in patients who did and did not receive HSCT during the study period; median (95% CI) OS was 24.1 (18.8–not estimable [NE]) and 7.4 (6.6–8.3) months, respectively (Mantel-Byar $p < 0.0001$). In patients who received vs did not receive HSCT, OS rates at 6, 12, 24 and 36 months were 92.5% vs 58.8%, 67.7% vs 26.0%, 50.3% vs 12.7%, and 44.9% vs 8.1%, respectively. Among gilteritinib-treated HSCT recipients who were relapse-free at day 60 post-HSCT, 54 resumed gilteritinib and 28 did not. Median OS (95% CI) was NE (16.8–NE) vs 10.1 (3.8–17.4) months in patients who did and did not resume gilteritinib, respectively. In patients who resumed vs did not resume gilteritinib, 6-, 12-, 24- and 36-month OS rates were 83.3% vs 59.6%, 68.5% vs 47.7%, 62.8% vs 26.0% and 60.8% vs 26.0%, respectively.

Conclusion:

In patients with R/R *FLT3*^{mut+} AML, long-term survival was strongly associated with receipt of HSCT, specifically for gilteritinib-treated patients who resumed gilteritinib post-HSCT.

Integrating leukemia stem cells into minimal residual disease evaluation predicts survival of acute myeloid leukemia

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Aims:

Multiparameter flow cytometry (MFC) immunotyping with different antibody combinations to detect minimal residual disease (MRD) has the characteristics of wide applicability, high sensitivity and strong specificity, which is of great value for the prognosis of AML patients and has been included in the clinical decision-making of AML. Although current MRD assessment by MFC includes the monitoring of leukemic myeloid progenitor cells, it may not accurately detect the relapse-initiating leukemia stem cells (LSCs) from the CD34⁺CD38⁻ pool. This study aimed to evaluate the performance of a one-tube-ten-color antibody panel detecting LSCs and the prognostic value of integrating LSCs into MRD in an AML cohort.

Methods:

A follow-up cohort containing 247 AML cases with MRD results by MFC was retrospectively reanalyzed for LSCs with known LSC markers (CD34, CD38, CD7 and CD56) included in the MRD panel. Meanwhile, a redesigned one-tube-ten-color panel including CD45, CD34, CD38, CD123, CD45RA, CLL-1, CD56, TIM-3, CD117 and CD7 was prospectively used to detect LSC in 99 newly diagnosed AML and a follow-up cohort containing 242 patients. Additionally, Kaplan-Meier curves were used to examine the prognostic value of LSCs combined with either MFC-MRD or molecular-MRD on leukemia-free-survival.

Results:

CD123, CD45RA, and CD56 demonstrated their diagnostic significance. LSCs integrated into MRD evaluation would more precisely stratify AML patients with differential overall survival. Furthermore, the heterogeneity of immunophenotypes of the CD34⁺CD38⁻ LSCs was revealed.

Conclusion:

LSCs may serve as a critical biomarker for risk stratification in AML patients. Monitoring the LSCs levels may provide important prognostic information, helping to classify patients based on their risk of relapse and overall survival outcomes. The expression of LSC markers can provide a basis for developing more precise and efficient MFC panel in the future. Our findings offer significant insights into personalized treatment planning for AML, improving clinical decision-making and patient outcomes.

AML with RAS pathway mutations is resistant to venetoclax but sensitive to GM-CSF neutralisation

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Aim:

Acute myeloid leukaemia (AML) with a monocytic phenotype is associated with resistance to venetoclax (Ven) therapy and poor survival. We have recently observed durable clinical and molecular responses to the anti-GM-CSF antibody therapy lenzilumab (Lenz) in combination with azacitidine (Aza) in patients with high-blast-count RAS pathway-mutant chronic myelomonocytic leukaemia (CMML) at increased risk of AML transformation in the PREcision Approach to CHronic Myelomonocytic Leukaemia (PREACH-M; ACTRN 1262100022383) clinical trial. We therefore aimed to investigate whether RAS pathway-mutant secondary AML (sAML) transformed from CMML may respond to Lenz in combination with Ven/Aza.

Method:

CRISPR-edited human cord blood-derived CD34+ cells and CMML/sAML patient mononuclear cells were assayed for proliferation and colony-formation in the presence of Ven, Aza and/or Lenz.

Results:

CRISPR-editing of RAS pathway-mutant genes conferred hypersensitivity to the pro-inflammatory cytokine GM-CSF, consistent with findings in patient-derived mononuclear cells, and this effect was abrogated by Lenz. We also confirmed that sAML (CMML>AML) is highly resistant to Ven (mean IC₅₀ 1.8±0.5 µM), but retains spontaneous colony-forming capacity that is sensitive to Lenz. Colony suppression by Lenz was significantly greater than Ven or Aza alone or in combination, but comparable to Ven/Aza/Lenz triple therapy. Based on these findings, a patient with sAML resistant to Ven/Aza after 8 cycles was treated with Ven/Aza/Lenz triple therapy. Treatment was well-tolerated and the patient showed a durable response following 10 cycles, remaining on therapy, transfusion-independent, with no acute admissions over 11 months.

Conclusion:

We demonstrate that venetoclax-resistant RAS pathway-mutant AML transformed from CMML is sensitive to GM-CSF neutralisation. Encouraging real-world clinical data of a patient with sAML safely receiving Lenz in combination with standard-of-care Ven/Aza supports GM-CSF neutralisation as a potential therapeutic strategy for Ven-resistant AML.

Development of same-day comprehensive molecular diagnostics in acute leukaemia using long-read sequencing

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Aim

Molecular diagnostics in acute leukaemia are fragmented across cytogenetics, FISH and targeted DNA/RNA next generation sequencing, with clinically impactful results often returned after commencement of empirical therapy. We aimed to develop a novel long-read wet lab and bioinformatic workflow to deliver integrated acute leukaemia genomic classification within hours of sample receipt (Fig. 1).

Methods

PCR-free library preparation was performed with adaptive sampling of 223 leukaemia-relevant loci, real-time base-calling and methylation inference was performed using the Oxford Nanopore P2-solo long-read sequencer with directly attached high-performance compute. Between January and April 2026, 30 suspected or confirmed acute leukaemia cases were analysed comprising 23 non-APL AML, 3 APL, 3 ALL and 1 DLBCL.

Results

Custom bioinformatic workflows addressing long-read diagnostic gaps and short-read limitations were developed including (i) adaptive-sampling-aware low-coverage whole genome copy-number calling (ii) automated structural-variant prioritisation inside adaptive loci, (iii) a novel tandem-duplication caller for *FLT3*-ITD and *UBTF*-TD. Dropout-aware methylation classification was performed across 38 acute leukaemia classes using the MARLIN neural network. DNA-to-result turnaround for karyotype and methylation class prediction was 6-10 hours across all samples. At 60 minutes of sequencing, adaptive-sampling-aware copy-number calling produced karyotype-concordant profiles in 18/18 evaluable cases and methylation classification assigned the correct disease category in 19/23. After 24 hours, structural-variant and tandem-duplication calling detected *UBTF*-TD in 4/4 cases and a novel *NAB2::RARA* fusion in a variant APL missed by methylation. Subgroup-defining driver lesions were detected in 29/29 cases, including *ZNF384*-R, *BCL11B*-R, *TLX1*-R, *PML::RARA*, *BCR::ABL1*, *CBFB::MYH11*, *RUNX1::RUNX1T1*, *KMT2A*-R, and *NPM1* and *CEBPA* variants.

Conclusion

Long-read sequencing with adaptive sampling enables integrated copy-number, methylation and structural-variant classification, allowing comprehensive molecular subclassification within 6-10 hours of DNA extraction – a potentially disruptive advance in acute leukaemia diagnostics. Prospective cohort expansion is underway to refine classifier thresholds for underrepresented subgroups and define orthogonal confirmation pathways for clinical deployment.

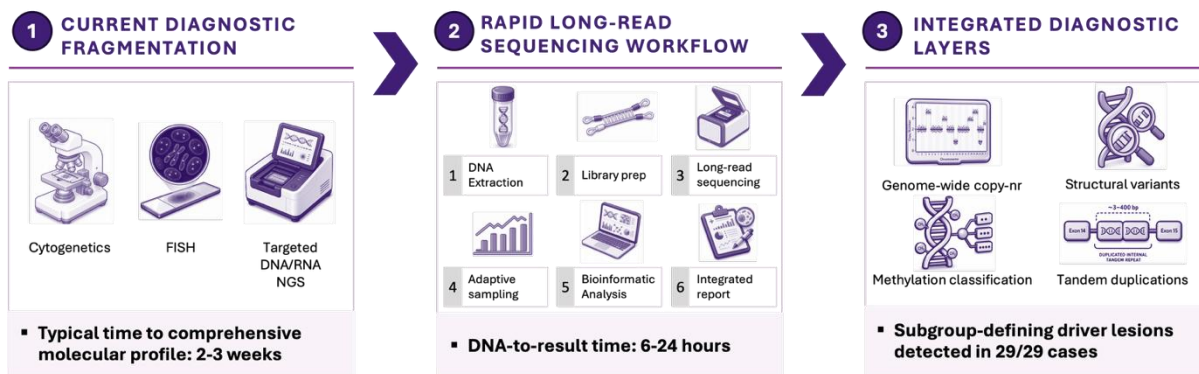


Figure 1. Long-read diagnostic workflow.

TGF- β Signalling Governs Quiescence and Chemoresistance in CD123^{High} Leukemic Stem Cells

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Aim:

Leukemic stem cells (LSCs) are a major driver of relapse and chemoresistance in Acute Myeloid Leukemia (AML) and are characterised by high IL-3R α (CD123) expression. This study investigated how microenvironmental inflammatory signalling regulates CD123 expression, quiescence, and therapeutic resistance in AML.

Method:

Cytokine stimulation, drug response, SMAD2 and SMAD4 knockdown and TGF- β 1 overexpression studies and TGF- β signalling pathway analyses were performed in AML cell lines, primary AML samples, and CD34⁺ stem cells using flow cytometry, qPCR, Western blotting, CFU assays, ChIP-PCR, and immunofluorescence. Cell cycle progression and Cytarabine resistance were assessed by PI and Annexin V/7-AAD staining.

Results:

TGF- β 1 induced IL-3R α /CD123 expression through TGF β RI/TGF β RII-mediated activation of SMAD2/4 signalling. Following TGF- β 1 stimulation, phosphorylated SMAD2 formed a complex with SMAD4 that localized to the *IL3RA* proximal enhancer containing a SMAD-binding motif. SMAD4 knockdown significantly impaired TGF- β 1-mediated CD123 upregulation, confirming dependence on canonical SMAD signalling.

Functionally, TGF- β 1 promoted chemoresistance by reducing cytarabine-induced apoptosis and enhancing clonogenic recovery after drug withdrawal. This effect was associated with suppression of IL-3-driven proliferation, induction of G0/G1 arrest, and increased p21 expression, consistent with an LSC-like quiescent state. Furthermore, IL-3 stimulation reinforced TGF- β signalling by increasing *TGF β RI* expression and SMAD2 phosphorylation, creating a feed-forward circuit that further enhanced CD123 expression.

FLT3-ITD AML patient samples demonstrated constitutive SMAD2 phosphorylation, which was reduced following TGF β RI inhibition or SMAD4 knockdown. Importantly, primary leukemic blasts and isolated LSCs became significantly more sensitive to cytarabine following TGF β RI inhibition.

Conclusion:

These findings identify a novel TGF- β 1–SMAD2/4 signalling axis that promotes CD123 expression, quiescence, and chemoresistance in AML LSCs, highlighting TGF β RI inhibition as a potential strategy to target minimal residual disease.

Investigating clonal haematopoiesis and risk factors for myeloid evolution (I-CHROME) study

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¹Department of Clinical Haematology, Peter MacCallum Cancer Centre & Royal Melbourne Hospital, Parkville, Australia, ²Division of Blood Cells and Blood Cancer, Walter and Eliza Hall Institute of Medical Research, Parkville, Australia, ³Department of Pathology, Peter MacCallum Cancer Centre, Parkville, Australia, ⁴Sir Peter MacCallum Department of Oncology, The University of Melbourne, , Australia

Aim:

To establish a prospective study to examine the natural history of clonal haematopoiesis (CH) and risk of progression to myeloid malignancy following cancer therapy.

Method:

Patients with prior cancer therapy were enrolled prospectively at Peter MacCallum Cancer Centre between March 2024 and November 2025. Genomic DNA isolated from blood and/or bone marrow from all patients was analysed by targeted next-generation sequencing. VAF cut-off was 1%. Descriptive statistics were expressed as counts, percentage frequencies, median, and range. All statistical analyses were performed using R (version 4.0.4).

Results:

A total of 125 patients have been enrolled in this study to date. This is an 18-month update on 66 patients with haematological malignancies (52% large B-cell lymphoma, 42% myeloma, 3% mantle cell lymphoma, 4% other). Median patient age was 69 years (range: 17-82), 56% were male. Median lines of prior therapy were 3 (range: 1-5). Among these, 50% had received prior CAR-T therapy, 47% lenalidomide (median duration 2.8 years, range: 0.4-6.3), and 45% had undergone prior autologous stem cell transplantation. Median follow-up time by the cut-off date (11-NOV-2025) was 12 months (range:1-20).

At study entry, 45 (68%) patients had 84 variants (vars) identified. Median number of vars per patient was 1 (range: 1-6), with 42% having 2+ vars. The most frequent CH variant involved *DNMT3A* (31%, n=26), followed by *TP53* (18%, n=15), *PPM1D* (10%, n=8), *ASXL1* (10%, n=8), and *TET2* (10%, n=8). *TP53* CH was present in 27% (n=12) of patients. Serial NGS (Fig 1) monitoring demonstrated that the expansion of the *TP53* clone preceded the clinical development of myeloid neoplasm by 6-12 months.

Conclusion:

CH post-cytotoxic therapy can be tracked longitudinally before the development of myeloid neoplasm through the I-CHROME study. This prospective CH clinic has established the spectrum of variants in this post-cancer therapy population and will continue to define the future risk of myeloid transformation within disease cohorts.

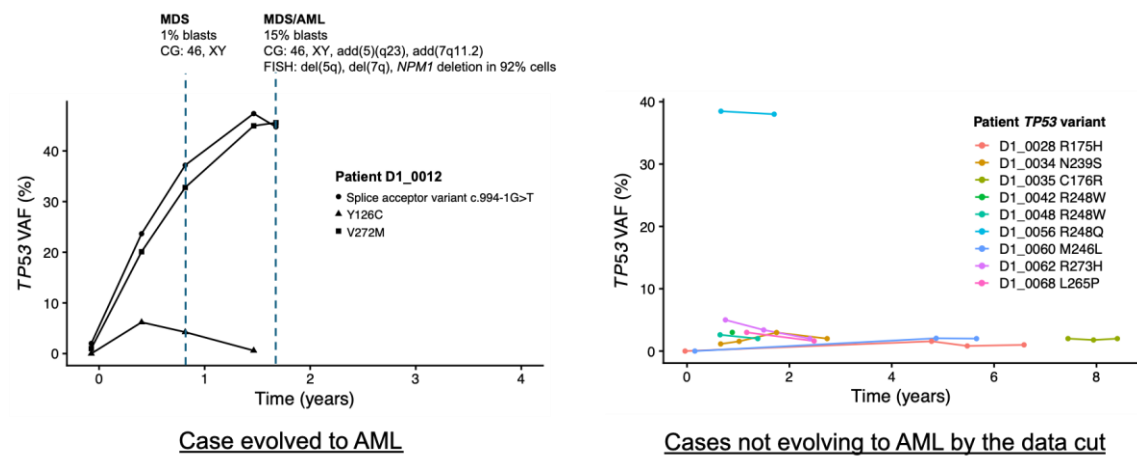


Figure 1: Longitudinal kinetics of *TP53* variants

Phase 1 study of SL0349, a bispecific nanobody based BCMA/GPRC5D CAR-T, in relapsed or refractory multiple myeloma

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Background: SL0349 is a bispecific nanobody-based chimeric antigen receptor T cell (CAR-T) product targeting both BCMA and GPRC5D, engineered with VHH binders and an optimized structure. This article reports preliminary data from a currently active phase 1 study (NCT07003568), evaluating the safety and efficacy of this therapeutic approach in heavily pretreated patients with RRMM..

Methods: This open label, single dose, exploratory phase I study was initiated on June 1, 2025, and was carried out at Shanghai Liquan Hospital (Shanghai, China). Patients were administered SL0349 at dose of 1.0×10^6 cells/kg.

Results: As of April 30, 2026, a total of 21 patients were infused with anti-BCMA/GPRC5D bispecific CAR T cells. The median age was 58.0 years old (Range 36-71). 14 (66.7%) were Caucasian and 7 (33.3%) were Asian respectively. 10 patients (47.6%) presented with extramedullary disease (EMD). 13 (61.9%) patients were diagnosed with high-risk cytogenetic profile.

Cytokine release syndrome occurred in 95.2% (20/21) patients, of which all cases were grade 1-2. Grade 1 immune effector cell-associated neurotoxicity syndrome occurred in 14.3% (3/21) patients.

The overall response rate was 100%, with sCR rate of 47.6% (10/21). The MRD negativity rate was achieved in 100% (21/21) assessed by bone marrow flow cytometry. For patients with EMD, 60% (6/10) achieved sCR and 40% (4/10) achieved PR

The median follow-up time for the 21 patients was 5.1 months (range, 0.7-11). Two patients died from relapse and pneumonia, respectively. While the others remained remission.

Conclusion: This analysis of the phase 1 study establishes a positive risk–benefit profile for a single low-dose infusion of SL0349, yielding early, deep responses in heavily pretreated RRMM patients, particularly for patients with high-risk cytogenetic features and/or EMD lesions.

Presence of end organ damage at commencement of second line therapy significantly impacts outcomes in Multiple Myeloma: An Australia and New Zealand Myeloma and Related Diseases Registry (ANZ MRDR) Analysis

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Aim: Consensus is lacking on treating relapsed multiple myeloma at clinical (CP) versus biochemical progression (BP). This study assesses real-world practices and outcomes across Australia and New Zealand (ANZ).

Method: We retrospectively reviewed 445 patients in the ANZ Myeloma and Related Diseases Registry (9 sites, 2013–Dec 2024) who progressed following first-line therapy. We analysed treatment timing (BP vs. CP), end organ damage (EOD) at 3–6 months, progression-free survival (PFS), and overall survival (OS) using Kaplan-Meier methods. Cox proportional hazards regression evaluated the EOD-survival association, adjusting for treatment site.

Results: Among 445 patients, 51% were treated at BP and 49% at CP. Both groups had similar baseline age, gender, ECOG status, stage (ISS-3), and high-risk cytogenetics. No differences existed in time to first progression (CP: 18.4 vs. BP: 19.7 months, $p=0.1$), time to initiate therapy (CP: 1.7 vs. BP: 2.1 months, $p=0.19$), or second-line regimens used ($p=0.94$).

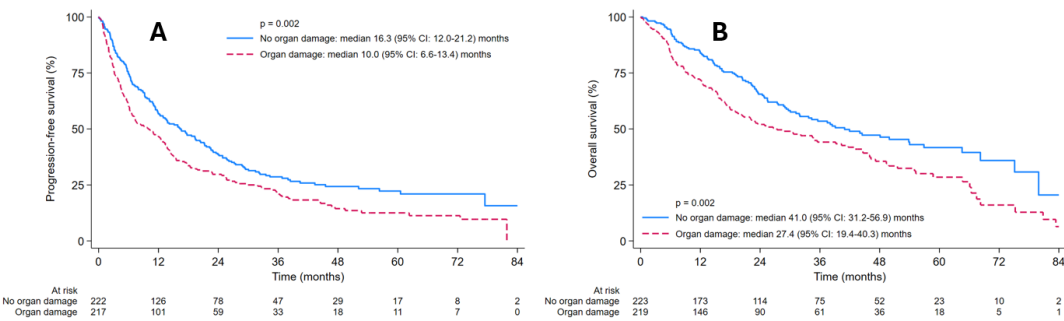
However, CP patients experienced more persistent EOD at 6 months, including significantly higher opioid requirements (24% vs. 10.3%, $p<0.001$) and mobility aid use (9.0% vs. 3.8%, $p=0.034$), though fracture rates were similar (8.8% vs. 7.5%, $p=0.64$). Among those with renal EOD, 68% lacked a 3-month renal response (IMWG criteria).

Crucially, treatment at CP resulted in significantly shorter survival from second-line therapy initiation versus BP (median PFS: 10.0 vs. 16.3 months, $p=0.002$; median OS: 27.4 vs. 41.0 months, $p=0.002$).

Conclusion: Despite similar initial disease characteristics and progression timelines, initiating second-line therapy at CP yields significantly worse clinical outcomes. CP treatment is associated with greater persistent EOD (increased opioid/mobility aid use and poor renal recovery) and inferior survival, resulting in a 6.3-month reduction in PFS and a 13.6-month reduction in OS compared to treatment at BP.

Figure 1.

A: PFS and B: OS by presence of organ damage at commencement of second-line therapy.
(No organ damage=Biochemical progression, Organ damage=Clinical progression)



Circulating plasma MYC/BCL2 RNA co-expression in newly diagnosed multiple myeloma identifies patients with a higher risk of early progression

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³Northern Health, Epping, Australia

Aim

MYC and BCL2 are established prognostic biomarkers across B-cell malignancies. This study evaluated the prognostic significance of circulating *MYC* and *BCL2* extracellular RNA (exRNA) and bone marrow MYC/BCL2 protein expression in newly diagnosed multiple myeloma (NDMM).

Methods

The study included 163 NDMM patients from the Myeloma and Related Disease Registry (MRDR). Plasma *MYC* and *BCL2* exRNA expression was quantified by digital PCR (dPCR) using QIAcuity platform and normalised to *GAPDH* and *HPRT1*. Immunofluorescence (IF) analysis was performed on 71 archival bone marrow trephines from Alfred Hospital, with HALO software quantifying the proportion of plasma cells expressing MYC and BCL2. Thirty-two patients have both liquid biopsy and immunofluorescence data available. Patients were stratified into expression tertiles, and Kaplan-Meier and Cox regression analysis were used to assess progression-free (PFS) and overall survival (OS).

Results

High *MYC* and *BCL2* exRNA expression were each associated with inferior PFS compared with low expression. (*MYC*: 28.3 vs 47.0 months; HR 1.68, 95% CI 1.05 – 2.71; *p*=0.032; *BCL2*: 28.3 vs 47.7 months; HR 1.72, 95% CI 1.05-2.83; *p*=0.032). Combine *MYC/BCL2* profiling further improved risk stratification, with median PFS ranging from 59.5 months in the low *MYC*/low *BCL2* group to only 23.3 months in the high *MYC*/ high *BCL2* group (*p*=0.0005) (Figure 1).

In contrast, bone marrow MYC and BCL2 protein expression assessed by IF did not independently predict PFS and OS (Figure 2A and 2B). However, concurrent low MYC and BCL2 IF expression identified a low-risk subgroup with significantly prolonged PFS compared with all other patients, suggesting negative predictive value for disease progression. No significant correlation was observed between circulating exRNA levels and corresponding bone marrow protein expression.

Conclusion

Circulating *MYC* and *BCL2* exRNA are strong prognostic biomarkers of disease progression in NDMM, whereas corresponding bone marrow protein expression lacks independent prognostic value but identifies a low-risk subgroup. Liquid biopsy-based *MYC/BCL2* profiling may provide a novel approach for risk stratification.

Figure

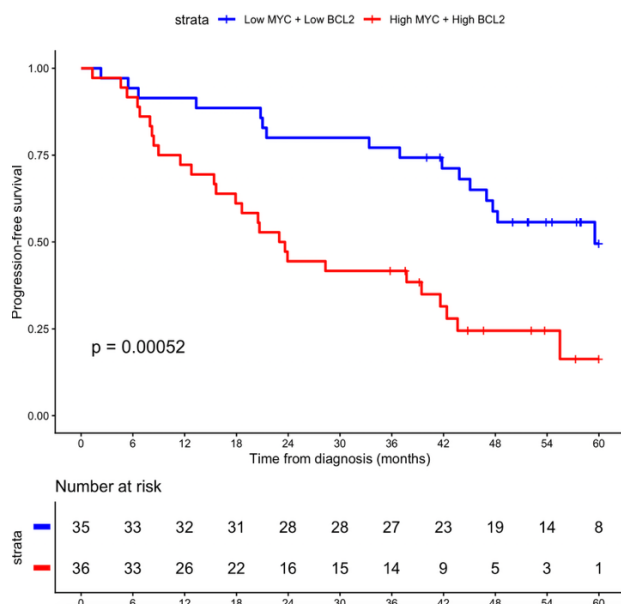


Figure 1. Kaplan-Meier PFS analysis demonstrating significantly inferior PFS in patients with combined high *MYC/BCL2* exRNA expression compared with low *MYC/BCL2* exRNA expression

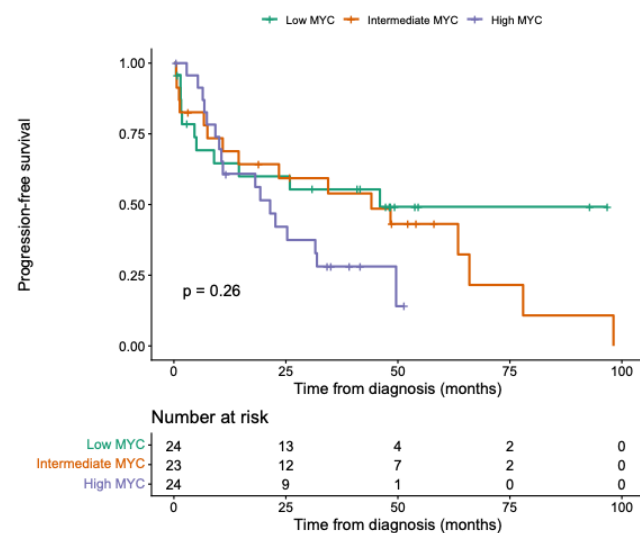


Figure 2A: Kaplan-Meier analysis of PFS by bone marrow MYC IF expression, showing no significant difference in PFS

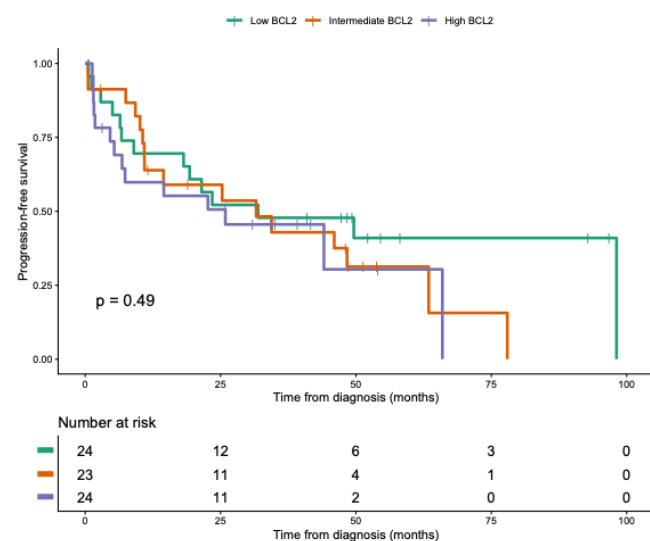


Figure 2B: Kaplan-Meier analysis of PFS by bone marrow BCL2 IF expression, showing no significant difference in PFS

Exploiting Glucocorticoid-Induced Leucine Zipper (GILZ) to deliver the anti-myeloma effects of steroids without metabolic toxicities

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¹Blood Cancer Therapeutics Laboratory, Department of Medicine, School of Clinical Sciences at Monash Health, Monash University, Clayton, Australia, ²Monash Haematology, Monash Health, Clayton, Australia, ³Rheumatology Research Laboratory, Department of Medicine, School of Clinical Sciences at Monash Health, Monash University, Clayton, Australia, ⁴Sir Peter MacCallum Department of Oncology, University of Melbourne, Parkville, Australia, ⁵Peter MacCallum Cancer Centre, Parkville, Australia

Aim:

Steroids are a pillar of multiple myeloma (MM) treatment but cause unwanted metabolic side effects, negatively impacting on patient quality of life. GILZ (TSC22D3) is a steroid induced effector protein which mediates anti-inflammatory effects of steroids entirely distinct from metabolic consequences (e.g., diabetes, osteoporosis). We hypothesised that the lymphotoxic properties of GILZ would translate to anti-myeloma activity and sought to determine the therapeutic potential of GILZ-based therapeutics.

Methods:

Doxycycline (Dox) inducible GILZ constructs were transduced into a panel of MM cell lines of varying dexamethasone (Dex) sensitivity including MM1.S and MM1.R (isogenic Dex sensitive and resistant lines where MM1.R lack the glucocorticoid receptor [GR]). To dissect the role of GILZ in Dex responses, GILZ knock-out (KO) was performed using CRISPR/Cas9 editing. Cellular responses were assessed by viability assays, RNASeq and Western blot.

Results:

Dox-induced GILZ caused growth inhibition and cell death across all MM cell lines including those with de novo (e.g., H929) and acquired (MM1.R) Dex-resistance. This correlated with reductions in mTOR pathway signalling and markers of apoptosis. Unexpectedly, the viability of Dex-treated MM cells was not attenuated by GILZ-KO. Dex-induced GILZ expression was augmented by proteasome inhibition but not IMiDs and synergised with bortezomib in cell death assays.

Conclusion:

GILZ induction induces myeloma cell death independent from the GR, bypassing GR-loss as a mechanism of Dex resistance. CRISPR-mediated GILZ KO did not ameliorate Dex toxicity to MM cells. Thus, GILZ induction is sufficient to kill MM but not necessary for Dex-induced MM cell death. As GILZ acts independently downstream of the GR, therapeutic strategies to deliver or augment GILZ offer the promise of steroid-like anti-MM activity without adverse metabolic consequence.

Word count: 273

Ethnic disparities in cytogenetic characteristics at diagnosis and survival of multiple myeloma patients within the Auckland region

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Aim:

New Zealand myeloma patients of Maori and Pacific Island (MPI) ethnicity have poorer outcomes. Moore et al. (2022) reviewed 138 MPI and 530 non-MPI patients between September 2012 and April 2021 from the Myeloma and Related Diseases Registry (MRDR), identifying a higher rate of t(4;14) as a potential cause. t(11;14) was not analysed. We aim to verify these findings in the Auckland region, given incomplete MRDR registration.

Method:

Patients who had a diagnostic bone marrow biopsy between 1 March 2011 and 1 March 2025 with FISH processed at LabPLUS and IGENZ, the laboratories servicing Auckland, were identified. Further patient identification and data collection is ongoing. Patients without FISH are not currently included.

We collected data on IGH translocations, TP53 aberrancy, +1q, -1p, -13q, age at diagnosis, sex, paraprotein type, ISS/R-ISS, bone marrow plasma cell burden, blood test indices, bone involvement and overall survival (OS). Data was analysed with R.

Results:

194 MPI patients and 613 non-MPI patients with FISH results were identified within the Auckland region. MPI patients had a lower median OS (5.2 years vs 7.3 years, $p=0.0009$) than non-MPI. Following Benjamini-Yakutieli false-discovery correction, an apparent increase in t(4;14) among MPI patients did not remain statistically significant (15.2% vs 9.2%, $p=0.03/p\text{-corrected}=0.22$). MPI patients demonstrated more frequent +1q (61.4% vs 40.5%, $p=0.0009/p\text{-corrected}=0.01$) and less frequent t(11;14) (8.2% vs 22.5%, $p=0.0001/p\text{-corrected}=0.0026$), with median OS seemingly lower with +1q (4.7 years vs 7.3 years, $p=0.2$) but less affected by t(11;14) (4.6 years vs 5.1 years, $p=0.3$).

Conclusion:

Auckland MPI patients have a significantly lower rate of t(11;14) and higher rate of +1q, but no detected significant difference in t(4;14). Their shorter OS may reflect non-translocation genetics, co-morbidities and/or treatment inequalities.

Effectiveness of bridging therapy corresponds to improved outcomes after ciltacabtagene autoleucel: phase 3 CARTITUDE-4 study of patients with relapsed, lenalidomide-refractory multiple myeloma

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Aim:

Effective tumour-burden reduction with bridging therapy (BT) correlates with improved PFS¹ and safety outcomes² in patients treated with ciltacabtagene autoleucel (cilta-cel). CARTITUDE-4 (median follow-up, 33.6 months) showed significant progression-free survival (PFS) benefit (HR weighted, 0.29 [95% CI, 0.22–0.39]) and overall survival (OS) benefit (HR, 0.55 [0.39–0.79]; P=0.0009) vs standard of care.³ We assessed the relationship between BT response before cilta-cel, with efficacy and safety outcomes post-infusion.

Method:

CARTITUDE-4 cilta-cel arm patients underwent apheresis, ≥1 investigator-choice BT cycle; either daratumumab, pomalidomide, dexamethasone (DPd) or pomalidomide, bortezomib, dexamethasone (PVd); lymphodepletion (cyclophosphamide/fludarabine), then a single cilta-cel infusion 5–7 days post-lymphodepletion initiation.⁴

Results:

Of 196 cilta-cel recipients (176 study treatment; 20 subsequent therapy), 172 (87.8%) received DPd and 24 (12.2%) received PVd during BT (median BT cycles 2; range 1–6). Pre-lymphodepletion responses were; 42 patients with very good partial response or better (≥VGPR), 70 with partial response (PR), 61 with minimal response/stable disease (MR/SD), 20 with progressive disease (PD), 3 were non-evaluable (NE). PFS at 30 months post-cilta-cel infusion (95% CI) was 75.9% (59.8–86.2) for ≥VGPR, 72.9% (60.4–82.1) PR, 56.5% (42.8–68.1) MR/SD, and 30.0% (12.3–50.1) PD. Thirty-month OS was 85.1% (69.9–93.0), 91.4% (81.9–96.1), 74.8% (61.6–84.0), and 40.0% (19.3–60.0), respectively. Safety results shown in table 1.

Table 1. Safety outcomes post-infusion (n=196)

	≥VGPR	PR	MR/SD	PD
Movement/neurocognitive adverse events (MNT)	0	0	1 patient SD (unconfirmed PD)	1 patient
Cranial palsy	11.9%	7.1%	8.2%	5.0%
Fatal infections	2.4%	4.3%	13.1%	15.0%
Prolonged* thrombocytopenia	9.5%	11.4%	11.5%	50%
Prolonged* neutropenia	2.4%	9.8%–15.7%		
Non-relapse mortality (NRM)	7.1%	8.6%	18.0%	30%

*Grade 3/4 cytopenia through day 60 post cilta-cel.

Conclusion:

Greater BT response before cilta-cel correlates with longer PFS/OS and lower rates of post-infusion adverse events, underscoring the importance of optimising BT for disease control prior to cilta-cel infusion.

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Long-term follow-up for safety and efficacy of zanubrutinib in elderly (≥80 years) treatment-naïve CLL/SLL patients, including those with del(17p): subgroup analysis from the SEQUOIA trial

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Aim:

Chronic lymphocytic leukemia (CLL) and small lymphocytic lymphoma (SLL) largely affect older adults, with a median age at diagnosis of 72y. Advancing age, comorbidities, and poor performance status can limit tolerability and effectiveness of treatment. However, clinical data in this population remain limited. This subgroup analysis of SEQUOIA (NCT03336333) assessed efficacy and safety of zanubrutinib in patients aged ≥80yrs with CLL/SLL.

Method:

SEQUOIA enrolled TN patients with CLL/SLL unsuitable for FCR, defined as age ≥65y and/or with significant comorbidities. In Cohort 1/1a, patients without del(17p) were randomized 1:1 to receive continuous zanubrutinib (Arm A) or six cycles of BR (Arm B). In Cohort 2 (Arm C), patients with del(17p) all received continuous zanubrutinib.

Results:

A total of 38 patients treated with zanubrutinib (Arm A: 28; Arm C: 10) were aged ≥80y at study entry, with a median age of 81y. Del(17p) and/or *TP53*^{mut} were present in 36.8% of patients and 57.9% had unmutated IGHV. As of 31-Oct-2025, median follow-up was 78.8mo. The overall response rate was 100%, with a complete response rate of 18.4%. Estimated PFS rate at 72mo was 63.8%. Estimated OS rate at 72mo was 75.8%.

TEAEs of interest (any grade/grade ≥3) included atrial fibrillation/flutter (15.8%/0%), major hemorrhage (21.1%/13.2%), hypertension (28.9%/18.4%), and infections (76.3%/36.8%). TEAEs leading to treatment discontinuation occurred in 39.5% of patients, and TEAEs leading to death were observed in 13.2% of patients. In total, 36.8% of patients remain on zanubrutinib.

Conclusion:

Patients aged ≥80 y achieved durable benefit from zanu despite advanced age and high-risk characteristics. The tolerability profile observed in this subgroup is as expected for a very elderly population and is comparable to the established safety profile reported for zanu. These results support the use of zanubrutinib as an effective first-line treatment for patients with TN CLL/SLL, including those aged ≥80y.

First-line treatment of CLL/SLL with the all-oral combination of sonrotoclax (sonro) and zanubrutinib (zanu) achieves undetectable minimal residual disease (uMRD) rates of >90%, including in patients with del(17p)/TP53

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Aim:

Oral, fixed-duration BTKi-BCL2i doublets are effective for first-line treatment of CLL. Upgrading the BCL2i component with sonro, a next generation BCL2i, may lead to improved uMRD rates. Here, we report updated data in patients with treatment-naïve CLL/SLL treated with zanu+sonro (320 mg cohort) in a phase 1/1b study (NCT04277637).

Methods:

Treatment consisted of lead-in zanu 320 mg QD for 8-12 weeks, after which sonro was added with ramp-up to 320 mg QD. Patients were treated until progression, unacceptable toxicity, or protocol-defined elective discontinuation after 96 weeks of combination treatment at target dose. Primary endpoint was safety. Secondary endpoints included ORR; exploratory endpoints included blood uMRD4 rates.

Results:

Of 86 patients enrolled in the 320 mg cohort, 40 (47%) discontinued sonro, most due to protocol-defined elective discontinuation (85%; n=34). The most common any-grade/grade ≥3 TEAE was neutropenia (38%/29%). No TLS occurred; no AEs led to death.

In 84 efficacy-evaluable patients, ORR was 100% (CR: 55%). Median time to response was 2.6 months (range, 1.5-9.1 months). No patients in the 320 mg cohort experienced progression.

The best uMRD4 rate assessed by flow cytometry was 99% (83/84) and 100% (10/10) in patients with TP53/del(17p) mutations. Median time from reaching sonro target dose to uMRD was 3.0 months (range, 2.3-27.4 months), and the best uMRD4 rates by weeks 24, 48 and 96 were 81% (69/85), 91% (63/69) and 98% (55/56), respectively. No patient with uMRD4 reverted to dMRD. Updated results to be presented.

Conclusions:

Sonro+zanu was well tolerated and achieved uMRD rates of >90%. The depth and kinetics of uMRD achieved with sonro+zanu highlights the improved potency and differentiated profile of this combination versus available combination therapies in first-line CLL. Sonro+zanu is being evaluated in two phase 3 clinical trials (NCT06073821, NCT07277231).

BCR neoantigens drive T-cell immunity and favourable outcomes in Chronic Lymphocytic Leukaemia

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Aim: Although IGHV mutational frequency (due to mutations in the B cell receptor 'BCR') are a well-established prognostic feature in CLL, the underlying mechanism remains unknown. Because BCR mutations are overlooked, CLL is considered a tumour with low mutational and neoantigen (neoAg) burden, with the latter uncharacterised in CLL. We hypothesised that BCR mutations encode neoAgS that elicit neoantigen-specific T-cell (NeoAgST-cells) responses that influence prognosis.

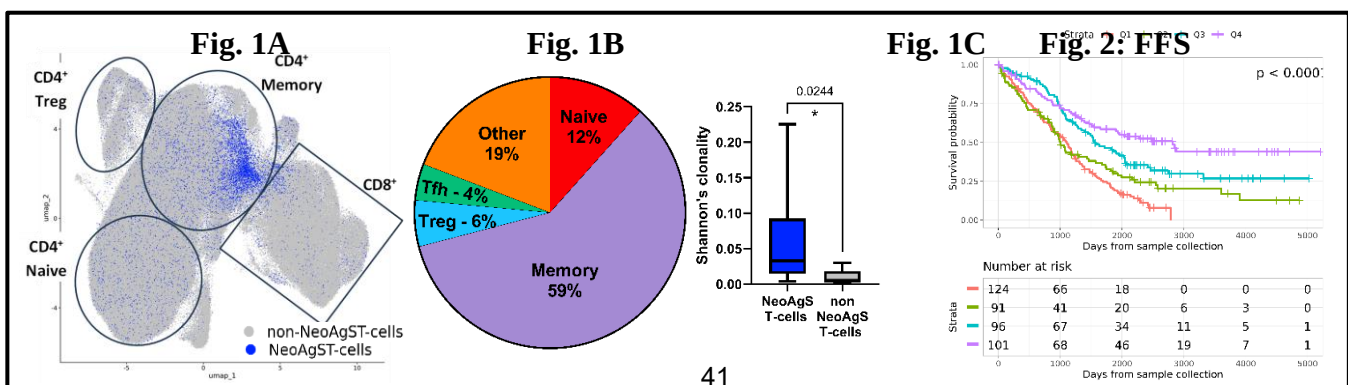
Method: Forty-five prospectively collected CLL cases drawn from Brisbane and Adelaide underwent paired whole-exome sequencing and bulk PBMC RNAseq. HLA-I/II neoAgS were called from BCR and somatic mutations and validated by MHC-immunoprecipitation and mass-spectrometry. Single-cell RNA/TCR sequencing (scRNA/TCRSeq) characterised NeoAg specific T-cell responses (n=12). Prognostic associations with neoAg burden were validated in an independent meta-cohort from NIH dbGaP (n=412).

Results: Somatic mutation burden was low (36, range 10-87) with only 21% of mutations expressed as mRNA. However, inclusion of BCR mutations, increased mutational burden by 30% (47, range 10-113). Furthermore, BCR mutations were uniformly expressed and were also more likely to be antigenic than somatic mutations (50% vs 8%, $p < 0.0001$), with neoAgS predominantly presented by HLA-II (62%). BCR neoAgS were temporally stable in 9/9 cases with serial samples. NeoAgST-cells responses were explored by scRNA/TCRseq. Consistent with HLA-II neoAg predominance, NeoAgST-cells were predominantly clonally expanded CD4⁺ memory T-cells (Fig 1A-C) with transcriptional signatures of activation, cytotoxicity and cell killing.

In an independent meta-cohort, BCR-neoAg burden was independently prognostic for OS and PFS (Fig 2) by univariate/multivariate analysis.

Conclusion:

BCR-neoAgS provoke a cytotoxic CD4⁺ T-cell response in CLL. This anti-tumour response may underpin the favourable clinical outcomes of mutated IGHV CLL and represents a promising target for personalised immunotherapy. Our group is currently developing a personalized mRNA vaccine against these targets in ex-vivo models.



MAP3K14 (NIK) synonymous variants drive altered splicing to activate NF-κB in mature B-cell malignancies

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Aim:

Genetic alterations activating NF-κB are described in mature B-cell malignancies, including loss of TRAF3, which liberates NF-κB-inducing kinase (NIK, encoded by *MAP3K14*) to drive non-canonical NF-κB (ncNF-κB) signalling. Here, we discovered and characterised synonymous variants (SVs, i.e. not predicted to change amino acid sequence) in *MAP3K14* that activate ncNF-κB via altered splicing, resulting in NIK disengagement from TRAF3.

Method:

We retrospectively reviewed diagnostic sequencing data from 2,224 patients with mature B-cell malignancies tested on the Peter MacCallum Cancer Centre AllHaem targeted DNA panel (September 2024–February 2026). Candidate variants were functionally characterised in OPM2 cells, in which SVs were introduced by prime editing (OPM2^{SV})¹.

Results:

MAP3K14 exon 2 variants clustering around the TRAF3-binding motif (Ile78-Ala84) were identified in 89/2,224 patients (4.0%, **Fig. 1A**); including patients with chronic lymphocytic leukaemia (CLL, 45/913, 4.9%), lymphoplasmacytic lymphoma/Waldenström's macroglobulinaemia (21/262, 8.0%), multiple myeloma (3/202, 1.5%) and mantle cell lymphoma (1/150, 0.6%). The most common were SVs c.99G>T and c.159A>T (69/89 patients). Long-read sequencing of patient CLL cells harbouring SVs revealed *MAP3K14* mRNA transcripts with an in-frame deletion removing the TRAF3-binding motif (**Fig. 1B**). Co-immunoprecipitation in HEK293T cells confirmed that SV-derived NIK had impaired TRAF3 binding. Prime-edited OPM2^{SV} cells exhibited a transcriptomic profile by RNA-seq similar to that of isogenic TRAF3-deficient cells. Functionally, OPM2^{SV} showed increased secretion of chemokines/cytokines, including IP-10 (recently proposed to attenuate cell killing by T-cell redirecting therapies)², and increased growth and survival. Finally, using unbiased cell-surface proteomics, we identified NF-κB-associated markers (e.g., CD132/IL2Ry), from which we developed a novel flow-cytometric assay measuring NF-κB activation, which we validated in OPM2^{SV} cells, additional B-cell malignancy cell lines, and primary CLL cells.

Conclusion:

This study expands the spectrum of genetic lesions that result in activation of NF-κB in mature B-cell malignancies, and highlights the importance of SVs as a driver of cancer biology that may be under-recognised in molecular diagnostics.

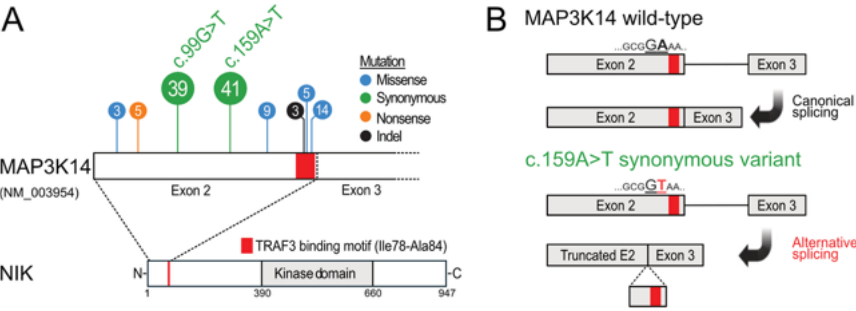


Figure 2. (A) Mutations observed in *MAP3K14* exon 2 across mature B-cell malignancies. (B) Schematic representation of canonical splicing of wild-type *MAP3K14* (upper) or altered splicing generated by the c.159A>T synonymous variant (lower). The new “GT” motif creates a novel splice donor site, driving alternative splicing resulting in the deletion of amino acids 54-86, including the TRAF3 binding motif (shown in red).

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Pirtobrutinib in post-cBTKi chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL): phase 1/2 BRUIN study with more than 5 years follow-Up (final update)

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Aim:

Pirtobrutinib a highly selective, non-covalent BTKi is approved for treating chronic lymphocytic leukemia (CLL) in adults in the EU and USA after prior BTKi treatment. We report the final efficacy and safety results of pirtobrutinib from the phase-1/2 BRUIN study with more than 5-years follow-up.

Method:

Patients with prior cBTKi-exposed chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL) were eligible for pirtobrutinib treatment. Overall response rate (ORR) per 2018 iwCLL criteria, ORR including partial response with lymphocytosis (PR-L), duration of response (DOR), and progression-free survival (PFS), IRC-assessed, overall survival (OS), and safety, were analyzed. Data-cut was 27Jan2025, (median study follow-up of 34.1-months; range:0.5-69.8).

Results:

282 patients post-cBTKi with CLL/SLL, 84.4%(238/282) received pirtobrutinib 200mg as the starting dose. Median age was 69years. Median number prior therapies; 4(45.4% received prior BCL2i, and 77.0% discontinued due to progressive disease (PD), 19.5% due to toxicity). High-risk features: unmutated IGHV 85.8%(193/225), mutated *TP53* 40.4%(99/245), and del(17p) 29.2%(59/202). ORR was 72.3%(95%CI:66.7-77.5). ORR including PR-L: 81.6%(95%CI:76.5-85.9). Median DOR and PFS (months, 95%CI): 18.4, 14.82-20.27 and 18.7, 16.6-21.8. 36-month DOR and PFS rate: 28.0%(21.6-34.7) and 25.0%(19.4-31.0), respectively. Among all CLL/SLL: median follow-up was 46.5-months, median OS was not estimable (NE) (95%CI:47.8-NE), 36-month OS rate: 62.0%(95%CI:55.8-67.7). Most frequent TEAEs, were fatigue (38.7%), neutropenia (35.8%), diarrhea (30.5%), cough (29.8%), COVID-19 (28.4%), and contusion (27.7%). Most frequent grade ≥ 3 TEAEs: infection (36.5%) and neutropenia (29.8%). Low rates of grade ≥ 3 TEAE of hypertension (5.3%), hemorrhage/hematoma (2.5%), and atrial fibrillation/flutter (2.1%) were observed. Grade-5 TEAEs, regardless of attribution, occurred in 35(12.4%) patients.

Conclusion:

In heavily pretreated R/R post-cBTKi CLL/SLL, pirtobrutinib continues to show favorable and durable efficacy and is well-tolerated, with low rates of grade ≥ 3 TEAE. Dose reductions/discontinuations were low. No new pirtobrutinib safety signals were identified with more than 5-years of follow-up.

BGB-16673, a Bruton tyrosine kinase degrader, in patients with relapsed/refractory chronic lymphocytic leukemia/small lymphocytic lymphoma in the CaDAnCe-101 study

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Aim:

BGB-16673 is a Bruton tyrosine kinase (BTK) degrader that blocks signaling by tagging BTK for degradation through the cell's proteasome pathway, leading to tumor regression. Here, updated safety and efficacy results are reported for patients with relapsed/refractory (R/R) chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL) in the phase 1 portion of the CaDAnCe-101 study (BGB-16673-101; NCT05006716).

Method:

Eligible patients had R/R CLL/SLL (≥ 2 prior therapies), Eastern Cooperative Oncology Group performance status of 0-2 (0-1 in the EU), and adequate organ function. BGB-16673 (50-500 mg) was administered orally QD.

Results:

At the December 15, 2025, data cutoff, 67 patients enrolled (median age, 70 [range, 47-91] years; median prior lines of therapy, 4 [range, 2-10]); most received prior covalent BTK inhibitors ($n=63$ [94.0%]). Median study follow-up was 24.1 (range, 0.3-37.7) months; 52.2% of patients remained on treatment at data cutoff. Any-grade treatment-emergent adverse events (TEAEs) occurred in 97.0% of patients, including fatigue (37.3%), contusion (32.8%), diarrhea (29.9%), and neutropenia (29.9%). Grade ≥ 3 TEAEs occurred in 61.2% of patients, including infections (34.3%), neutropenia (25.4%), and thrombocytopenia (7.5%). TEAEs led to death in 7.5% of patients. The ORR ($\geq$ partial response [PR] with lymphocytosis) was 85.1%, $\geq$ PR rate was 77.6%, and complete response (CR)/CR with incomplete marrow recovery rate was 3.0% (200-mg dose: ORR, 94.1%; 1 CR). Promising ORRs were seen in high-risk subgroups (*del*(17p)/*TP53* mutated, 79.5% [35/44]; IGHV unmutated, 86.5% [32/37]; complex karyotype [≥ 3 abnormalities], 73.9%, [17/23]; *BTK* mutated, 76.0% [19/25]; *PLCG2* mutated, 90.0% [9/10]). Median time to first response was 2.8 (range, 2.0-19.4) months; median duration of response was 20.7 (range, 0-27.6) months. The 18-month PFS rate was 65.2% (95% CI, 50.9%-76.2%).

Conclusion:

BGB-16673 has a manageable safety profile with durable responses in patients with difficult-to-treat R/R CLL/SLL. ©EHA2026.

Potential for treatment free remission in newly diagnosed chronic phase chronic myeloid leukaemia initially achieving major molecular response on dasatinib and then transitioned to imatinib. Results of the phase 2 kinase inhibition with sprycel startup (KISS) study

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Aim:

Frontline second-generation TKIs achieve faster and deeper molecular responses than imatinib but have an increased risk of significant long-term side effects. This study assessed if imatinib can be used to maintain a major molecular response (MR^{3.0}) achieved on initial dasatinib treatment in patients with newly diagnosed chronic phase chronic myeloid leukaemia (CP-CML).

Method:

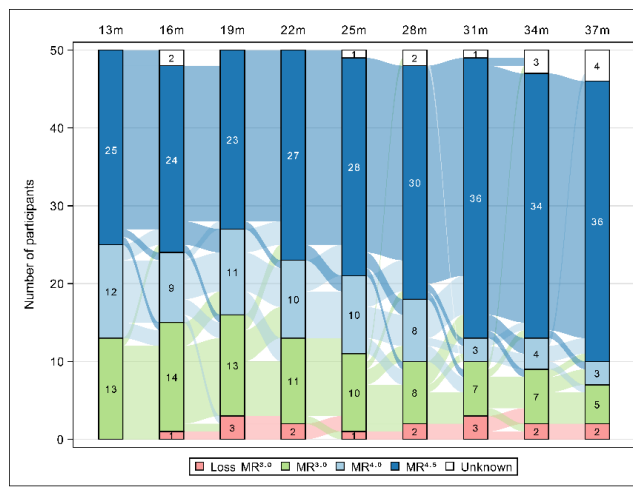
Multicentre, prospective, open-label phase II trial of dasatinib followed by imatinib, in treatment naïve CP-CML. Participants were followed up for two years post transition to imatinib.

Results:

96 participants were recruited from 9 centres in New Zealand from 2017 to 2022. 93 were confirmed eligible and commenced dasatinib. At 12 months, 56 participants remained on dasatinib and achieved MR^{3.0}, of which 50 consented to imatinib switch. 43 (84%) participants retained MR^{3.0} during the 2-year treatment period with imatinib (95%CI, 65-93%). At time of imatinib switch, 12/50 (24%) of participants were in MR^{4.0} and 25/50 (50%) were in MR^{4.5}. At the end of study follow-up, 3/46 (7%) were in MR^{4.0} and 36/46 (78%) were in MR^{4.5}. There were lower rates of dose interruptions or reductions due to toxicity with imatinib compared with dasatinib. 7 participants lost MR^{3.0} following switch. 5 subsequently regained MR^{3.0} with dasatinib or improved imatinib adherence. 2 did not regain MR^{3.0}. PFS, FFS and OS at 3 years were 98% (95%CI, 89-100%), 86% (95%CI, 73-94%) and 100% (95%CI, 93-100%) respectively.

Conclusion:

This treatment strategy effectively maintained MR^{3.0} achieved on dasatinib, with majority of participants experiencing further deepening of response following imatinib switch. Durable deep molecular response ($\geq$ MR^{4.0}) with reduced long-term toxicity on imatinib suggests this may serve as a more tolerable algorithm to generate a population that is potentially eligible for treatment-free remission. An extension study is underway to collect 5-year-follow-up data in this cohort to assess eligibility for a trial of TKI discontinuation.



Selinexor plus ruxolitinib in JAK inhibitor–naïve myelofibrosis: Phase 3 SENTRY trial

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Aim: SENTRY (NCT04562389) evaluated treatment with selinexor plus ruxolitinib (S+R) in patients with JAK inhibitor (JAKi)–naïve myelofibrosis.

Method: 353 patients with JAKi-naïve myelofibrosis were randomized 2:1 to selinexor 60 mg weekly plus ruxolitinib (n=235) or placebo plus ruxolitinib (n=118), stratified by DIPSS risk, spleen volume, and platelet count. Eligible patients had spleen volume ≥ 450 cm³, active myelofibrosis symptoms, DIPSS Int-1 or higher, and platelets $\geq 100 \times 10^9$ /L. Co-primary endpoints were spleen volume reduction $\geq 35\%$ (SVR35) and absolute mean change in total symptom score (AbsTSS; excluding fatigue) at Week 24. Hierarchical testing (one-sided $\alpha=0.025$) was applied. Secondary endpoints included safety and overall survival (OS). Variant allele frequency (VAF) changes were exploratory.

Results: SVR35 was achieved in 49.8% of patients with S+R vs 28.0% with ruxolitinib (OR, 2.58; 95% CI, 1.60, 4.17; $P<0.0001$) at Week 24, 49.4% vs 20.3% at Week 12, 46.9% vs 23.0% at Week 36, and 67.7% vs 44.9% at any time. Mean (95% CI) AbsTSS change at Week 24 was -9.9 (-11.2 , -8.6) vs -10.9 (-12.6 , -9.1); adjusted mean difference was 0.97 (-1.07 , 3.02; $P=0.825$).

As of Feb 20, 2026, 224 (95.3%) patients in S+R and 106 (89.8%) in ruxolitinib were alive. With median follow-up of 11.6 and 12.6 months, OS HR was 0.43 (95% CI, 0.19, 1.00; nominal $P=0.022$). VAF percent reduction $\geq 20\%$ at Week 24 occurred in 32.0% vs 23.9% and was associated with SVR35.

TEAEs were 99.1% in S+R and 97.4% in ruxolitinib (grade ≥ 3 in 70.1% vs 50.0%). TEAEs leading to treatment discontinuation were 14.5% and 8.6%. TEAEs leading to death occurred in 0.9% vs 2.6%. Confirmed leukemic transformation was 1.7% in both.

Conclusion: S+R significantly improved SVR35 vs ruxolitinib alone, with comparable symptom improvement from baseline, manageable safety profile, and promising OS and VAF reductions, supporting S+R as a novel frontline strategy for myelofibrosis.

Update from phase 2 RESTORE trial of elritercept in patients with myelofibrosis receiving ruxolitinib

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Aim:

We report updated findings from the phase 2 RESTORE trial in patients with MF (NCT05037760).

Method:

RESTORE (NCT05037760) is an open-label, phase 2 study of elritercept monotherapy, or with ruxolitinib, in patients with myelofibrosis and anemia. Eligible patients were transfusion-dependent (TD; ≥ 3 RBC units/12 weeks) or non-transfusion-dependent (NTD; < 3 RBC units/12 weeks with Hgb < 10 g/dL). We report data for patients receiving elritercept starting at 3.75 mg/kg Q4W with ruxolitinib. Primary endpoint was safety/tolerability; other endpoints included hematologic parameters, spleen size, MF-SAF-TSS, and gene mutations.

Results:

As of July 2025, 38 patients receiving ruxolitinib were treated with elritercept ≥ 3.75 mg/kg. Baseline: median age 71 years (45–80); 27 (71%) had spleen volume ≥ 450 cm³; median Hgb 8.5 g/dL, platelets 121×10^9 /L; median RBC transfusion requirement 4 units/12 weeks (0–17), with 23 (61%) TD. Median elritercept exposure was 10.9 months (1.2–20.6); 21 (55%) up-titrated to 5 mg/kg. Common adverse events were diarrhea (24%, none grade ≥ 3), thrombocytopenia (18%, grade 3: 10.5%), and fatigue (18%, grade 3: 5%). By week 24, 8 (35%) TD patients achieved RBC transfusion independence (TI) ≥ 12 weeks, 13 (57%) had $\geq 50\%$ transfusion reduction over 12 weeks, and 4 (17%) achieved TI with mean Hgb increase ≥ 1.5 g/dL. Among NTD patients, 5/14 (36%) and 7/14 (50%) achieved Hgb increases ≥ 1.5 and ≥ 1 g/dL over any 12-week period. At week 24, 16/38 (42%) had platelet increase $\geq 30 \times 10^9$ /L. Spleen volume reduction $\geq 25\%$ occurred in 5/24 (21%) and MF-SAF TSS reduction $\geq 50\%$ in 13/27 (48%). JAK2 V617F allele burden reduction $\geq 50\%$ occurred in 3/19 at week 24 and persisted at week 52.

Conclusion:

Elritercept add-on to ruxolitinib showed improvements in transfusion burden, spleen volume, platelet counts, and symptoms in patients with myelofibrosis, supporting further evaluation.

Encore: Outcomes with momelotinib in patients with intermediate-1(int-1)–vs intermediate-2 (int-2)–/high-risk myelofibrosis (MF): post hoc analyses of the phase 3 SIMPLIFY-1 and MOMENTUM trials

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Aim:

Momelotinib is a JAK1/JAK2/activin A receptor type 1 inhibitor approved for the treatment of patients with intermediate- or high-risk MF with moderate-severe anaemia based on the phase 3 SIMPLIFY-1 and MOMENTUM trials in JAK inhibitor–naïve and –exposed patients, respectively. Here we report results on spleen, symptom, and anaemia-related benefits of momelotinib in patients with int-1– vs int-2–/high-risk MF.

Method:

SIMPLIFY-1 (NCT01969838) and MOMENTUM (NCT04173494) were randomised, double-blind, phase 3 trials of momelotinib vs ruxolitinib or danazol, respectively. This post hoc analyses focus on the momelotinib arms of the intent-to-treat populations. Week 24 endpoints summarised descriptively were spleen volume reduction $\geq 35\%$ from baseline (SVR35), total symptom score reduction $\geq 50\%$ from baseline (TSS50), transfusion independence (TI; no transfusions nor haemoglobin < 8 g/dL in the previous 12 weeks), and achievement of dual SVR35+TI.

Results:

In SIMPLIFY-1, 46/215 (21%) momelotinib-randomised patients were int-1 risk (by International Prognostic Scoring System; IPSS), while in MOMENTUM, only 7/130 (5%) were int-1 risk (by Dynamic IPSS), reflecting the advanced disease stage of JAK inhibitor–exposed, anaemic population. In SIMPLIFY-1, the response rate was higher in the int-1 vs int-2/high risk subgroup across multiple endpoints: TSS50 (39% vs 25%); TI (83% vs 62%) and SVR35+TI (26% vs 24%). Similarly, in the MOMENTUM trial, int-1 demonstrated higher response rates than int-2/high risk subgroup: SVR35 (29% vs 22%); TSS50 (57% vs 23%); TI (57% vs 29%) and SVR35+TI (29% vs 10%).

Conclusion:

Spleen, symptom, and anaemia-related benefits of momelotinib were observed across all risk assessment categories. Higher TSS50 and TI rates in the int-1–risk population suggests that earlier initiation of momelotinib treatment may be associated with better outcomes. These findings support momelotinib use in int-1–, int-2–, and high-risk patients for which it is approved.

Funding: GSK.

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Plasma cell-free DNA monitoring of myelofibrosis following allogeneic stem cell transplantation

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Aim: Allogeneic stem cell transplantation (allo-SCT) is the only curative therapy for myelofibrosis, yet ~40% of patients will relapse. Post-transplant monitoring of residual disease currently relies on morphological assessment of bone marrow (BM). We investigated whether genomic monitoring of BM, plasma-derived cell-free DNA (cfDNA) or whole blood (WB) would provide alternate methods to monitor disease post-allo-SCT.

Method: Ten patients with myelofibrosis (7 *JAK2*^{V617F}, 1 *CALR*, 2 triple-negative) undergoing allo-SCT had blood and BM samples collected pre-transplant and followed up to 2 years post-transplant. Cellular DNA was extracted from BM and WB, and cfDNA from plasma using Qiagen kits. Mutations were assessed using the Oncomine Myeloid MRD DNA Assay (LOD 0.05%) on an Ion S5 Sequencer, with the Torrent Suite Software and Ion Reporter.

Results: Pre-transplant analyses identified 15 mutations in 9 genes, including driver (VAF of BM 73.1-84.4%, WB 55.8-88.2%, cfDNA 87.6-95.3%) and high-molecular risk (HMR) mutations (BM 36.3-43.1%, WB 29.0-46.6%, cfDNA 42.6-49.6%). Following allo-SCT, all patients achieved remission and engrafted with donor chimerism ≥96%. At day 100, driver and HMR mutations were still detectable in BM and cfDNA (4 patients) but not in WB, with VAFs having decreased by >99%; by 461 days (mean 287) these were no longer detectable. A new *DNMT3A*^{R882C} mutation was detected in cfDNA and WB at 100 days in one patient, with no significant changes in VAF by 560 days (0.27-0.44%). An *U2AF1*^{Q157P} mutation (0.06%) was acquired in another patient at latest point of sampling (260 days). All patients continue in remission.

Conclusion: cfDNA and BM were more sensitive than WB in detecting low-level driver and HMR mutations post-allo-SCT. Concordance between cfDNA and BM suggests cfDNA may be suitable for genomic monitoring. Ongoing monitoring will provide further data to determine the suitability of cfDNA for post-transplant surveillance of driver and HMR mutations in myelofibrosis.

Dual-epitope targeting enables precision therapy for type 1 versus type 2 CALR-mutant MPN

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Aim:

Somatic frameshift mutations in the gene encoding calreticulin (CALR) give rise to myelofibrosis and are classified as Type 1 (del52) or Type 2 (ins5) according to the degree of wildtype sequence retained adjacent to the neopeptide, with Type 2 associated with more aggressive disease. Targeting strategies specific for Type 1 vs Type 2 mutations would have enormous clinical utility in the treatment and prevention of myelofibrosis as responses to tyrosine kinase inhibitors are not durable nor mutation-specific.

Results:

Here we show that dual targeting of Type 1 (del52) mutant CALR with two monoclonal antibodies directed against distinct epitopes in CALR have significant advantages compared to single agent treatment in the eradication of primary patient megakaryocyte progenitors in vitro and in a humanised microenvironment with improved survival in xenograft models. Significantly we observed depletion of CALR+wWF+CD45lo mutant megakaryocytes after ex vivo treatment of primary progenitor cells engrafted into human ossicles created from healthy mesenchymal stromal cells. Dual targeting was superior in blocking constitutive STAT5 and ERK phosphorylation induced by del52 and prevented accumulation of JAK2 phosphorylation, overcoming ruxolitinib resistance. In contrast, Type 2 mutations showed increased CALR dimer formation and cell surface binding due to an extra cysteine encoded by the neopeptide. Type 2 cells were partially resistant to antibody targeting across multiple patients but could be impacted by a ruxolitinib triple combination.

Conclusions:

Together, our data demonstrate an ultra-precision medicine approach tailored to either Type 1 or Type 2 mutation classes will be required for maximal efficacy and complete blockade of JAK/STAT signalling, with far-reaching implications for patient management.

The time has arrived to address long-term care needs in myeloma: a nurse-and-pharmacist-led intervention of a Living Better with Myeloma clinic

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Aim:

People living with multiple myeloma (MM) are at increased risk of cardiovascular disease, infection and secondary primary malignancies¹. There is an unmet need for models of care to address these complex survivorship needs. We tested the feasibility and acceptability of implementing a nurse-and-pharmacist-led survivorship clinic at a tertiary cancer centre.

Method:

A two-phase mixed-methods pilot feasibility study was conducted. In Phase 1, focus groups were undertaken. The *Action, Actor, Context, Target, Time* (AACTT) framework, guided specific behaviours required to implement the clinic into routine care². Phase 2, assessed the feasibility and acceptability of implementing the clinic. Feasibility indicators included the following core components: completion of patient-reported outcome measures (PROMs) pre-clinic, pharmacist-led and nurse-led reviews, care plan development and written communication to GP and primary consultant. Acceptability was evaluated through semi-structured interviews with patients and healthcare professionals (HCPs) guided by the Theoretical Framework of Acceptability (TFA) and Theoretical Domains Framework³. Quantitative findings were analysed descriptively and qualitative data used deductive structured coding.

Results:

A total of 14 HCPs participated in focus groups. Patients with stable MM on maintenance treatment were identified as targets for the intervention. Twenty-six patients consented (72.2% participation). The clinic was feasible to deliver, with all (100%) core components completed. Seventeen referrals to specialities resulted from identified unmet needs. Twenty patients (76.9%) had medications changed following pharmacy review. Nine patients (35 %) were up to date with recommended national cancer screening and seventeen (65%) with recommended vaccinations. The clinic was highly acceptable to patients, who described positive experiences and HCPs who valued the patient-centred holistic approach.

Conclusion:

This study demonstrates that the Living Better with Myeloma clinic is feasible and acceptable to both patients and HCPs. Moreover, it offers a model of care to address the complex needs of people living with myeloma.

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Supporting the Shift: Inpatient Review of BCMA CAR-T Therapy in Multiple Myeloma Reveals Early Safety and Feasibility for a Nurse Lead Outpatient Model of Care

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Aim: BCMA-directed CAR-T therapy has improved outcomes in multiple myeloma but is traditionally inpatient due to toxicity risks. As 4-1BB products show delayed onset, outpatient monitoring may be feasible. This retrospective observational study reviewed incidence, timing, and severity of post-infusion toxicities and evaluated the safety and feasibility of a nurse-led outpatient model of care.

Method: A retrospective consecutive review of 39 MM patients receiving BCMA-directed CAR-T was performed. Two high-risk patients ($\geq 50\%$ marrow infiltration and/or progressive disease despite bridging therapy) and two treated with Abecma® were excluded, leaving 35 patients for evaluation. Data was collected by the CAR-T data manager and included age, gender, ECOG, line of therapy, cytokine release syndrome (CRS) onset, immune effector cell-associated neurotoxicity syndrome (ICANS) onset, and $\geq$ Grade 3 cytopenias within the first five days. Statistics assessed the incidence, timing, and severity of early complications within the first five days to inform feasibility and safety of a nurse-led outpatient model.

Results: The median onset of CRS was Day +7 (range Day +5 - 13), with ICANS also occurring at Day +7. No severe immune-related toxicities or cytopenias necessitating emergency presentation or unplanned admission were observed within the first five days post-infusion. Grade ≥ 3 cytopenias were identified early but were effectively managed with standard supportive measures.

Conclusion: Early complications post-BCMA CAR-T were infrequent and manageable, with CRS and ICANS consistently occurring on or after Day +5. A nurse-led outpatient model from lymphodepleting chemotherapy through Day +5, incorporating daily ambulatory reviews (blood tests, ICE scoring, neurological evaluations) coordinated by an Advanced practice nurse, has been successfully piloted, with four patients safely infused. Transition to admission on Day +5 enables high-risk monitoring during peak CAR-T expansion. This model has been accepted institutionally as the new standard of care, enhancing patient-centred delivery. It supports healthcare sustainability and will reduce hospitalisation by up to six days per patient.

Balancing profound responses with toxicity: real-world experiences with elranatamab in relapsed/refractory multiple myeloma highlight the critical need for advanced, nurse-led supportive care.

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Aim: Elranatamab, a B-cell maturation antigen bispecific antibody is approved for relapsed/refractory multiple myeloma (RRMM) patients with at least three prior lines of therapy including a proteasome inhibitor, immunomodulatory agent and anti-CD38 monoclonal antibody. We describe the implementation and patient outcomes of elranatamab at a single tertiary centre highlighting the essential role of a Multiple Myeloma Nurse Practitioner (MMNP)-led supportive care program.

Method: Drug access was via an early access program or Pharmaceutical Benefits Scheme. Patients received elranatamab step-up dosing during a 5-day inpatient admission or as an outpatient (n=3) with prophylactic tocilizumab. REDCap database was utilised for standardised data entry, including prior therapy, adverse events, and treatment response. Descriptive statistics were used to describe the clinical outcomes and adverse events.

Results: To date 25 patients received elranatamab treatment. The median age was 67 (range 49-78) years. Patients received a median of 5 (range 3-10) prior lines of therapy with a median of 5 (range 1-22) years since diagnosis. 68% of patients achieved a very good partial response or better with an 84% overall response rate. PET scans were performed in 10 patients and 4 achieved complete metabolic response at 6 months post-treatment. Adverse events included cytokine release syndrome (56%, all grade 1-2); multiple infections including cytomegalovirus with 24% requiring therapy; grade 4 neutropenia (56%) requiring filgrastim; skin toxicities including desquamation (11%) and injection site reactions (24%); and fatigue (68%).

Conclusion: A MMNP-led elranatamab delivery model is feasible, safe, and effective in the management of RRMM patients. Elranatamab achieves high response rates in heavily pre-treated patients, and an MMNP-led model enables rapid identification and management of adverse events. This model supports high-quality, coordinated care for both inpatient and outpatient step-up dosing with reduced healthcare resource use and cost burden for outpatient delivery. Further evaluation of patient outcomes is planned as outpatient delivery participation increases.

From data to decisions: Developing a clinical dashboard to support VTE prevention and anticoagulation management

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Background:

Venous thromboembolism (VTE) is a potentially preventable cause of significant morbidity and mortality in hospitalised patients. Appropriate VTE prophylaxis significantly reduces the risk of hospital-acquired VTE. However, inconsistent documentation of VTE risk assessments, and inappropriate prescribing and monitoring of anticoagulants remains common. These gaps highlight the need for proactive, system-wide anticoagulation stewardship. Funding was secured for a 12-month quality improvement project for an anticoagulation stewardship pharmacist to design and implement a clinical dashboard to support real-time identification of patients at risk of VTE or anticoagulant-related harm.

Aim:

To develop a prototype anticoagulation stewardship dashboard integrated within the electronic medical record (EMR) to identify hospitalised patients at increased risk of VTE or anticoagulant-related harm.

Method:

Hospital-acquired complication data, anticoagulation prescribing data, VTE risk assessment completion rates, and medication incident reports were reviewed to identify key problems and preventable factors. Based on these findings, predefined clinical rules were developed to proactively identify at-risk patients using real-time EMR data. Once built, the prototype was user-tested to guide further improvements.

Evaluation:

Evaluation focused on the initial dashboard build and iterative refinement of its design, layout, and underlying clinical logic. User testing with an anticoagulation stewardship pharmacist assessed usability, clarity of information display and appropriateness of rule thresholds. Feedback informed refinement of rule logic, prioritisation of risk indicators, and optimisation of dashboard navigation to support efficient oversight of unit level signals and individual patient review.

Conclusion:

This project demonstrates the potential of EMR-embedded, real-time identification of anticoagulation-related problems to strengthen anticoagulation stewardship. Unlike retrospective audits or externally hosted dashboards, this EMR-integrated tool enables timely, targeted intervention within the same system. Future work will focus on implementing a formal model of care to support sustained and scalable use of the dashboard in clinical practice.

Evaluating a universal calibrator to exclude significant levels of apixaban and rivaroxaban: A blinded, multisite interlaboratory validation study.

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Aim: The direct oral anticoagulants (DOACs) rivaroxaban and apixaban are not reliably excluded by standard coagulation tests, posing challenges in the emergency setting where rapid decision-making is required. A universal assay to reliably exclude clinically significant levels of drug would guide use of reversal agents and safety for procedures. Chromogenic anti-Xa assays using a low molecular weight heparin (LMWH) calibrator are widely available, and have demonstrated strong correlation with drug-specific anti-Xa activities. However, this correlation varies across analyser/reagent/calibrator combinations, and no real-world validation data between laboratories using different analysers are available.

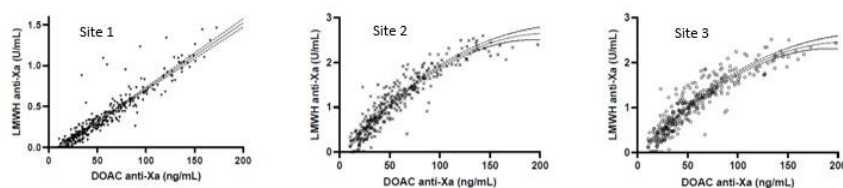
This study aimed to determine and validate clinically relevant LMWH anti-Xa cutpoints correlating to apixaban or rivaroxaban levels of 50ng/mL (primary endpoint), 30ng/mL, and 75ng/mL across 3 separate laboratories.

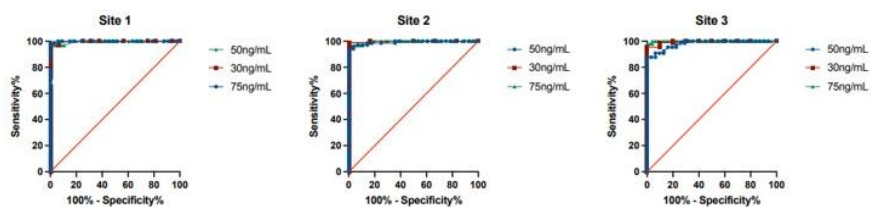
Method: We performed anti-Xa activities on stored plasma samples from patients on rivaroxaban or apixaban using drug-specific and LMWH calibrators at three laboratories with different analyser/reagent/calibrator combinations in Melbourne, Australia (n=314). LMWH anti-Xa activity thresholds corresponding to pooled DOAC levels of 30ng/mL, 50ng/mL and 75ng/mL were derived, and prospectively validated through a blinded inter-laboratory sample exchange (n=297). Regression analysis, receiver operator curves, Pearsons correlation coefficient and R-square values were used to determine optimal models and cutpoints.

Results: Strong correlations were observed between LMWH and drug-specific combined DOAC anti-Xa activities across all sites. LMWH anti-Xa cut points for 30ng/mL, 50ng/mL, and 75ng/mL were derived at each laboratory for prospective validation (figure 1). Sensitivity of these cut-points was 93.3%-98.7% for 50ng/mL, 95.6-98.3% for 30ng/mL, and 90.5-97.5% for 75ng/mL.

Conclusion: This is the first multisite prospective study validating the use of a LMWH-calibrated anti-Xa activity to accurately exclude clinically significant levels of rivaroxaban and apixaban. This supports the use of a LMWH calibrated anti-Xa assay as a universal, accessible tool for DOAC assessment in the emergency setting, optimising clinical decision-making and resource utilization.

Figure 1. Anti-Xa correlations and ROC analyses by site





VTE-STOP: Improving venous thromboembolism prevention through targeted risk assessment and prescribing interventions

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Aim:

Hospital-acquired venous thromboembolism (VTE) is a major cause of preventable morbidity and mortality. VTE-STOP aimed to improve VTE and bleeding risk assessment documentation and appropriate thromboprophylaxis prescribing through targeted interventions in a non-EMR Acute Medical Unit (AMU), with a goal of achieving ≥85% compliance in line with VicTAG Anticoagulation Stewardship indicators.

Method:

VTE-STOP was implemented as a 12-week quality improvement initiative (October 2025–January 2026) in the AMU of a tertiary metropolitan hospital using paper-based prescribing. A pre-implementation staff survey identified key barriers, including time pressures, limited confidence, and unclear clinical responsibility, which informed intervention design. Interventions included a simplified decision-support tool available as quick-reference lanyard cards and in patient folders, updated admission documentation with embedded prompts, targeted education, and engagement strategies supported by a medical registrar VTE champion. Baseline audit data (August 2025) were compared with mid- and post-implementation audits using a standardised VTE prevention audit tool. Staff awareness was assessed through pre- and post-implementation surveys. Changes were analysed using two-proportion z-tests.

Results:

Documentation of VTE risk assessment increased from 2.9% at baseline to 61.1% post-implementation ($p < 0.001$), with completion within 24 hours improving from 2.9% to 58.3% ($p < 0.001$). Appropriateness of thromboprophylaxis improved from 74.3% to 91.7% ($p = 0.057$). Staff awareness of VTE prevention practices improved markedly, achieving 100% awareness of the local VTE prevention policy and risk assessment tool post-implementation.

Conclusion:

VTE-STOP demonstrated that a co-designed, stewardship-led intervention can significantly improve VTE prevention practices in a high-turnover, non-EMR clinical setting. Following success in the AMU, the program has expanded into Haematology and Oncology services, with implementation in Gerontology underway. Feedback from VTE-STOP is informing collaboration to update the statewide paper Anticoagulation Medication Chart, supporting scalability beyond electronic solutions.

Establishing the broad assay of complement overactivation (BACON) as a potential diagnostic test

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Aim:

We have developed a cell based functional assay to detect complement overactivation in serum. The assay is based on the modified HAM developed by Gavrilaki et al¹ but is distinctly different in its simplicity and adaptability to the diagnostic laboratory. The aim of this study was to validate our assay using samples from patients with clinically diagnosed complement mediated thrombotic microangiopathy (CM-TMA) compared to those with non-complement mediated TTP and normal controls.

Methods:

Participants (21 normal, 14 CM-TMA, 5 TTP) were recruited from 6 tertiary hospitals. Serum samples were stored at -80°C and transferred to the central research laboratory for testing. Positive controls were constructed by spiking normal serum with shiga toxin 1, B subunit. Heat inactivated serum was used as a negative control for each sample. Serums were incubated with a complement sensitive cell line for 3h and the percentage of cells with permeabilised plasma membranes quantified by flow cytometry using a viability dye. Clinical accuracy was assessed by ROC analysis.

Results:

Normal serum was used calculate intra- and inter- assay variabilities of 1.08% (n=10) and 1.23% (n=23), respectively, and establish a lower cut-off of 6.2%. All shiga toxin spiked controls produced positive BACON results with an average of $91.15 \pm 3.34\%$ (n=21) permeabilised cells (inter assay CV=3.67%, n=9). Testing of clinical samples revealed 9 true positives (8 active CM-TMA and 1 poorly controlled despite ravulizumab therapy) and 7 true negatives (3 CM-TMA patients on C5 inhibition and 4 TTP patients). There was 1 false positive and 4 false negatives. Overall clinical accuracy was 86% with ROC AUC= 0.784 (95%CI: 0.634 – 0.894, P=0.005).

Conclusion:

BACON is a quick and reliable way to detect fluid phase complement overactivation in patient serum and may be a useful tool to aid in the diagnosis of conditions such as CM-TMA.

1. Gavrilaki, E., et al., *Modified Ham test for atypical hemolytic uremic syndrome*. Blood, 2015. **125**(23): p. 3637-46.

Implementation and evaluation of a proactive anticoagulant stewardship service across a large metropolitan health service: a quality improvement initiative

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Aim:

To evaluate the 12-month outcomes of the Metro South Health (MSH) Anticoagulant Stewardship (ACS) service - a proactive, risk-stratified surveillance model designed to reduce anticoagulant-related harm across a metropolitan health service.

Method:

A prospective quality improvement evaluation was conducted across four MSH hospital sites (22 April 2025 - 3 April 2026). The service comprised of 0.8 FTE Haematologist and 1.0 FTE Pharmacist. An electronic dashboard was customised to proactively identify patients prescribed anticoagulants meeting pre-specified high-risk criteria (including <50kg/120kg, eGFR<30, platelet <50, 2+ anticoagulation orders, home anticoagulation withheld). Multidisciplinary virtual rounds occurred three-times-weekly, with pharmacist-led surveillance on remaining days. Steering Committee-endorsed KPIs were monitored: service utilisation, clinical interventions, clinician receptiveness, reported clinical incidents and Hospital-Acquired Complications (HACs: PE HAC 7.1, DVT HAC 7.2, haemorrhagic disorders HAC 10.2).

Results:

The dashboard captured 6,000–6,500 patients weekly, with 25% meeting high-risk criteria. Clinical interventions averaged 44/week (range 18–69; total 2233), 33% were referrals and 67% from dashboard screening. Common categories requiring ACS-initiated intervention included weight extremes (34%), (2+ anticoagulants (21%), UFH (13%), and eGFR <30 (10%). Clinician receptiveness was high: 82% of recommendations accepted within 24 hours, and only 5% not accepted. No SAC 1 incidents were recorded; SAC 3-4 incidents trended downward from 42/month (April 2025) to 16/month (March 2026). Quarterly HAC data showed reductions in hospital-acquired PE (34 vs 25), DVT (25 vs 17), and anticoagulation-related haemorrhage (28 vs 21). The service received permanent funding in February 2026.

Conclusion:

The MSH ACS service demonstrated strong reach, high clinician engagement, and sustained stewardship activity, with encouraging trends in anticoagulant-related HACs and incident data. The model supports NSQHS Standard 4 compliance and offers a scalable framework for anticoagulant stewardship. Extended resourcing to outpatient and satellite sites would further reduce organisation-wide anticoagulant-related harm.

Butterfly: The safety and acceptability of a subcutaneous catheter for the administration of low molecular weight heparins

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Aim: Certain patient groups require long term low molecular weight heparin (LMWH) therapy for the treatment or prevention of blood clots. Long term injections carry morbidity due to pain and anxiety. A subcutaneous catheter can reduce the injection burden, and is frequently used in the paediatric and palliative care settings. This study evaluates the safety, feasibility and acceptability of a subcutaneous catheter for LMWH administration in adults.

Methods: A prospective crossover study for patients receiving prophylactic and therapeutic doses of LMWH. The catheter remained in place for up to 1 week, and drug exposure was assessed using serial anti-Xa assessments via both methods (catheter and direct injections). Site complications, duration of catheter lifespan, and patient preferences were assessed. Descriptive statistics and paired t-test were used for analysis.

Results: 12 patients completed the initial study crossover period, 6 in the prophylactic arm and 6 in the therapeutic arm. Median age was 33.9years, and all enrolled patients were female, 7 of whom were pregnant. There was no clinically or statistically significant difference in anti-Xa assessments between methods for either prophylactic ($p=0.77$) or therapeutic ($p=0.54$) groups, with a mean difference in anti-Xa exposure of $<0.1\text{IU/mL}$. 11/12 patients preferred the subcutaneous catheter due to less impact on daily life, and reduced discomfort and anxiety related to injections. The main complications related to the device were local bruising, and 2 patients experienced local bleeding at removal of the device which resolved with pressure. The majority of patients (9/10) wished to continue using the subcutaneous catheter. See table 1 for additional information.

Conclusion: An indwelling subcutaneous catheter appears safe and feasible for patients requiring long-term LMWH therapy with no significant difference in drug exposure between administration methods. Catheter-related complications were minor, with less negative impact on daily life as compared to subcutaneous injections.

Table 1. Patient characteristics

Patient characteristics	Prophylactic arm (n=6)	Therapeutic arm (n=6)
Age (median, IQR)	33 years (30, 37)	56 years (38, 61)
Weight (median, IQR)	106.7kg (88.8, 111.1)	82kg (73.4, 89.1)
BMI (median, IQR)	39.0 (31.0, 40.6)	29.8 (29.5, 30.0)
Pregnant (%)	5 (83.3%)	2 (33.3%)
Day of catheter removal*	Day 7 (5.5, 7)	Day 8 (7, 8)
Complications related to catheter (%)	6 (100%)	3 (50%)
Bruising	4 (66.7%)	2 (33.3%)
Bleeding	0 (0)	2 (33.3%)
Pain	1 (16.7%)	3 (50%)
Erythema	2 (33.3%)	1 (16.7%)
Swelling / induration	0 (0)	1 (16.7%)
Infection	0 (0)	0 (0)
Mean difference in mean anti-Xa exposure	0.004IU/mL	0.043IU/mL
Percentage difference in mean anti-Xa exposure	2.7%	13%

*day of insertion is day 1

Durable efficacy of lenzilumab plus azacitidine in newly diagnosed proliferative CMML patients: Interim analysis after four years of study commencement

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Introduction:

Proliferative chronic myelomonocytic leukemia (CMML) is an increasingly recognized blood cancer involving pro-inflammatory monocytes with no approved treatments in Australia or United Kingdom. The PREcision Approach to CHronic Myelomonocytic Leukemia (PREACH-M; ACTRN12621000223831) trial investigates novel CMML therapies directed by molecular profiling. Lenzilumab, a first-in-class monoclonal antibody that neutralizes GM-CSF.

Methods:

PREACH-M is a Phase 2/3 non-randomized, uncontrolled, open-label trial in 54 adults aged at least 18 years, newly diagnosed CMML stratified according to mutation. Subjects exhibiting RAS-pathway mutations (NRAS, KRAS, CBL, PTPN11, NF1, BRAF) receive 24 cycles (every 28 days) of AZA (SC; 75 mg/m² for 7 days) and LENZ (IV; 552 mg; d1 & d15 of cycle 1 and d1 only for all subsequent cycles); while those with only TET2 mutations receive the same AZA regimen and sodium ascorbate (IV; 30 g for 7 days; PO 1.1g on all other days).

Results:

As of Oct 31, 2025, 36 patients were enrolled in the LENZ-AZA arm of the study. Of 29 patients that had response data available within 12 months of study commencement, 25 out of 29 (86%) had either a complete remission or a marrow complete response (bone marrow blasts less than 5%) according to IWG 2006 criteria at some point within 12 months.

The most common mutations that showed durable decreases in VAF were *CBL*, *NRAS*, *KRAS*, *SRSF2* with some modest decreases in *ASXL1* and *TET2* observed in the first 3 months. In contrast, mutations in *TP53*, *RUNX1*, *STAG2*, *MPL* and *FLT3* increased while patients were on study.

Conclusion:

Interim analysis of the PREACH-M trial shows promising results with LENZ/AZA resulting in durable complete responses beyond 12 months with 86% of subjects achieving a complete remission or marrow complete remission without significant LENZ related toxicity.

Clonal architecture and microenvironmental drivers of donor-derived haematological neoplasm after allogeneic haematopoietic stem cell transplant

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Aim: Donor-derived haematological neoplasm (DDHN) is an increasingly recognised, but poorly understood complication of allogeneic HSCT. We performed an integrated clinical and biological analysis to elucidate DDHN burden, clonal evolution and pathogenesis.

Method: We screened 811 patients transplanted at the Royal Adelaide Hospital between 1990–2023 to determine DDHN incidence. We characterised clonal evolution by next-generation sequencing and microenvironmental contributions in vitro using expanded bone marrow mesenchymal stromal cells (BM-MSC) collected at serial timepoints.

Results: Thirteen (1.6%) cases of DDHN were identified locally, a >10-fold higher incidence than prior European and Japanese registry studies. Notably, two cases were initially misclassified as relapse, suggesting some presumed relapses may represent unrecognised DDHN. Median time to diagnosis was 33.6 months (95% CI, 16.3–61.3), and two-year overall survival was 40.1% (95% CI, 47.4–99.8). Given the rarity of DDHN, we augmented our cohort with five additional cases (total 18 cases) from collaborating centres to facilitate comprehensive molecular profiling. The DDHN cases were enriched for adverse-risk cytogenetic lesions (44%), including monosomy/derivative-7 (17%) and complex karyotype (17%); and for mutations in epigenetic regulators (67%), with *DNMT3A^{mut}* (39%) and *TET2^{mut}* (17%) most frequent (Figure 1A). Interestingly, *DNMT3A^{mut}*- and *TET2^{mut}*-DDHN exhibited distinct evolutionary kinetics: *DNMT3A^{mut}* had paradoxically shorter latency despite slower steady-state clonal expansion, whereas *TET2^{mut}* evolved later despite faster steady-state growth. Paired donor-recipient analyses demonstrated accelerated recipient-biased clonal expansion and divergent malignant evolution from shared ancestral clones. Strikingly, our stromal profiling demonstrated that DDHN-derived BM-MSCs were profoundly senescent (Figure 1B) and secreted excessive levels of pro-inflammatory senescence-associated secretory phenotype mediators, including IL-1 β ; with subsequent in vitro modelling in *TET2*-knockout CD34+ cells exhibiting preferential growth in pro-inflammatory DDHN-derived BM-MSC conditioned media (Figure 1C) that had considerably elevated IL-1 β levels.

Conclusion: Collectively, these findings demonstrate DDHN are substantially under-recognised and supports a model in which donor clonal fitness is shaped by recipient inflammatory bone marrow niche selection post-alloHSCT. Targeting senescence-associated pathways may offer a strategy to disrupt disease evolution.

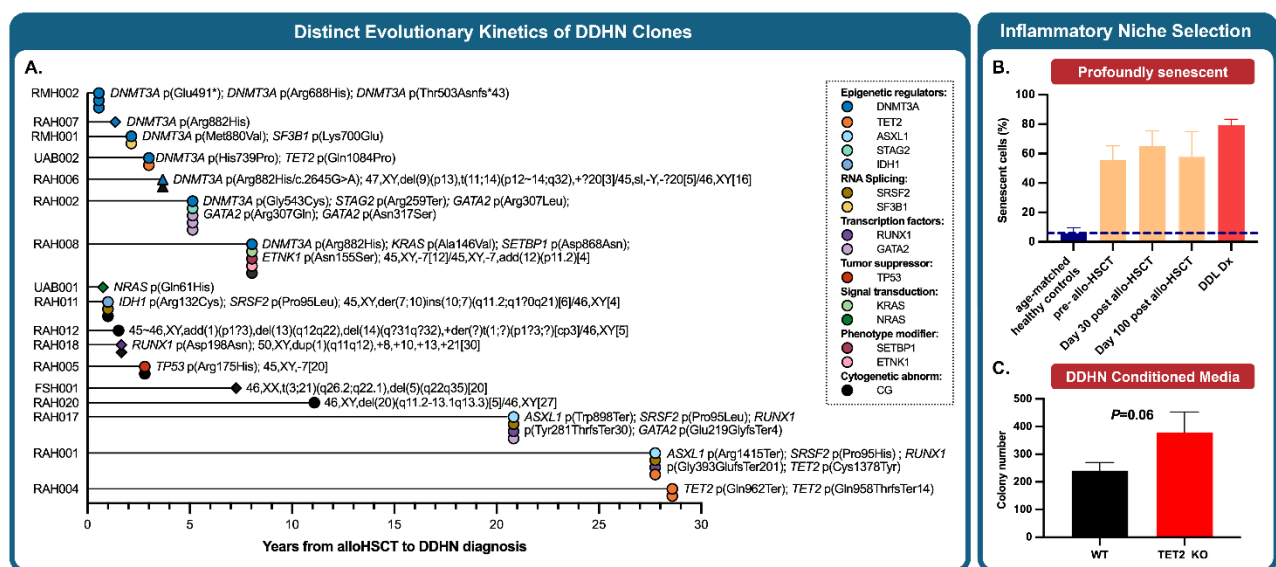


Figure 1: Characterisation of DDHN clonal architecture and bone marrow microenvironment. (A) Distinct molecular profile of DDHN cases by time to diagnosis (years) and adverse-risk cytogenetic enrichment. (B) Profoundly senescent phenotype in DDHN bone marrow mesenchymal stromal cells (BM-MSC) assessed by the percentage of β -galactosidase-positive cells at passage 3. (C) Colony numbers of wild-type (WT) and TET2-knockout (KO) CD34⁺ cells cultured for 2 days in 50% DDHN-derived BM-MSC conditioned media, followed by MethoCult culture for 12–15 days.

Development of an allogeneic CAR-T cell therapy for mature T cell Lymphomas

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Background:

Relapsed or refractory T cell lymphoma (TCL) is an aggressive blood cancer with limited treatments and poor outcomes. Although CAR-T cell therapy shows promise, no approved therapies exist for TCL. Challenges include shared antigens on healthy and malignant T cells, leading to toxicity; low numbers of healthy T cells; and antigen escape. Developing TCL-specific CAR-T therapies is urgently needed.

Aims:

To create an allogeneic CAR-T therapy targeting KIR3DL2, which is highly expressed on tumour cells but minimally on healthy T and NK cells. Additionally, to combine pharmacologic approaches with CAR-T cells to address tumour heterogeneity and antigen escape.

Methods:

We developed second-generation KIR3DL2 CAR-T cells and evaluated their efficacy in murine xenograft models of cutaneous and leukemic T-cell lymphoma. These allogeneic CAR-T cells were generated via CRISPR-Cas9 HDR, inserting the CAR into the *TRAC* locus and HLA-E into the *B2M* locus. A high-throughput-drug-screen was performed to boost KIR3DL2 expression on tumour T cells, aiming to enhance CAR-T effectiveness against antigen-low tumour cells.

Results:

KIR3DL2-CAR-T cells effectively controlled tumour growth, with 80% of mice surviving beyond 60 days compared to 12 days in controls (n=6; p<0.0001, Mantel-Cox test). Due to manufacturing limitations, allogeneic CAR-T cells were produced with over 50% double knock-in and 80% double knock-out efficiencies, with robust expansion. These cells demonstrated high cytotoxicity against TCL patient tumour samples at a 2:1 effector-to-target ratio (n=8). The drug screen identified HDAC inhibitors as top candidates for upregulating KIR3DL2, thereby countering antigen-low escape.

Conclusion:

We developed an off-the-shelf CAR-T therapy for TCL by employing a multi-pronged approach that includes careful target selection, CRISPR-HDR, and drug screening. Our KIR3DL2 CAR-T cells showed increased efficacy and specificity in preclinical models. Drug screening expands potential applications across TCL subtypes. These results indicate our platform could be an innovative, much-needed treatment to improve patient outcomes.

Matrix stiffness drives dysfunctional megakaryopoiesis in a novel human 3D model of primary myelofibrosis

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Aim:

Primary myelofibrosis (PMF) is characterised by fibrotic remodelling of the bone marrow and abnormal megakaryopoiesis, yet the contribution of extracellular matrix stiffness to megakaryocyte dysfunction remains poorly understood. We aimed to establish a tunable three-dimensional (3D) culture system to investigate how matrix stiffness regulates human megakaryocyte maturation and whether fibrotic-like mechanical conditions recapitulate features of PMF-associated megakaryopoiesis.

Method:

Synthetic polyisocyanide hydrogels functionalised with integrin-binding peptides were engineered to model soft marrow-like and stiffer fibrotic-like microenvironments. Primary human CD34⁺ haematopoietic stem/progenitor cells, isolated from donor leukoreduction filters, were cultured in hydrogels with defined stiffness. Megakaryocyte maturation was assessed by confocal microscopy, flow cytometry, ploidy analysis, and quantitative RT-PCR. Statistical analyses included Student's t-test and ANOVA with post hoc testing.

Results:

The findings supported the hypothesis that increased matrix stiffness disrupts human megakaryocyte maturation and induces features of fibrotic megakaryopoiesis. Soft hydrogels supported coordinated megakaryocyte maturation, including cytoplasmic expansion, cytoskeletal remodelling, proplatelet formation, and increased CD42b expression. In contrast, increased matrix stiffness impaired cytoplasmic maturation and reduced expression of integrins involved in matrix sensing, while permitting ongoing nuclear polyploidisation. Megakaryocytes cultured in stiff hydrogels were smaller, exhibited impaired spreading and reduced cytoskeletal reorganisation, yet showed increased ploidy with occasional giant cells. Stiffer matrices also delayed immunophenotypic maturation, with persistence of CD34⁺ progenitors and significantly reduced acquisition of CD42b (66% in soft versus 33% in stiff hydrogels; $P = 0.014$).

Conclusion:

We establish a novel tunable human 3D model of fibrotic megakaryopoiesis that provides mechanistic insight into the role of the marrow microenvironment in PMF pathogenesis. Matrix stiffness directly regulates human megakaryocyte maturation and reproduces key features of dysfunctional megakaryopoiesis observed in PMF, supporting an active role for fibrotic marrow remodelling in PMF progression. Our platform offers a clinically relevant system for studying disease mechanisms and evaluating microenvironment-targeted therapies in myeloproliferative neoplasms.

Real-world application of the IMS/IMWG consensus genomic staging criteria for high-risk multiple myeloma: a report from the Australia and New Zealand Myeloma and Related Diseases Registry

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Aim:

The International Myeloma Society/International Myeloma Working Group consensus genomic staging (IMS/IMWG CGS) criteria were recently proposed to define high-risk multiple myeloma (Avet-Loiseau et al., 2025). This study evaluated the real-world validity of a modified IMS/IMWG definition and compared its predictive performance with established staging systems.

Method:

We conducted a retrospective cohort analysis of patients diagnosed between 2012-2025 from the Australia and New Zealand Myeloma and Related Diseases Registry. Due to lack of availability, routine next-generation sequencing data for TP53 mutation and biallelic del(1p32) were excluded from the modified IMS/IMWG criteria. We assessed the association of CGS risk groups with overall survival (OS) and progression-free survival (PFS) in the overall cohort, and in transplanted, frail and renal impairment subgroups. We also evaluated the performance of the modified CGS against the ISS, R-ISS and R2-ISS in predicting functional high-risk disease (FHR; defined as PFS-1 <18 months).

Results:

Of 832 patients, 567 (68%) had determinable modified CGS status (166 high-risk, 401 standard-risk). High-risk disease conferred a near doubling of the hazard of death (HR 1.90, $p < 0.001$). This association was strongest in transplant-eligible (HR 2.73, $p < 0.001$), non-frail (HR 3.22, $p < 0.001$) and normal renal function (HR 2.33, $p < 0.001$) subgroups, but was attenuated and not statistically significant in transplant-ineligible (HR 1.32, $p = 0.18$), frail (HR 1.36; $p = 0.11$), and renal impairment (HR 1.50, $p = 0.09$) subgroups. Modified IMS/IMWG CGS high-risk status was associated with early progression (OR 2.17; $p < 0.001$), but did not clearly outperform ISS (OR 2.36, $p < 0.001$), R-ISS (OR 3.29, $p < 0.001$) or R2-ISS (OR 3.34, $p < 0.001$) in predicting FHR disease.

Conclusion:

A modified application of the IMS/IMWG CGS identified high-risk disease at rates comparable to previous reports and predicted inferior survival in this real-world cohort. However, its prognostic performance appears reduced in transplant-ineligible, frail and renal impairment populations. FHR disease remains poorly predicted, highlighting the continued importance of dynamic response-based assessments.

Table 1: Odds ratios for association with early progression in high-risk disease as defined by the ISS, R-ISS and IMS/IMWG CGS-HR criteria with associated positive and negative predictive values						
Risk Scoring System	Odds Ratio for PFS-1 <18m (95% CI)	p-value†	AUC (95% CI)	PPV	NPV	n
ISS III vs non-ISS III	2.36 (1.62–3.45)	<0.001	0.597 (0.553–0.640)	44%	75%	539
R-ISS III vs non-R-ISS III	3.29 (1.97–5.52)	<0.001	0.585 (0.545–0.625)	56%	72%	446
R2-ISS III/IV vs non R2-ISS III/IV	3.34 (2.09–5.33)	<0.001	0.64 (0.591–0.689)	44%	81%	380
IMS/IMWG CGS-HR vs CGS-SR	2.17 (1.41–3.32)	<0.001	0.583 (0.538–0.628)	43%	74%	500
Key: ISS, International Staging System; R-ISS, Revised International Staging System; R2-ISS, The Second Revision of the International Staging System; IMS/IMWG CGS-HR, consensus genomic staging as defined by the International Myeloma Society (IMS)/ International Myeloma Working Group (IMWG) in 2025. †Hypothesis testing using a logistic regression model.						

A cytokine-based biomarker model to predict the onset of moderate to severe chronic graft-versus-host disease

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Aim

Chronic graft-versus-host disease (cGVHD) affects 10–20% of allogeneic stem cell transplant (alloSCT) recipients and can cause irreversible multisystem damage if not identified early. We aimed to develop a day 100 (D100) cytokine biomarker model to predict moderate-to-severe (M-S) cGVHD risk and inform surveillance and prophylaxis strategies.

Methods

D100 serum samples were prospectively collected from consecutive alloSCT recipients at The Alfred Hospital (January 2022–January 2024). Cytokines were quantified using a 9-colour LEGENDplex™ assay on the CYTEK Northern Lights platform. cGVHD was defined by 2014 NIH consensus criteria. Candidate cytokines were screened by receiver-operating-characteristic (ROC) analysis and incorporated into a multivariable logistic regression model. The model optimal cutoff value was determined by ROC analysis.

Results

Seventy-seven patients were included (median age 61 years; IQR 46–68), with 14% developing M-S cGVHD. 23 (28.5%) received matched related donors, 28 (36%) matched unrelated donors, and 26 (33.7%) haploidentical donors. 87% received post-transplant cyclophosphamide as GVHD prophylaxis. Among the nine cytokines tested, TNFα, IL-6, and TGF-β1 demonstrated satisfactory predictive signal via ROC analysis (area-under-curve (AUC) >0.6) and were integrated into a multivariable model:

$$\text{logit}(P) = -1.38 + 1.02 \cdot \log(\text{TNF}\alpha + 1) - 1.58 \cdot \log(\text{IL-6} + 1) + 0.51 \cdot \log(\text{TGF}\beta 1 + 1)$$

where P = probability score

The model showed strong discrimination (AUC 0.81) and effectively stratified patients using a cutoff of 0.18 (Figure 1). To enable external applicability, a standardised cytokine probability score (CPS) was derived:

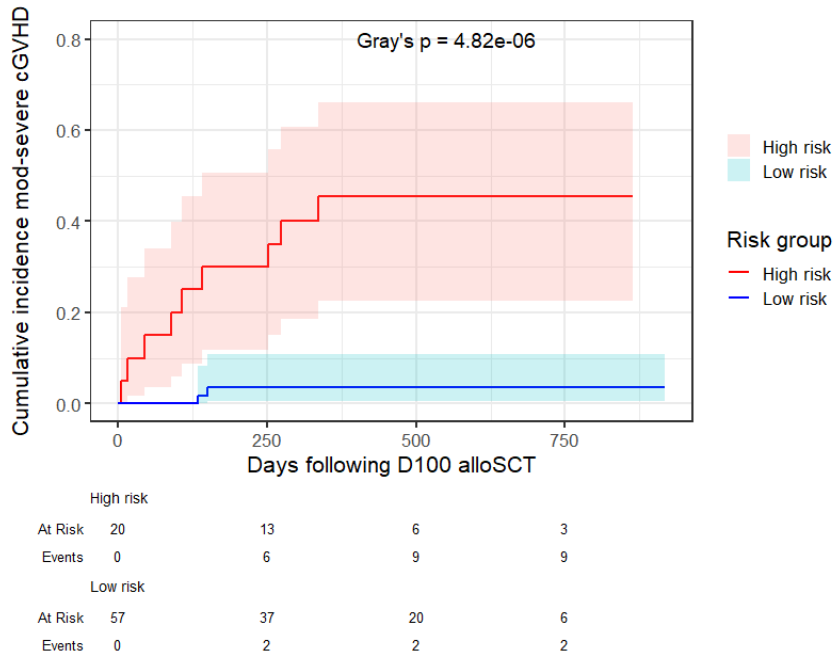
$$\text{CPS} = 1.02 \cdot Z^{\text{TNF}\alpha} - 1.58 \cdot Z^{\text{IL-6}} + 0.51 \cdot Z^{\text{TGF}\beta 1}$$

where $Z = (\log(x+1) - \mu)/\sigma$ represents the number of standard deviations from the cohort mean.

Conclusion

We present a novel cytokine signature that predicts M-S cGVHD from a single D100 sample with strong discriminatory performance. This approach enables early identification of high-risk patients and provides a practical framework for risk-adapted monitoring and pre-emptive intervention. Future collaborative studies would be useful in validating this algorithm.

Figure 1: Cumulative incidence plot demonstrating separation of groups according to M-S cGVHD risk as predicted by the model.



Upfront mycophenolate in newly diagnosed ITP is highly effective and well tolerated with durable responses

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Aim:

To assess real-world durability of responses in newly diagnosed ITP treated with mycophenolate plus prednisolone.

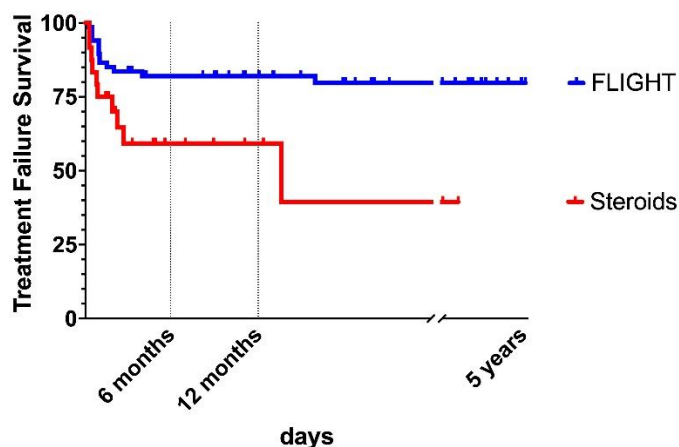
Method:

A single-centre case review was conducted of all consecutive patients newly diagnosed with primary ITP from January 2020 to December 2025, mycophenolate was routinely added to prednisolone 1mg/kg for all newly diagnosed patients. Mycophenolate was started at 500mg bd for the first week, then increased to 1000mg bd if tolerated and ceased without taper after 6 months. Prednisolone was fully tapered within 8 weeks. Patients were monitored weekly by phone review with full blood counts until one week post prednisolone cessation and then monthly until one month post mycophenolate cessation with second monthly follow up until 1 year. Subsequent phone contact and blood counts were performed to determine ongoing remission status. Real-world comparisons are made with an alternative tertiary referral hospital treating with steroids as first-line.

Results:

67 patients were treated over a 6 year period with median follow up of 611 days with a 88.0% (59/67) response rate. These responses were maintained at 12 months with an overall response rate 92.3% (48/52) and complete response rate 84.6% (44/52) by IWG criteria. Mycophenolate was well tolerated and 88.7% (55/62) completed scheduled treatment. Seven patients ceased mycophenolate within the first 4 weeks due to intolerance. Only five patients were refractory to therapy and required treatment change within 6 months.

Amongst patients in complete remission at 12 months, only one patient relapsed after median follow-up 736 days. Thus the durable complete remission rate is 82.7% (43/52), and the 12 month treatment failure survival rate is 82.0% compared to 59.2% with standard-of-care/steroids.



Conclusion:

Response rates in our real-world cohort are very similar to the prospective FLIGHT study (88.0% vs 91.5% Bradbury et al NEJM 2021). However, our longer term follow-up confirms excellent durability, and supports a potential disease-modifying role of upfront mycophenolate added to steroids for newly diagnosed ITP.

Use of data-independent mass spectrometry (DIA-MS) to identify plasma proteomic profiles associated with major adverse cardiovascular events in chronic kidney disease patients

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Aim:

Cardiovascular disease (CVD) is the leading cause of mortality in chronic kidney disease (CKD), yet accurate risk prediction remains elusive. We aim to characterise plasma proteomic differences between CKD patients who experienced a major cardiovascular adverse event (MACE) and those who did not.

Method:

We conducted a case-control biomarker discovery study using plasma samples from 60 CKD patients (eGFR<30ml/min/1.73m²) enrolled in a prospective observational cohort at Northern Health, Australia. Thirty-nine patients with MACE (myocardial infarction, stroke/transient ischaemic attack, or cardiovascular death) were matched to 21 patients without events. Baseline demographics and plasma were collected at recruitment.

Optimised on-bead enzymatic digest protocols were applied to plasma samples and unbiased proteomic profiling was performed using high-resolution data-independent acquisition mass spectrometry on a Bruker timsTOF HT platform. Data were processed using Spectronaut, and protein-level abundance estimates derived using limma. Gene ontology biological process enrichment was assessed via gene set enrichment analysis (GSEA), with normalised enrichment scores calculated. Processes with false discovery rate <0.05 were considered significant.

Results:

Sixty patients (median age 64.5 years; 65% males) were included. Between groups eGFR did not differ (p=0.28) but more MACE patients were dialysis-dependent (57.1% vs 89.7%, p=0.003).

To elucidate functional implications of proteomic findings, GSEA was performed on the 11 differentially expressed proteins (adj p-value < 0.05). We observed significant upregulation of key biological pathways related to proteasome-mediated ubiquitin-dependent protein catabolic processes, cell cycle regulation, and mitochondrial repair pathways, suggesting heightened proteostatic and cellular stress. Conversely, lipid and cholesterol transport pathways including cholesterol efflux and HDL particle remodelling were significantly downregulated, indicating impaired HDL functionality and dysregulated lipid metabolism.

Conclusion:

CKD patients with MACE demonstrated distinct plasma proteomic signatures marked by impaired lipid metabolism, increased proteasome activity and cellular stress pathways. These

findings highlight potential mechanisms of CVD and opportunities for biomarker development and targeted intervention.

Erp57 regulates Von Willebrand factor production

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Aim: The production of secreted proteins is under the control of chaperones and foldases in the endoplasmic reticulum¹ such as endoplasmic reticulum 57 (ERp57).² The aim of this project was to identify megakaryocyte and platelet protein substrates of ERp57 and how these affect thrombus formation.

Method: We used mice with megakaryocyte-specific ERp57 deficiency (conditional knockout, CKO) and human immortalized megakaryocytes (imMKCLs) with CRISPR-mediated ERp57 deletion. Platelets were isolated from mice and the protein content was analysed by mass spectrometry. Mouse plasma was collected to measure circulating Von Willebrand factor (vWF) level and function. Mouse femur bones were harvested to measure vWF expression in megakaryocytes. Platelet production in ERp57 CKO mice was measured by flow cytometry following platelet depletion assays with injection of R300 (anti-GPIb α) antibody. Proplatelet formation in ERp57 deficient imMKCLs was measured by immunohistochemistry. vWF in mouse platelets, mouse megakaryocytes and imMKCLs was measured by immunofluorescence confocal microscopy. Thrombus formation in ERp57 CKO mice was studied using a laser-induced venous thrombosis model³ and an electrolytic injury-induced carotid artery thrombosis model.

Results: ERp57-deficient mouse platelets exhibited markedly decreased amount of vWF which was consistent with our finding of decreased vWF expression in human ERp57-deficient imMKCLs (**Fig. 1A**). ERp57 CKO mice had decreased amount of plasma vWF. In vivo, ERp57 CKO mice demonstrated reduced vWF accumulation at sites of both venous and arterial injury (**Fig. 1B**). Platelet turnover was unchanged between ERp57 CKO and control mice, indicating that decreased platelet vWF was not due to altered platelet lifespan.

Conclusion: These findings identify ERp57 as a key regulator of vWF biosynthesis in maturing megakaryocytes, potentially through effects on protein folding or glycosylation. Defective ERp57 function may affect vWF production and function which may have implications in von Willebrand disease.

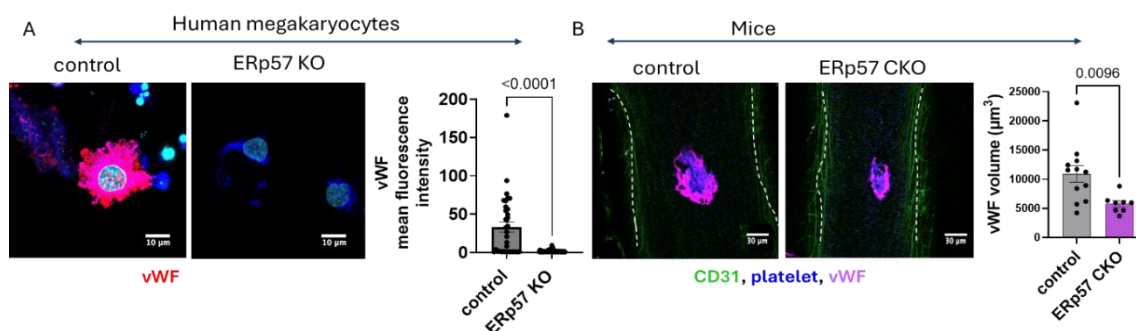


Figure 1.
ERp57

deficiency decreases vWF production. A. Immunostaining of vWF in wild type (control) versus ERp57 knockout immortalized megakaryocytes, Mann-Whitney test. vWF is shown in red. **B.** Detection of vWF in vivo at the site of mesenteric vein injury in mice with ERp57 deficient platelets versus control mice, n=3 mice per group, Mann-Whitney test. vWF is shown in magenta.

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Persistent rural inequities in anticoagulation management for atrial fibrillation in the DOAC era

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Aim:

To determine whether contemporary anticoagulation management for atrial fibrillation (AF) differs according to geographic remoteness in Australia despite universal healthcare and subsidised direct oral anticoagulant (DOAC) therapy.

Method:

We analysed data from the 45 and Up Study, Australia's largest population-based longitudinal cohort, with linkage to Pharmaceutical Benefits Scheme prescribing and mortality data. Participants with self-reported AF were included. Geographic remoteness was classified using the Modified Monash Model into urban (MM1), non-urban (MM2–MM7), and rural/remote (MM4–MM7) groups. Anticoagulant prescribing, cardiologist review, stroke, bleeding, heart failure, and mortality outcomes were evaluated using logistic and multinomial logistic regression adjusted for age and sex.

Results:

Among 8,193 participants with AF, 4,147 (50.6%) lived in urban areas and 4,046 (49.4%) in non-urban areas. Overall anticoagulant use was similar across regions, but substantial differences in anticoagulant type and specialist access were observed. Compared with urban participants, non-urban participants were significantly less likely to receive apixaban (odds ratio [OR] 0.72, 95% confidence interval [CI] 0.61–0.85, $p < 0.001$), rivaroxaban (OR 0.77, 95%CI 0.65–0.92, $p = 0.01$), or dabigatran (OR 0.79, 95%CI 0.65–0.97, $p = 0.02$) relative to warfarin. Similar findings were observed in rural/remote participants. Cardiologist review was also lower in non-urban (OR 0.81, 95%CI 0.66–0.99, $p = 0.04$) and rural/remote populations (OR 0.70, 95%CI 0.54–0.90, $p = 0.01$). Heart failure risk increased with remoteness, while stroke, bleeding, and mortality rates were similar across groups.

Conclusion:

In Australia's universal healthcare system, major geographic inequities in anticoagulation management persist. Rural and remote populations were significantly less likely to receive evidence-based DOAC therapy and specialist cardiology review despite similar overall anticoagulation rates. These findings highlight an important gap in equitable anticoagulation care delivery and support anticoagulation education and specialist access pathways to improve uptake of contemporary anticoagulant therapy.

Single-dose self-amplifying mRNA encoding an activated platelet-specific scFv provides thromboprophylaxis for one week

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Aim: Long-term thromboprophylaxis remains constrained by bleeding risk, short drug half-lives and the need for repeated dosing. To overcome these limitations, we developed a programmable mRNA-based strategy to transiently express an activated platelet-specific single-chain variable fragment (scFv) targeting activated GPIIb/IIIa, using conventional mRNA or self-amplifying mRNA (samRNA) delivered by a proprietary liver-targeted lipid nanoparticle (LNP).

Method: *In vitro*, scFv expression, secretion, activated platelet selectivity and antiplatelet activity were assessed by western blotting, flow cytometry, platelet aggregometry and microfluidic flow assays. LNP biodistribution and hepatic expression were evaluated by IVIS imaging and liver immunohistochemistry. *In vivo* thromboprophylactic efficacy was tested across doses and time points in a FeCl₃-induced murine carotid artery thrombosis model. Haemostatic safety was assessed by tail bleeding, and systemic tolerability by haematology, liver and kidney function tests, cytokine profiling and organ histology.

Results: Transfection with scFv mRNA produced secreted, functional scFv that selectively bound activated GPIIb/IIIa and inhibited platelet aggregation under static and flow conditions. Following single intravenous administration, conventional mRNA significantly prolonged carotid artery occlusion time for up to 24 hours, whereas samRNA extended antithrombotic protection for up to 7 days compared with controls ($P < 0.05$). Importantly, neither mRNA nor samRNA treatment prolonged bleeding time, unlike the clinically used non-selective GPIIb/IIIa inhibitor eptifibatide ($P < 0.05$). No major abnormalities were detected in inflammatory cytokines, haematology, liver or kidney function, or organ morphology after treatment.

Conclusion: Self-amplifying mRNA extended activated platelet-specific thromboprophylaxis to one week after a single intravenous dose, while conventional mRNA provided shorter 24-

hour protection. By selectively targeting activated platelets without prolonging bleeding time or causing systemic toxicity, this platform provides proof-of-concept for a sustained, programmable antithrombotic strategy that may overcome key limitations of current repeated-dose thromboprophylaxis.

High-throughput flow cytometry platelet functional phenotyping for diagnosis of bleeding disorders

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Background and Aim:

Platelet function testing is an essential tool in the diagnosis of bleeding disorders. Common methods, such as aggregometry (LTA) or PFA-100 require specialised equipment and have limited performance in thrombocytopenia. We refined a flow cytometric protocol incorporating functional and glycoprotein measurement.

Method:

Whole blood from patients suspected of inherited bleeding disorder (median ISTH-BAT 6; IQR: 10); and healthy controls were collected as part of Sydney Platelet Group project. Platelet activation was measured: alpha granule (CD62P); dense granule (CD63) and αIIbβ3 activation (PAC-1) - in response to ADP, thrombin receptor activating peptide (TRAP), and cross-linked collagen related peptide (CRP-XL) at increasing concentrations. 12 surface makers quantified include GPIIb/IIIa (CD41/61), Ia/IIa (CD49b/29), Ib/IX (CD42b/42a), IV (CD36), VI using BD-Quantibrite™. Comparisons between BD Fortessa and Beckman-Coulter DxFlex and CytoFlex were made.

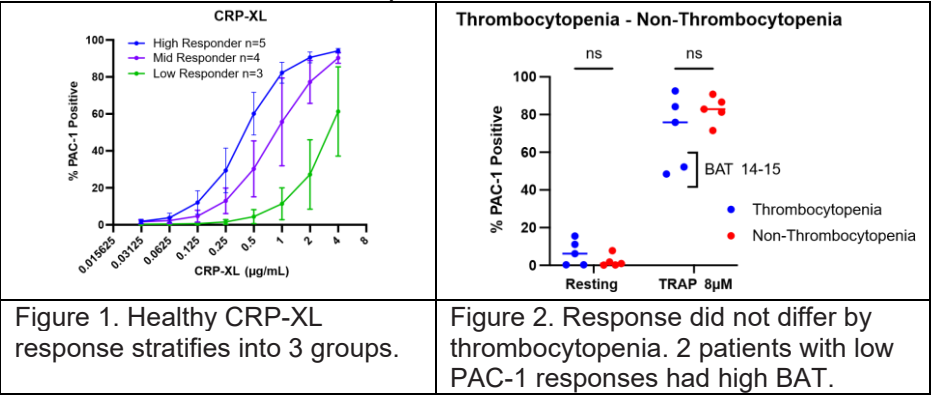
Results:

10 patients (platelet: 11-338 x10⁹/L) and 12 healthy controls with normal platelet counts were successfully measured. Abnormal glycoprotein expression was detected in 5/10 patients.

In functional evaluation, consistent with known GP6 polymorphisms, healthy donor platelet activation to CRP-XL segregated into three groups by k-means clustering, establishing stratified reference intervals (Figure 1). As opposed to LTA, thrombocytopenic patients with low BAT generated normal responses indicating the method can detect preserved function despite severe thrombocytopenia (Figure 2). Notably, maximal PAC-1 binding to TRAP was lower in patients with higher BAT (14 - 15) indicating reduced responses may reflect true clinical abnormalities. Matched samples (n=4) between cytometers – BD and BeckmanCoulter - demonstrated high concordance ($R^2 = 0.89 - 0.98$, $p < 0.001$).

Conclusion:

Flow cytometric platelet phenotyping is a comprehensive method that overcomes many deficits of traditional techniques. The method is transferable to most clinical cytometers.



Autologous stem cell harvests are compromised by high platelet load

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Aim: To determine the impact of high platelet concentrations on viable CD34⁺ cell (vCD34) recovery and engraftment time following autologous peripheral blood haemopoietic progenitor cell (HPC) collection, cryopreservation and transplantation.

Method: We retrospectively analysed 498 HPC collections between 1st January 2016 and 31st December 2025 for post-thaw vCD34 recovery. Post-transplant engraftment times were evaluated in 200 transplanted patients.

Prospectively we examined platelet-cell interactions (CD34/CD41) and platelet activation (CD62P/P-selectin) in n=22 fresh and post-thaw HPC samples by flow cytometry. Platelet-derived mediators (sTLT-1, sGPVI, PF4), and inflammatory cytokines in HPC supernatants were measured by enzyme-linked immunosorbent assay.

Results: Platelet concentrations correlated negatively with post-thaw vCD34 recovery ($P<0.0001$, Figure A). Harvests containing high platelet concentrations ($\geq 1000 \times 10^9/L$) yielded significantly lower vCD34 recovery than harvests with $<1000 \times 10^9/L$ ($68.8 \pm 11.8\%$ vs $79.1 \pm 14.1\%$; $P<0.0001$).

Recipients transplanted with harvests containing high platelet counts experienced slower neutrophil engraftment (11.43 vs 10.94 days; $\Delta 0.49$ days; $P=0.002$, Figure B), however platelet engraftment and hospital length of stay following transplant were unaffected by the platelet load.

Increased numbers of CD34/CD41 events post-thaw confirmed CD34 cell-platelet interactions during processing and cryopreservation. Platelet-CD34⁺ cell aggregates increased by 27% following freeze-thaw ($P<0.0001$). Harvest supernatants consistently featured platelet activation and degranulation with increased sTLT-1, sGPVI and PF4 following processing and cryopreservation.

Importantly, peripheral platelet counts strongly predicted harvest platelet load ($R^2=0.82$, $P<0.0001$) and inversely predicted vCD34⁺ recovery ($R^2=0.21$, $P<0.0001$), enabling pre-apheresis risk stratification.

Conclusion: Platelets in HPC transplant products become activated, bind directly to CD34⁺ cells, and release mediators that impair stem cell viability and prolong neutropenia. Targeted platelet-reduction strategies guided by peripheral platelet counts could represent an immediately translatable intervention to improve graft quality, reduce remobilisation, and accelerate granulocyte recovery after HPC transplant. The full impact of platelet burden in harvest products warrants further investigation.

Figure A

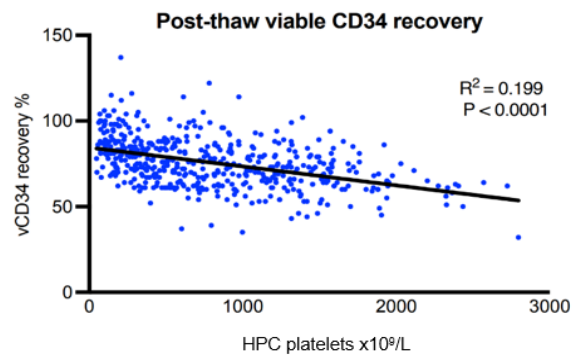
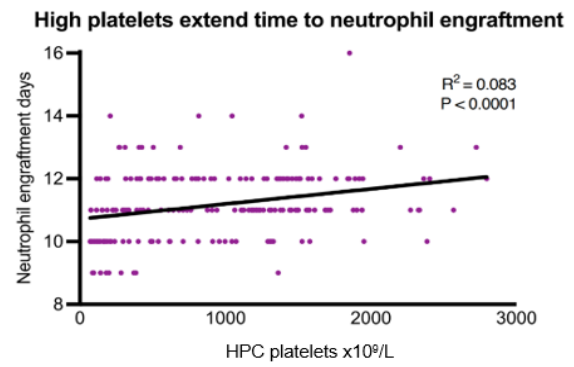


Figure B



Post-allogeneic stem cell transplant outcomes in myelofibrosis in a New Zealand cohort

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¹Te Whatu Ora, Auckland, New Zealand

Aim:

Allogeneic haematopoietic stem cell transplantation (allo-HSCT) is the only potential curative therapy for primary or secondary myelofibrosis (MF). Historically, allo-HSCT for MF was associated with high-rates of non-relapse mortality and morbidity. This retrospective review of a large single centre cohort of MF patients between 2020-2024 aims to identify pre-transplant characteristics that correlate with post-allo-HSCT outcomes and describe modern transplant outcomes in the New Zealand setting.

Method:

We conducted a retrospective audit at Auckland City Hospital of adult patients (>18 years) with MF undergoing allo-HSCT between 2020 and 2024. 42 eligible patients were identified. Data was collected on standard patient and transplant variables. The primary outcome was graft-versus-host disease relapse free survival at 1 year (GRFS) with key secondary outcomes including overall survival (OS), day 100 chimerism, and graft failure.

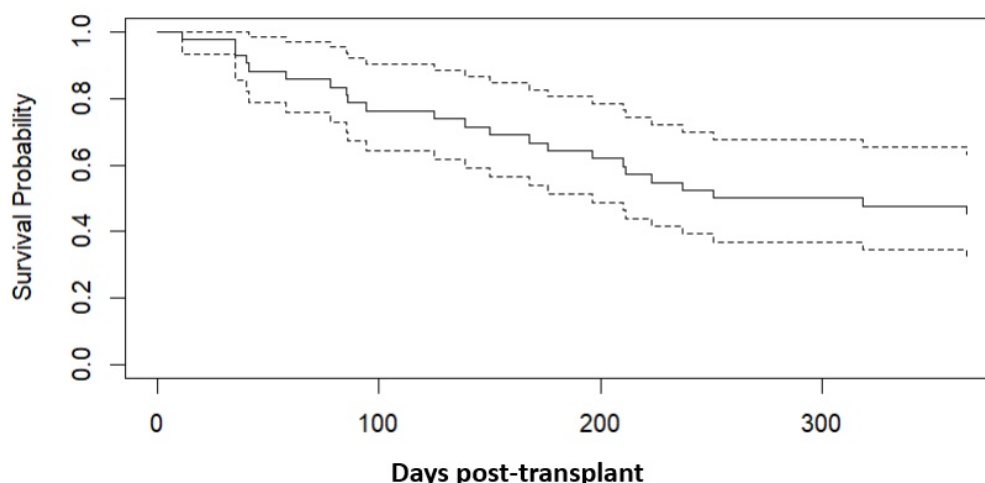
Results:

The median age at initial diagnosis of myelofibrosis (primary or secondary) was 51.5 years, with the median age at allo-HSCT being 61 years. 76% of patients had a JAK2 and 19% had a CALR mutation. 54.7% of patients were classified as high/very high risk by MIPSS score and the median HCT-CI was 2. Pre-transplant ruxolitinib was used in 85.7% of patients for a median of 10 months. The 1 year GRFS was 45.2% (CI 95% 32.4%-63.1%). The estimated 1 year OS was 73.8% and early mortality (prior to D100) was 16.7%. Complete donor chimerism at day 100 was achieved in 64.3% of patients, with primary graft failure seen in 1 patient and secondary graft dysfunction in 9.5% of patients.

Conclusion:

Outcomes in this cohort reflect the improvement in survival seen in the modern era, however the high early mortality reflects the challenges of transplanting patients with myelofibrosis and the importance of careful timing and candidate selection.

1-year graft-versus-host disease-free, relapse-free survival (GRFS)



Kaplan–Meier estimate of GRFS for the full cohort (n = 42). The solid line represents the estimated probability of GRFS, and the dotted lines indicate the 95% confidence interval. The 1 year GRFS was 45.2% (CI 95% 32.4%-63.1%). The steepest decline in GRFS occurred within the first 100 days post-transplant.

Renal function at the time of stem cell infusion predicts cyclosporine associated acute kidney injury in alloHSCT recipients receiving PTCy–CsA based GVHD prophylaxis

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Aim

To determine whether renal function at Day 0 (stem cell infusion) predicts cyclosporine associated acute kidney injury (AKI) and the need for renal sparing immunosuppression in alloHSCT recipients receiving PTCy–CsA based GVHD prophylaxis.

Method

A retrospective study was conducted in adult patients undergoing alloHSCT between 2015 and 2024 at a single tertiary centre. All patients received PTCy and cyclosporine for GVHD prophylaxis. Baseline renal function was calculated using the CKD-EPI 2021 race-free equation (BSA-adjusted). AKI was graded according to KDIGO grading (Stage 1, 2, and 3). Clinical documentation was reviewed to identify reasons for cyclosporine cessation or conversion to renal-sparing immunosuppression.

Results

A total of 112 patients were included (median age 60.9 years; 69% male). Baseline renal function was preserved (median creatinine 68 $\mu\text{mol/L}$; median CKD-EPI 99 mL/min/1.73 m²). Day 0 CKD-EPI categories were: >90 mL/min/1.73 m² (60%), 60–89 (22%), 30–59 (18%), and <30 (<2%).

During cyclosporine therapy, 41% of patients developed AKI (Stage 1: 17%; Stage 2: 11%; Stage 3: 13%), typically within 3–6 weeks of transplant. There was a graded correlation between CKD-EPI category and AKI severity: patients with Day 0 CKD-EPI >90 mL/min/1.73 m² predominantly developed Stage 1 AKI, while those with CKD-EPI 30–59 mL/min/1.73 m² were disproportionately represented among Stage 3 events. The cumulative incidence of Stage 3 AKI by CKD-EPI category is shown in Figure 1.

Conversion to sirolimus was reserved for progressive or severe AKI. Eight patients required conversion to sirolimus, of whom six (75%) had a baseline CKD-EPI of 30–59 mL/min/1.73 m². Severe AKI was associated with increased treatment-related mortality (TRM), as shown in Figure 2.

Conclusion

These findings support prospective assessment of Day 0 CKD-EPI to guide individualised GVHD prophylaxis selection, with consideration of CNI-free regimens in patients with pre-existing renal impairment.

Figure 1. CKD-EPI category and cumulative incidence of Stage 3 acute kidney injury.

Figure 2. Severe acute kidney injury and association with treatment-related mortality.

Figure 1. CKD-EPI and cumulative incidence of Stage 3 acute kidney injury

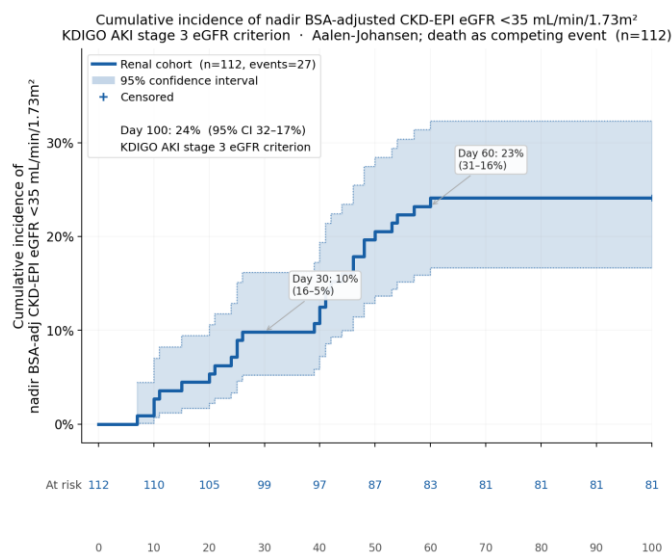
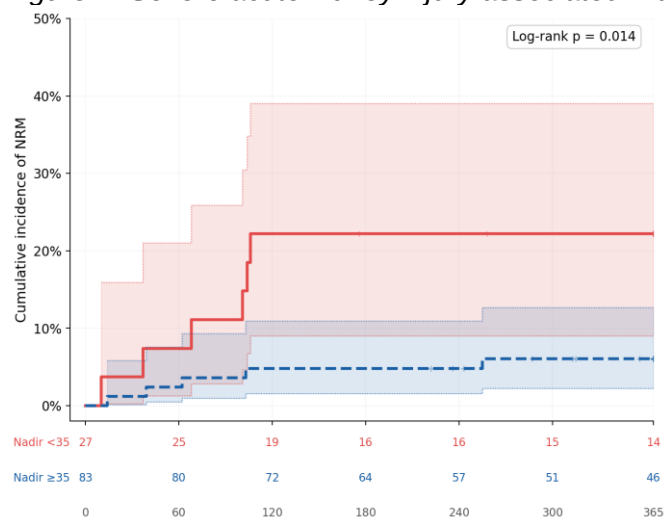


Figure 2. Severe acute kidney injury associated with increased TRM



HLA evolutionary divergence (HED) in Allogeneic stem cell transplantation: A time-varying bidirectional effect on relapse, chronic GvHD, and survival

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BACKGROUND

HLA Evolutionary Divergence (HED) quantifies the amino-acid distance between HLA sequences, reflecting the breadth of presented antigens. Higher HED may amplify graft-versus-leukaemia (GvL) effects at the expense of graft-versus-host disease (GvHD). However, its significance in 10/10 matched unrelated donor (MUD) allogeneic stem cell transplantation (alloSCT) remains undefined. We evaluated whether patient-donor HED scores predict clinical outcomes in a contemporaneous 10/10 MUD cohort.

METHODS

This retrospective single-centre study included 193 adults undergoing first 10/10 MUD alloSCT (2010–2024). HED was calculated using Grantham amino-acid distances across Class I and II loci. Patients were categorized as HED-matched(n=69) or HED-divergent(n=124) using median split (3.78) and upper quartile. Multivariable Cox and Fine–Gray competing-risk models adjusted for standard transplant covariates.

RESULTS

Median follow-up was 26 months. Class II HED was independent of baseline risk factors(all $p > 0.20$). In the full cohort, the overall survival (OS) effect was null (HR 0.922, $p = 0.40$) but violated proportional hazards assumptions ($p = 0.010$), supporting a time-varying effect.

Before day+100, divergent HED recipients demonstrated inferior outcomes, including a numerically increased early mortality hazard(HR 4.40, 95% CI 0.98–19.7, $p = 0.052$), lower 100-day OS (85.3% vs 97.1%, $p = 0.014$). primary graft failure occurred exclusively in the divergent group (9.3% vs 0%, $p = 0.009$).

Conversely, D+100 landmark analysis demonstrated superior long-term outcomes among divergent recipients, with a 56% reduction in late mortality hazard (HR 0.44, 95% CI 0.24–0.82, $p = 0.009$). Three-year OS from D+100 was 69.0% for divergent versus 60.1% for matched recipients. Progression-free survival was similarly improved (HR 0.557, $p = 0.028$; median PFS 65.0vs52.3 months).

Divergent HED was associated with increased moderate-to-severe cGvHD (36-month cumulative incidence 16.7%vs3.7%, $p = 0.025$) alongside reduced relapse risk in myeloid malignancies (HR 0.660, $p = 0.029$).

CONCLUSION :

HED demonstrates a bidirectional, time-varying effect in 10/10 MUD alloSCT, with increased early toxicity but improved late survival among day-100 survivors. These findings support prospective validation of HED as a donor selection biomarker.

Faecal microbial transplantation for graft-versus-host disease

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Aim:

Graft-versus-Host Disease (GVHD) remains a life-threatening complication of allogeneic haematopoietic stem cell transplantation (HSCT), where disease frequency and severity are linked to reduced gut microbial species diversity. Faecal Microbial transplantation (FMT) represents a novel GVHD therapy, utilising transfer of diverse microbial populations from healthy donors. We report a pilot trial of FMT after allo-HSCT, using the Australian Red Cross Lifeblood Microbiome product.

Method:

9 participants with steroid-refractory (SR) and steroid-dependent (SD) GVHD received a single FMT via naso-jejunal tube. All standard of care treatments, including Ruxolitinib, were permitted.

Results:

At 7 days post-FMT 2 (22%) participants achieved a complete response (CR) and 3 (33%) a partial response (PR), giving an overall response rate of 55%. CR increased to 3 (33%) at day 14 and 4 (44%) at day 28. No aspiration events occurred. 1 participant experienced a blood stream infection with a coliform organism potentially related to FMT, however had previously cultured this organism during a prior episode of sepsis.

Distinct microbiome trajectories were related to clinical response. Low gut microbial diversity persisted in non-responders, whereas CR demonstrated gradual recovery of alpha diversity. Recovery of bacterial diversity was associated with increased abundance of *Flavonifractor plautii* and *Copromorpha* sp900549125, while a strong inverse relationship was observed between response and *E. faecium* abundance. Decreases in *E. faecium* correlated with increased diversity and favourable clinical outcomes.

FMT was associated with upregulation of serum IL-15 and downregulation of programmed cell death protein 1 and CD-40 ligand.

Conclusion:

Use of FMT in immunosuppressed patients with SR and SD GVHD is safe and feasible in second line and a CR rate of 44% was observed. *E. faecium* was identified as a key opportunistic pathobiont where capacity for antimicrobial resistance, niche colonisation, and competitive exclusion of commensal bacteria may be linked to adverse clinical responses to FMT.

Plerixafor administration within three hours prior to apheresis results in successful haematopoietic stem cell collection

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Aim: Plerixafor, a CXCR4 inhibitor, improves haematopoietic stem cell (HSC) mobilisation when combined with G-CSF in poorly mobilised patients, resulting in high collection success rates. Plerixafor is approved for patients with peripheral blood (PB) CD34+ count <10x10⁶/L or apheresis CD34+ yield <1x10⁶/kg. Recommendations advise administration 6-11 hours pre-apheresis, based on studies demonstrating peak CD34+ mobilisation 9-11 hours post-plerixafor. However, this necessitates logistically challenging late-evening administration. Pharmacodynamic studies demonstrate rapid HSC egress post-plerixafor, with increased PB CD34+ counts as early as 3-hours post-injection. Our centre adopted an early-morning plerixafor strategy (<3hr) with staged apheresis rate up-titration 3 hours from plerixafor administration. This study evaluates apheresis outcomes according to plerixafor timing.

Method: Adult patients at a tertiary hospital receiving plerixafor were identified from an autologous HSC transplant database between May 2023 and April 2026. Demographics, treatment and apheresis outcome data were collected from the medical record.

Result: Of 87 patients undergoing HSC apheresis, 22 (25%) required plerixafor (Table 1). Indication for plerixafor included low PB CD34+ count in 17 (77.3%) and low apheresis yield in 5 (22.7%). Those with low PB CD34+ count pre-apheresis had a median count of 4.9x10⁶/L (range: 1.3-8.8). Fourteen patients (63.6%) received plerixafor ≤3hr pre-apheresis, 5 (22.7%) 9-11hr pre-apheresis, and 3 (13.6%) ≥12hr pre-apheresis. Successful HSC harvest was achieved in 13/14 (92.9%), 5/5 (100%) and 2/3 (66.7%) patients respectively, with a median of 2, 2 and 1 apheresis days required. Median CD34+ yield post-plerixafor was 2x10⁶/kg (0.5-16.4), 4.2x10⁶/kg (0.5-7.6) and 9.4x10⁶/kg (0.7-10.7), with median total HSC yields of 4.3x10⁶/kg (1.1-16.4), 5.4x10⁶/kg (3.1-18.1) and 9.4x10⁶/kg (1.4-10.7) respectively (Figure 1). Median collection efficiency was highest in the ≤3hr cohort (72.5% vs. 56% vs. 42%).

Conclusion: Our data demonstrates that plerixafor administered ≤3hr prior to apheresis, with staged up-titration apheresis flow rates, achieve successful HSC harvest outcomes, comparable to standard ≥9hr plerixafor dosing.

Figure 1

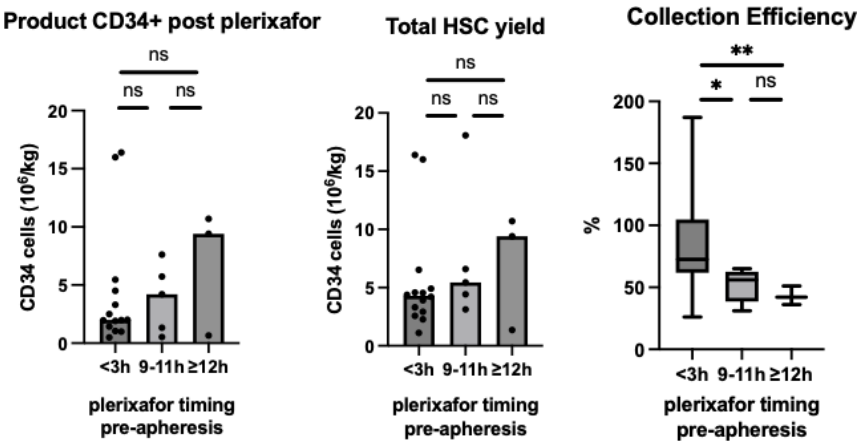


Table 1.
Demographics and Treatment data

Male (n,%)	13 (59%)	Age (median, range)	64 (20-72)
Diagnosis (n,%)		Most recent treatment (n,%)	
• MM/amyloidosis	12 (54.5%)	• Chemoimmunotherapy	13 (59%)
• DLBCL	4 (18.2%)	• Lenalidomide based therapy	8 (36.4%)
• MCL	3 (13.6%)	• Pembrolizumab	1 (4.5%)
• HL	2 (9.1%)		
• Germ cell tumour	1 (4.5%)		

Butterfly trial: The efficacy and acceptability of low molecular weight heparin (LMWH) administration via a subcutaneous catheter vs subcutaneous injections in both prophylactic and therapeutic settings

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Aim:

To demonstrate that a subcutaneous catheter is a safe and acceptable alternative to subcutaneous injections for LMWH administration in prophylactic and therapeutic settings. To assess which method was preferred by participants and to identify any catheter-related issues.

Method:

A prospective crossover study to assess efficacy of different dosing methods for LMWH. The initial subcutaneous catheter, 'Insuflon', was replaced by the 'Neria guard' in July 2025 due to discontinuation by the manufacturer. Participant surveys assessing impact on daily life, preference for the catheter vs subcutaneous injections, and drawbacks of either method were collected at several time points during the initial crossover period. Nursing assessments of the catheter sites were conducted at multiple time points throughout the study and long-term extension (LTE) period and recorded using a standardised assessment tool.

Results:

12 participants have been enrolled at the primary site, all female. 11 completed the interventional study. 6 were on prophylactic LMWH, 5 were on treatment dosing. All 11 participants reported minimal impact on daily activity of the catheter, and 90% reported reduced anxiety with the catheter as compared to subcutaneous injections. All participants that were eligible for LTE were assessed and approved, 6 of whom proceeded. Nursing site assessments during LTE revealed that most mild site issues (ie. redness or bruising) occurred in the first 4 weeks then resolved. No site related infection have been seen to date.

Conclusion:

At the end of the interventional study, majority of participants indicated they preferred the subcutaneous catheter, due to lower impact on daily life. The few complications that were seen were minor and reduced over time, supporting this as a safe and acceptable alternative for patients.

When the off-switch fails: Understanding haemophagocytic lymphohistocytosis (HLH)

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Case study:

Haemophagocytic Lymphohistocytosis (HLH) is a rare, life-threatening hyperinflammatory syndrome, characterised by excessive immune activation and progressive organ dysfunction (Konkol et al., 2026; Hsu et al., 2026). Defects in cytotoxic T-cells and natural killer (NK) cells, unregulated macrophage activity triggers a catastrophic, systemic cytokine storm. Etiology is divided into Primary and Secondary HLH. Primary HLH (pHLH) occurs due to germline genetic predispositions affecting cytotoxicity function, typically presenting in paediatric populations. Conversely, Secondary HLH (sHLH) more commonly presents in adults, triggered and driven by an underlying issue, such as infection, malignancy or autoimmune disease. Because its clinical presentation mimics a sepsis-like phenotype, sHLH is significantly underreported and frequently progresses to rapid multiorgan failure (La Rosee et al., 2019).

Through a comparative lens, this oral presentation evaluates three recent single-center cases - one of primary HLH and two secondary cases driven by Diffuse Large B-cell Lymphoma and rheumatologic disease - to examine differences in disease drivers, clinical presentation, diagnostic complexity and therapeutic management. Addressing a central dilemma in adult HLH care regarding the historical reliance on paediatric frameworks, this session contrasts the diagnostic evolution from the initial clinical indicators of the HLH-94 protocol to the expanded criteria and revisions introduced in the HLH-2004 framework. It highlights why applying these paediatric-derived protocols to adults poses severe risks of overtreatment and toxicity.

Furthermore, the session details therapeutic strategies utilising immunosuppressive and cytotoxic therapies, alongside an analysis of contemporary targeted biologic agents such as Anakinra and Emapalumab. Haematology nurses will learn to recognise clinical warning signs and key nursing interventions required to support timely escalation and optimal patient outcomes.

Conclusion

By connecting these distinct patient journeys to clinical rationales, this session equips nursing staff to identify treatment toxicities, monitor complex complications and facilitate rapid interventions essential to positive patient outcomes.

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Practical guidance for the administration of glofitamab: managing small-volume and prolonged administration time

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Aim:

To provide local operational guidance for the administration of glofitamab during small volume step-up dosing with a 4-hour administration time

Background:

Glofitamab is a CD20xCD3 bispecific antibody, for the treatment of diffuse large B-cell lymphoma. Since March 2026, glofitamab has been listed on the Australian Pharmaceutical Benefits Scheme, and is now accessible outside of clinical trials and larger centres. Currently there are no practical guidance for the administration for nurses and pharmacists, which provides challenges to smaller and regional centres with limited experience. Technical complexity exists due to the small volume of the first dose and 4- or 8-hour administration time. Rapid administration may increase the risk of infusion related reaction (IRR), cytokine release syndrome (CRS) and other immune-mediated toxicities due to abrupt T-cell activation.

Method:

Two sites (Barwon Health and Peter MacCallum Cancer Centre) completed a validation process of the administration of 25ml over 4-hour infusion time for glofitamab. Considerations for each site were; assessment of administration line to determine safe priming volume, dead-space of the priming volume, chair time utilisation, consideration of the overage in the infusion bag, flush volume to ensure full dose received, patient safety and risk of bolusing glofitamab.

Results:

Assessment of administration lines identified that increased chamber volume can prolong glofitamab infusion time, emphasising the need for careful priming. Validation of total line volume enabled safe, rapid priming with glofitamab with the aim to reduce outpatient chair time and reduce risk of toxicity such as IRR/CRS with correct administration. Accounting for line deadspace ensures full delivery of the prescribed dose to the patients and is therefore an important consideration when developing infusion guidelines.

Conclusion:

This practical advice, aims to reduce practice variation and support wider adoption of glofitamab across regional hospitals and smaller centres, enabling continued service development and improved patient access to novel therapies

Early outcomes of a weight adjusted immunoglobulin dosing strategy in New Zealand

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Aim: To evaluate the clinical and economic impact of implementing a weight-adjusted dosing strategy for immunoglobulin (Ig) using ideal body weight (IBW) and dose-determining weight (DDW), compared with actual body weight (ABW) dosing, at a national blood service.

Background: Ig usage is growing in New Zealand at approx. 11% per annum, exceeding population growth (0.7% in 2025). Almost 750 000g was issued to over 2000 patients from 1 January 2025 to 31 December 2025.

In December 2025, New Zealand Blood Service implemented a national Ig dosing strategy recommending IBW/DDW-based calculations in place of ABW, with clinician opt-out permitted where clinically justified. This approach aimed to improve stewardship of a high-cost, limited therapy and reduce dose-related AEs, particularly in patients with obesity.

Method: A retrospective analysis compared Ig utilisation, dosing and AEs during the 6 months pre- and post- implementation. Outcomes included total grams dispensed, percentage change in Ig issued and AE rates, expressed as rate of AE determined as possible/likely/certain per 100kg of Ig. Linear regression analysis was conducted to assess monthly reduction in Ig grams issued per patient.

Results:

	Actual Body Weight (pre-implementation)	Weight-adjusted (post-implementation)	P value
Adverse events rate of possible, likely or certain AE per 100kg of Ig			
• Privigen	23	3	0.006
• Privigen NZ	14	10	0.215

This early post-implementation analysis has shown that the utilisation of a weight-adjusted strategy was associated with a marginally significant reduction in grams per patient issued per month ($p=0.053$) with a negative trend of -0.54g per patient per month. The AE rate ratio of 0.62 (95% CI, 0.37 – 1.05), indicating an overall reduction in clinically meaningful AE rates following implementation. However, the lack of statistical significance reflects limitations due to small sample size and event counts at this early stage.

Conclusion: Implementation of a national weight-adjusted Ig dosing strategy was anticipated to reduce Ig utilisation, improved safety outcomes, and lower direct product costs. These early findings support weight-adjusted dosing as an effective stewardship intervention for Ig; ongoing evaluation is required to confirm.

Introducing emergency group O RhD positive red blood cells (RBC) into a regional Victorian hospital that utilizes satellite blood fridges. Do the benefits outweigh the risks?

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Aim:

With the release of the National Blood Authority recommendation for the emergency use of group O RBC in Victoria, consideration was given to including O RhD positive RBC into the satellite blood fridges alongside the current O RhD negative RBC. Transfusion nurses aimed to establish safe access to both options in emergency situations and monitor compliance.

Method:

Data from previous critical bleeding incidents found the majority of patients met the criteria for O RhD positive RBC use. Consultations were held with relevant stakeholders to discuss findings and agree on safety strategies to implement this change.

An education program was implemented, where staff were provided with training and relevant new protocols, prior to implementation of O RhD positive RBC being stocked in the fridges. Visual posters were displayed across clinical areas and colour coded tags were allocated to differentiate RhD RBC type. Each emergency RBC used is audited by the transfusion nurses for appropriate use.

Results:

Table 1 highlights the reduction in Group O RhD negative RBC used. However, the criteria breaches demonstrate ongoing safety concerns. Often the breaches were due to locum doctors being unfamiliar with the recommendation criteria, despite being alerted by nursing staff.

Table 1: Emergency Group O RBC accessed from satellite blood fridge

	Total units	O negative	O positive	Criteria breaches
2021	53	53		
2022	51	51		
2023	25	25		
2024*	54	30	24	7
2025	53	21	42	5
2026 (Jan-March)	23	3	20	1
*Emergency O positive RBC available from August 2024				

Conclusion:

Despite significant reduction in O negative usage, the risk of human error is still present. As the organisation becomes more acute, a business plan is being developed to investigate removal of satellite fridges with all blood being dispensed from the laboratory.

Human factors and systems safety analysis of Wrong Blood in Tube risks in pre-transfusion blood sample collection

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Aim:

Wrong Blood in Tube (WBIT) events, where a blood specimen is collected from the wrong patient and labelled with the intended patient's details or blood that is taken from the intended patient but labelled with another patient's identifiers, are infrequent but high-risk patient safety incidents that may result in serious harm, including incompatible transfusion. This project aimed to identify system-level vulnerabilities that contribute to WBIT risk during pre-transfusion blood sample collection in South Australian public hospitals and to develop recommendations to improve safety and workflow reliability.

Method:

A statewide, two-phase, proactive patient safety review was conducted across metropolitan and regional South Australian public hospitals. Phase one utilised Human Factors analysis using the Systems Engineering Initiative for Patient Safety (SEIPS) framework, incorporating site visits, cognitive walkthroughs, process mapping, and stakeholder engagement to examine differences between "work as imagined" and "work as done" in specimen collection workflows. Phase two involved a Healthcare Failure Mode and Effects Analysis (HFMEA) with 64 multidisciplinary stakeholders, including clinicians, pathology staff, safety and quality representatives, and consumers. Failure modes, workflow variability, contributory factors, and potential mitigation strategies were systematically analysed across the pre-transfusion specimen collection process.

Results:

The review identified multiple interacting socio-technical contributors to WBIT risk, including workflow desynchronisation, interruptions, workload pressures, technology and printer reliability issues, variation in specimen labelling practices, informal workarounds associated with electronic medical record workflows, and inconsistencies in positive patient identification processes. Twenty-two system-focused recommendations were developed targeting workflow redesign, technology optimisation, standardisation, simulation-based training, consumer engagement, and improved alignment between clinical workflows and electronic systems.

Conclusion:

WBIT risk emerges from interactions between human, technological, environmental, and organisational factors within complex healthcare systems. Human factors and HFMEA methodologies identified potential system vulnerabilities and opportunities for pragmatic statewide redesign to strengthen transfusion safety and support safer real-world clinical workflows.

More than reporting: How the STIR expert group adds value to Haemovigilance

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Aim:

Review STIR (Serious Transfusion Incident Reporting) activities and outcomes to understand the quality and educational role of the STIR Expert Group (EG).

Method:

The STIR system receives notifications of adverse events from 4 jurisdictions, Victoria, Tasmania, ACT and NT. The reports are validated and investigation forms sent to health services to complete. All investigations are then analysed by a member of the STIR EG.

Results:

EG members are volunteer medical specialists, transfusion scientists and transfusion nurses whose expertise is instrumental in reviewing incidents and deriving recommendations for improvements for better, safer transfusion practice.

The EG members:

- review, analyse and validate serious transfusion adverse events. High-acuity cases or those with uncertain reaction type or imputability are reviewed by the whole group in a 3-monthly meeting
- contribute to the STIR annual report, which includes analyses and data-driven recommendations for improved transfusion safety
- develop and review educational material (bulletins, newsletters, checklists and posters) to support frontline staff
- share information widely at conferences and other professional, educational and scientific meetings
- participate in horizon scanning by sharing literature, reports and new developments with other relevant groups (e.g. Blood Matters wider program, national Haemovigilance Advisory Committee).

From financial years 2015-2023, 1492 cases were submitted by hospitals:

- 111 were excluded after EG review, leaving 1381 cases for analysis.
- 297 cases underwent a second review
- 99 had a change in diagnosis (commonly TRALI reclassified to TACO),
- 193 the severity or imputability was changed
- Approximately 10% of reports are determined to not be transfusion-related
- The reporter is notified of all major changes by the EG.

Conclusion:

The STIR EG adds value, by providing program governance, enhancing the quality of the analyses and reports, along with education and mentoring functions. It also undertakes horizon-scanning activities and functions as a peer-support and expert network for members, STIR staff, and participating hospitals.

Cultural definition of blood from an Aboriginal and/or Torres Strait Islander perspective

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Background:

Blood is commonly understood within the Western biomedical frameworks as only being a physiological substance (American Society of Hematology, 2021). However, for Aboriginal and/or Torres Strait Islander peoples blood holds much broader cultural meanings. To date there has been limited research in this area and this could contribute to gaps in the provision of Culturally Safe healthcare to Aboriginal and/or Torres Strait Islander peoples (Perry, 2025).

Aim:

To explore how Aboriginal and/or Torres Strait Islander peoples define and understand blood from a cultural perspective.

Methods:

This qualitative study was underpinned using Indigenous Knowledges methodology (Rigney, 1999). Individual yarning was undertaken with Aboriginal and/or Torres Strait Islander participants (n=12). The yarns were analysed thematically, privileging Indigenous ways of knowing, being, and doing (Rigney, 1999).

Results:

Blood was understood as more than a biological entity, meanings were deeply connected to identity, kinship, family, and Country. Participants described blood as relational, extending beyond the individual body to collective and ancestral connections. Blood was associated with belonging, continuity, and responsibility, reflecting connections between past, present, and future generations. These cultural definitions shaped participants' understandings of health, illness, and interactions with healthcare systems.

Conclusion:

Aboriginal and/or Torres Strait Islander people's beliefs about blood are varied. A new cultural definition of blood was formed from the themes uncovered during the yarns. The overall cultural definition of blood which came from the author's Doctor of Philosophy is that 'blood is culture, family, kinship, Community, Country, health and needs to be delivered in a culturally safe manner' (Perry, 2025) Incorporating this overall definition into clinical practice and communication may improve trust, engagement, health outcomes and provide Culturally Safe care for Aboriginal and/or Torres Strait Islander peoples.

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A rapid amplification-free method for transgene sequence, insertion site and methylation analysis for gene therapies (TALISMAN)

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Aim: Transgene integration is central to chimeric antigen receptor (CAR) T-cell and lentiviral vector (LVV)-based haemoglobinopathy gene therapies. Efficacy and adverse effect risk, including rare transgene-containing malignancies, may be influenced by transgene insertion site and methylation. Existing methods to characterise transgenes demand multi-day workflows and cannot simultaneously capture transgene sequence, insertion site, and methylation status. We designed and evaluated TALISMAN (Targeted Amplification-Free Long-Read Sequencing for Transgene Intity, Insertion Site and Methylation Aalysis), a rapid method for comprehensive transgene characterisation.

Method: TALISMAN employs CRISPR/Cas9 cleavage at a conserved transgene sequence to enrich transgenic and flanking genomic regions for long-read nanopore sequencing (~4 hours wet-lab preparation), and was compared with non-enriched (rapid barcoding) nanopore sequencing. Both were applied to a clonal CAR-transduced cell line and polyclonal primary CAR T-cells generated using LVVs. Read concordance was assessed against Sanger-verified transgene sequence, and insertion sites mapped to human genome using minimap2. Cytosine methylation, called using Dorado, was benchmarked against published Illumina EPIC array data (Pearson correlation), and compared between transgene-containing and -absent reads (Wilcoxon rank-sum).

Results: CRISPR/Cas9-directed cleavage provided up to ~200-fold enrichment of transgene-containing reads versus non-enriched sequencing. Transgene identity could be determined in CAR T-cell products bearing one or two separate transgenes (single-read accuracy 93–99%). Up to 100 individual transgene insertion sites were mapped per sequencing run, and mapped predominantly to intronic or intergenic regions. CAR T-cell gene methylation profiles correlated strongly with those of CD4⁺ and CD8⁺ T-cells (Pearson's $r > 0.6$), but not with unrelated cell types. Transgenic and flanking non-transgenic regions exhibited significantly lower methylation than non-transgene-containing reads, consistent with localised epigenetic remodelling driven by the transgenic EF1 α promoter.

Conclusion: TALISMAN can simultaneously determine transgene sequence, insertion site, and methylation status within CAR T-cell products, and may be of utility for product release, mechanistic investigation, and/or assessment of suspected transgene-related adverse events.

Disruption of ROS and NETs as a therapeutic target for anti-HNA-3a antibody-mediated TRALI

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Aim:

Antibodies against HNA-3a have been associated with severe and fatal transfusion-related acute lung injury (TRALI). Neutrophil activation, resulting in neutrophil extracellular trap (NET) and reactive oxygen species (ROS) release, have been shown to be essential in models of TRALI caused by other antibodies. However, the role of these processes in anti-HNA-3a antibody-mediated TRALI is unclear. The aim of this study was to determine the importance of these steps in anti-HNA-3a mediated TRALI, using inhibitors of activation (IL-10), NETs (DNase), and ROS (superoxide dismutase; SOD)

Method:

HNA-3a/a neutrophils were seeded onto glass coverslips in plates. Neutrophils were treated with LPS (2µg/mL; 30 minute) before treatment with antibody-negative control serum or serum containing anti-HNA-3a antibodies ± IL-10 (10ng/mL), SOD (25U/mL), or DNase (1U/mL). After 180mins, neutrophils were fixed and stained with antibodies against neutrophil elastase, histones and a DNA stain. Images were acquired microscopically and NETs was quantified.

Confluent human lung microvascular endothelial cells (HLMVECs) were treated with LPS (2µg/mL, 30 minutes). HNA-3a/a positive neutrophils ± inhibitors (as above) were then added. After 30mins, either control serum or anti-HNA-3a serum was added. Following 30mins, trypan blue staining and microscopy was used to count viable HLMVECs.

Results:

In the presence of LPS, anti-HNA-3a serum induced significantly higher NET release compared to control serum ($11.1 \pm 2.2\%$ vs $0.58 \pm 0.375\%$; $P=0.0424$). Treatment with IL-10 ($1.1 \pm 0.9\%$; $P < 0.0001$), SOD ($1.7 \pm 1.3\%$; $P=0.0002$) or DNase ($1.6 \pm 0.3\%$; $P=0.0002$) significantly decreased anti-HNA-3a serum mediated NET formation.

Anti-HNA-3a serum reduced HLMVEC viability compared to control serum ($60.3 \pm 9.6\%$ vs $88.6 \pm 2.2\%$; $P=0.0240$). Pretreatment with SOD ($85.8 \pm 6.4\%$; $P=0.0283$) or DNase ($83.7 \pm 10.7\%$; $P=0.0304$) improved HLMVEC viability whereas IL-10 did not ($62.9 \pm 21.4\%$; $P=0.9471$).

Conclusion:

Exposure to anti-HNA-3a antibody resulted in NET release that was dependent upon neutrophil activation and ROS release. Both ROS and NET release contributed to reduced HLMVEC viability in the in vitro TRALI model; however, this was independent of neutrophil activation. Therefore disruption of ROS and/or NETs may be viable therapeutic targets for anti-HNA-3a mediated TRALI.

Proof-of-principle for detecting wild-type fetal RHD sequences against a maternal RHD variant background using next-generation sequencing

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Aim:

Fetal *RHD* screening programs, using non-invasive prenatal testing (NIPT), are routine for RhD-negative pregnancies to predict fetal RhD blood group status and guide RhD immunoglobulin (RhD-Ig) prophylaxis. However, 2–5% of cases remain inconclusive, due to maternal *RHD* variants (e.g. *RHD-CE-D*), and are administered RhD-Ig despite the possibility that the fetus is RhD-negative. This study demonstrates proof-of-principle for next-generation sequencing (NGS)-based NIPT to determine fetal RhD status in the presence of maternal RhD variant genotypes.

Method:

To simulate a NIPT model, two genomic DNA (gDNA) samples, from female blood donors with *RHD-CE-D* hybrid variant genotypes (*RHD*01N.04* and *RHD*06*), were spiked with gDNA from wild-type *RHD* male donors to mimic circulating fetal DNA within maternal gDNA. Male gDNA (n=8) samples included duplicates of each wild-type *RHD*-positive (R1r/R2r) and *RHD*-negative (r'r/r'r) phenotypes. NGS and bioinformatic analysis was performed using a panel targeting *RHD* exons 4, 5, 7 and 10. *SRY* was used to confirm the presence of spiked gDNA.

Results:

The un-spiked DNA samples had low *SRY* mean coverage (3–11×) compared to the spiked samples (140–304×). The un-spiked *RHD*01N.04* sample mean coverage, at *RHD* exons 4, 5, and 7, was 37–74×. *RHD*01N.04* (n=8) samples spiked with RhD-negative or RhD-positive gDNA had a mean coverage of 28–106× and 242–588×, respectively. The un-spiked *RHD*06* sample mean coverage, at *RHD* exons 4 and 5, was 31–69×. *RHD*06* samples (n=8) spiked with RhD-negative or RhD-positive gDNA had a mean coverage of 28–86× and 270–477×, respectively. In all D-positive spiked samples (n=8) the mean coverage increased at the interrogated regions.

Conclusion:

Wild-type *RHD* signals were detected in all female *RHD* variant samples spiked with RhD-positive gDNA. This study supports further validation using clinical maternal gDNA and fetal cell-free DNA samples to resolve inconclusive cases from *RHD* screening programs.

A 2-year shelf-life for human platelet lysate and precipitate

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Aim: Human Platelet Lysate (HPL) and Human Platelet Precipitate (HPP) are platelet-derived products made by repeated freeze-thawing of platelet concentrates. These products are abundant in growth factors and cytokines that promote cell growth and wound healing. There are no standardised production methods for these products and therefore methods vary between manufacturing sites. There are also no current quality or storage guidelines mandated for these products. The aim of this study was to establish a shelf-life for HPL and HPP manufactured at our blood centre.

Method: Apheresis platelets in plasma underwent a series of freeze-thaw cycles to manufacture HPL and HPP. HPL and HPP units were stored at -80°C for <1, 3, 6, 12, 18 or 24 months, n=3 per time point. Products were thawed at 37°C and tested for fibrinogen, growth factors [epidermal growth factor, fibroblast growth factor, platelet-derived growth factor, transforming growth factor β 1 (TGF- β 1)] and total protein. Results at each time point were compared using one-way ANOVA with appropriate *post-hoc* tests. A p-value of <0.05 is considered significant.

Results: Fibrinogen was stable over the 2-year storage period for HPL (p=0.504) and HPP (p=0.359), and consistently met our HPP concentration specification of ≥ 5 g/L. The mean post-thaw recovery of fibrinogen in HPP (75 $\pm$ 18%) was similar to the fresh units, frozen and stored for <1 month (77 $\pm$ 12%). The mean total protein concentration was 52.1 $\pm$ 2.7 g/L for HPL and 56.9 $\pm$ 2.5 g/L for HPP, with no significant difference over the 24-months of storage (p=0.472 and p=0.772 respectively). The most abundant growth factor in HPL and HPP was TGF- β 1, with mean concentrations of 98.6 $\pm$ 11.4 ng/mL and 219.8 $\pm$ 31.5 ng/mL respectively. Growth factor concentrations did not alter significantly throughout storage in either product.

Conclusion: A 2-year shelf-life is appropriate for both HPL and HPP manufactured at our blood centre when stored at -80°C.

Territory Pathology transfusion laboratory and patient blood management operations: The 2026 Katherine flood disaster response

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Aim:

To describe Territory Pathology's coordination, preparedness and recovery activities supporting continuity of laboratory and transfusion services during the March 2026 Katherine flood disaster response. We highlight operational lessons in communication, logistics, service restoration and disaster preparedness for pathology services in a remote regional setting.

Method:

A retrospective review of Territory Pathology's operational response during the Katherine flood event was undertaken, including the period of emergency evacuation, extended hospital closure, interim service continuity arrangements, staged hospital re-opening and restoration of local pathology services. We collated relevant records and operational information relating to communication pathways, transport logistics, cold chain and inventory management, transfusion support arrangements, staffing considerations, service continuity planning, quality requirements and recovery actions. Operational challenges and mitigation strategies were identified through debriefing, incident reporting and multidisciplinary communication.

Results:

Territory Pathology supported continuity of essential laboratory and transfusion services through early communication, escalation and coordination with key stakeholders, including Katherine Hospital, Royal Darwin Hospital, Lifeblood, clinicians and the deployed response capability. Key activities included pre-event planning, maintaining communication pathways, transfusion stock and cold chain considerations, coordinating transport and supply chain requirements, access to laboratory information and records where possible, and planning for staged restoration of local services. Challenges included disrupted infrastructure, access limitations, communication complexity, transport delays, blood product and consumable management, and the need to safely transition services back to Katherine Hospital. Lessons identified informed updates to local flood planning, laboratory business continuity arrangements, communication pathways and recovery processes.

Conclusion:

The 2026 Katherine flood response demonstrated the importance of pathology service continuity planning, clear communication pathways, defined escalation processes, and strong coordination between local, regional and deployed health response teams. Territory Pathology's experience highlights practical lessons for transfusion laboratory preparedness, recovery planning and service restoration in remote regions affected by natural disaster.

Beyond ISBT quality indicators: A detailed analysis of donor deferral patterns at New Zealand blood service

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Aim:

ISBT Quality Indicators (QIs) for donor deferral provide a useful benchmarking framework, but their broad design may obscure important operational differences. This study aimed to examine donor deferral data at New Zealand Blood Service (NZBS) to identify additional indicators and analytical approaches that better inform quality improvement.

Method:

NZBS donor deferral QIs were calculated for whole blood and apheresis donations over a 12-month period from 1 May 2025. Exploratory data analysis was undertaken to investigate deferral patterns by deferral location, staff role, individual staff members, and region.

Deferrals were also categorised by duration to assess potential implications for donor return.

Results:

Initial ISBT QIs indicated a high overall donor deferral rate of 0.938 per donation. When deferrals applied by the nursing team responsible for donor assessment outside of donation sessions were excluded, deferral rates were substantially lower (total 0.343; temporary 0.298; permanent 0.0448), highlighting the importance of understanding where and by whom deferrals are applied. A strong correlation ($r = 0.834$) was observed between the number of interviews conducted and deferrals applied by individual staff members. However, marked variability was present. The median staff deferral rate was 6.8% and was not normally distributed. Regional differences were observed in both deferral rates and deferral types. Categorisation by deferral duration identified variation that may influence donor return behaviour.

Conclusion:

ISBT QIs are valuable for benchmarking, but meaningful interpretation requires deeper analysis and contextual understanding of staff roles and operational processes. Stratifying deferrals by location, staff activity, and duration provides insights beyond headline QI values and supports more targeted quality improvement initiatives. Monitoring trends over time, rather than relying on single aggregate indicators, enhances the utility of QIs for decision-making in blood services.

Divergent T-cell trajectories distinguish refractory and late-relapse DLBCL: integrated profiling of paired diagnostic and relapse biopsies

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Aim:

The genetic landscape of DLBCL has been well characterised, with overall limited genetic divergence at relapse. A large comprehensive assessment of the tumour microenvironment using paired DLBCL biopsies has not been undertaken to date. We hypothesised that immune attrition would be evident from diagnosis to later timepoints, but that late relapsing patients could represent a subset of patients with relative preservation of T cell health given historically demonstrated improved outcomes.

Method:

We conducted a large integrated analysis of 140 rrDLBCL patients between 2004-2021. 87 patients had matched diagnostic and relapse biopsies, inclusive of 16 with 3-5 biopsies. We performed Nanostring PanCancer Immune profiling, TCR sequencing and spatial transcriptomic analysis.

Results:

Serial T-cell attrition as evidenced by reduced T cell abundance and activation was seen from diagnosis through to first relapse and subsequent timepoints. Immune gene profiling showed coordinated downregulation of T-cell activation and PD-L1–pathway genes (adj p<0.044), aligning with reduced overall T-cell abundance scores, particularly CD8 T-cell subtypes at relapse (p=0.015). This was supported by spatial whole transcriptome gene set enrichment analysis of tumor enriched segments demonstrating suppression of TCR and antigen processing pathways at relapse.

Late relapsing (LR) patients, however, demonstrated a different TME at baseline compared to early relapsing and refractory patients, with accumulative disparity over time. LR patients demonstrated higher baseline T-cell abundance with preservation at relapse, and greater T cell repertoire throughout disease. LR was associated with markedly improved overall survival at relapse (p=0.0005), consistent with prior findings.

Conclusion:

This study identifies T-cell attrition as a key feature of DLBCL relapse; however, late relapsing patients represent a distinctive subset of patients with markedly superior outcomes and relative preservation of intratumoral T-cell abundance and repertoire. These TME differences could account for differences in chemotherapy resistance and may impact CAR-T and bispecific antibody response rates.

Ibrutinib, rituximab, valaciclovir and third-party EBV-specific virus specific T-lymphocytes for EBV-positive immunosuppression-associated lymphoproliferative disorders: Results of the ALLG TREBL1 phase 1 investigator-initiated trial

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Aim:

EBV-positive Immunosuppression-associated lymphoma (IA-LPD) arise in patients with significant pre-existing comorbidity and carry a predilection for advanced stage and central nervous system (CNS) involvement¹. Those refractory to or unfit for immunochemotherapy have few effective treatment options². TREBL-1 was a phase 1 multicentre trial evaluating the safety, feasibility and preliminary efficacy of combination ibrutinib, rituximab, valaciclovir and third-party EBV-specific virus specific T-lymphocytes (VSTs) in this setting.

Method:

Eligible patients had EBER-ISH+ IA-LPD (13 LBCL, 3 HL, 4 other) relapsed/refractory or unsuitable for standard first-line therapy. The regimen comprised ibrutinib 560 mg/day (weeks 1–78), rituximab 375 mg/m² (weeks 1–4, 20, 30, 40, 50), valaciclovir 1g four times daily (weeks 1–8), and HLA-matched third-party EBV-specific VSTs (weeks 10–13, 3×10⁷/m²).

Result:

Twenty patients were enrolled between June 2019–July 2021. Median age was 63 years (range 38–75); 60% were male. The majority presented with CNS involvement (PCNSL n=6 (30%), SCNSL n=5 (25%)). 20 received ibrutinib; 17 (85%) received VSTs. Of those with unsuccessful delivery, two lacked an HLA match and one withdrew prior to VST. Grade ≥3 adverse events occurred in 17 patients (85%) which included infection (30%), febrile neutropenia (20%), diarrhoea (25%) and arrhythmia (10%). There were no severe AEs associated with VST infusion.

The overall response rate (ORR) was 55% (11/20; complete response [CR] 35%) (Fig 1). Amongst CNS-involved patients, ORR was 72% (CR 36%). Median duration of response was 44 weeks (95% CI 10.6-NR). Of patients demonstrating early response (<8 weeks), 7/10 maintained/ deepened their

response post VST infusion. The 12-month survival was 45% (9/20). EBV clearance in peripheral blood was associated with response.

Conclusion:

TREBL-1 demonstrated a manageable safety profile and meaningful clinical activity in patients with EBV+ IA-LPD, including those with CNS involvement. These results support further evaluation of EBV-directed combination immunotherapy in this challenging high-risk population.

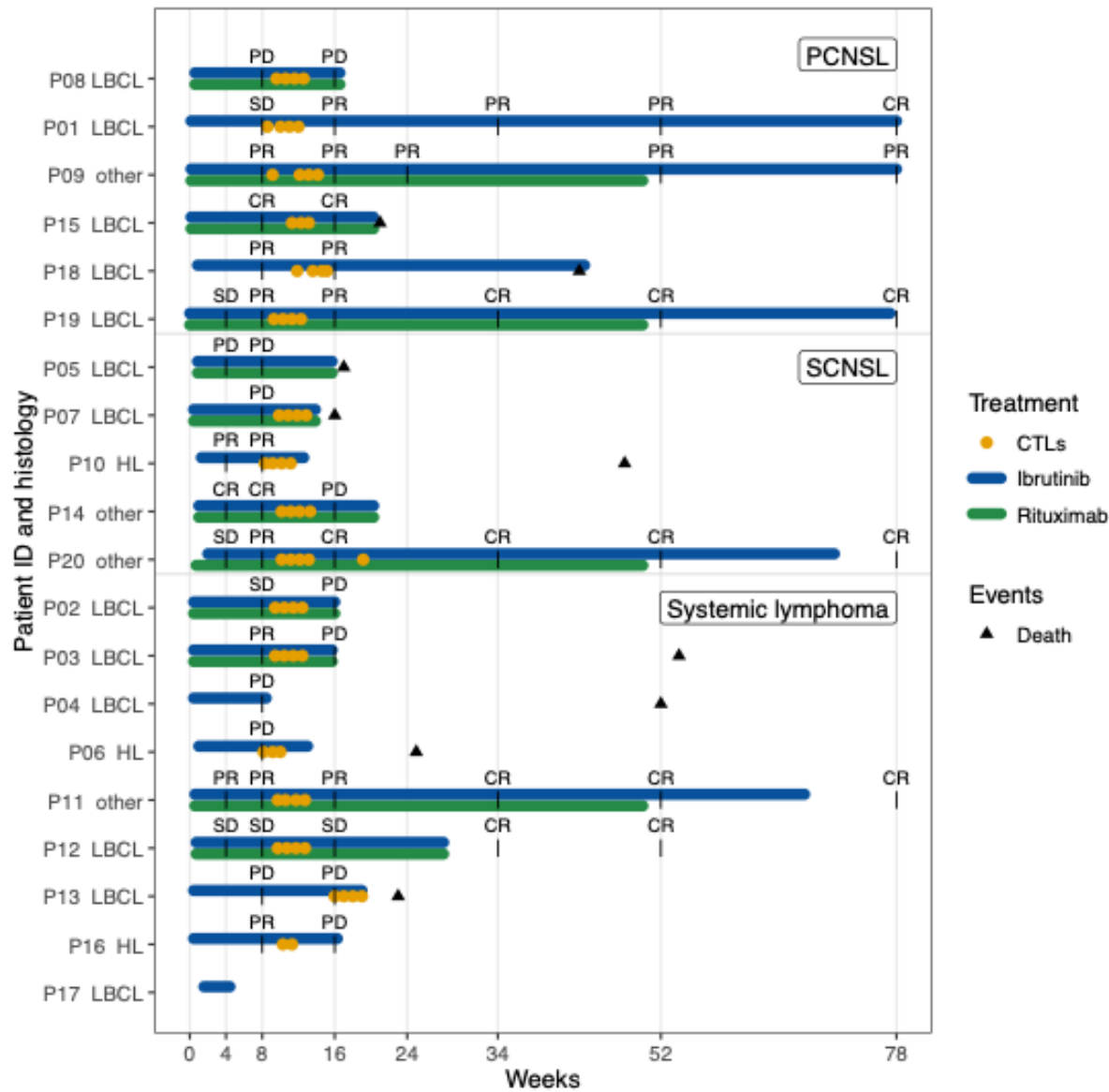


Figure 1: Swimmers plot demonstrating treatment and response dynamics in EBV+ IA-LPD patients treated with Ibrutinib, rituximab, valaciclovir and third-party EBV-specific cytotoxic T lymphocytes on TREBL1 clinical trial.

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Distinct immune checkpoint landscapes in PCNSL and SCNSL revealed by single-nucleus profiling

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Aim:

Immune evasion is a hallmark of central nervous system lymphomas (CNSL), yet detailed immune maps of primary (PCNSL) and secondary CNS lymphoma (SCNSL) remain limited due to disease rarity and technical constraints. We sought to generate the largest single-cell atlas of the CNSL tumour microenvironment (TME) to compare and contrast CNSL to systemic DLBCL without CNS spread.

Method:

We performed single-nucleus RNA sequencing (snRNA-seq) using the 10x Genomics FLEX platform on fresh frozen and FFPE biopsies from 20 PCNSL, 4 SCNSL, and 5 systemic only DLBCL patients.

Results:

We identified 16 major cell types spanning malignant B-cells, T-cells, myeloid, glial and neuronal cells, and endothelium. TME composition was broadly similar across CNSL subtypes. Except, PCNSL displayed increased DCs, extracellular-matrix-remodelling (ECM) macrophages, TREGs and NK cells compared with SCNSL. Whereas Cytotoxic CD8 and Th1 were increased in SCNSL. Relative to DLBCL, PCNSL showed significantly fewer M1-like macrophages, C1Q+ macrophages, and dendritic cells but increased immune suppressive myeloid populations (adj-p<0.05). Compared with DLBCL, PCNSL T-cell states were characterised by reduced naïve CD4⁺/CD8⁺, TH1, and exhausted CD8⁺ populations, alongside increased Tfh cells (adj-p<0.05).

Ligand–receptor analysis revealed markedly expanded immune checkpoint interactions in PCNSL and SCNSL (72 and 58 interactions) relative to DLBCL (23; PCNSL vs DLBCL p=0.0051; SCNSL vs DLBCL p=0.0128). PCNSL and DLBCL predominantly engaged PD-L1/PD-1 and PD-L2/PD-1 signalling, whereas SCNSL displayed dominant Gal-9/TIM-3 interactions, also present but less prominent in PCNSL and absent in DLBCL. A major driver of suppression in PCNSL is a population of ECM microglia. This program is also highly immunosuppressive in SCNSL but is shared between both ECM macrophages and ECM microglia.

Conclusion:

This work identifies CNS-specific immune checkpoint interactions (PD-L1/PD-1/PD-L2/PD-1; PCNSL vs *Gal-9–TIM-3*; SCNSL) and enriched *SPP1*⁺ myeloid populations in PCNSL. These findings highlight distinct immune-suppressive programs as potential therapeutic targets for rational immunotherapy development in CNSL.

Evolving bridging strategies for CD19 CAR T-cell therapy in aggressive B-cell lymphoma: a 7-year single-centre experience

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Aim: Most patients awaiting CD19 CAR T-cell therapy for large cell lymphoma (LCL) receive bridging therapy (BT). Optimal modality and the practical logistics of BT delivery are not well described. We characterised changes in bridging strategy, response, radiotherapy (RT) field, and location of delivery.

Method: We retrospectively reviewed all patients infused with axicabtagene ciloleucel or tisagenlecleucel for LCL at a single Australian centre between Sep 2020 and Apr 2026. Bridging regimens were classified hierarchically by modality. RT focality (unifocal vs multifocal), pre-infusion response (CR/PR/SD/PD), and location of BT delivery (referring centre vs CAR-T centre) were recorded.

Results: 229 patients were infused. Bridging utilisation rose from 75% (2020) to 100% (2026); overall 212/229 (93%) were bridged. RT alone became the dominant modality, rising from 25% (2020) to 59% (2026); any RT-containing bridging accounted for 51% of bridged patients, of whom 88% received unifocal RT. RT monotherapy led to the highest pre-infusion CR (22%) and ORR (57%); chemotherapy ORR was 50%. ORR rose from 39% (2023) to 71% (2026); CR from 6% to 19%. Notably, 169/212 (80%) of all bridging therapy was delivered at referring sites rather than the CAR-T centre — a proportion that has remained consistently high (67–88%) across years and was observed across all modalities.

Conclusion: Bridging strategies for CAR-T have evolved; there is increasing use of effective unifocal RT in DLBCL, likely coinciding with 2L treatment for persistent single sites of disease. Most bridging still occurs at referring sites, guiding resource planning for radiation oncology and chemotherapy infrastructure. This underscores the need for close collaboration between referring sites and the CAR-T centre to ensure safe, timely delivery. Further work is needed to establish the impact of bridging response on CAR-T outcomes.

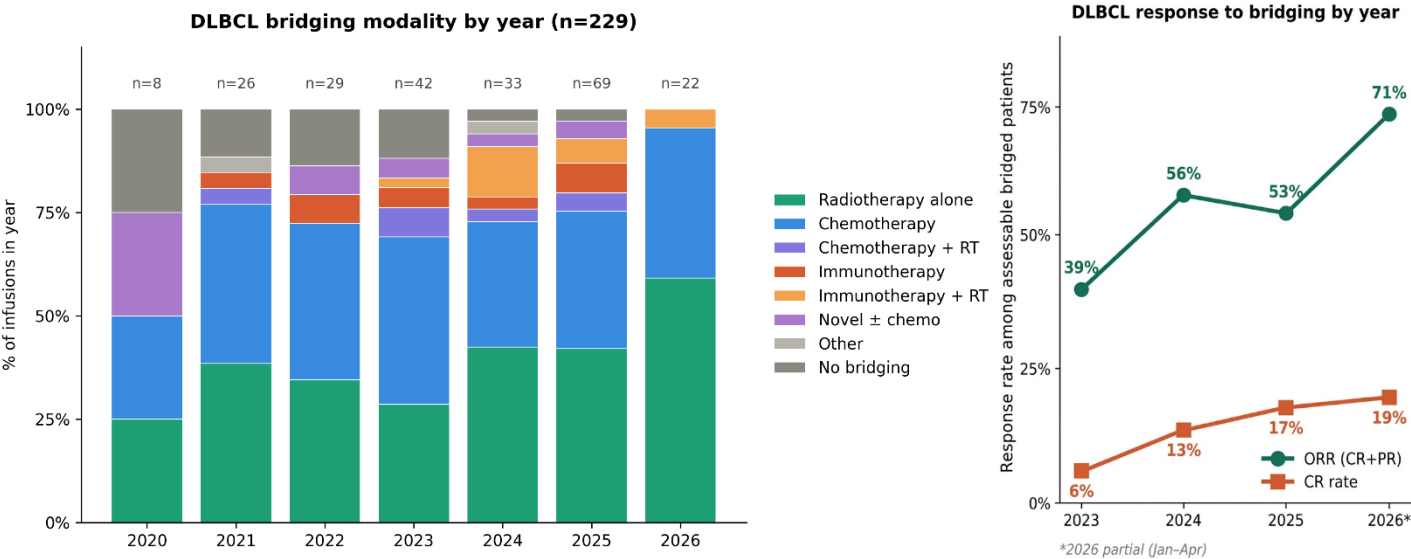


Figure. (A) DLBCL bridging modality by year, full cohort. 'Novel ± chemo' includes regimens with polatuzumab plus venetoclax/lenalidomide/selinexor/pembrolizumab; 'Other' includes single cases of surgery and chemo+RT+novel. (B) Response to bridging by year (assessable bridged patients)

Divergent immune ecosystems in immune-privileged diffuse large B-cell lymphomas

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Aim:

Primary testicular lymphoma (PTL) and primary CNS lymphoma (PCNSL) are rare, aggressive extranodal DLBCLs arising in immune-privileged sites. Despite shared oncogenic drivers (*MYD88/CD79B* mutations, MCD/C5 molecular subtypes) their immunological equivalence has not been systematically examined. Understanding immune architecture is critical to rationally deploying checkpoint inhibitors, bispecific antibodies, and CAR-T therapies.

Methods:

We performed multiomic profiling of PTL (n=18) and PCNSL (n=47), incorporating whole-exome sequencing, NanoString immune transcriptomics, GeoMx spatial transcriptomics, single-nucleus RNA-sequencing, and bulk TCR- β sequencing.

Results:

Despite a conserved oncogenic backbone, PTL and PCNSL diverged profoundly in immune microenvironment. PTL exhibited higher tumour mutational burden (34.18 vs 17.04 mutations/Mb; $p=0.0007$), enrichment for proliferative CD8 T-cell states, higher T-cell infiltration by TCR sequencing and selective macrophage PD-L1 upregulation, hallmarks of adaptive immune resistance amenable to checkpoint inhibition. PCNSL was characterised by suppressive macrophage predominance, microglial reprogramming with *SPP1/TREM2* expression, reduced antigen presentation, and significantly more oligoclonal T-cell repertoires than PTL, consistent with immune exclusion. Spatial transcriptomics confirmed myeloid immune suppression in PCNSL, with reduced antigen presentation in CD8 regions and elevated *SPP1:CXCL9* in macrophage compartments. In a PTL case with CNS relapse, dissemination recapitulated the cohort-level PCNSL immune phenotype, with CD8 contraction, PD-L1 loss, and clonal TCR focusing. Conserved resident macrophage programs across sanctuary tissues define a common immune substrate, upon which site-specific reactive immune states determine the balance between cytotoxic engagement and myeloid restraint.

Conclusion:

PTL and PCNSL share tumour genetics but are immunologically distinct. These findings support a two-tier model of immune privilege, a conserved resident macrophage substrate overlaid by a site-specific reactive layer, arguing against treating these entities as interchangeable and supporting immune subtyping over genotype alone to guide therapeutic selection. PTL resembles a T-cell-inflamed phenotype likely responsive to PD-1 blockade, while PCNSL requires myeloid-directed strategies to overcome immune exclusion before T-cell therapies can be effective.

Incidence, predictors and impact of immune effector cell associated haematotoxicity (ICAHT) post Axi-cel for LBCL: An analysis from the AusCART consortium

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Aim:

Immune effector cell-associated haematotoxicity (ICAHT) is a poorly understood complication of chimeric antigen receptor T (CAR-T) cell therapy. We aimed to evaluate (i) the incidence and predictors of ICAHT, (ii) its association with progression-free survival (PFS) and overall survival (OS), and (iii) the impact of chemotherapy bridging intensity.

Method:

Patients with LBCL treated with axicabtagene ciloleucel (axi-cel) between 01/08/2021 and 31/12/2025 across six Australian sites were included. The primary endpoint was incidence of grade 3-5 (Gr3-5) early neutrophil ICAHT (N-ICAHT)¹. Logistic regression was performed to assess baseline predictors. Associations between Gr3-5 N-ICAHT and PFS/OS were evaluated using Cox proportional hazards. Chemotherapy bridging was categorised as “high” (platinum-based salvage or high-dose cytarabine-containing) or “low” intensity. Propensity score-based inverse probability of treatment weighting (IPTW) was used to assess impact of bridging intensity on Gr3-5 N-ICAHT and PFS.

Results:

A total of 593 patients were included; 64% male, 77% 3L+, 11% bone marrow [BM] involvement; 43% CAR HAEMATOTOX high (≥ 2) at lymphodepletion (LD). Gr3-5 N-ICAHT occurred in 27% (159/593) of patients. On univariable analysis, Gr3-5 N-ICAHT was significantly associated with 3L+ vs 2L therapy (OR 1.64, 1.04-2.66, $p=0.038$), bulk $>10\text{cm}$ (OR 2.478, 1.49-4.10, $p<0.001$), BM involvement (OR 3.12, 1.75-5.61, $p<0.001$) and high CAR-HAEMATOTOX score ≥ 2 (OR 2.55, 1.53-4.26, $p<0.001$). Patients with G3-5 N-ICAHT had inferior PFS (HR 1.33, 1.03-1.71, $p=0.029$) and OS (HR 1.46, 1.07-1.99, $p=0.016$). A total of 111 patients were included in the propensity score-weighted IPTW analysis (74 low intensity vs. 37 high-intensity). In this analysis, high intensity bridging was associated with a higher incidence of Gr3-5 ICAHT (49% vs. 29%, OR 2.71, 1.19-6.25, $p=0.018$) and similar PFS (HR 0.97, 0.56-1.68, $p=0.907$) (Figure 1).

Conclusion:

Gr3-5 early N-ICAHT occurs in approximately one quarter of patients treated with axi-cel for R/R LBCL and is associated with inferior PFS and OS. High-intensity chemotherapy bridging is associated with increased Gr3-5 ICAHT.

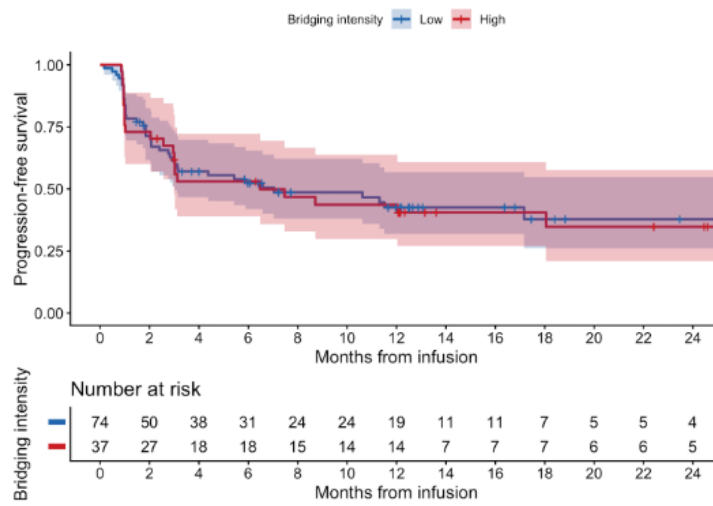


Figure 1: PFS according to intensity of bridging chemotherapy with propensity score matching

References:

1. Rejeski K, Subklewe M, Aljurf M, et al. Immune effector cell–associated hematotoxicity: EHA/EBMT consensus grading and best practice recommendations. *Blood*. 2023;142(10):865-877. doi:10.1182/blood.2023020578

Bridging the trans-Tasman gap in blood cancer care: findings from New Zealand's first State of Blood Cancer report

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Aim:

To evaluate the burden of blood cancer in New Zealand and assess the actions required to deliver care aligned with international standards.

Method:

A mixed-methods national analysis was undertaken using New Zealand Cancer Registry data, Health New Zealand datasets, Statistics New Zealand's Integrated Data Infrastructure (IDI), epidemiological analyses from the University of Auckland, and surveys of 744 patients/carers and 85 clinicians. Analyses examined epidemiology, survival, treatment access, health service utilisation, workforce participation, financial burden, and system capacity. Comparative benchmarking against Australian survival outcomes and treatment access was undertaken.

Results:

An estimated 27,000 people are living with blood cancer in New Zealand, with over 3,000 new diagnoses annually. Blood cancer is the third leading cause of cancer death and one of the fastest growing contributors to cancer mortality. Unlike other major cancers, combined blood cancer mortality has remained largely unchanged over 15 years despite major therapeutic advances.

IDI analysis showed that the impact of blood cancer extends well beyond the health system. In 2023, hospital-based care cost approximately NZD \$209 million, while over half of people living with blood cancer accessed social support in 2024, totalling more than NZD \$56 million. Linked income data demonstrated a marked post-diagnosis reduction in workforce participation, highlighting the significant wider economic and societal burden of blood cancer. Comparative benchmarking identified lower survival across several blood cancers relative to Australia, alongside reduced access to internationally standard therapies including targeted therapies, bispecific antibodies, and CAR T-cell therapies. Patient-reported findings reinforced this impact, with 45% reporting significant out-of-pocket costs and 69% drawing on life savings.

Conclusion:

New Zealand's first whole-of-system assessment of blood cancer demonstrates a measurable trans-Tasman gap in care, with delayed access to innovation and constrained system capacity likely contributing to poorer outcomes. Coordinated national planning and improved access to modern therapies will be critical to closing this gap.

Baseline neurological vulnerability predicts immune effector cell-associated neurotoxicity following CAR-T cell therapy: a prospective cohort study

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Aim:

To evaluate the association between clinical baseline neurological factors and the development of ICANS following CAR-T cell therapy.

Methods:

We conducted a prospective cohort study of 203 adult patients undergoing CAR-T cell therapy for haematological malignancies at a tertiary CAR-T referral centre in Melbourne, Australia. All patients underwent structured baseline neurological assessment and brain MRI prior to infusion, with longitudinal neurological follow-up for up to two years post-infusion. Associations between baseline clinical variables and the risk of any-grade and high-grade ICANS (grade ≥ 3) were evaluated using univariable and multivariable logistic regression. Pre-existing central nervous system (CNS) comorbidity was defined as a clinically significant CNS abnormality (based on history or MRI evidence), according to specialist neuroimmunology consensus. CNS involvement of the underlying haematological disease was analysed separately and excluded from this definition.

Results:

Patients had a median age of 67.7 years and 65.0% were male. The majority had lymphoma (73.4%), followed by multiple myeloma (22.2%) and B-cell acute lymphoblastic leukaemia (4.4%). ICANS occurred in 65 patients (32.0%), including 25 cases of high-grade ICANS (12.3%). On multivariable analysis, baseline CNS comorbidity was independently associated with ICANS (OR 3.49, 95% CI 1.42–9.09, $p=0.008$) and high-grade ICANS (OR 5.35, 95% CI 1.84–15.46, $p=0.002$). In a secondary lymphoma-only analysis, CNS comorbidity remained the only variable associated with all-grade ICANS (OR 4.62, 95% CI 1.71–14.13, $p=0.004$) and was also associated with high-grade ICANS (OR 5.69, 95% CI 1.79–19.01, $p=0.004$). Full results and forest plots will be presented.

Conclusion:

Pre-existing CNS comorbidity was the most consistent clinical predictor of both the occurrence and severity of ICANS following CAR-T cell therapy. These findings highlight the importance of structured baseline neurological evaluation prior to CAR-T treatment, which may help identify individuals at increased risk of neurotoxicity and support tailored monitoring and management strategies.

Intensive care unit utilisation amongst chimeric antigen receptor T-cell recipients: a single centre experience

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Aim:

Chimeric antigen receptor (CAR) T-cell therapy is now standard-of-care (SoC) for certain relapsed/refractory B cell leukemias, lymphomas and recently multiple myeloma. The therapy is complicated by immune-related toxicities, including cytokine release syndrome (CRS), immune effector cell associated neurotoxicity syndrome (ICANS), and immune effector cell-associated haematotoxicity (ICAHT), that may require intensive care unit (ICU) support. Here we describe ICU resource utilisation and outcomes amongst SoC CAR-T recipients within 28 days of infusion.

Method:

We retrospectively reviewed all approved commercial CAR-T recipients at our centre between July 2019 and December 2025. Descriptive statistics were used to summarise ICU resource utilisation, and survival analyses were performed using the Kaplan-Meier method.

Results:

In contrast to the Pivotal trials only 58 (19%) of 308 CAR-T recipients were admitted to ICU, across a total of 79 episodes (13 patients were admitted twice; 4 three times). The median age was 65 (interquartile range 56–72); 69% were male; haematological diagnosis was diffuse large B-cell lymphoma (DLBCL) 90%, mantle cell lymphoma (MCL) 7% and B-cell acute lymphoblastic leukemia (B-ALL) 3%. 14 patients (24%) experienced grade $\geq$ 3 CRS; 39 (66%) experienced grade $\geq$ 3 ICANS; 14 (24%) experienced grade $\geq$ 3 ICAHT. Median ICU length-of-stay was 2.7 days (range 0.5–58.0 days). Invasive mechanical ventilation (INV) was delivered in 18 (23%) of episodes, non-invasive ventilation in 6 (8%), vasopressor/inotrope in 31 (39%) and renal replacement therapy in 2 (3%). No specific organ support was delivered in 44 episodes (56%). Only 2 patients (3%) died in ICU/within days of ICU discharge. 12-month progression-free survival (PFS) was 42% and 12-month overall survival (OS) was 60%.

Conclusion:

ICU resource utilisation in CAR-T patients was significantly less than that reported in the pivotal trials, with acceptable short and long-term outcomes. Over half of ICU admissions did not require specific organ support, suggesting that there are opportunities to optimise ward-based protocols for heightened observation to reduce the need for ICU admissions.

Preventing Infections after CD19-directed Chimeric Antigen Receptor T-cell Therapies for Lymphoma: A Consensus Practice Statement

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⁴Peter MacCallum Cancer Centre, Melbourne, Australia, ⁵Austin Health, Melbourne, Australia,

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Aim:

Chimeric antigen receptor (CAR) T-cell therapies directed against the B-cell antigen CD19 are a standard of care for the treatment of relapsed or refractory large B-cell and mantle cell lymphomas. Infection is the leading cause of death after CAR T, and this risk persists for months to years after treatment. Predisposing factors include prior lymphoma therapy, lymphodepletion, anti-cytokine therapies, hypogammaglobulinaemia and late cytopenias. We aimed to develop an evidence-based approach to preventing, investigating and managing infections before and after receipt of CD19-directed CAR T-cells for lymphoma.

Method:

A panel of haematologists, infectious disease specialists, and specialist nurses identified key questions. A literature review was conducted using Medline, consensus recommendations were agreed, and evidence quality and recommendation strength determined using the AGREE-II tool and Grading of Recommendations Assessment, Development and Evaluation (GRADE) framework.

Results:

The following key topics were defined: 1. screening for infectious agents before CAR T-cell therapy; 2. indications for CAR T-cell deferral in the event of active infection; 3. vaccination before CAR T-cell therapy; 4. use of granulocyte-colony stimulating factor; 5. antimicrobial prophylaxis; 6. diagnosis and monitoring of infection; 7. immunoglobulin replacement; 8. venous access, dietary recommendations and lifestyle advice; 9. vaccination following CAR T-cell therapy. Moderate and strong consensus recommendations were agreed within each topic, and evidence strength graded. The panel noted that many recommendations relied on low quality evidence, often extrapolated from other clinical scenarios.

Conclusion:

This Australasian practice statement provides practical evidence- and expert-informed recommendations for the prevention, investigation and management of infections among recipients of CD19-directed CAR T-cell therapies for lymphoma. There is an ongoing need for studies to refine risk factors and define optimal infection management strategies in this setting.

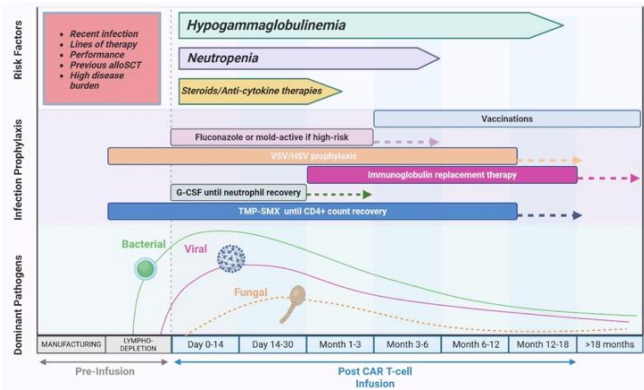


Figure: Risk factors, prophylactic measures and dominant pathogens following CD19-directed CAR T-cell therapy

Early empirical antibiotic discontinuation in patients with high-risk febrile neutropenia: a systematic review and meta-analysis of randomised controlled trials

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Aim:

Febrile neutropenia (FN) leads to significant morbidity and mortality in high-risk groups, including those with haematological malignancies. While initial empirical antibiotics may prevent life-threatening infections, continued therapy increases antibiotic resistance while delaying and reducing effectiveness of treatment. In response, guidelines have revised antibiotic regimens, suggesting more conservative usage. However, recommendations between them remain unclear especially amongst high-risk groups. This systematic review and meta-analysis examine early antibiotic discontinuation in high-risk groups.

Method:

Embase, PubMed and Cochrane Library databases were systematically searched for randomised controlled trials (RCTs) comparing early discontinuation with continuation of empirical antibiotics in clinically stable, high-risk FN patients. Mortality, treatment success rate and recurrence of fever were analysed. Where possible, data was pooled and synthesised using a random-effects meta-analysis. A risk of bias analysis and certainty of evidence was performed.

Results:

Seven RCTs with 1078 distinct patients (546 discontinuation and 532 continuation) were analysed. The most common diagnosis and treatment was acute leukemia and induction or reinduction chemotherapy respectively. Pooled estimated mean neutropenia days across both groups was approximately 13.5 days. There was no statistical difference between groups across mortality (RR=0.76; 95% CI=0.32 – 1.81; I²=18%; p=0.54), treatment response rates (RR=0.99, 95% CI=0.92–1.06; I²=0%; p=0.81) or fever recurrence (RR =1.10, 95% CI=0.91–1.32; I²= 0%; p=0.33). Heterogeneity was low across all outcomes.

Conclusion:

Early discontinuation of empirical antibiotics in clinically stable, afebrile patients with high-risk FN appears to be safe, with no observed differences in mortality, treatment success, or fever recurrence. These findings provide moderate-certainty evidence supporting guideline recommendations to encourage early discontinuation practises.

Evaluating the impact of a communication skills workshop for health care professionals on the early introduction of palliative care in patients with haematological malignancies

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Aims:

This study aimed to explore healthcare professionals' experience of a communication skills workshop (CSW), specifically focusing on its content, delivery and relevance to their clinical practice in facilitating discussions about early Palliative Care (PC) introduction in patients with haematological malignancies. The study evaluated the impact of CSW participation on clinicians' confidence and communication skills for PC introduction.

Methods:

The participants were sixteen clinicians, including specialists, trainees, and nurses working in PC and haematology. Participants completed pre- and post-workshop surveys on the day of the workshop. Survey responses were collected before and after the workshop using a Likert scale. Statistical analyses were undertaken using GraphPad Prism v10.0 (Boston, Massachusetts, USA). Paired samples were compared utilising a Wilcoxon signed-rank test. Semi-structured interviews were conducted later using Microsoft Teams and were audio-recorded and transcribed. Inductive data analysis was performed using reflexive thematic analysis.

Results:

Analysis of the survey responses identified a statistically significant improvement in all survey questions after the workshop. Analysis of the qualitative interview data identified five key themes: 1) perceived barriers faced by haematology clinicians in initiating early PC discussions; 2) the impact of perceived barriers on delayed PC introduction; 3) the benefits of early PC and challenges experienced by PC clinicians; 4) the benefits of an individualised, tailored workshop on promoting early PC involvement; and 5) the impact of the CSW on clinicians' confidence and communication practices.

Conclusion:

PC and haematology clinicians described the effectiveness of the CSW in introducing early PC referrals for patients with haematological malignancies. Participants discussed the benefits of the diverse communication tasks they performed and the positive influence of the tailored workshop on their self-reported improvement in confidence and communication skills regarding the early introduction of PC.

Transfusion truths: Nursing knowledge and decision making across the blood transfusion process — implications for patient safety in New Zealand hospitals

Miss Katerina Hodgson¹

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Aim:

This study aimed to measure New Zealand (NZ) nurses' knowledge and decision-making across the blood transfusion process and identify potential risks to patient safety.

Method:

A prospective cross-sectional quantitative study was conducted across NZ hospitals (Auckland Health Research Ethics Committee approval: AH28223). A total of 130 registered nurses completed an anonymous 32-item online questionnaire distributed via a newsletter and a postgraduate nursing platform between December 2024 and March 2025. The survey captured demographic characteristics and assessed knowledge and decision-making across domains including general transfusion knowledge, blood sampling, pre-transfusion responsibilities, complication management, and during/post-transfusion care. Data were analysed using IBM SPSS to identify descriptive and inferential trends.

Results:

Participants achieved an average knowledge and decision-making score of 60% across 23 questions, indicating significant gaps in safe transfusion practice. The lowest-performing domains were blood sampling (38%) and complication management (36%), areas strongly associated with preventable transfusion errors and patient harm. Higher performance was observed in questions related to during and after transfusion (85%).

Self-reported confidence and prior attendance at blood transfusion education were analysed; however, many associations were not statistically significant. Although 79% of participants reporting feeling confident or very confident, confidence did not correlate with accuracy. In one question addressing monitoring for adverse transfusion reactions, lower-confidence participants outperformed higher-confidence participants ($p = 0.006$). Prior attendance at transfusion education was significantly associated with better performance on independent double-checking ($p = 0.020$) and the first action during a transfusion reaction ($p = 0.042$). These results suggest confidence is not a reliable indicator of competence, whereas targeted education may improve knowledge.

Conclusion:

NZ nurses demonstrated inadequate knowledge and variable decision-making across the blood transfusion process, particularly in high-risk domains such as blood sampling and complication management. The mismatch between confidence and competence, combined with inconsistent educational impact, highlights the need for future research into education frequency, format, and retention.

Preventing iatrogenic anaemia in malignant haematology inpatients: A pilot randomised controlled trial

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Aim:

Iatrogenic anaemia from frequent blood sampling is common among inpatients with haematological malignancies and may contribute to transfusion dependence. While patient blood management (PBM) strategies have reduced blood loss in other inpatient populations, feasibility data in malignant haematology is limited. This study evaluated the feasibility and acceptability of a tailored PBM intervention and explored its preliminary effects on phlebotomy blood loss and transfusion-related outcomes.

Method:

A single-centre, parallel-group, pilot randomised controlled trial was conducted at a tertiary cancer centre in Brisbane, Australia. Adult (≥ 18 years) inpatients receiving intravenous chemotherapy via a central venous access device (CVAD) where a nadir was expected, were randomised 1:1 to standard of care or a PBM intervention. The intervention included reduced CVAD discard volumes, small-volume blood sampling tubes, and documentation of phlebotomy loss. Primary outcomes assessed feasibility and clinician acceptability. Secondary outcomes included phlebotomy volumes, haemoglobin change, red blood cell transfusions, length of stay, and patient-reported outcomes. Analyses were descriptive and conducted on an intention-to-treat basis.

Results:

Of 103 patients screened, 62 were randomised (control $n=32$, intervention $n=30$). Recruitment was 60%, with high retention and minimal withdrawal. Clinician acceptability was high. Mean daily phlebotomy loss was lower in the intervention group (18.9mL/day vs 28.8mL/day), with reduced cumulative blood loss (340mL vs 541mL). No consistent between-group differences were observed in transfusion-related outcomes. No adverse events were reported.

Conclusion:

A targeted PBM intervention is feasible, acceptable, and safe in malignant haematology inpatients and substantially reduces phlebotomy-related blood loss, supporting progression to a multicentre trial.

Development and impact of a nurse-led subcutaneous immunoglobulin (SCIg) program

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Background:

Increasing use of B-cell directed therapies, via clinical trial and standard of care, has led to increased demand for immunoglobulin (Ig) replacement therapy and outpatient infusion care. Patients eligible for SCIg who are receiving intravenous Ig contribute to this demand. An expanded nurse-led SCIg program was established at a large metropolitan hospital offering an alternative to intravenous delivery. One full-time SCIg Clinical Nurse Consultant was appointed following approval of business case.

Aim:

To describe the development and evaluation of the impact of a nurse led SCIg program.

Method:

Scoping of the existing SCIg process was performed. Using eight domains of National Blood Authority governing requirements¹, service gaps were identified and SCIg guidelines were updated. Referral and patient flow pathways, and patient and staff education were developed. Eligible patients were identified and offered the opportunity to commence SCIg. Program development was managed and activity tracked using Microsoft Excel. At the time of commencement, block funding was provided by the Victorian Department of Health via the SCIg Access Program, which has changed to an activity-based funding model. After one year patient experience was evaluated using a Microsoft Forms survey and data were analysed using descriptive statistics.

Results:

From October 2024-March 2026 n=253 eligible patients were referred to the service. N=131 (52%) commenced SCIg: n=75 changed from IVIg to SCIg, freeing 275 hours of outpatient chair time; n=56 commenced Ig replacement using SCIg, preventing referral to outpatient services. N=31 patients stopped SCIg. Medical subspecialties serviced: haematology 88% (n=115), respiratory 8% (n=11), neurology 4% (n=5).

Patients reported reduced travel costs; less disruption to work; decreased time in hospital; increased time at home; greater autonomy in their care.

Conclusion:

A nurse led SCIg program improves patient experience while optimising hospital resources. It reduces outpatient demand by freeing chair capacity and reducing new referrals.

Reference:

1. SCIg Program: getting started flowchart <https://www.health.vic.gov.au/patient-care/subcutaneous-immunoglobulin-scig-program-tools-and-resources>

Empowering care at home - patient-reported experiences of a nurse-led subcutaneous immunoglobulin (SCIg) program

Miss Karen Sadler¹, Tim Chestney¹, Danielle Lee¹, Ellen Heywood¹, Miss Cassie Abbott¹

¹The Alfred Hospital, Melbourne, Australia

Background:

Increasing use of B-cell directed therapies has led to increased demand for immunoglobulin replacement therapy and outpatient infusion care. An expanded nurse-led SCIg program was commenced at a large metropolitan hospital to offer an alternative to intravenous delivery.

Aim:

To evaluate the utility, practicality and patient experience of a nurse-led SCIg program and identify areas for future improvement.

Method:

A Microsoft Office forms survey was developed and distributed via email or text to n=114 patients who took part in the SCIg program from 1 Oct 2024 – 30 Nov 2025. Questions were a mixture of closed, open-ended and free text. Topics encompassed education and training, obtaining medication and consumable supplies and experience of SCIg at home. All responses were collected anonymously. Descriptive statistics were used to analyse survey responses, and a content analysis was conducted for open ended responses.

Results:

Forty-nine (43%) complete responses were received. Length of time on SCIg therapy: 1-3 months n=9 (18%), 4-6 months n=9 (18%) and >6months n=31 (63%). 100% patients rated SCIg education clear and easy to understand. 94% felt confident administering SCIg post training. N=8 (16%) patients reported side effects, including infusion site reactions and/or mild systemic reactions. N=48 (98%) patients found ordering medication via outpatient pharmacy very easy or somewhat easy. All patients found ordering infusion consumable supplies very easy or somewhat easy. There were no major or minor improvements suggested. Participants rated their overall experience of administering SCIg at home as easy or somewhat easy n=47 (96%). Participants reported the best aspects of the SCIg program as 'the time saved'; 'being at home'; and 'having control over their own care'.

Conclusion:

Overall, participants provided positive feedback about the nurse-led SCIg program and were empowered through education and support to self-administer SCIg at home, leading to time savings and agency over their healthcare.

T cell subsets in HIT reveal broad immune dysregulation persisting beyond clinical resolution

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Aim:

Heparin-induced thrombocytopenia (HIT) is a highly prothrombotic immune complication of heparin therapy, driven by antibodies against platelet factor 4 (PF4)-heparin complexes. Although HIT is classically considered an antibody mediated disorder, the broader immune response accompanying acute disease and recovery remains poorly defined. To address this gap, we aimed to determine circulating T cell populations in patients with HIT at diagnosis and after recovery.

Method:

Peripheral blood mononuclear cells were collected from patients with clinically and laboratory-confirmed HIT during acute presentation and at three-month follow-up, alongside heparin-exposed HIT-seronegative controls over 2 years. The cohort includes 12 patients with confirmed HIT, 2 follow-ups and 5 HIT-seronegative controls. A 17-marker spectral flow cytometry panel was used to assess T cell phenotype, activation status and correlate with anti-PF4 titre determined by STAGO-ELISA. Data were normalised using CytoNorm and analysed using high-dimensional clustering. Biologically annotated T cell populations were compared as proportions of total CD3+ T cells.

Results:

T cell subsets were broadly preserved across groups; however, HIT samples showed measurable shifts in the relative abundance of several annotated T cell populations. These changes were most evident in memory, helper-associated, and activation-linked populations, suggesting that HIT is accompanied by adaptive immune remodelling beyond the pathogenic anti-PF4 antibody response. Importantly, differences were also observed in three-month follow-up samples, raising the possibility that immune perturbation may persist beyond platelet count recovery and clinical resolution.

Conclusion:

These preliminary data provide, to our knowledge, the first evidence that circulating T cells are affected in HIT, supporting the concept that HIT is not solely an B cell dependent disorder. Further studies will determine whether a T cell signature can be used to support the diagnosis of HIT and to identify immune mechanisms underlying HIT pathogenesis and recovery.

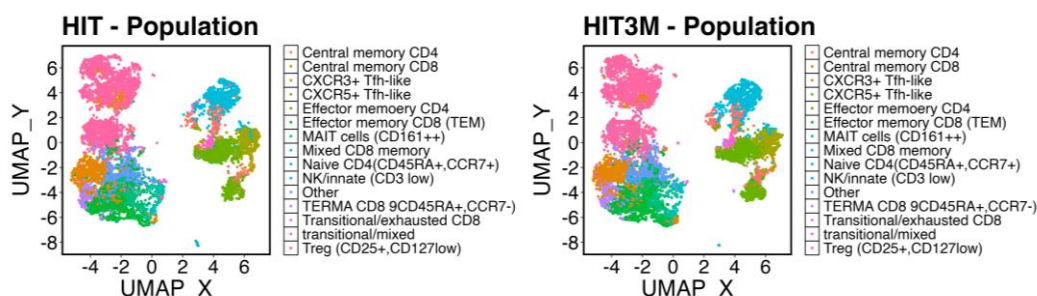


Figure 1. UMAP projection of T cell populations in acute HIT and three-month (HIT3M) follow-up samples.

Identification of ABO(H) blood group antigen carrying platelet glycoproteins

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Aim:

Thrombosis and haemorrhage are among the leading causes of death worldwide. ABO blood group is a risk factor for thrombosis and bleeding; however, the mechanisms of this association are not fully understood. Platelets are known to be modified by the antigens that define ABO blood types (A, B, and H), but the full repertoire of glycoproteins that carry these epitopes remains unknown.

We hypothesize that ABO(H) antigens on platelet glycoproteins contribute to the association of thrombosis and bleeding with ABO blood type. We aim to identify platelet glycoproteins that carry ABO(H) antigens to better understand their involvement in haemostasis and thrombosis.

Method:

We employed specific antibodies to immunoprecipitate glycoproteins from human type O platelets that carry the blood group antigen H. The isolated glycoproteins were identified via tandem mass tag mass spectrometry. The experiments were performed in triplicate for three donors. Furthermore, we developed a workflow to confirm the presence of ABO(H) antigens on glycoproteins of interest by Western blot.

Results:

Our proteomics analysis confirmed prior reports that glycoproteins such as platelet endothelial cell adhesion molecule (PECAM1), platelet glycoprotein (GP) IIb (GPIIb), GPIV and GPV are modified with ABO(H) antigens. Furthermore, we have identified over 200 protein candidates not previously known to carry ABO(H) antigens. We verified the presence of these antigens on several proteins which are highly important for platelet function, for example P-Selectin, Integrin alpha-5 and Integrin alpha-6.

Conclusion:

We have shown that ABO(H) antigens are present on many more platelet glycoproteins than previously described. Many of these glycoproteins play critical roles in blood clot formation. By further investigating platelet glycoproteins that carry the ABO(H) antigens, new insights will be gained for diagnosis, prevention and treatment of thrombosis and bleeding.

Platelet-leukocyte aggregates a potential new target in antiphospholipid syndrome-related thrombosis

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Aim:

Pathophysiology of thrombosis in antiphospholipid syndrome (APS) is heterogeneous, and personalised adjuncts to anticoagulation may improve outcomes. The role of platelet-leukocyte aggregation (PLA) in APS remains unclear. We sought to determine if PLA could be induced by APS patient sera and be prothrombotic.

Method:

APS patient serum was heat-inactivated (HI) and incubated with fresh healthy donor whole blood (HDWB) with/without collagen-related peptide (CRP) stimulation prior to measuring PLA by flow cytometry. PLA were defined as the proportion of leukocytes (including neutrophils, PNA) positive for platelet marker, CD41, with absolute change in percentage compared to autologous HI serum reported. APS sera with increased PLA formation by flow cytometry were tested in a collagen-coated ex vivo microfluidic model of thrombosis with/without PLA inhibitor, crizanlizumab.

Results:

Incubation with APS HI serum increased PLA proportions in HDWB compared to healthy control sera: mean $\pm$ SD increase $3.0 \pm 6.9\%$ (n=30) and $0.3 \pm 0.9\%$ (n=8), respectively (p=0.047). There was a trend to increased PLA with APS sera after stimulation with CRP $4 \mu\text{g/mL}$ (p=0.09). The increased PLA were primarily due to PNA (p=0.03), with a subset (4/30) of APS HI sera inducing a pronounced increase (>11%) in PNA. The PNA induction in this subset was completely reversed by crizanlizumab in CRP-stimulated HDWB: vehicle control mean $46.6 \pm 16.0\%$, crizanlizumab $20 \mu\text{g/mL}$ mean 0.2 ± 1.1 (n=4, p=0.008). In the ex vivo thrombosis model, APS sera (n=4) increased fibrin formation, particularly in 3/4, compared to healthy control sera (n=3): fibrin mean integrated density 1839768 ± 1690336 and 131215 ± 61596 , respectively (p=0.14), reduced when APS sera-treated HDWB was preincubated with crizanlizumab (mean integrated density 349594 ± 392789 , n=4).

Conclusion:

Heat-inactivated serum from a subset of APS patients can induce PLA and increase fibrin formation in an ex vivo model. These results indicate PLA inhibition in these APS patients may reduce thrombus formation with potential implications for recurrent thrombotic risk.

Objective platelet kinetics and emerging Post-COVID challenges in HIT diagnostics

Dr Michel Lu^{1,2}, Dr Freda Passam^{3,4}, Dr Silvia Zheng^{1,2}

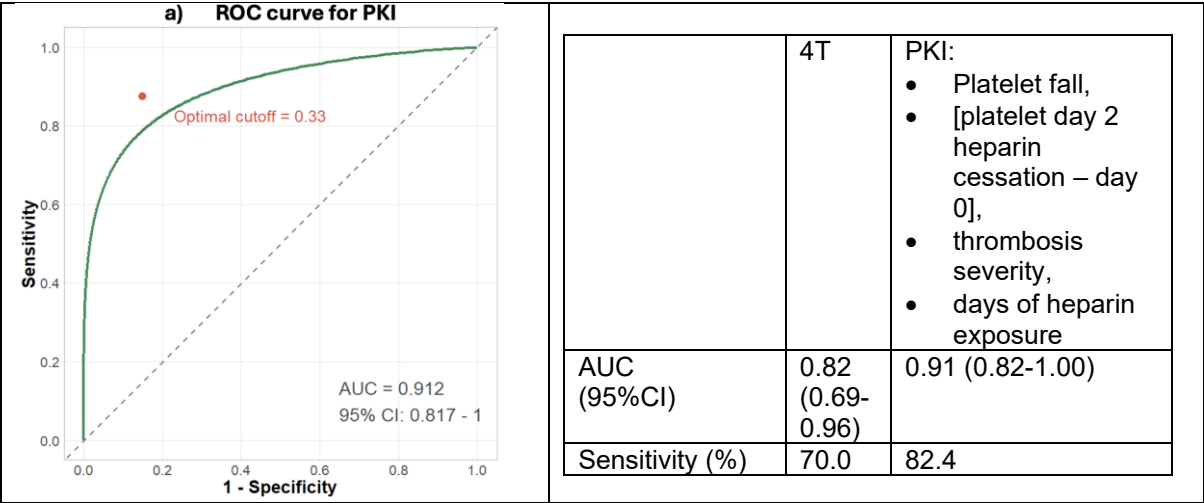
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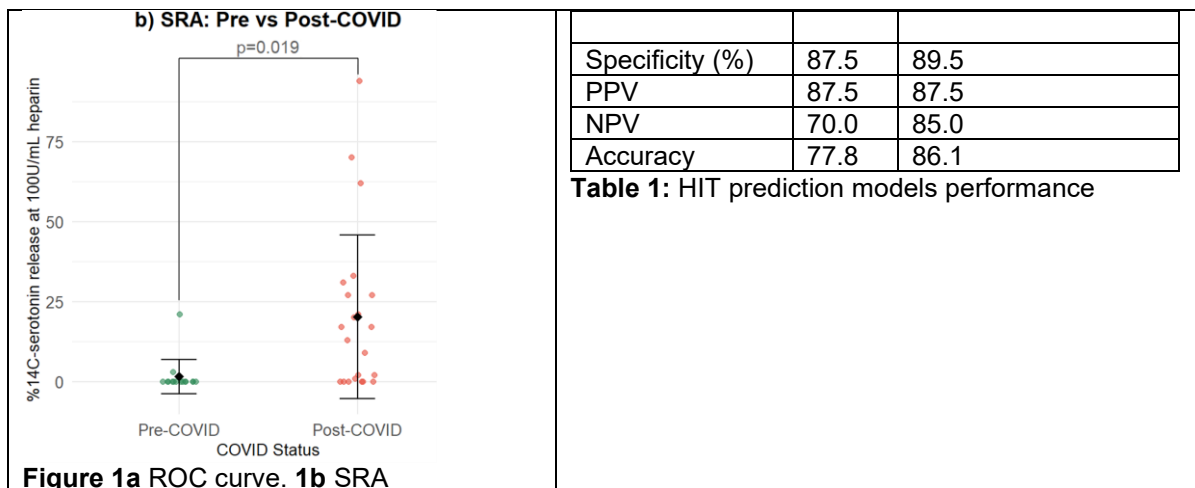
Aim: Heparin-induced thrombocytopenia (HIT) is a rare but serious adverse reaction to heparin caused by autoantibodies against the heparin–platelet factor 4 complex. Clinical diagnosis is supported by the 4T score, a pretest clinical probability score with significant inter-operator variability.¹ Screening tests are sensitive but non-specific. Confirmatory serotonin release assays (SRAs) remain the gold standard but are costly and labour-intensive.^{2,3} We aimed to develop an objective and clinically applicable diagnostic support tool for HIT.

Methods: A retrospective single-centred analysis was conducted of suspected HIT cases investigated with ELISA and SRA during the pre-COVID (2018-2019) and post-COVID (2023-2024) periods. Clinical and laboratory variables were extracted and analysed using statistical software R.

Results: Thirty-seven patients were identified. Multiple variables were analysed using univariate and LASSO regression to develop the Platelet Kinetics Index (PKI) HIT prediction model. At a cutoff of 0.33, it demonstrated clinically meaningful discrimination and outperformed the 4T score in predicting HIT (Figure 1a, Table 1). Firth logistic regression demonstrated ELISA OD>1 as a strong predictor of HIT (AUC 1.00, p < 0.001). Samples tested in the post-COVID era (n=22) demonstrated significantly higher serotonin release at 100U/mL heparin (p=0.019), suggesting altered SRA patterns and increased non-specific platelet activation (Figure 1b).

Conclusion: PKI is a promising objective measure for HIT prediction that may improve risk stratification compared with the 4T score. ELISA OD>1 strongly predicted HIT positivity in this cohort and may refine prioritisation for confirmatory testing. Altered SRA patterns observed in the post-COVID era highlight emerging challenges in functional assay interpretation and warrant further investigation in larger cohorts.





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Vorticity-facilitated platelet aggregation: insights from a high expansion-ratio stenotic microfluidic platform

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Aim:

The specific hemodynamic factors that govern platelet activation and aggregation within stenotic vascular geometry in arterial thrombosis remain unclear. Understanding how complex flow patterns, specifically the contribution of vorticity — the rotational component of fluid flow, regulate thrombus formation is critical for improving device design to prevent vortex-induced clotting.

Method:

We developed a microfluidic platform featuring a double stenosis followed by expansion regions with different expansion angles (β) to systematically modulate downstream vorticity under defined shear conditions. Computational fluid and Ghost Particle Velocimetry visualization were employed to characterize and quantify the flow patterns. The kinetics of thrombus formation, such as real-time detection of von Willebrand factor (vWF) accumulation, platelet integrin $\alpha\text{IIb}\beta 3$ intermediate activation, and intracellular calcium signalling, were detected by differential interference contrast and confocal microscopies under varying vorticity magnitudes.

Results:

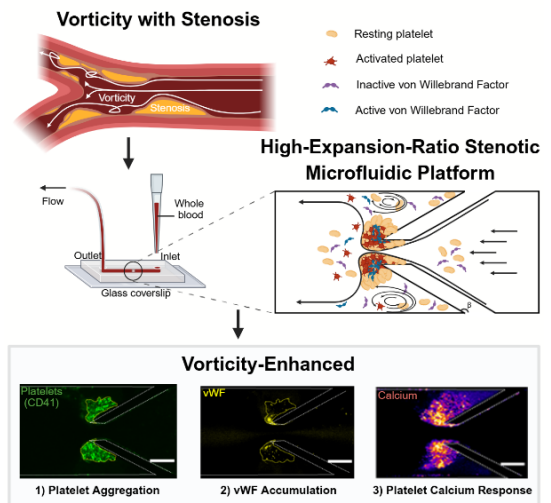
The distinct vortical flow zones of high expansion-ratio geometries were confirmed by flow analysis. There is a strong correlation between thrombus formation and vorticity magnitude ($r = 0.6698$), which is independent of conventional shear-rate effects. High-vorticity conditions produced thrombi up to fourfold larger than in low-vorticity geometries. This was accompanied by at least a twofold increase in vWF deposition, a twofold enhancement in intermediate $\alpha\text{IIb}\beta 3$ activation, and significantly elevated calcium signaling within vortical regions. In addition, platelet aggregation is almost completely abolished with the inhibition of the vWF–GPIIb interaction.

Conclusion:

These findings provide direct mechanistic evidence that vorticity, beyond shear-rate magnitude alone, plays a critical hemodynamic factor in thrombus initiation and progression. Our microfluidic model offers a powerful tool to dissect biomechanical contributors to thrombosis in complex arterial flow, and provides new insights into the design of antithrombotic strategies and vascular devices with improved hemocompatibility.

Schematic abstract: Vorticity-enhanced arterial thrombosis in an *in vitro* microfluidic model

Vorticity-Enhanced Arterial Thrombosis in an *in vitro* Microfluidic Model



A platelet $\beta 3$ integrin phenotype that is associated with heavy menstrual bleeding

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Aim: Heavy menstrual bleeding (HMB) is a common manifestation of a bleeding disorder (BD) of often unknown cause. The platelet integrin αIIb and $\beta 3$ subunits are constitutively produced as multiple partially disulfide-bonded states. Notably, the C177-C184 disulfide bond in the $\beta 3$ headpiece is particularly unformed. Our aim is to elucidate the function of $\alpha IIb\beta 3$ integrin missing the $\beta 3$ C177-C184 disulfide bond and test for association of this platelet phenotype with patients with a history of HMB and BD.

Method: Redox state of the platelet $\beta 3$ C177-C184 disulfide bond was determined by cysteine alkylation and mass spectrometry. Function of the disulfide-ablated integrin was investigated in BHK cells. Molecular dynamics simulations revealed how the missing disulfide bond influences ligand binding. Venous blood was collected from females (n=22, 29-73 years) with a history of HMB with an abnormal ISTH bleeding assessment tool (BAT) score and compared to healthy controls (5 F, 3 M, 20-80 years).

Results: The $\alpha IIb\beta 3$ integrin missing the $\beta 3$ C177-C184 disulfide bond is a nonfunctional receptor as it is unable to bind its RGD ligands. Ablation of the disulfide bond results in destabilizing effects around the MIDAS site, which accounts for the loss of ligand binding. The $\beta 3$ C177-C184 disulfide bond was significantly more unformed in the HMB cohort ($55 \pm 13\%$ of the total integrin pool) when compared to healthy controls ($45 \pm 4.2\%$ of the total integrin pool).

Conclusion: The state of the $\beta 3$ C177-C184 disulfide bond in platelets may act as barometer of platelet function. Individuals with low or high levels of unformed C177-C184 bond have relatively reactive or unreactive platelets, respectively. This thesis is supported by a higher unformed state of the bond in women with HMB and an abnormal BAT score.

Diamond Blackfan anaemia resulting from polyadenylation variants

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¹Australian Regenerative Medicine Institute, CLAYTON, Australia, ²Molecular Haematology Laboratory and Wilson Centre for Blood Cancer Genomics, Peter MacCallum Cancer Centre, Melbourne, Australia

Aim:

Diamond Blackfan anaemia (DBA) is a rare inherited bone marrow failure syndrome characterised by macrocytic anaemia, congenital abnormalities and cancer predisposition. Approximately 80% of cases are due to heterozygous loss-of-function mutations in ribosomal protein genes. However, 20% still lack an identified genetic cause. We sought to identify pathogenic variants in non-coding regions in unresolved DBA cases.

Method:

Extended genomics analysis was performed as part of the IBMDx clinical study (NCT05196789). Following leads from clinical scenarios, we used gene editing in zebrafish to model the functional effect on erythropoiesis of disruptions in the PAS sequence of three ribosomal protein genes.

Results:

A 16-year-old male with DBA was found to carry a de novo heterozygous 2 nucleotide deletion within the Polyadenylation Signal (PAS) motif of the RPL31 gene, recognised by transcriptome analysis after whole genome sequencing did not initially establish a genetic diagnosis. He had low total RPL31 transcript expression and extended transcripts terminating at multiple downstream alternative PAS sites. To strengthen the causality of this variant/disease pairing, a functional assay was needed. We chose zebrafish disease modelling to link a clinically-aligned phenotype with the molecular lesion.

Zebrafish heterozygous for a RPL31 PAS-disrupted allele had reduced RPL31 expression, extended RPL31 transcripts terminating at assorted downstream PAS motifs, and were significantly anaemic. PAS-disruption in the zebrafish orthologues of two other DBA genes (RPL27, RPS26/RPS26L) also resulted in anaemia, demonstrating that PAS-disruption was a generic cause of functional DBA gene haploinsufficiency.

Conclusion:

To our knowledge, these are the first animal models of genetic disease caused by PAS variant alleles. The zebrafish models functionally confirm that PAS variant alleles in three DBA genes are sufficient to cause anaemia. PAS variant alleles are likely an overlooked cause of DBA in conventional genomic diagnostic approaches, and also a likely cause of many other genetic diseases.

299 words / 300 allowed

Evaluating a novel FcRn blocking monoclonal antibody as a preventive strategy in red cell alloimmunised pregnancies at risk of severe HDFN

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Aim:

Hemolytic disease of the fetus and newborn (HDFN) results from maternal-fetal red blood cell antigen incompatibility, in which maternal immunoglobulin G (IgG) alloantibodies cross the placenta via the neonatal Fc receptor (FcRn) and cause fetal hemolysis. Severe HDFN may lead to fetal anemia, hydrops fetalis, or fetal/neonatal death. Current management remains reactive, relying on monitoring and treating fetal anemia with intrauterine transfusions (IUTs). A novel FcRn-blocking monoclonal antibody is currently under investigation as a potential preventive therapy for pregnancies at risk of severe HDFN. This ongoing Phase 3 clinical trial aims to evaluate the safety and efficacy of the investigational product in pregnancies at risk of severe HDFN.

Method:

Eligible participants are aged 18 to 45 years and have a history of severe HDFN in a prior pregnancy. Participants are randomised in a 2:1 ratio to receive investigational product or placebo. The treatment period consists of weekly intravenous infusions for up to 23 weeks. Following delivery, participants enter a safety follow-up period of 24 weeks for mothers and 104 weeks for infants.

Result:

Recruitment for the study is ongoing, and data collection is currently in progress.

Conclusion:

Emerging evidence from preclinical and early clinical studies suggests this investigational product may offer a preventive management approach in pregnancies at risk of severe HDFN, with the potential to reduce disease burden and improve maternal and fetal outcomes. Findings from this Phase 3 trial will further define the efficacy and safety profile of this therapy and its potential role in future clinical practice.

Initial Reflections following the introduction of Newborn screening for Sick Cell disease in an Australian population (September 2025-May 2026): A retrospective review of implementation and clinical utility.

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Aim:

As the first Australian state to implement newborn bloodspot screening (NBS) for Sick Cell Disease (SCD), we aimed to evaluate the program's initial effectiveness. In particular, we sought to assess the rate of detection compared to existing antenatal screening pathways and evaluate the diagnostic utility of the chosen methodology.

Method:

This retrospective review analysed the demographic characteristics and outcomes of all infants identified during the first eight months following implementation of the newborn screening for SCD in Victoria.

Data was collected from all screen positive infants who were screened through the statewide NBS program and referred for confirmatory testing. Screening results, confirmatory test results, diagnostic subtype, demographic distribution and available antenatal screening results and postnatal management plans were reviewed. Comparative analysis was performed to determine the proportion of cases that would not have had an antenatal and/or postnatal diagnosis in the absence of NBS.

Results:

Out of 47,183 individuals screened, 13 cases were referred for further evaluation. Although data collection remains ongoing, preliminary analysis confirmed SCD in 3 out of the 13 referrals (23%). The use of capillary electrophoresis (CE) as the primary screening methodology also provided diagnostic benefit beyond SCD; most notably in the detection of severe beta thalassaemia which accounted for approximately 30% of all referrals. Notably, 33% (n=1/3) of these confirmed SCD cases and 25% (n=1/4) of the severe beta thalassaemia cases had not been identified as being at risk by prior antenatal screening, highlighting gaps in current obstetric screening pathways.

Conclusion:

Implementation of NBS for SCD in Victoria has successfully identified high risk infants who may have faced delayed diagnosis. Our findings also demonstrate that CE methodology offers additional utility in detecting other clinically significant haemoglobinopathies. These results provide the framework for other Australian jurisdictions to optimise screening pathways and emphasise that NBS is an important safety net for the detection of SCD and related disorders in a diverse population. A formal health economic assessment is recommended to further evaluate these potential benefits.

Insufficient erythropoiesis drives early mortality in warm autoimmune haemolytic anaemia

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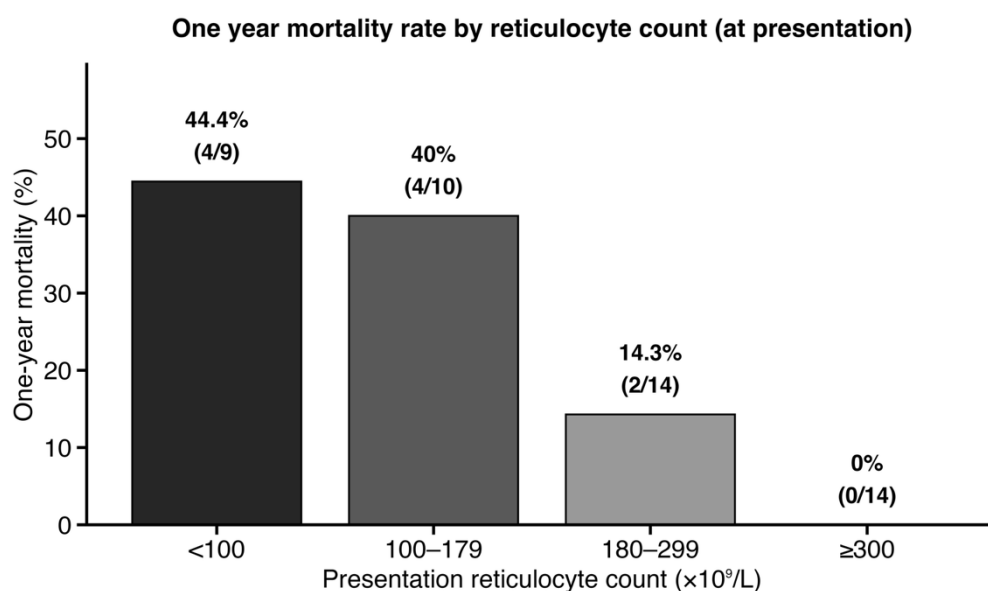
Aim: Warm autoimmune haemolytic anaemia (wAIHA) is a rare acquired anaemia associated with substantial morbidity and mortality, but poorly defined predictors of outcome. We evaluated clinical and laboratory variables for mortality in patients with wAIHA at an Australian tertiary centre.

Method: We performed a retrospective cohort study of adults newly diagnosed with wAIHA between 1 January 2018 and 11 November 2022. Mixed, Evans, cold agglutinin disease and relapses were excluded. Baseline renal function (eGFR), early erythropoietic response (peak absolute reticulocyte count within 14 days), and haemoglobin recovery metrics (time-weighted haemoglobin, time to haemoglobin ≥ 100 g/L, and haemoglobin change to day 14) were analysed. Associations with mortality were assessed using non-parametric comparisons and Spearman correlation.

Results: Overall mortality was 21.3% at 1 year and 31.9% at median follow-up (1518 days). Patients who died had lower absolute reticulocytes within 7 days of presentation (141 vs 246, $p=0.013$). Early reticulocytes correlated with haemoglobin recovery, including time-weighted average haemoglobin to 120 days ($p=0.449$,

$p=0.004$) and time to haemoglobin ≥ 100 g/L ($\rho=-0.386$, $p=0.027$). Delayed haemoglobin recovery, rather than nadir haemoglobin, was associated with mortality (time-weighted average haemoglobin to 120 days $p<0.001$). Baseline eGFR was lower in patients who died (66 vs 83, $p=0.015$) and positively correlated with early reticulocyte response ($\rho=0.379$, $p=0.019$).

Conclusion: Impaired early erythropoietic compensation and reduced renal function are key determinants of mortality in wAIHA. Adverse outcomes appear driven not only by haemolysis severity, but by failure of erythropoietic compensation, identifying a high-risk phenotype for targeted intervention. The association between renal impairment and blunted reticulocyte response raises the possibility that haemolysis-associated renal injury disrupts erythropoietin production, further limiting compensatory erythropoiesis. Early risk stratification may provide an opportunity for renal-protective or erythropoietin replacement strategies alongside rapid control of haemolysis.



Endocrinopathy in transfusion-dependent thalassaemia: A retrospective cohort analysis from an Australian Tertiary Referral Centre

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Aim:

To review patient characteristics, iron burden, and lifetime prevalence of endocrinopathies in a large cohort of transfusion-dependent thalassaemia (TDT) patient in an Australian tertiary referral centre.

Method:

We conducted a retrospective cohort study of TDT patients receiving care at a major tertiary referral centre in Sydney, Australia, from 2000 to May 2025. Lifetime prevalence of comorbidities, treatment exposure, serum ferritin, MRI T2* results, and endocrine comorbidities were determined by examining all patient diagnosis codes, medical records and clinician correspondence.

Results:

Seventy-four patients met inclusion criteria. Age tertiles (T1 18.26–33.83 years, n=25; T2 33.94–47.24 years, n=24; T3 47.72–58.65 years, n=25) demonstrated expected anthropometric differences by sex and age. Skeletal disease predominated: osteoporosis in 38/73 (52.1%), osteopenia in 29/73 (39.7%), and fragility fractures in 11/73 (15.1%). Other endocrinopathies included diabetes in 16/74 (21.6%), hypogonadism in 22/74 (29.7%), hypothyroidism in 15/74 (20.3%), hypoparathyroidism in 6/74 (8.1%), and adrenal insufficiency in 1/74 (1.4%). Logistic regression showed each 10-year increase in age was associated with higher endocrinopathy burden (OR 2.55, 95% CI 1.62–4.02; p=0.0001). Cardiac T2* medians were within acceptable range (>20 ms) across all subgroups, while median liver T2* values were in the mild iron range (5–11 ms). Median serum ferritin declined from 2009–2015 to 2019–2025 in every subgroup (Friedman $\chi^2 = 31.2$, p<0.001). Deferasirox was the predominant chelation agent in younger and middle-aged patients.

Conclusion:

Despite marked improvements in iron control and widespread use of oral chelation, endocrine morbidity remains almost universal in this Australian TDT cohort, with skeletal disease predominating and central axis dysfunction common. Age is the principal correlate of burden, while average ferritin and liver/cardiac T2* did not independently predict risk. These findings support embedding endocrine pathways within haemoglobinopathy services and prospective studies evaluating organ-specific iron burden, chelation intensity, and endocrine outcomes.

Microbial–host metabolic signatures underlying acute graft-versus-host disease in post transplant cyclophosphamide-treated transplant recipients

Dr Joanne Tan¹, Dr Tiffany Khong¹, Dr Sean Byars², Dr Katy Jeppe³, Dr Christopher Barlow³, Dr Sridurga Mithraprabhu², Prof Andrew Spencer¹

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Aim

Acute graft-versus-host disease (aGVHD) is a major inflammatory complication affecting 20–50% of allogeneic stem cell transplant (alloSCT) recipients, driven by donor immune-mediated tissue injury. While post-transplant cyclophosphamide (PTCy) is increasingly used as GVHD prophylaxis, metabolic signatures of aGVHD in this population remain poorly defined. We therefore profiled the serum metabolome of recipients receiving PTCy to define aGVHD-associated metabolic signatures.

Methods

Serum samples were collected from PTCy-treated alloSCT recipients at aGVHD onset (pre-treatment) and from matched PTCy-treated controls at day 100 post-transplant. Untargeted metabolomic profiling was performed using high-performance liquid chromatography–mass spectrometry. Partial least squares discriminant analysis (PLS-DA) identified metabolites associated with aGVHD, and pathway enrichment analysis was performed using MetaboAnalyst v6.0.

Results

Seventy-two patients were analysed (29 aGVHD, 43 controls), across 1,224 metabolites. Median age was 60 years (range 46–68), with donor types including matched related (27.7%), matched unrelated (42.6%), and haploidentical (29.7%). Tryptophan metabolism was the only pathway significantly altered after multiple-testing correction (Holm-adjusted $p=0.01$), indicating disruption of microbiota-associated metabolic processing. Host- and microbial-associated metabolites demonstrated a distinct discriminatory profile in aGVHD (Figure 1), consistent with microbial dysbiosis and epithelial barrier dysfunction. Microbial-derived tryptophan metabolites were reduced in aGVHD, including indole-3-acetate (fold change [FC] 0.53, $p=0.001$) and indolelactic acid (FC 0.72, $p=0.017$). PLS-DA also identified several host–microbial interface metabolites as key discriminators of aGVHD, including citrulline (FC 0.73, $p<0.0001$; AUC 0.74), hydroxyphenylpropenoic acid (FC 0.55, $p<0.0001$; AUC 0.77), and pyrrole-5-carboxylic acid (FC 0.67, $p<0.0001$; AUC 0.74).

Conclusion

aGVHD is characterised by a distinct serum metabolic signature reflecting disruption of host–microbiome interactions in PTCy-treated alloSCT recipients. Longitudinal metabolomic and microbiome studies are warranted to further define the mechanistic role of host–microbial metabolic dysregulation in aGVHD and support development of microbiome-targeted

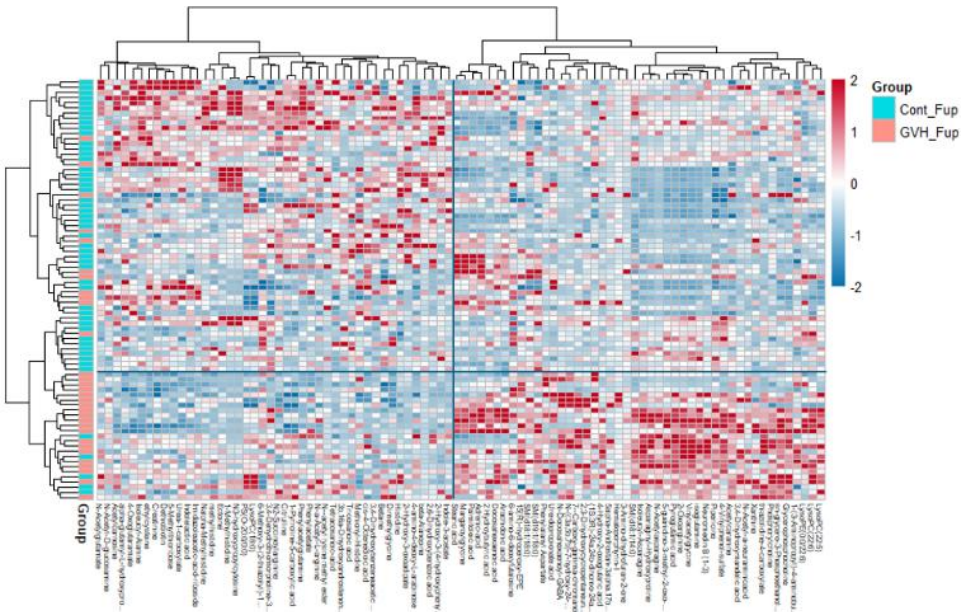


Figure 1: Clustered heat map of discriminatory metabolites comparing the host and microbiome metabolic signature of PTCy patients. (GVH_Fup – cases, Cont_Fup – controls). Samples (y-axis) and metabolites (x-axis) are hierarchically clustered based on their scaled abundance profiles. Heatmap colours denote standardised metabolite intensities (z-scores), with red indicating higher and blue lower relative abundance compared with the mean level of each metabolite.

therapies.

Clonal determinants of haematopoietic stem cell engraftment in ageing and clonal haematopoiesis

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Aim:

To define the clonal programmes governing HSPC engraftment, determine how these are altered by ageing and clonal haematopoiesis, and identify strategies to enhance stem cell fitness.

Method:

HSPCs were labelled using SPLINTR, a lentiviral barcoding system that introduces unique heritable barcodes into individual stem cells. These barcodes are inherited by daughter cells, allowing clonal fate to be tracked after transplantation and linked to pre-transplant single-cell transcriptional profiles. Barcoded HSPCs were transplanted into recipient mice to assess engraftment, persistence and lineage bias. Young and aged donor/recipient combinations were used to separate cell-intrinsic ageing from microenvironmental effects. SPLINTR was used to link post-transplant clonal outcomes to single-cell transcriptomes.

Results:

Stem cell clones showed reproducible lineage bias and output across replicate mice, demonstrating that fate is governed by cell-intrinsic programmes. Long-term engrafting clones identified an engraftment-associated transcriptional signature that was conserved across two genetically distinct mouse strains and remained evident in aged HSPCs. Ageing reduced chimerism and clonal contribution, with aged HSPCs showing clonal attrition and impaired regenerative output despite similar baseline immunophenotypic and transcriptional features. Interestingly, distinct clones were favoured by different recipient microenvironments, with some engrafting exclusively in young niches and others in aged niches. In clonal haematopoiesis models, mutant clones showed altered engraftment and competitive behaviour, demonstrating that genetic context also reshapes clonal fitness. To improve stem cell engraftment, we evaluated the engraftment signature genes using an *in vivo* CRISPR activation screen combined with SPLINTR-barcoded HSPCs. Remarkably, several genes conferred engraftment capacity and long-term multilineage output in clones that do not normally engraft. This resulted in an almost tenfold increase in polyclonality of actively contributing clones.

Conclusion:

HSC engraftment is shaped by definable clonal programmes that can be molecularly modified. We identified several genes that markedly increased the number of engrafting clones, demonstrating a strategy to improve stem cell fitness after transplantation.

Word count: 299 without headings (300 limit)

Detection of acute leukaemia and APML in peripheral blood using blast-enriched weakly supervised machine learning

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Aim: Acute promyelocytic leukaemia (APML) is a life-threatening subtype of acute myeloid leukaemia (AML) requiring urgent treatment, yet diagnosis remains time- and labour-intensive. We aimed to develop a machine learning model to detect acute leukaemia (AL) and APML in peripheral blood smear images from a clinically heterogeneous cohort, using self-supervised pre-training and blast-enriched attention-based multiple-instance learning (aMIL).

Method: We conducted a single-centre, retrospective study of cases from January 2011 to June 2025. Images from 397 AML, 67 APML, 139 other AL, 461 non-AL (including myelodysplastic and myeloproliferative neoplasms, reactive and lymphoid conditions) and 149 normal controls were scanned using CellaVision DM1200. A stratified train/validation/test split was used. An EfficientNetB0 backbone was pretrained using SimCLR self-supervised learning on 729,000 cell images. A supervised blast classifier was trained on 224,843 cells. Two aMIL models were trained: one discriminating AL from non-AL (AL detector) using blast-informed attention, and another discriminating APML from other AML (APML detector) using bags restricted to blast cells. Performance was evaluated on a held-out test set using bootstrapped area under the receiver operating characteristic (AUROC) curve, sensitivity, and specificity.

Results: The blast classifier achieved AUROC 0.973 with 87.7% sensitivity. The AL detector achieved AUROC 0.956, with sensitivity 91.0% and specificity 88.7% (AUROC 1.000 for AL vs normal, comparable with published literature). The APML detector achieved AUROC 0.993, sensitivity 97.5% and specificity 95.1%. Ablation analyses confirmed improved detection with SimCLR pretraining and blast enrichment (Fig 1).

Conclusion: Our model achieves high diagnostic performance for AL and APML detection from peripheral blood smear images in a heterogeneous cohort, a more challenging task than the curated genetic subtypes underlying published AUROCs of 0.94-0.97. As a screening tool, the APML detector sensitivity of 97.5% is promising. Limitations include modest cohort size and single-centre design. Prospective validation is warranted to enable clinical integration.

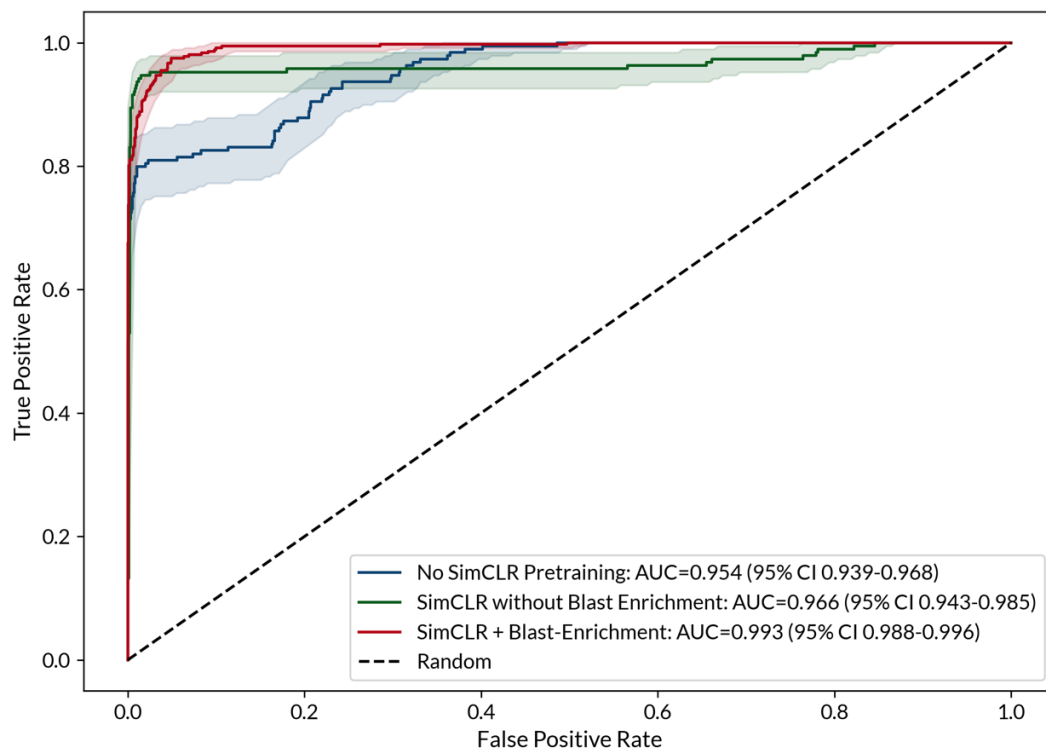


Figure 1: Receiver Operating Characteristic (ROC) Curve for APML Detector

Detection of CAR-T cells within the LBCL tumour microenvironment following CD19 CAR-T therapy using multimodal single-cell spatial transcriptomic and proteomic analysis

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Aim:

Understanding the immune milieu of the LBCL tumour microenvironment (TME) is essential to inform novel immunotherapies. CAR-T cells *in situ* remain uncharacterised due to limited spatially resolved detection methods. We aimed to characterise the LBCL TME and detect CAR-T cells *in situ* in patients treated with CD19 CAR-T immunotherapy.

Method:

Spatial multiomic approaches were applied to FFPE lymphoid tissue biopsies using complementary spatial transcriptomic and proteomic platforms, Xenium and Phenocycler-Fusion (PCF) respectively, incorporating custom CAR-T detection probes and antibodies.

Results:

15 pt biopsies and 7 tonsil controls were analysed by PCF. Samples were collected pre-CAR-T infusion (n=7) and post-infusion (n=8), including 4 paired cases, spanning D-7 to D+69. Best response was CR in 6 pts and non-CR in 9 pts (PR=2, PD=5, SD=2). CAR-T cells were detected *in situ* in 4/7 post-infusion samples using the custom CAR-T antibody (Figure 1A). Xenium analysis was performed on 8 samples from this group (2 pre-infusion, 6 post-infusion). Best response was CR in 4 pts and non-CR in 4 pts (PR=1, PD=1, SD=2). CAR-T cells were identified *in situ* using custom Xenium probes (Figure 1B). Regions enriched for CAR-T cells by proteomic analysis corresponded to areas with CAR-T transcripts, with overall cell numbers correlating between platforms. No clear relationship was observed between CAR-T cell abundance and sampling timepoint. Spatial context analysis demonstrated variable cell populations surrounding CAR-T cells at different distances (Figure 2). Quantitative single-cell results across both spatial platforms will be presented.

Conclusion:

Integrated spatial proteomic and transcriptomic profiling enables a new capability to detect and characterise CAR-T cells *in situ* within the LBCL TME. This multiomic approach will provide crucial insights into LBCL TME architecture in patients receiving CD19 CAR-T therapy to guide the development of future targeted interventions.

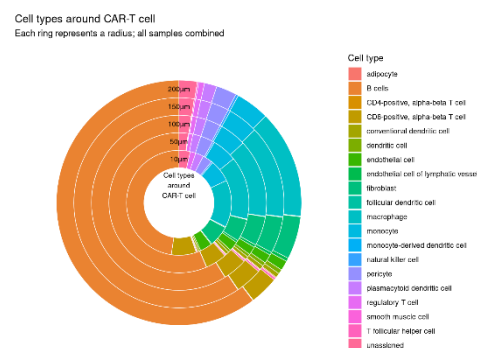
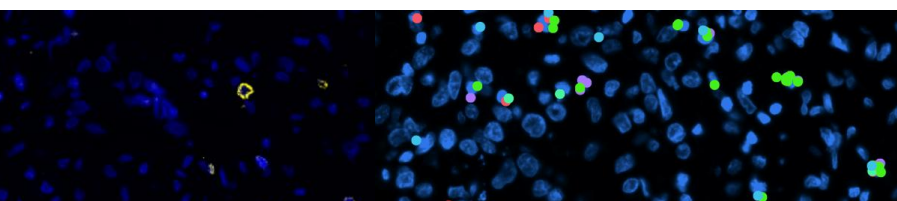


Figure 1: Detection of CAR-T cells by PCF (yellow) (A) and distinct CAR-T transcripts by Xenium, shown as differently coloured dots (B)

Figure 2: Proportions of cell types at increasing distances from CAR-T cells

Pathological megakaryocyte biology in myelofibrosis.

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Introduction:

Megakaryocytes are central mediators of fibrosis and myeloproliferative neoplasms (MPN), yet the biological mechanisms underpinning progression to myelofibrosis (MF) remain poorly defined. Further, the impact of MF therapies on megakaryocyte biology is unclear. We characterised megakaryocyte proliferative, endomitotic and apoptotic proteomic pathways, and evaluated their association with MPN, MF progression and response to MF-directed therapies.

Methods

Archival bone marrow biopsies from 204 patients with MPN (polycythaemia vera=37; essential thrombocythaemia=93; myelofibrosis=74) and normal controls (n=304) were assessed by immunohistochemistry for proliferative (Ki67, GATA1), endomitotic (AURKA, AURKB) and apoptotic (Bcl2, Bcl-XL, BNIP3, survivin, caspase-8, caspase-9, Diablo, p53) biomarkers. Megakaryocyte expression was quantified and analysed by MPN subtype and driver mutation using Mann-Whitney U-tests, Kruskal-Wallis ANOVA and post-hoc Dunn's tests. Serial biopsies from 10 MF patients treated with ruxolitinib and/or navitoclax were evaluated for changes in proliferative and apoptotic signalling.

Results

MPN megakaryocytes were characterised by hyperproliferation, abnormal endomitosis and apoptotic resistance compared with controls. Proliferative Ki67 expression was increased 3-fold in MPN ($p<0.001$), with increased AURKA, but unchanged AURKB. Megakaryocytes showed a dominant anti-apoptotic phenotype characterised by increased Bcl-XL and survivin, together with reduced BNIP3 (all $p<0.001$). There was concurrent upregulation of caspase-8, caspase-9, Diablo and p53 suggesting cellular stress and compensatory pro-apoptotic signalling, despite ineffective downstream apoptotic activation. In MF, apoptotic dysregulation was most pronounced (reduced BNIP3 and caspase-9: $p<0.001$), while GATA1 did not differ from other MPN subtypes. These proliferative and anti-apoptotic signalling signatures persisted with ruxolitinib and/or navitoclax treatment. Driver mutation status had minimal impact on megakaryocyte profiles.

Conclusion

Megakaryocytes in MPN show marked hyperplasia and apoptotic resistance. Anti-apoptotic mechanisms are accentuated in MF without further proliferative activation. These pathological pathways persist despite treatment with ruxolitinib and/or navitoclax and are largely independent of driver mutation status. Future therapies should target these megakaryocyte abnormalities to achieve meaningful disease modification.

Validating a novel multiplex capillary electrophoresis assay for UBTF-TD and FLT3-ITD detection.

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Aim:

Acute myeloid leukaemia (AML) with *UBTF* tandem duplications (UBTF-TD) is an under-recognised entity seen predominantly in children and young adults and associated with dysplasia, normal karyotype/trisomy 8, *FLT3* internal tandem duplications (FLT3-ITD) and/or *WT1* variants. Its prognosis is similar to European Leukaemia Network 2022 intermediate/adverse risk genomic abnormalities¹. Recognition is important for prognostication and treatment options including allogeneic transplant and menin inhibitors. The aim is to validate a novel multiplex capillary electrophoresis (CE) methodology for UBTF-TD and FLT3-ITD detection in AML.

Method:

Forty samples including 27 blood/bone marrow internal samples, 10 specimens shared from external diagnostic laboratories, 1 FLT3-ITD reference standard, and 2 FLT3-ITD quality assurance program specimens were assessed across eight runs. Extracted genomic DNA was amplified in a multiplex polymerase chain reaction (PCR) targeting *FLT3* exons 14-15 (NM_004119.3) and *UBTF* exon 13 (NM_014233.4) using fluorophore-labelled primers and AmpliTaq Gold 360 master mix on the VeritiPro 96 Well Thermocycler (Thermo Fisher Scientific). PCR products were analysed by CE with a 600bp or 1200bp LIZ size standard on a SeqStudio Genetic Analyzer (Thermo Fisher Scientific). Serial dilutions were performed for lower limit of detection assessment. DNA input was 15ng.

Results:

The assay detected 100% of FLT3-ITD positive samples (27/27), 100% of UBTF-TD positive samples (10/10), and 100% of samples with concurrent UBTF-TD and FLT3-ITDs (8/8). For large UBTF-TD fragment sizes, 2/3 samples showed concordant orthogonal CE sizes (results not available for one sample), though all samples showed minor 6bp size discrepancy compared to orthogonal massive parallel sequencing.

Intra-run, inter-run, and inter-operator concordance were 100%, demonstrating excellent reproducibility. Specificity was 100% (3/3 samples with no FLT3-ITD or UBTF-TD). Dilution experiments demonstrated a lower limit of detection of mutant allele was ~2%.

Conclusion:

Multiplexed UBTF-TD and FLT3-ITD CE demonstrates excellent sensitivity/specificity and is useful in the diagnostic and therapeutic work-up of an uncommon intermediate/adverse prognostic AML subgroup.

References:

1. Duployez N, et al. (2023). *UBTF* tandem duplications define a distinct subtype of adult de novo acute myeloid leukaemia, *Leukaemia*, 37, 1245 – 1253.

Pirtobrutinib in relapsed/refractory (R/R) mantle cell lymphoma (MCL): results from the phase 1/2 BRUIN study (final update)

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Aim:

Pirtobrutinib, a highly selective, non-covalent BTKi and was safe and effective in the phase-1/2 BRUIN study in R/R MCL. We report final pirtobrutinib efficacy and safety in R/R MCL assessed >5 years in the phase-1/2 BRUIN study.

Method:

Patients who received ≥ 1 prior therapy (including BTKi) were eligible. Endpoints: overall response rate (ORR), duration of response (DOR) and progression-free survival (PFS) (all IRC-assessed/Lugano 2014 criteria). Data-cutoff:27Jan2025 (median follow-up:17.5-months[0.5-69.6]).

Results:

A total of 153/166 patients received pirtobrutinib 200mg/day. 92% received prior cBTKi, of which 84.2% discontinued due to progressive disease [PD], and 10% due to toxicity. Median age of cBTKi-pre-treated patients: 70yrs(range:46-88). Median number of prior therapies: 3(range:1-9); 11(7.2%) were cBTKi pre-treated and 6(42.9%) cBTKi-naïve patients remained

on-treatment. ORR of cBTKi pre-treated patients: 49.3%(95%CI:41.1-57.6), with 15.8% complete responses (CR)(n=24) and 33.6% partial responses (PR)(n=51). Median DOR (n=75) of 21.6-months(95%CI:9.2-27.2) at a median follow-up of 24-months. ORR was 43.0% and 93.3%, among PD and toxicity groups. Median PFS/OS for cBTKi pre-treated pts: 5.6(95%CI:5.3-9.2) and 23.9-months(95%CI:17.3-51.5). ORR of cBTKi-naïve patients: 85.7%(95%CI:57.2-98.2), with 50.0% CR (n=7) and 35.7% PR (n=5); median DOR 42.7-months(95%CI:25.8-NE) at a median follow-up of 43-months. Median PFS/OS of cBTKi-naïve patients: 44.6-months(95%CI:16.7-NE) and not reached (95%CI:33.5-NE). Most frequent TEAEs (n=166): fatigue (31.9%), diarrhea (22.9%), anemia (18.1%), and dyspnea (18.1%). Most common Grade $\geq$ 3 TEAE: neutropenia (13.3%), Grade $\geq$ 3 infections (21.1%). There were 13 (7.8%) fatal TEAE, with 4 (2.4%) infections; 8 (4.8%) dose reductions, 6 (3.6%) pirtobrutinib discontinuations.

Conclusion:

Pirtobrutinib continues to demonstrate efficacy in heavily pre-treated R/R MCL regardless of cBTKi use. Safety profile of pirtobrutinib remained favorable with a low-rate of dose reductions/discontinuations due to drug-related toxicity. No new safety signals were identified after up to 5 years of follow-up.

Real world outcomes in hairy cell leukaemia (HCL): A single centre experience

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Aim:

HCL is a rare indolent B-cell neoplasm with distinct biology and therapy. While cladribine remains the standard first-line therapy, approaches to relapsed/refractory diseases are heterogeneous. We sought to examine real world outcomes of patients with HCL diagnosed at Monash Health between 2011-2026.

Method:

Data from individual case records of patients with HCL identified via pathology database were collected. Clinical characteristics, treatment, and outcomes were analysed. Response was defined according to established criteria (Niang et al.) Key endpoints included overall response rate (ORR), progression-free survival (PFS), and response to subsequent therapies.

Results:

A total of 39 patients were identified with a median age at diagnosis of 54 years and 79% male predominance. 2/8 females were diagnosed during pregnancy. The median follow up of surviving patients was 46 months. At time of reporting 5 patients had died. Frontline therapies included Cladribine (26), Pegylated interferon alfa-2a (2), Fludarabine (1) and IV R-CVP (2) with initial watch and wait (8).

The ORR was 90% with a CR rate of 77%. 2 patients had primary refractory disease. Median PFS was not reached with 79% remaining progression-free at 5 years. 9 patients relapsed with a median time to relapse of 53 months. Second-line therapies included: rituximab-monotherapy (3), Rituximab-Fludarabine (1), Rituximab-Gemcitabine Oxaliplatin (1), Cladribine (1), BGB-3111 clinical trial (1) and pegylated interferon (2).

Second-line therapy was associated with durable disease control. Pegylated interferon alfa-2a was highly effective with no patients front or later line progressing or ceasing due to toxicity. It was particularly successful in pregnancy.

Overall the most common grade ≥ 3 toxicities were neutropenia and infections, with a minority requiring hospitalisation. Deaths were infrequent and predominantly attributable to infection or comorbid conditions rather than progressive HCL.

Conclusion:

Cladribine remains highly effective frontline therapy, achieving high remission rates and durable disease control. Relapse occurs in a minority, typically after several years, and remains highly responsive to second-line therapies including rituximab and pegylated interferon alfa-2a.

BGB-16673, a Bruton tyrosine kinase degrader, in patients with relapsed/refractory Waldenström macroglobulinemia in the CaDAnCe-101 study

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Aim:

BGB-16673 is a Bruton tyrosine kinase (BTK) degrader that blocks signaling by tagging BTK for degradation through the cell's proteasome pathway, leading to tumor regression. Here, updated safety and efficacy results are reported for patients with relapsed/refractory (R/R) Waldenström macroglobulinemia (WM) in the phase 1 portion of the CaDAnCe-101 study (BGB-16673-101; NCT05006716).

Method:

Eligible patients had R/R WM with ≥ 2 prior therapies (including an anti-CD20 antibody and covalent BTK inhibitor) and an Eastern Cooperative Oncology Group performance status of 0-2 (0-1 in the EU). BGB-16673 (100-350 mg) was administered orally QD.

Results:

At the December 15, 2025, data cutoff, 43 patients enrolled (median age, 72 [range, 46-81] years; median number of prior therapies, 3 [range, 2-11]); 83.7% of patients discontinued prior BTK inhibitor due to progressive disease. Median study follow-up was 14.3 (range, 0.2-37.3) months. At data cutoff, 60.5% of patients remained on treatment. Any-grade treatment-emergent adverse events (TEAEs) occurred in 95.3% of patients and included neutropenia (37.2%), diarrhea (30.2%), and contusion (27.9%). Grade ≥ 3 TEAEs occurred in 60.5% of patients and included neutropenia (34.9%), infection (18.6%), and anemia (14.0%); 7.0% of patients died due to TEAEs. The overall response rate (ORR; $\geq$ minor response) was 85.7% (36/42), major response rate ($\geq$ partial response) was 76.2% (32/42), and very good partial response rate was 31.0% (13/42). Median time to first overall response was 1.0 (range, 0.9-8.2) months and to best overall response was 2.8 (range, 1.0-12.2) months. High ORRs were seen in patients with disease bearing *CXCR4* mutations (100% [19/19]), *TP53* mutations (91.3% [21/23]), *BTK* mutations (100% [13/13]), and *PLCG2* mutations (100% [3/3]). The 15-month PFS rate was 70.4% (95% CI, 52.6%-82.5%).

Conclusion:

BGB-16673 has a manageable safety profile with substantial antitumor activity in heavily pretreated patients with R/R WM, including high-risk disease. ©EHA2026.

Follicular lymphoma with Clinically aggressive features, Discordant to the Indolent Histology has greater risk of transformation.

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Aim:

A subset of follicular lymphoma (FL) is known to exhibit clinically aggressive features but with discordant indolent histology (CDIH).¹ We evaluated treatment and outcomes of CDIH in an Australian multicentre cohort.

Method:

We retrospectively analysed FL patients from three tertiary centres in the last 10 years. CDIH was defined as grade 1-3A FL with at least one aggressive feature: B symptoms; elevated LDH; SUVmax >14; Ki67 >30%; atypical extranodal disease (bone, pleura, central nervous system, soft tissue, or lung); necrosis on CT scan; and/or discrete lesions in liver or spleen¹. We analysed treatment patterns and compared histologic transformation, progression-free survival (PFS), overall survival (OS) and progression of disease within 24 months (POD24) post chemoimmunotherapy (CIT).

Results:

Among 273 newly-diagnosed FL patients, a high proportion (61%) were classified as CDIH. FLIPI score was ≥ 3 in 27% (38% in CDIH and 11% in non-CDIH). At median follow-up of 61 months (IQR 38 – 83 months), overall rates of progression, transformation, and death were 27%, 9%, and 12%, respectively.

24% were observed, 52% received CIT, and 24% received other therapies. CDIH patients more likely required treatment (87% vs 59%, $P < 0.001$) and had shorter time to first treatment (HR 12.9, $P < 0.001$). Amongst those treated, CDIH patients more likely had CIT (77% vs. 50%, $P < 0.001$) with higher rates of CHOP/CVP rather than bendamustine based CIT in both CDIH and non-CDIH groups (77% and 71% respectively).

Independent of FLIPI ≥ 3 , CDIH was associated with higher transformation risk (12.6% vs 3.8%, aHR 3.5, $P = 0.029$) and shorter time to transformation (aHR 3.8, $P = 0.016$). CDIH had inferior OS (HR 5.6, $P = 0.018$), yet PFS and POD24 rates did not differ significantly.

Conclusion:

CDIH is common and associated with higher and earlier risk of transformation to high-grade disease, independent of FLIPI. This under-recognised subgroup may benefit from alternative monitoring and treatment strategies.

Reference:

1. Cabanillas F, Rivera N, Pardo W. Indolent Lymphomas That Present With Clinically Aggressive Features: A Subset of Low-Grade Lymphomas With a Behaviour Inconsistent With the Histologic Diagnosis. *Clinical Lymphoma Myeloma and Leukemia*. 2016;16(10):550-7.

Centroblast score companion biomarker improves FDG-PET prognostication to guide frontline therapy in follicular lymphoma

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Aim: FDG-PET is widely used to guide frontline therapy selection in follicular lymphoma (FL), yet remains an unreliable predictor of outcome as it may reflect both malignant B cell and lymphoma microenvironment (LME) activity. We aimed to develop a complementary transcriptomic biomarker to refine PET-based risk stratification and identify FL subsets that safely benefit from bendamustine-containing regimens.

Method: A retrospective real-world cohort of 129 FL patients treated with first-line bendamustine ICT was collected from 13 Australian academic institutions. Baseline clinical, laboratory and FDG-PET indices including centrally-reported SUVmax were collected. Bulk RNAseq was performed to derive B-cell functional gene expression signatures (fGES) including a centroblast (CB) score, with immune cell deconvolution quantifying the LME. A combined model integrating SUVmax and CB score was evaluated for prognostic stratification. Spatial proteomic analysis (Akoya Phenocycler) was performed in a subset (n=24) to further characterise the LME.

Results: Among 129 bendamustine-treated FL patients (median follow-up 46.4 months), SUVmax alone did not predict PFS (p=0.59). A CB_{HI} score (split by median) was a strong independent predictor of inferior PFS (HR 2.51, 95% CI 1.29–4.87; p<0.01) and early progression/transformation (OR 4.03, p=0.03), correlating incompletely with higher Ki-67 and histopathologic grade. Combined SUVmax and CB score markedly improved risk stratification. In the high SUVmax subgroup, 4-year PFS was 48% in CB_{HI} vs 100% in CB_{LO} patients (p<0.001), with no early relapses in the CB_{LO} group, identifying a biologically low-risk subset with favourable outcomes on bendamustine. RNASeq deconvolution and spatial proteomic analysis identified communities enriched for extrafollicular macrophages and reduced CD4 T-cells in CB_{HI} cases.

Conclusion:

A low CB score demonstrated favourable response to bendamustine-based therapy, including patients with high SUVmax. Patients with high CB score had inferior outcomes and correlated with a depleted TME. Future studies should explore the role of immunotherapies in this biologically distinct cohort.

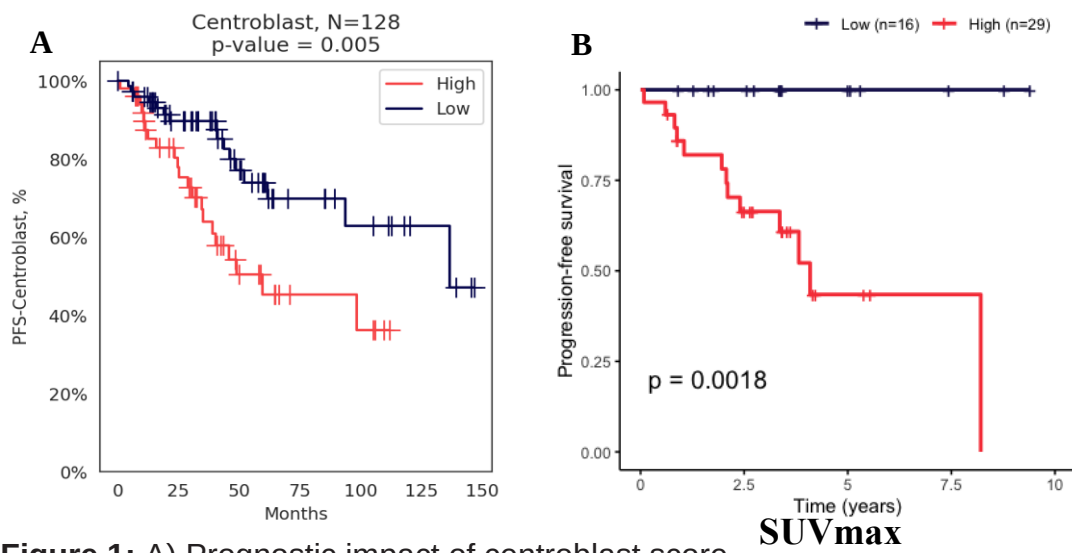


Figure 1: A) Prognostic impact of centroblast score
B) Prognostic impact of centroblast score in high SUVmax (>12) cases

HAVCR2-associated subcutaneous panniculitis T-cell lymphoma in Auckland – A quality improvement audit and next steps

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Introduction

Germline *Hepatitis A Virus Cellular Receptor 2* (HAVCR2) is a driver of haematological diseases, particularly subcutaneous panniculitis-like T-cell lymphoma (SPTCL) which can lead to hemophagocytic lymphohistiocytosis (HLH). HAVCR2 p.Tyr82Cys (Y82C) is described in Asian populations, and anecdotally in New Zealand patients particularly the Pasifika and Maori populations. We aimed to characterise the relationship between HAVCR2 and SPTCL within New Zealand patients.

Methods

Quality improvement audit across two centres, Middlemore Hospital and Starship Hospital, to understand the burden of HAVCR2-associated haematological disease. Retrospective chart review of patients with SPTCL from 2004 onwards. HAVCR2 was tested since 2018.

Results

Twenty-three patients with SPTCL were identified; 83% were Pasifika, and 14% Māori. Mean age was 30.7 years (range 10-72 years). Nine patients developed HLH (39%) of whom six received HLH-directed therapy. Two patients have died (9.5%), two lost to follow-up, with an average follow-up of 7.5 years (range 1-21). Eighty-three percent used ciclosporin as first-line therapy with the other 17% commencing on HLH-directed therapy. Eight required second-line therapy of whom 5/23 (21%) received tacrolimus, and 2/23 (9%) had CHOEP chemotherapy followed by allogeneic haematopoietic stem cell transplant. Patients present with fevers, inflamed skin lumps/panniculitis sometimes mistaken for cellulitis. Other features include deranged LFT's, systemic inflammation (high CRP, hyperferritinaemia, hypergammaglobulinaemia, and HLH in advanced cases), DIC, and cytopenias (lymphopenia and monocytopenia is common). Of the 13 patients diagnosed after 2018, 77% had HAVCR2 p.Tyr82Cys (Y82C). Nine were homozygous, and one heterozygote with HAVCR2 p.Arg140Leu.

Discussion

HAVCR2-related haematological disease in particular SPCTL in New Zealand are unique with excellent prognosis with appropriate treatment. Further investigations into these patients in New Zealand is warranted. We are collaborating with Māori and Pasifika health experts and the Aplastic Anaemia and Other Bone Marrow Failure Registry (AAR) (aaregistry.org.au) to establish a national snapshot of disease prevalence and outcomes.

Nurse-led implementation and service evaluation of 30-minute intravenous rituximab infusions in a haematology unit

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Aim:

To evaluate the safety and feasibility of a nurse-led 30-minute rituximab infusion protocol based on published evidence supporting accelerated infusion rates (Wahlin et al., 2025).

Method:

Following a service development process, a 30-minute rituximab infusion protocol was introduced in September 2025. Patients were eligible once they had tolerated a 90-minute infusion without dose interruption or infusion-related reaction (IRR). Premedication comprised paracetamol 1g and loratadine 10mg; steroids were given when part of a chemotherapy regimen. Vital signs were recorded before and after each infusion. We subsequently conducted a retrospective analysis of patients treated between July 2024 and May 2026 comparing IRR before and after implementation. IRR was graded according to CTCAE criteria and incidence reported as a proportion with exact 95% confidence intervals (Clopper-Pearson); cohorts were compared using Fisher's exact test.

Results:

In the post-implementation cohort, 30 patients received 69 doses of 30-minute rituximab with zero IRRs (0%; 95% CI 0–5.2%). Diagnoses included diffuse large B-cell lymphoma (n=11), follicular lymphoma (n=8), and other B-cell malignancies or immune conditions (n=11). Twenty-five doses (36%) were administered with concurrent steroid-containing chemotherapy. In the pre-implementation cohort, 100 patients received 322 doses with 6 IRRs (1.9%; 95% CI 0.7–4.0%). IRR incidence did not differ significantly between cohorts (Fisher's exact, p=1.0). No grade 3–4 adverse events occurred in either cohort. Each 30-minute infusion saved one hour of chair time.

Conclusion:

This service evaluation confirms that 30-minute rituximab infusions can be safely implemented. Combined with biosimilar rituximab, this protocol offers a cost-effective alternative to subcutaneous formulations. Limitations include the retrospective design and modest cohort size. The low IRR rate may support out-of-hours administration without on-site haematology staff for selected patients who have tolerated prior standard-rate infusions.

Reference:

Wahlin, B. E., Ljungqvist, M., Falk, O., Rådman, T., Lindé, S., & Sonnevi, K. (2025). A 30-minute intravenous infusion of rituximab is safe and cost-effective (SpeedR). *Annals of Hematology*, 104(11), 5929–5933. <https://doi.org/10.1007/s00277-025-06521-9>

Developing a nurse-led e-learning program to support safe delivery of bispecific antibodies in lymphoma care

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Aim:

To develop and evaluate an evidence-based e-learning program to improve nursing knowledge and confidence to support the safe administration of bispecific antibodies in lymphoma care, particularly in regional and non-tertiary settings.

Method:

This educational project will be conducted by Lymphoma Australia in 2026. An online learning package including recorded expert webinars, interactive modules, a written clinical resource, and knowledge assessments will be developed and reviewed by specialist lymphoma nurses. Key content areas include mechanism of action, patient education, safe administration, and management of adverse events such as cytokine release syndrome and neurotoxicity. Pre- and post-intervention surveys will be provided to a pilot sample of nurses to assess learning outcomes, measuring changes in knowledge scores related to the safe administration and patient management of bispecific antibodies for lymphoma. Qualitative feedback will be analysed thematically to assess usability and clinical relevance. Once the platform has been launched to the wider community of haematology nurses across Australia, analytics will capture engagement and completion rates. A Likert scale to rate self-reported confidence in the safe administration of bispecific antibodies among nurses will be utilized in this phase of the project.

Results:

It is hypothesised that participation in the program will result in self-reported increased nurse confidence in delivering bispecific antibody therapies. The program is also expected to demonstrate strong engagement from regional nurses, supporting its accessibility and the effectiveness of a structured, nurse-led e-learning approach in improving readiness for the delivery of novel lymphoma therapies.

Conclusion:

This project will support the knowledge and confidence of nurses administering bispecific antibodies for lymphoma thereby improving patient management and workforce capability, particularly in regional settings. The findings will inform future education models and contribute to more equitable access to advanced lymphoma therapies, enabling patients to safely receive treatment closer to home.

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A review of current Australian practices of antifungal prophylaxis therapeutic drug monitoring for adults with acute myeloid leukaemia

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Aim:

In February 2025, the Australian National Acute Myeloid Leukaemia (AML) Clinical Guideline was published. One key recommendation was the implementation of systematic antifungal prophylaxis (AFP) therapeutic drug monitoring (TDM). The aim of this project was to review current practice relating to TDM of AFP agents across Australian institutions where adult patients with AML are treated.

Method:

An attempted census of all members of the Haematology Society of Australia and New Zealand (HSANZ) undertaken with a 17-point questionnaire developed and validated with an expert panel. Quantitative data from closed-ended questions were analysed using descriptive statistics to identify common practices and emerging trends across sites. Qualitative data from open-ended questions were summarised and presented to identify any variations or similarities in approach, or perceived barriers or facilitators to TDM use.

Results:

Responses have been received that represent 12 institutions across Australia to date. The majority of sites use TDM (58%), while the remainder (42%) relied on standard dosing. Among the sites that used TDM, initial monitoring practices were consistent, but ongoing monitoring frequency varied. Only three sites identified having formal guidelines for TDM. Institutions not using TDM cited barriers including perceived limited clinical value, difficulty obtaining accurate levels, and workflow challenges.

Conclusion:

Significant variation was identified in the use of posaconazole TDM across institutions treating adult patients with AML across Australia, highlighting the need for a structured, evidence-based approach to support consistent practice. The results also identify barriers to TDM that need to be addressed to support effective implementation in practice.

Novel dried blood spots protocol enable qualitative fusion transcript detection in leukemia: proof-of-concept validation with long-term frozen biobanking

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Aim:

To evaluate dried blood spots (DBS) as an alternative sample matrix for RNA-based fusion transcript detection in leukemia using a novel protocol, circumventing cold-chain and phlebotomy barriers that limit access to molecular diagnostics in resource-limited tropical settings.

Method:

In this prospective proof-of-concept study conducted at ICMR–NICHR, New Delhi, paired DBS and whole blood samples from 110 leukemia patients across collaborating centres were analysed for qualitative fusion transcript detection using RT-PCR-based commercial fusion panels for BCR-ABL1 (p210/p190/p230), AML-associated targets, and ALL-associated targets. Novel DBS extraction was matched against whole blood RNA extraction. Pre-analytical stability under tropical conditions evaluated through deliberate exposure to varying environmental conditions (25–45°C temperature, 40–90% humidity, and storage duration of 2–96 hours). Long-term biobanking feasibility was also assessed using frozen DBS samples.

Results:

Across 110 paired patient samples, DBS-derived RNA was successfully extracted and amplified for qualitative molecular analysis., demonstrated complete concordance with matched whole blood analysis (100% concordance), with equivalent positive and negative classification for leukemia-associated transcripts including BCR-ABL1, E2A-PBX1, TEL-AML1, AML-ETO, PML-RARA, NPM1, FLT3-ITD, MLL rearrangements, and other recurrent fusions. RNA quality remained stable despite exposure to variable tropical environmental conditions, showing no significant effect of temperature (25–45°C) or humidity (40–90%) on assay performance. Long-term frozen storage further demonstrated preserved RNA amplifiability and stable qualitative detection, supporting DBS biobanking feasibility.

Conclusion:

The novel DBS-derived RNA protocol demonstrates robust qualitative concordance with venous whole blood for leukemia fusion transcript detection, while maintaining stability under challenging tropical temperature and humidity conditions and during long-term frozen storage, support practical and scalable platform for decentralised molecular diagnostics and expanded access to precision haematology in resource-limited settings.

Next-generation-sequencing-based UBTF tandem duplication measurable residual disease (UBTF-MRD) in patients with MDS and AML

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Aim: UBTF tandem duplication (UBTF-TD) defines a molecular subgroup of MDS/AML enriched in children and young adults. We evaluated the clonal stability and clinical utility of UBTF-TD as a measurable residual disease (MRD) biomarker.

Method: Fifty-three patients (pts) with UBTF-TD MDS/AML were identified from institutional databases. Paired diagnosis-relapse bone marrow (BM) samples underwent mutation profiling. A next-generation-sequencing (NGS)-based UBTF-MRD assay targeting exon 13 (NM_014233.3) region was developed for longitudinal monitoring. UBTF MRD were compared with multiparametric flow-cytometry (MFC-MRD) and FLT3-ITD NGS MRD where available.

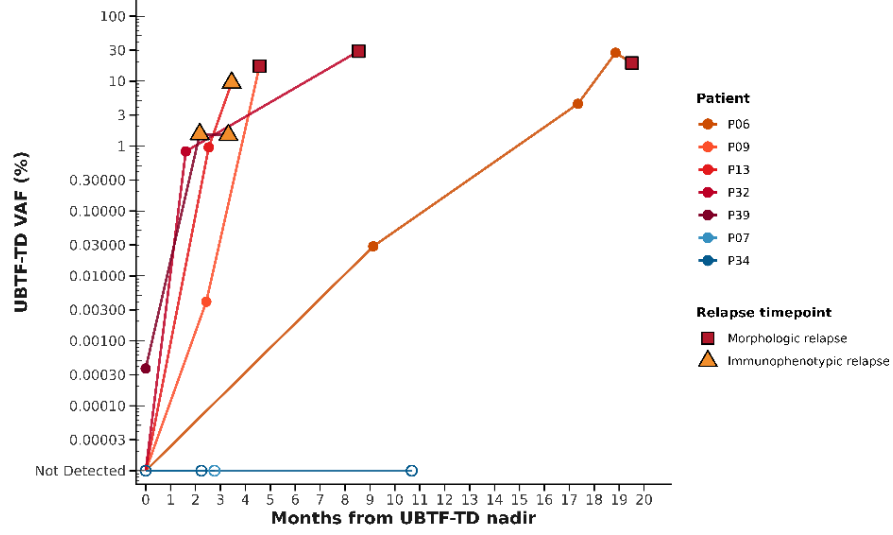
Results: The cohort had a median age of 26 years (range 7–79) with frequent trisomy 8, FLT3-ITD, and WT1 co-mutations. All 19 paired diagnosis-relapse samples retained the same UBTF-TD, which remained the dominant lesion by VAF at relapse, whereas 4/12 (33%) FLT3-ITD-positive pts became FLT3-ITD-negative at relapse.

Twenty-eight pts had 56 morphologic remission BM samples (<5% blasts). 16/28 (57%) pts had at least one remission sample with UBTF-TD >2.5% VAF (median 33.8%, range 5.7-52%), supporting persistence of a pre-leukaemic compartment. Among the remaining 12 patients, 11/15 paired samples were MFC-negative/UBTF-positive (VAF 0.0003-1.1%), and 3/4 paired samples were FLT3-negative/UBTF-positive (VAF 0.006-0.025%).

Given presence of pre-leukaemic UBTF-TD, we evaluated UBTF-MRD in 11 pts undergoing allogeneic transplant (allo-HCT). Compared to pre-transplant levels, UBTF-MRD decreased at Day-30 in all seven evaluable pts. Rising UBTF-MRD occurred in all five pts who subsequently relapsed, increasing from nadir 2-7 months before morphologic (n=3) or immunophenotypic relapse (n=2) at 0.51-0.94 log10/month (**Figure 1**). In contrast, two pts with durable remission (4-7 years follow-up) maintained UBTF-MRD negativity.

Conclusion: UBTF-TD was a clonally stable lesion while FLT3-ITD was frequently lost at relapse. While pre-leukaemic UBTF-TD may limit interpretation of single-timepoint UBTF-MRD positivity, rising UBTF-MRD from post-transplant nadir was associated with subsequent relapse, supporting further prospective evaluation of UBTF-MRD as a monitoring biomarker in MDS/AML.

Figure 1. Rising UBTF-TD precedes post-allo-HCT relapse



Post-induction MRD in NPM1 AML by molecular methods: a cross-validation ultra-sensitive NGS vs. RT-qPCR study from the UK NCRI AML17 trial

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Aim:

To cross-validate the prognostic impact of post-course 2 (PC2) *NPM1* measurable residual disease (MRD) using next-generation-sequencing (NGS), as an alternative technology to reverse-transcription quantitative polymerase-chain-reaction (RT-qPCR).

Method:

NPM1 AML patients from the landmark AML17 trial cohort (Ivey et al. NEJM 2016) who were in remission at PC2 with stored DNA sample were included. Retrospective ultra-sensitive ($\geq 5 \times 10^{-5}$) *NPM1* NGS MRD was performed (700 ng input) with correlative RT-qPCR results available. Discordant results between the two platforms were resolved by 'best-of-three' consensus NGS testing. Cumulative relapse (CIR) and overall survival (OS) were evaluated.

Results:

247 patients contributed 170 blood (PB) and 145 bone marrow (BM) PC2 samples for NGS MRD: MRD-negativity was attained in 79% and 37%, respectively. Due to word limits, only PB results are presented in this abstract. Patients who were NGS MRD- had lower 5-y CIR compared to those MRD+ (37% vs. 58%, HR 2.03) with a trend for improved OS. Meanwhile, RT-qPCR MRD-negativity was associated with both lower 5-y CIR (36% vs. 76%; HR 4.07) and superior OS (73% vs. 35%, HR 3.08). Regression of paired NGS/RT-qPCR results demonstrated modest correlation ($R^2=0.340$), with identification of NGS MRD+ discrepant cases in 5% (i.e., NGS Test 1 MRD+, 'best-of-three' consensus MRD-); these patients actually had comparable CIR and OS to concordant NGS/RT-qPCR MRD- cases. Threshold analysis revealed VAF of 0.0034% as optimal for prognostication by NGS in the PB (Fine-Gray $\chi^2 = 10.95$ vs. 6.55 with undetectable as threshold): compared to MRD-low patients ($< 0.0034\%$), MRD-high patients ($\geq 0.0034\%$) had significantly worse 5-y CIR (82% vs. 39%; HR 5.60) and OS (18% vs. 73%; HR 5.95). Indeed, all NGS MRD+ discrepant cases above had VAF $< 0.0034\%$. Finally, time-dependent analysis demonstrated CR1 allograft benefit, restricted to those NGS MRD+ (any level; 5-y OS 100% vs. 50% without).

Conclusion:

Post-induction *NPM1* MRD by RT-qPCR was more prognostic overall than NGS for outcomes prediction. For the latter, predictive value may be augmented by the application of an optimised threshold (VAF 0.0034%) and resolution of NGS MRD+ discrepant cases.

Role of whole transcriptome sequencing and artificial intelligence in subtyping of B-cell acute lymphoblastic leukemia (B-ALL) in an Indian cohort

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Aim:

B-cell acute lymphoblastic leukemia (B-ALL) is characterized by distinct genetic alterations that drive prognosis and therapeutic stratification. Despite the identification of established subtypes (e.g., BCR::ABL1), a significant proportion of cases remain classified as "B-other," lacking defining drivers. Whole transcriptome sequencing (RNA-seq) offers a comprehensive view of gene fusions and expression profiles. This study aimed to integrate RNA-seq with machine learning (ML) algorithms to deconvolute the heterogeneity of B-other ALL and identify genetic subtypes with potential prognostic significance.

Method:

This ambispective study enrolled 360 B-ALL cases (209 pediatric, 151 adult; median age 16 years; M:F 2:1) diagnosed between 2021-2024. Conventional RT-PCR detected recurrent fusions in 107 cases (30%), leaving 253 (70%) categorized as B-other. Eighty-nine priority cases, enriched for high-risk features, underwent Whole Transcriptome Sequencing. RNA-seq analysis employed STAR-Fusion, FusionCatcher, and Arriba for fusion detection, complemented by mutation analysis via GATK pipeline and copy number variation detection using RNASeqCNV. Machine learning classifiers (ALLCatchR, MD-ALL, ALLSorts) assigned gene expression-defined subtypes according to WHO-HAEM5/ICC classifications. Subtype-defining fusions were validated by RT-PCR and Sanger sequencing.

Results:

RNA-seq successfully classified 83 of 89 (93%) B-ALL cases into distinct molecular subtypes. The analysis identified 14 distinct genetic subtypes: Ph-like B-ALL (18%), Ph (16%), PAX5-altered (12%), DUX4-rearranged (11%), hyperdiploid (14%), and rare entities including CDX2/UBTF (3%), iAMP21 (3%), and ZNF384-rearranged (1%). The study identified 16 novel fusion events missed by conventional methods. ML classifiers also enabled identification of fusion-negative variants e.g. DUX4-like lacking canonical rearrangements and rare subtypes like CDX2/UBTF.

Conclusion:

Integrating machine learning with whole transcriptome sequencing effectively refines risk stratification in B-ALL by identifying high-risk subtypes like Ph-like and CDX2/UBTF that are missed by routine workups, but also highlights the utility of ML in automating complex transcriptomic data interpretation. These findings support the routine implementation of RNA-seq for accurate classification and personalized management of B-ALL.

TET2 Loss in human monocytes and macrophages drives inflammasome activation and promotes clonal expansion in CMML

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Introduction

Mutations in the epigenetic regulator *TET2* are common in age-related clonal haematopoiesis and chronic myelomonocytic leukemia (CMML), a disease characterized by inflammatory monocytosis. While *TET2*-deficient murine macrophages show increased IL-1 β production following lipopolysaccharide (LPS) stimulation, the functional consequences in human monocytes/macrophages (mono/mac) remain poorly defined. This study investigates the impact of *TET2* loss in human mono/mac.

Methods

TET2 was knocked out (KO) in cord blood CD34⁺ HSPCs using CRISPR/Cas9 targeting exon 3, with AAVS1-targeted cells as controls (WT). Proliferation and CFU assays were performed. HSPCs were differentiated into mono/mac over 21 days and characterized by flow cytometry. Inflammatory responses were assessed following LPS/ATP stimulation by measuring IL-1 β , IL-6, TNF- α , and NLRP3 (western blot, ELISA). Effects of conditioned media and cytokines (IL-1 β , IL-6) on CFU formation were evaluated. Clinical relevance was assessed using CMML patients.

Results

Efficient *TET2* KO (~90%) was confirmed. *TET2*-KO HSPCs showed increased proliferation, colony formation, and myeloid skewing. Differentiated mono/mac expressed CD14, CD11b, CD206, CD68, and upregulated CD80 upon stimulation. *TET2*-KO mono/mac exhibited increased IL-1 β and IL-6 secretion after LPS/ATP stimulation, with no significant change in TNF- α . NLRP3 levels were elevated at baseline and significantly after stimulation. Both conditioned media from *TET2* KO mono/mac and cytokine treatment favoured CFU formation in *TET2*-KO HSPCs. Clinically, *TET2* mutations were detected in 78% of CMML patients, with a trend toward increased IL-1 β .

Conclusion

TET2 deficiency promotes a hyper-inflammatory mono/mac phenotype with enhanced inflammasome activation, supporting a model in which *TET2*-mutant mono/mac drive a pro-inflammatory microenvironment that favours expansion of *TET2* mutant clones in CMML.

Multiparametric immuno-flowFISH enables sensitive detection of IGH rearrangements in multiple myeloma without plasma cell enrichment

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Aim:

Assessment of immunoglobulin heavy chain (*IGH*) rearrangements in multiple myeloma is routinely performed by interphase fluorescence *in situ* hybridisation (FISH) following plasma cell enrichment of bone marrow aspirate samples. However, this may fail in poor-quality samples or cases with low plasma cell burden, reducing assay sensitivity and limiting detection of rare clones. We evaluated a multiparametric imaging flow cytometry-based assay for enrichment-free detection of *IGH* rearrangements in plasma cells.

Methods:

Bone marrow samples from 50 patients with myeloma were analysed. Following red cell lysis, cells were incubated using CD38/CD138/CD319-AF647 to identify plasma cells and CD3-BV510 (control). After DNA denaturation, cells were hybridised with *IGH* breakapart and partner locus specific probes (*MYEOV*, *FGFR3*, *MAF*). Samples were acquired on an ImageStream imaging flow cytometer and analysed using quantitative fusion algorithms.

Results:

Between 10,000 and 300,000 cells were acquired per sample, with plasma cells comprising 0.1-53.2% of events. *IGH* abnormalities were detected in 22 cases, to as low as 0.08%. Partner chromosomes were identified in 17 cases, including *CCND1/MYEOV* (n=11), *FGFR3* (n=4) and *MAF* (n=3) with balanced, unbalanced and complex translocation patterns observed. Two abnormalities not detected by conventional FISH were identified: (1) an emergent signal pattern indicative of clonal evolution (10% plasma cells); and (2) concurrent *IGH::CCND1/MYEOV* (90% plasma cells) and *IGH::MAF* (10%) translocations within the same samples, demonstrating detection of rare co-existing sub-clones.

Conclusion:

Multiparametric immuno-flowFISH enables sensitive, enrichment-free single-cell detection of *IGH* rearrangements in myeloma. By integrating plasma cell immunophenotyping with automated image analysis and constitutional control normalisation, this reduces subjectivity while enabling detection of rare sub-clones (<0.1%). Analysis of large cell populations improves detection of sub-clones and permits evaluation of poor-quality or low cellularity specimens without plasma cell enrichment. This approach has potential to improve detection of *IGH* rearrangements, sub-clones and other chromosomal abnormalities in myeloma.

Consensus recommendations for delivering bispecific antibody therapy in multiple myeloma: an evidence-based framework. On behalf of the Haematology Society of Australia and New Zealand Myeloma Specialist Practice Network (HSANZ M-SPN)

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Background:

Bispecific antibodies (BsABs), including elranatamab, teclistamab and talquetamab, are increasingly used in the treatment of multiple myeloma (MM). Initial exposure during step-up dosing (SUD) phase is associated with cytokine release syndrome (CRS), immune effector cell-associated neurotoxicity syndrome (ICANS), infections and other adverse drug reactions. Current recommendations include hospitalisation during SUD to enable close monitoring and timely toxicity management. Emerging consensus guidance has identified factors that support safe ambulatory BsAB delivery models.

Aim:

The Myeloma Specialist Practice Network (M-SPN) established a multidisciplinary working group to develop consensus recommendations for BsAB delivery in MM. The aim was to produce a practical, evidence-based resource to support nurses and healthcare services in developing local models of care and guiding safe patient management.

Methods:

A consensus-based expert review approach was used. The working group included advanced practice MM nurses, including Clinical Nurse Specialists, Clinical Nurse Consultants and Nurse Practitioners. Literature reviewed included licensing studies for elranatamab, teclistamab and talquetamab, alongside evidence relating to CRS, ICANS, infection risk and ambulatory BsAB delivery. M-SPN members completed a survey identifying educational and practice needs relating to BsAB therapy. Findings from the literature review and survey informed document structure and section allocation according to clinical expertise. Draft recommendations were developed collaboratively and refined through regular meetings. External review was undertaken by three international MM Nurse Practitioners and two Australian haematologists.

Conclusions:

Consensus recommendations were developed across five domains: (1) stakeholder and service preparation; (2) factors supporting ambulatory SUD delivery; (3) CRS mitigation strategies; (4) administration considerations including pre-medications, dosing and scheduling; and (5) nursing and supportive care considerations including care coordination, monitoring, communication pathways, documentation and patient education. These recommendations provide a practical resource to support implementation of BsAB therapy across diverse clinical settings.

Double-Check, Zero Harm: The state of embedding pretransfusion double independent checking in practice

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Aim:

To assess if health services policies and practice align with the Australian and New Zealand Society of Blood Transfusion (ANZSBT) guidelines for positive patient identification and double independent pretransfusion checking.

Method:

A two-part audit of 109 public and private health services in Victoria, Tasmania, Australian Capital Territory and Northern Territory

Part A: Desktop audit of health service pretransfusion checking procedure: 82 (75%) responses.

Part B: Observation of each element of the pretransfusion checking procedure according to guidelines for up to 20 transfusions: Resulting in 778 transfusions from 71 health services audited.

Results:

Part A: All 82 had a policy for pretransfusion checking; 58 (71%) stated double independent checking must occur.

Part B:

Check performed	Double independent (%)	Shared (%)
Patient identification: State/spell full name, DOB, checked against ID band, prescription	162 (21)	611 (79)
Blood component: Patient ID, donation number, blood groups, expiry, pack integrity	282 (36)	496 (64)
All pretransfusion checks (patient and component)	137 (18)	641 (82)

Results adjusted for conscious/competent patients and N/A elements

Auditor stopped the pretransfusion checks for process failure 123 (16%) times.

The gold standard for pretransfusion checking includes:

- Double independent checking, patient ID and component - 137 (18%)
- Performed at the bedside – 743 (96%)
- No attempt to spike prior to completion - 761 (98%)

Gold standard pretransfusion checks occurred in 135 (17%) observational audits.

Conclusion:

There is an opportunity for health services to align policy and practice with current guidelines by including and clearly outlining patient identification and double independent pretransfusion checking, including each step of the process. Clinical staff must have a clear understanding of this process to ensure best practice and patient safety.

Implementing a national framework to improve access and compliance for unapproved Cellular Therapy products in New Zealand

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Demand for unapproved cellular therapy products in New Zealand is increasing, particularly for therapies such as Virus Specific T cells (VSTs) accessed under Section 29 of the Medicines Act 1981. Within the New Zealand Blood Service (NZBS), the absence of a formalised framework for procurement, importation, and storage created variability in practice, limited governance, and increased regulatory risk. Delays in accessing these therapies may also affect timely patient care and clinical outcomes.

Method:

A national, cross-functional programme was undertaken to develop a standardised framework for managing unapproved cellular therapies. This included formal policies and standard operating procedures, a future-state process map, and a structured clinical request pathway. A responsibility matrix (RACI) was introduced to clarify roles and accountabilities across Clinical programs, Quality and Regulatory Affairs, Technical Services, Information Services, and Finance, as well as Te Whatu Ora. Risk and impact assessments, system configuration, stakeholder engagement, and targeted training were incorporated to support safe and effective implementation.

Results:

The framework established a clear end-to-end process for the importation, storage, and management of unapproved cellular therapies. This resulted in improved governance, enhanced traceability, and strengthened regulatory compliance. Defined roles and standardised processes improved coordination across teams and with external stakeholders. Additionally, better visibility of service activity has improved understanding of costs and supports sustainable service delivery, reducing delays and uncertainty in accessing therapies.

Conclusion:

This initiative addresses a critical gap in the management of unapproved cellular therapies within New Zealand. The framework provides a scalable, regulatory compliant model that improves operational efficiency and supports timely patient access to treatment. It also has potential application across other advanced therapy pathways in regulated healthcare settings.

Impaired early erythropoietic compensation identifies high transfusion burden in warm autoimmune haemolytic anaemia

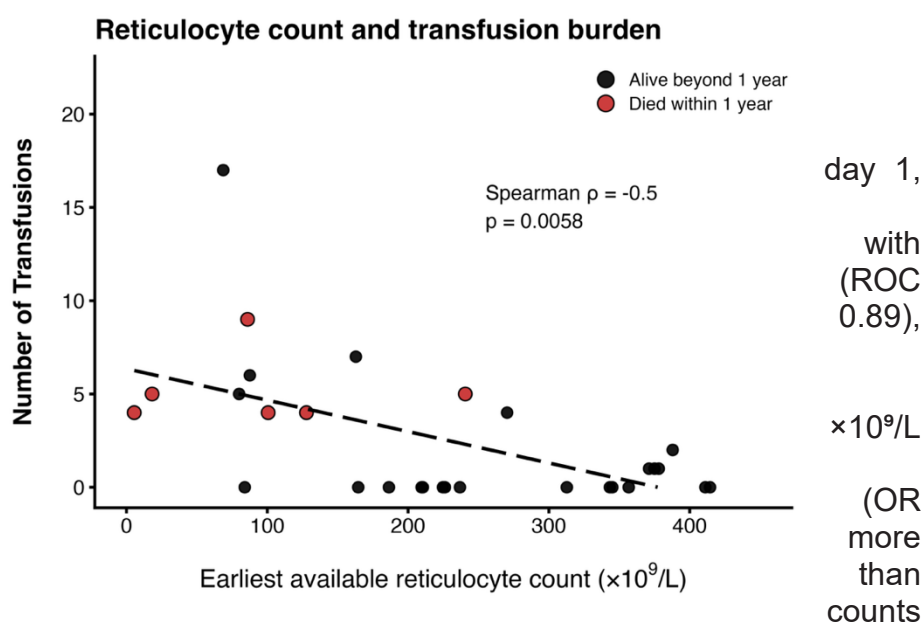
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Aim: Transfusion support in warm autoimmune haemolytic anaemia (wAIHA) is complicated by pan-reactive autoantibodies and delays in compatibility testing. Early identification of patients likely to require substantial transfusion support may assist compatibility investigation and transfusion planning. We evaluated whether earliest available reticulocyte count, as a marker of erythropoietic compensation, predicts transfusion dependence in wAIHA.

Method: We performed a single site retrospective cohort study of adults admitted with newly diagnosed wAIHA (1 January 2018 and 11 November 2022). Earliest available absolute reticulocyte count was defined as the first available reticulocyte measurement following presentation. Logistic regression and ROC analyses were performed. Patients were subsequently stratified using a prespecified threshold $180 \times 10^9/L$. Haemoglobin recovery was assessed using time to haemoglobin ≥ 100 g/L. Comparisons were performed using Fisher exact, Wilcoxon rank-sum and Spearman correlation analyses.

Results: Twenty-nine patients with available transfusion status were included. Earliest available reticulocyte count (median mean 1.41 days) predicted transfusion dependence moderate discrimination AUC 0.67, 95% CI 0.46–optimal threshold $164 \times 10^9/L$. Patients with reticulocyte counts <180 had increased odds of transfusion dependence (9.0, $p=0.018$) and were likely to require transfusion patients with reticulocyte $\geq 180 \times 10^9/L$ (81.8% vs 33.3%, Fisher exact $p=0.021$). Low-reticulocyte patients demonstrated substantially greater transfusion burden (median 5 vs 0 transfusions, Wilcoxon $p=0.001$) and delayed haemoglobin recovery (55 vs 22 days, Wilcoxon $p=0.021$). Reticulocyte count inversely correlated with transfusion burden (Spearman rho -0.50 , $p=0.0058$). All one-year deaths occurred in transfused patients (50.0% vs 0%, Fisher exact $p=0.006$).



Conclusion: Abrogated erythropoietic compensation at presentation identifies a high transfusion burden phenotype in wAIHA associated with substantial transfusion dependence and mortality. Reticulocyte counts at presentation may assist transfusion planning and prognosis in wAIHA.

Red cell exchange efficiency and metrics to guide timing and predict outcome

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Background:

Red cell exchange (RCE) is a therapeutic intervention for sickle cell disease.

The efficiency of RCE can be assessed by measuring whether the expected reduction in HbS% is achieved. The Spectra Optia Apheresis system predicts the fraction of the patients red cells remaining (FCR) (calculated FCR). An actual FCR (determined using measured pre- and post-HbS%)-to-calculated FCR ratio of 0.75-1.25 is considered acceptable.(1)

The predicted FCR can be used to calculate the expected post-procedure HbS%. However, this requires the pre-procedure HbS% which may not yet be available. Metrics to estimate the pre-procedure HbS% have been reported – the production rate index (PRI)(2), or daily rate of rise (RoR)(3). Another metric, the reduction efficiency index (REI)(2) has been proposed, to predict the reduction in HbS% expected per unit of RBC.

Aim:

1. Review the efficiency of RCE at a paediatric centre.
2. Assess the accuracy of RoR in determining the pre-procedure HbS%
3. Compare the predictive accuracy of FCR and REI for post-procedure HbS%.

Method:

An audit of RCE procedures was conducted from July 2024 to April 2026. The actual-to-calculated FCR was calculated as was the ROR and REI. The calculated pre-procedure HbS% using the RoR was compared to the measured pre-procedure HbS%. The post-procedure HbS% was predicted using the REI and the calculated FCR. The predicted post-procedure HbS% by both methods was compared with the measured post-procedure HbS%.

Results:

118 RCE procedures were performed, 116 had data available to review efficiency. All procedures achieved an actual-to-calculated FCR within the acceptable range.

RoR and REI could be calculated for 93 procedures. Pre-procedure HbS% estimated using the RoR correlated with the measured pre-procedure HbS% (R^2 0.82). The post-procedure HbS% estimated using the FCR more closely correlated with the measured post-procedure HbS% than that calculated using the REI (R^2 0.89 and 0.54 respectively).

Conclusion:

The RoR can be used to predict the pre-procedure HbS% which may help to optimise procedure scheduling and blood ordering. Using the FCR to predict the post-procedure HbS% is more accurate than the REI.

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Towards precision transfusion: Red cell genotyping in paediatric sickle cell disease (SCD)

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Aim:

To review serological and molecular testing results for paediatric patients with SCD locally and develop individualised transfusion support plans.

Method:

A single-centre, retrospective review of blood group serological and genotyping investigations in children with SCD in Melbourne. Serological results were reviewed from the laboratory information system. Australian Lifeblood Red cell reference reports for HEA BeadChip™, RHD Beadchip™, RHCE Beadchip™ and next generation sequencing (NGS) were evaluated. Ethnicity was categorized using the Australian Standard Classification of Cultural and Ethnic Groups.

Results:

96 SCD patients, mean age 9.7 years (SD 5.4), with 53% female. Most patients were HbSS (67%), HbS beta thalassaemia (17%) and HbSC (12%). Most patients were of African descent (Sub-Saharan African and African - unspecified) (79%), followed by Northern African and Middle Eastern (18%). The majority were group O (47%), then A (30%), B (18%) and AB (4%). Rare blood types included 2 patients (Jsb-), 1 patient (U variant), 1 patient rare Dombrock phenotype (Joa-, Hy-) and 2 patients (Coa-).

RHD variants were detected in 30/81 (37%), and were only present in individuals of African descent. In 10% (8/81) the RHD variant present resulted in the D type being changed to negative (serologically 12/12).

RHCE variants were detected in 29/32 (90%) who underwent targeted testing, the most common variants were the RHCE*ce733G (82%) and RHCE*ce48C (59%).

11/91 (12%) patients developed alloantibodies of which 7 were transfusion-related with specificities of D, C, M, K, possible Sc9, auto/allo-anti-e and possible anti-Ce or hrB.

Transfusion support plans were developed for all patients still in attendance with sufficient serological and molecular testing.

Conclusion:

Australia's paediatric sickle population has not previously been described with respect to their serological and molecular testing. As we see more children identified with SCD through newborn screening, there is anticipated to be significant complexity in their transfusion needs.

Intra-apheresis lymphocyte count: A Practical approach to predict lymphocyte yield in leukapheresis product for autologous CART-cell therapy

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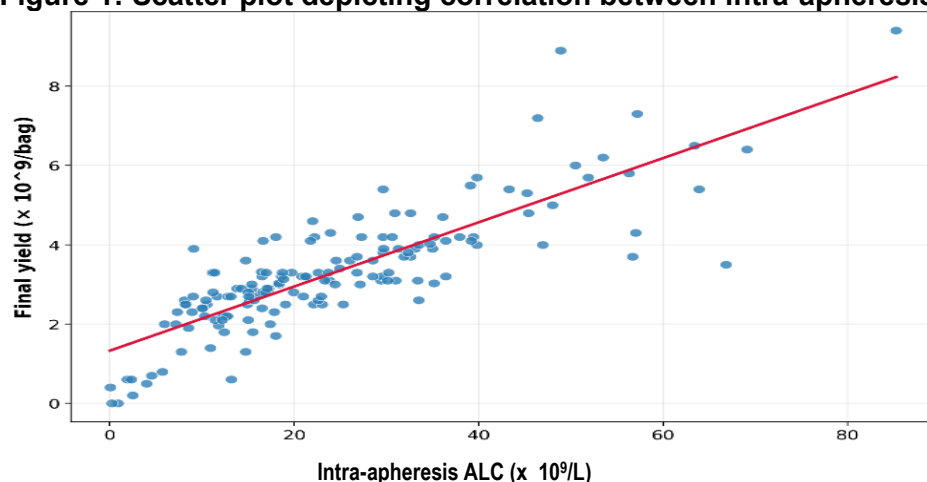
Aim: To evaluate the association between intra-apheresis absolute lymphocyte count (ALC) and lymphocyte yield in the final leukapheresis product for autologous CAR T-cell therapy.

Methods: This institutional ethics committee(IEC)-approved retrospective observational study was conducted at a tertiary care oncology centre from January 2024 to December 2025 and included all leukapheresis procedures performed for CAR T-cell therapy. Intra-apheresis samples were collected from the sample tube of the product bag under strict aseptic precautions and analyzed for ALC. Leukapheresis procedures were performed using Spectra Optia cell separator (Terumo BCT,USA) and Complete Blood Count(CBC) were performed either on Sysmex XN-10(Sysmex Corporation, Japan) or Advia 2120i hematology analyzer. Final lymphocyte yield was calculated for each apheresis product, with a minimum target yield of 2×10^9 lymphocytes per bag considered adequate for manufacturing. Statistical analysis was performed using the SPSS software, Version 29.0(IBM Corp., Armonk, NY,USA). Correlation between intra-apheresis ALC and final lymphocyte yield were analysed, with $p < 0.05$ considered statistically significant.

Results: A total of 159 leukapheresis procedures from 147 patients were included in the study. The mean intra-apheresis ALC was $24.3 \pm 15.3 \times 10^9/L$. The mean final lymphocyte yield obtained per bag was $3.3 \pm 1.5 \times 10^9$ cells, which was above the target yield for CAR-T cell production. Statistical analysis demonstrated a strong positive correlation between intra-apheresis ALC and final product lymphocyte yield ($p < 0.0001$) [Figure 1]. The intra-apheresis ALC values consistently correlated with the final lymphocyte yield, suggesting that intra-apheresis ALC monitoring help to predict collection adequacy during leukapheresis.

Conclusion: Real-time assessment of ALC during the apheresis procedure may aid in estimating the blood volume required to be processed to achieve the target lymphocyte yield and can serve as a practical predictor of collection efficiency and adequacy. This may help optimize leukapheresis procedures, ensure adequate collections, optimise resource utilization in CAR-T cell manufacturing.

Figure 1: Scatter plot depicting correlation between intra-apheresis ALC with final yield



Therapeutic apheresis activity in Aotearoa New Zealand: First report from the New Zealand Therapeutic Apheresis Registry

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Aim:

The New Zealand Blood Service (NZBS) is the primary provider of therapeutic apheresis in Aotearoa New Zealand. In 2025, NZBS established the National Therapeutic Apheresis Registry (TAR) to systematically collect data on all therapeutic apheresis procedures nationwide, supporting clinical decision-making, adverse event surveillance, and research. Herein, we present the first report from the TAR.

Methods:

We performed a retrospective descriptive analysis of non-identifiable TAR data for all therapeutic apheresis procedures undertaken by NZBS across six centres between April 2025 and March 2026. Variables included patient demographics, procedure characteristics (procedure type, number of procedures, processed volumes), and adverse events. Categorical data are reported as counts and percentages.

Results:

A total of 1,566 therapeutic apheresis procedures were performed in 797 patients. Therapeutic plasma exchange (TPE) accounted for 56% of procedures, followed by haematopoietic stem cell collections (34%), lipid apheresis (4.5%), and other procedures (4.5%). The most common indications for TPE were thrombotic thrombocytopenic purpura (16.6%), myasthenia gravis (16.5%), renal transplant rejection (9.8%), and chronic inflammatory demyelinating polyneuropathy (8.4%). The overall adverse event rate was 10.1%, with 99.2% of those classified as non-severe. The most frequent adverse events were citrate toxicity (34%), allergic reactions (14.6%), vasovagal episodes (11%), and vascular access issues (9.5%). No TPE-related deaths were reported. Regional variability was observed in indications, adverse event rates, and procedural practices. Most procedures were performed in Auckland (37%), Hamilton (26%), and Christchurch (16.8%).

Conclusions:

TPE is the most frequently performed therapeutic apheresis procedure in New Zealand, largely for neurologic immune-mediated conditions, and with a favourable safety profile. National registry data highlight regional practice variation and provide a foundation for quality improvement, standardisation of care, and optimisation of patient safety.

Lipid Apheresis for Familial Hypercholesterolemia in Aotearoa New Zealand

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Title:

Aim:

Familial hypercholesterolemia (FH) is associated with extreme cardiovascular risk, including premature myocardial infarction and aortic valve stenosis. While LDL-lowering therapies have advanced, access to newer agents remains limited, and some patients require additional interventions. Lipid apheresis (LA) removes LDL and lipoproteins from circulation using techniques such as double filtration and immunoadsorption. In New Zealand, LA is provided by the New Zealand Blood Service (NZBS) in a single region for patients with refractory or treatment-intolerant FH. This study aimed to evaluate the safety, efficacy, and clinical outcomes of LA in New Zealand.

Methods:

A retrospective observational review was conducted using non-identifiable data from the New Zealand National Therapeutic Apheresis Registry. Adult patients (>18 years) who underwent LA between January 2025 and February 2026 were included. All procedures used double-filtration plasmapheresis. Data collected included patient demographics, procedural details, LDL reduction, adverse events, and clinical outcomes. Descriptive statistics were applied.

Results:

Four patients (mean age 48 years) underwent 77 LA procedures, averaging 19 procedures per patient at 2.7-week intervals. Mean plasma volume processed was 1.5 L per session. Mean LDL levels decreased from 7.1 mmol/L pre-procedure to 1.8 mmol/L post-procedure, representing a 75% reduction. The adverse event rate was 11.6%, with 66% attributed to citrate toxicity; no severe events were recorded. Calcium prophylaxis was administered in 97.5% of sessions. Only one patient achieved guideline-recommended LDL targets (<2.6 mmol/L). All patients survived the follow-up period.

Conclusion:

LA effectively reduces LDL levels in FH but was insufficient alone to achieve recommended targets in most patients, highlighting the need for combination strategies. Limited-service availability suggests inequitable access across New Zealand.

Therapeutic Venesection in Aotearoa New Zealand

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Aim

Therapeutic venesection (TV) is an effective treatment for patients with iron overload disorders, porphyria cutanea tarda, and polycythaemia, reducing disease burden and associated complications. In some localities of NZ, these procedures are delivered by the New Zealand Blood Service (NZBS). This study describes the demographic and clinical characteristics of patients receiving TV through NZBS.

Methods

We conducted a retrospective observational review of non-identifiable electronic records from adults (≥18 years) undergoing TV at NZBS between January 2024 and February 2026. Patients were classified as: type 11 (TV only, not eligible to donate), type 26 (donor-eligible with higher-than-standard frequency), or type 33 (donor-eligible at standard frequency). Blood from types 26 and 33 was suitable for transfusion. Descriptive statistics were performed. Statistical analyses were performed using R (v4.1.1)

Results

A total of 2,831 patients (42% type 11, 22% type 26, 36% type 33) underwent 15,829 venesections, with a mean of 5.6 procedures per patient (type 11: 5.9; type 26: 6.3; type 33: 4.8). 93% of the venesections were due to hereditary haemochromatosis-related iron overload. Regional variation in patient classification was observed. Five percent of collections used a closed drainage system (Medinorm HVS). The overall adverse event rate was 1.7%, predominantly vasovagal reactions (61%) and haematomas (34%); no severe adverse events occurred. These venesections generated 8,793 whole blood units for processing and transfusion, representing 3.3% of total whole blood collections during the study period.

Conclusion

Therapeutic venesection delivered by NZBS is safe and contributes to the national blood supply. Donor-eligible TV patients represent an important dual benefit for individual patient care and transfusion services. Its dual impact should be optimised by increasing the localities offering the service and through partnership with other providers who are also performing such therapies but discarding the blood component.

A retrospective multicentre evaluation of apheresis using peripheral venous access: an Australian experience

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Aim: To assess the feasibility and safety of peripheral venous access (PVA) as an alternative to central venous catheters (CVC) for hospital-based apheresis.

Methods: We retrospectively reviewed all therapeutic plasma exchange (TPE) and continuous mononuclear cell collection (CMNC) procedures performed at three hospital-based apheresis centres from 2021–2024. Procedures were grouped by vascular access (PVA vs CVC). Feasibility outcomes included procedure completion and conversion from PVA to CVC. Planned outcomes included access-related infection, hospital length of stay, cost, and patient satisfaction. Analyses were conducted in R (v4.1.2). Continuous variables were summarised as mean (SD) or median (IQR) and compared using appropriate tests; categorical variables were compared using chi-square or Fisher's exact tests. Multivariable modelling and sensitivity analyses were planned to adjust for covariates and assess robustness.

Results: A total of 3,171 procedures were reviewed (2,658 TPE; 513 CMNC). PVA was used in 60% of TPE procedures (1,595/2,658) and 90% of CMNC procedures (463/513) across all centres. Preliminary review indicates high completion rates with PVA and infrequent conversion to CVC. These findings are consistent with published evidence demonstrating reduced infection rates, shorter hospital stays, lower costs, and improved patient satisfaction with PVA.

Conclusion: In this multicentre cohort, PVA was the predominant access method for both TPE and CMNC, supporting its feasibility in routine practice. Together with established evidence of lower infection risk, reduced length of stay, cost advantages, and higher patient satisfaction, these results support PVA as a safe and effective alternative to CVC for apheresis. Ongoing analyses will further define comparative safety, resource use, and patient-reported outcomes.

Neonatal Alloimmune Thrombocytopenia (NAIT): patient characteristics, management and outcomes--an update from the Australian NAIT Registry

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Aim:

Describe treatment and outcomes for NAIT, an uncommon cause of severe haemorrhage due to profound thrombocytopenia in the fetus/neonate, using data from the Australian NAIT registry.

Method:

All cases registered from 2009 to April 2026 were included, defined as: pregnant women treated antenatally for NAIT, regardless of laboratory results; and/or fetus/newborn with thrombocytopenia and maternal HPA antibodies. Analysis was performed with available data, therefore denominators vary.

Results:

The registry holds information on mothers, their pregnancies and neonates across 29 Australian sites. Examining NAIT pregnancies by anticipated/not anticipated, data for 199 pregnancies (144 mothers, 200 neonates) were analysed. NAIT was not anticipated in 62% of pregnancies, while 93% of anticipated cases were treated with antenatal IVIg.

	Not anticipated	Anticipated
Pregnancies	124	75
Neonates	123	77
Maternal antenatal IVIg	4/122 (3%)	66/71 (93%)
Neonatal platelet transfusion	86/116 (76%)	16/55 (29%)
HPA-matched platelet transfusion	10/86 (12%)	7/16 (44%)
Neonatal IVIg	55/115 (48%)	13/56 (23%)
Neonatal platelet counts (x 10 ⁹ /L) [median, IQR]		
First	19 [9, 42] n= 119	138 [70, 224] n=76
Lowest	16 [7, 29] n= 119	106 [45, 189] n= 75
Neonatal ICH	11/117 (9%)	1/58 (1.7%)

Neonates in whom NAIT was unanticipated had lower platelet counts, required more platelet transfusions, and greater incidence of bleeding than in anticipated cases. 102 cases received neonatal platelet transfusions; 17% were HPA-matched. Median [IQR] pre-transfusion platelet count (N = 97) was 13 x10⁹/L [6, 21]. Twelve intracranial haemorrhages (ICH) (7% of babies), and 4 deaths were recorded.

Conclusion:

Most NAIT cases are unanticipated. Antenatal treatment in anticipated cases results in lower neonatal complication rates than in unanticipated cases. Further research on long term outcomes and optimal treatment strategies is required.

HAPPI KIDS - A translational paediatric haemostasis platform: feasibility of continuous coagulation reference ranges and application to in-vitro evaluation of novel anticoagulants

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Aims: Interpretation of paediatric coagulation assays in the setting of rapid age related physiological change is limited by reporting using discrete age partitions. Continuous paediatric reference ranges (CRRs) offer enhanced interpretability by modelling physiological changes as a continuous function of age. Concurrently, there is increasing demand for high-quality paediatric samples to evaluate novel anticoagulants in neonates and children, where ethical and logistical constraints limit clinical studies.

To demonstrate the feasibility of deriving CRRs for coagulation tests using the HAPPI Kids biobank, and to highlight its application as a translational platform for in-vitro evaluation of emerging drugs in paediatric populations.

Method: HAPPI Kids recruits healthy neonates, infants, children, adolescents and adults undergoing minor elective procedures, enabling acquisition of well-phenotyped, high-quality venous samples. Samples are processed under standardised conditions and used to (1) develop CRRs for PT, aPTT, fibrinogen, factor assays and global haemostasis tests using continuous modelling approaches (e.g., quantile regression); and (2) support in-vitro anticoagulant studies by providing age-specific baseline samples for dose–response, pharmacodynamic, and comparative assay analyses. Feasibility indicators include recruitment efficiency, age-coverage density, and assay completeness.

Results: HAPPI Kids has demonstrated strong feasibility, achieving broad age representation (0- 62 years) and sample quality sufficient for both reference interval generation and anticoagulant testing (fig 1). Ninety age-specific CRR were developed. In-vitro studies using HAPPI Kids samples have enabled age-specific characterisation of four anticoagulant effects, supporting preclinical evaluation and regulatory submissions to the FDA and EMA.

Conclusion: HAPPI Kids is a scalable paediatric haemostasis platform capable of generating CRRs and enabling rigorous in-vitro evaluation of novel anticoagulants in neonates and children. This dual capability positions the platform as a valuable resource for diagnostic manufacturers and pharmaceutical partners aiming to optimise paediatric assay performance and therapeutic development.

Category	Total Days	Approached	Consented (Rate)	Sample Obtained (Rate)
Neonates	1,622	12,453	2,201 (17.7%)	1,615 (73.4%)
Children	2,069	9,822	8,093 (82.4%)	7,414 (91.6%)
Adults	60	60	60 (100%)	60 (100%)
Total	3723	22,307	10,325 (66.7%)	9,061 (88.3%)

First-in-human investigation of HMB-002: a subcutaneous antibody for prophylactic management of Von Willebrand disease

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Aim:

To evaluate safety, tolerability, pharmacokinetics (PK), and pharmacodynamics (PD) following a single subcutaneous dose of HMB-002.

Method:

VELORA Pioneer (NCT06754852) is an ongoing Phase 1/2, open-label, dose-escalation study evaluating HMB-002 in adults with VWD (baseline VWF activity ≤ 40 IU/dL, FVIII ≤ 70 IU/dL). The study consists of Part A (single ascending dose) and Part B (multiple dose assessment). Part A evaluated single ascending subcutaneous doses (20, 50, 150 mg) in sequential cohorts.

Results:

PD effect was evident from a dose-dependent accumulation of VWF and FVIII. In cohort A2 (50 mg), $>150\%$ change in VWF and FVIII was achieved and maintained for at least 8-10 days. Restoration of thrombin generation to the normal range and shortening of APTT were observed, with stable multimer distribution. PK analysis showed dose-dependent increases in HMB-002 plasma concentrations and prolonged exposure with subcutaneous dosing. HMB-002 demonstrated a favorable safety profile with no reported related treatment-emergent adverse events, injection site or hypersensitivity reactions, changes in D-dimer levels or inflammatory markers, or detectable antidrug antibodies at any timepoint. Data for cohort A3 (150 mg) are accruing; updated results will be presented at the congress.

Conclusion:

HMB-002 was well-tolerated and produced sustained dose-dependent increases in PK, and PD (VWF and FVIII), supporting proof of mechanism and the potential for infrequent subcutaneous dosing. These interim results support continued dose escalation to further evaluate PD magnitude and durability.

Geographic variation in clot kinetics following major trauma

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Aim:

Most evidence evaluating viscoelastic haemostatic assays (VHA) in trauma is derived from major trauma services (MTS), despite half of patients with major trauma presenting to non-MTS, with differing resources and resuscitation strategies. The aim of this study was to compare VHA-derived clot kinetics across trauma centre designation.

Method:

This was a retrospective statewide cohort study and included patients with major trauma undergoing VHA testing on hospital arrival across Queensland, Australia (2019–2025). Clot kinetics were stratified by MTS status and hospital geography.

Results:

Among 3590 patients with major trauma, 1102 underwent VHA testing on hospital arrival, including ROTEM (n=1052, 95%) and TEG (n=50, 5%). Overall, 674 (61%) patients were managed at MTS. Compared with non-MTS, patients managed at MTS demonstrated greater injury severity (median ISS 25 vs 22, $p<0.001$), greater aeromedical retrieval use (25% vs 17%, $p=0.002$), and more frequent intubation (38% vs 15%, $p<0.001$). Hyperfibrinolysis was more common in patients managed at MTS (40% vs 25%, $p<0.001$). While hypocoagulability was similar between groups (62% vs 64%, $p=0.6$), patients managed at MTS more frequently demonstrated multiple concurrent VHA abnormalities ($p=0.028$). Specific VHA clot kinetics deficiencies (fibrinogen, platelet, coagulation factor) were similar across trauma centre designation and hospital geography (all $p>0.05$).

Conclusion:

Patients managed at MTS demonstrated higher rates of hyperfibrinolysis and multiple concurrent VHA abnormalities, reflecting greater injury severity. However, substantial clot kinetic abnormalities were detected among patients managed at non-MTS. These findings support equitable consideration of haemorrhage resuscitation strategies across trauma systems.

Albumin use in Australian intensive care units: A retrospective observational data linkage study from the National Transfusion Dataset and Australian and New Zealand Intensive Care Society Adult Patient Database

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Aim:

Evidence-based guidelines restrict albumin therapy to specific critical care populations. The aim of this study was to describe patterns of albumin use in Australian intensive care units (ICU), including associated patient and clinical characteristics.

Method:

We conducted a retrospective observational study of 39,899 adult ICU patients admitted to two Australian tertiary hospitals between 2017 and 2024. Patients were identified through linked data from the National Transfusion Dataset and the Australian and New Zealand Intensive Care Society Adult Patient Database. The first ICU admission and first episode of albumin administration per patient were included. Patients were stratified into clinically relevant subgroups, including traumatic brain injury (TBI), cardiac surgery, sepsis, chronic liver disease, renal replacement therapy and burns. Descriptive analyses were performed and multivariable logistic regression identified factors associated with albumin administration, including age, comorbidities, illness severity and albumin level.

Results:

There were 7,945 episodes of albumin administration (20% of patients). 20% albumin accounted for 4,668 episodes (60%), while 4-5% albumin accounted for 2,968 (37%), the remaining 3% were unknown. Albumin use was more common in surgical than medical patients (53% vs 47%, $p < 0.001$). Among recipients, cardiac surgery was the largest subgroup ($n=1,917$, 24%), followed by sepsis ($n=1,652$, 21%). Of 3259 patients with TBI, 228 (7%) received albumin. Overall, use increased from 20% in 2017 to 24% in 2024. When compared to patients without disease, independent predictors of albumin use included sepsis (adjusted odds ratio (aOR) 1.55, 95% CI 1.42 – 1.68) and chronic liver disease (aOR 5.29, 95% CI 4.38 – 6.41).

Conclusion:

Albumin remains widely used across diverse Australian ICU populations, including TBI and cardiac surgery patients, where evidence supporting routine use in volume resuscitation remains limited. These findings highlight the need for further research evaluating specific indications for albumin use and associated patient outcomes.

Implementation of a therapeutic venesection clinic at NZ Blood and Organ Service (NZBS) donor centre

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Aim:

In response to increasing demand within Te Whatu Ora/Health NZ the Palmerston North Haematology service partnered with NZBS to establish a therapeutic venesection (TV) clinic at the Palmerston North Donor Centre. The aim was to improve local access to therapeutic venesection, reduce pressure on hospital services, integrate eligible patients into the whole-blood donor panel, and deliver a safe, efficient, and high-quality service supported by trained staff.

Method:

A multidisciplinary project team was formed, including NZBS clinicians, nursing, quality and operational staff alongside Te Whatu Ora/Health NZ Clinicians.

The service was implemented under the NZBS change management framework with an approved action plan encompassing stakeholder engagement, process mapping, risk management, workforce training, communication planning, contractual arrangements with Health NZ, and post-implementation evaluation.

Regular project meetings were held to manage and monitor progress.

Results:

The TV clinic opened on 01/12/2026 with four patients treated on the first day. Since implementation, the patient panel has increased to 71 individuals, with 150 therapeutic venesection procedures performed. Of these procedures, 31 were undertaken from patients eligible to donate whole blood, supporting expansion of the local donor panel. Five nursing staff and three administration staff were trained to deliver and support the service. A formal post implementation review is scheduled for July 2026 and will include stakeholder feedback and review of incidents, complaints and adverse events.

Conclusion:

Establishing a therapeutic venesection clinic within an NZBS donor centre successfully improved access to care, supported donor recruitment, enhanced workforce capability, and reduced service burden within Te Whatu Ora/Health NZ. This collaborative approach demonstrates how therapeutic services can be effectively integrated within blood collection settings while maintaining patient safety and high standards of care.

Anti-Kpa-Mediated Haemolytic disease of the fetus and newborn – a case report of antenatal treatment

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Aim:

To describe a case of haemolytic disease of the fetus and newborn (HDFN) caused by anti-Kp^a antibodies.

Background:

Kp^a red cell antigens within the Kell blood group system, are present in <2% of Caucasians and virtually absent in other ethnic groups.³ Anti-Kp^a alloimmunisation rarely causes HDFN, mediated via extravascular haemolysis.^{2,3} However, anti-Kp^a detection is challenging due to sporadic inclusion in routine antibody screening.^{1,4}

Case:

A 40-year-old woman, G4P1M2, presented in 2024 in early pregnancy after a prior live birth (2019), miscarriage at 19 weeks (2023) with hydrops fetalis (no other cause found) and miscarriage at 6 weeks gestation (early 2024). Anti-Kp^a was identified post-2023 pregnancy (no titres). Comorbidities included well-controlled type 1 diabetes (T1DM) and Hashimoto's thyroiditis.

Management was multidisciplinary, involving maternal-fetal medicine, haematology, endocrinology and coordination with a regional infusion centre given patient's rural residence. Maternal anti-Kp^a titres were monitored throughout pregnancy and rose from 1:16 preconception to 1:64 at 8 weeks gestation. Although traditionally anti-K titres do not always correlate with clinical severity, her history of miscarriage with hydrops fetalis raised concern that this antibody titre rise reflected an immunogenic reaction to the fetal Kp^a antigen, which is expected to be present from approximately 6 weeks gestation.¹ Paternal genotyping demonstrated Kp^a heterozygosity conferring 50% likelihood of fetal inheritance. Non-invasive prenatal testing (NIPT) in second trimester detected fetal Kp^a antigen.

Weekly IVIg (1mg/kg) from 10 weeks to birth at 38 weeks was complicated by adverse effects, including headaches and hyponatraemia, necessitating steroid premedication which exacerbated T1DM control. Serial ultrasounds monitored for fetal anaemia. At birth, biochemical evidence of fetal immune-mediated haemolysis was present: DAT2+, raised indirect bilirubin (159umol/L).

Conclusion:

Clinically significant HDFN due to anti-Kpa is rare. Successful antenatal treatment with weekly IVIg was undertaken with live birth. Rare antigens should be considered when investigating for HDFN.

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False positivity in the era of sensitive serology: A comparative study of Column Agglutination Technique (CAT) and Conventional Tube Technique (CTT) in DAT Evaluation

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False Positivity in the Era of Sensitive Serology: A Comparative Study of Column Agglutination Technique (CAT) and Conventional Tube Technique (CTT) in DAT Evaluation

Aim:

To evaluate the significance of Direct Antiglobulin Test (DAT) positivity detected by Column Agglutination Technique (CAT) compared with Conventional Tube Technique (CTT) in oncology patients and identify factors associated with false-positive DAT results.

Methods:

This retrospective cross-sectional study (IEC approved) was conducted in the Department of Transfusion Medicine at a tertiary care oncology centre. DAT-positive blood samples (by CAT) from oncology patients between January 2023 and April 2025 were analyzed. All DAT-positive samples detected by CAT (grades 0.5+ to 4+) were further tested using CTT (grades 1+ to 4+) and categorized as false positive (FP; CAT positive/CTT negative) or true positive (TP; CAT positive/CTT positive). Patient's demographic details, diagnosis, transfusion history, medication history, and laboratory parameters were reviewed. Statistical analysis was performed using Chi-square and Mann-Whitney U tests.

Results:

Of 251 DAT-positive results, 89.6% (225/251) were classified as FP and 10.4% (26/251) as TP. DAT reaction strength differed significantly between groups. TP showed significantly higher median CAT grades than FP (3 [IQR 3–4] vs 1 [IQR 0.5–2], $p < 0.001$). Similarly, CTT grades were significantly higher in TP (1 [IQR 1–2] vs 0 [IQR 0–0], $p < 0.001$). Medication history was present in 99.1% (223/225) of FP results compared with 42.3% (11/26) of TP results suggesting strong association between medication exposure and DAT false positivity ($p < 0.001$). These findings indicate that certain drugs (Table 1) may interfere with DAT interpretation, causing clinically insignificant positive reactions detected only by highly sensitive CAT methods.

Conclusion:

Most DAT-positive reactions in oncology patients represented false-positive findings detected only by CAT, highlighting the risk of overinterpretation with highly sensitive methods. Stronger DAT grades and concordant CTT positivity were associated with clinically significant DAT positivity. Correlation with clinical findings, hemolytic markers and medication history is essential to avoid misdiagnosis of autoimmune hemolytic anemia and ensure appropriate transfusion management.

Table 1: Medications observed to be associated with DAT positivity in oncology patients

Sr. No	Medications observed to be associated with DAT positivity in oncology patients
1	Cisplatin
2	Carboplatin
3	Oxaliplatin
4	Fludarabine
5	Rituximab
6	Daratumumab
7	Amikacin
8	Bendamustine

9	Doxorubicin
10	Pembrolizumab
11	Nivolumab

Anti-D prophylaxis during pregnancy and early postpartum – equity in remote settings via a collaborative model of care

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Background:

Anti-D prophylaxis within 72 hours of a sensitising event and routine antenatal Anti-D prophylaxis (RAADP) at 28 and 34-weeks' is standard therapy for pregnant women | wāhine with a RhD negative blood group, to protect the unborn baby | pēpi and future children | tamariki from haemolytic disease of the fetus and newborn.

Southern Health New Zealand | Te Whatu Ora (HNZ) delivers health care to a diverse population, across Otago and Southland. In addition to the main centres and rural communities, HNZ serves both Queenstown and Wānaka. As areas of outstanding beauty their populations grow, albeit quicker than the health infrastructure. For RhD negative wāhine in Wānaka, accessing Anti-D prophylaxis required three hours of travel, often in challenging alpine weather conditions. The barrier of distance and cost affected Anti-D prophylaxis.

Aim:

To provide equity to RhD negative wāhine in Wānaka by providing access to Anti-D in the Wānaka Primary Birthing Unit | Rākai Kahukura to mitigate anti-D alloimmunisation.

Method:

A model of care was developed, underpinned by a strong partnership between HNZ and the New Zealand Blood Service (NZBS) in Dunedin. Local access to Anti-D was a four-fold process covering Cold-Chain Certification; Cold-Chain and Inventory Kapapa | Guidelines; Competency Training and Logistics.

Once approved via NZBS quality processes the facility to hold and administer Anti-D in Wānaka could commence.

Results:

A whānau-centred model of care has reduced the financial and time burden of travel to access Anti-D, thereby providing equity and choice. The uptake of RAADP has increased and the ability to birth in a remote setting with access to Anti-D has changed the post-partum period.

Conclusion:

Equity shouldn't depend upon geography. The risk of anti-D alloimmunisation has been further mitigated by having the right blood at the right place; whilst protecting the taonga of blood by shared kaitiakitanga.

Home-based blood product transfusion in Australia: A qualitative study of existing programs

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Aim: Home-based transfusion programs have been operating around the world for several decades, including long-standing programs in Europe, North and South America. These are less common in Australia. Previously identified barriers include safety concerns, cost and staffing. This study aims to identify and characterise existing Australian home transfusion programs and explore their conception, implementation and sustainability.

Method: Descriptive qualitative study with semi-structured interviews conducted online using a researcher-developed interview guide. Participants were recruited through word-of-mouth and haematology or Hospital-in-the-Home (HITH) professional networks. Interviews were conducted to data saturation, and recorded, transcribed and analysed using content analysis.

Results: Six interviews were conducted with participants from 5 home transfusion programs across 3 Australian states (Table 1). Most were initiated to improve capacity in day centres and to keep patients out of hospital. Oversight, funding and administration were predominantly (4/5) provided by the tertiary centre HITH in metropolitan areas. Various logistical models were described, for example, for HITH staff to obtain the blood product for infusion, such as a courier to the patient's home vs HITH staff pick up from the blood bank. Perceived benefits of the program are summarised in Table 2. The services provided extra staff time for red cell transfusions, with all programs having a nurse present throughout the transfusion. All had mandatory staff training, escalation protocols and informed patient consent. Two services had conducted program evaluation with internal staff/patient surveys, one had formally evaluated their safety data (no significant issues reported) and one had commenced a preliminary economic analysis.

Conclusion: Home transfusion programs are operating in Australia with patient and staff-reported benefits contributing to program continuity. We found similar reasons for commencement, but with differing logistical models in each program. Areas for future research include further formal evaluation of safety, costs, and exploration of acceptability to patients and staff.

Table 1: Demographics

	State or territory	Interviewee	Duration of program	Blood product(s)	Population	Administering team
1	South Australia	Nurse manager	<5 years	Red cells, platelets, albumin, IVIg	Paediatrics	HITH
2	South Australia	Nurse manager Nursing director (2 interviews)	10-15 years	Red cells, platelets, albumin, IVIg	Adults at home or aged care, priority for those with "frailty"	Private nursing
3	Victoria	Nurse manager	5-10 years	Red cells	Aged care residents	HITH
4	Queensland	Nurse manager HITH physician	5-10 years	Red cells	Aged care residents	HITH
5	Queensland	Nurse manager	<5 years	Albumin	Paediatrics with a specific condition	HITH

*IVIg = intravenous immunoglobulin

Table 2: The perceived benefits of home transfusion, with selected quotes

Benefit to	Quote	Program
Patients	"... we were able to get them back as a family unit, back home... we felt passionate about it"	5
Patients	"We do it on the weekends, we do it on public holidays, these times and dates were not offered to ... this particular cohort before we started."	1
Patients	"...we come in at 3:30 in the afternoon. So he's done a full day at school, mum just has to leave work an hour earlier. We transfuse, he has his dinner and then we go home."	1
Patients	"We do see that it stops elderly, frail people going into a hospital site."	2
Patients	"...in nursing homes... it's quite the journey for them to find their way into hospital. It can take the better part of a day, including waiting for ambulances and all that..."	4

Staff	<i>"I sit near the HITH team and I see them coming in and I hear them, and I think that they actually enjoy that time with a patient. It's 1:1 with the family."</i>	5
Staff	<i>"it's a good service and the staff do enjoy it..."</i>	2
Cost	<i>"The preliminary data is showing that it's more cost-effective for us to provide this service in the home than in the clinic space, which blew my mind...."</i>	1

Phenotypic spectrum of RhD and RhCcEe variants among Omani blood donors

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Aims:

This study aims to define and characterize the phenotype of RhD and RHCE in RhD-negative Omani blood donors attending a hospital based Blood Bank with donor-based and transfusion facilities in Oman.

Methods:

An analytical prospective descriptive observational cross-sectional study design was employed. Eligible RhD-negative Omani blood donors were invited for enrolment in the study. Serological phenotype on of the obtained EDTA samples was performed using standardized blood banking methods and BioRad reagents within 24 hours of collection. Weak D testing was performed using indirect antiglobulin methods (IAT) by standard blood bank techniques. Obtained phenotypes were recorded as per the Wiener classification. Descriptive statistics was done and frequencies were reported. Ethical approval was secured and informed consent was obtained from each donor.

Results:

Among 12,457 donations between April 20th 2025 and April 25th, 2026, a total donor of 453 RhD negative donors were recruited and enrolled (3.6%). The frequencies of the blood groups O-, A-, B- and AB- among RhD negative blood donors were 62.3%, 21%, 14.6%, and 2.2% respectively. The most frequent RhCE phenotypes were rr (84.34%), r'r (13.02%), r''r (2.65%), r'r' (0.22%), r''r' and r'r'' (0.26% each). In combination with RhCE phenotype, rrK- phenotype was the commonest (78.1% of the donors), followed by r'rK- (12.8%), rrK+ (4.2%) and r''rK- (2.4%). No weak D variants were found.

Summary/Conclusions:

Overall, the rr and r'r were the commonest phenotypes among studied population. This distribution is consistent with patterns reported in other populations in the region, indicating that RhD and RhCE phenotype- frequencies in our Rh-negative donor pool largely reflect the genetic background of the Eastern Mediterranean population. Further studies are required to assess the underlying genetic profile and molecular characterization of the RhD and RhCcEe blood group system in the Omani blood donors.

Enhancing Saturday plasma donor attendance at the New Zealand Blood Service, Dunedin, through targeted communication

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Aim:

To evaluate the impact of a structured communication intervention on donor attendance and efficiency in Saturday plasma collections and assess its sustainability.

Method:

A retrospective service evaluation of Saturday plasma donation collections at the Dunedin Donor Centre was undertaken from January 2025 to March 2026 as part of a Southern initiative, with particular emphasis on outcomes specific to the Dunedin Donor Centre.

The following phases were analysed:

- Baseline: Jan–May 2025
- Intervention: Jun–Dec 2025
- Sustainability: Jan–Mar 2026

In June 2025, a structured communication intervention was introduced and implemented by the Dunedin Donor Relations team. This included targeted Wednesday SMS reminders emphasising demand and the impact of missed appointments, supported by social media and in-centre promotion. Outcomes measured included appointment attendance (confirmed, did not attend [DNA], late cancellations <24 hours), donor mix, age range, and plasma units collected.

Results:

Phase	Appointments (n)	Attendance	DNA	Age (range, typical)	Donor Mix (Sex at Birth)
Baseline	103	68.9%	31.1%	18–72 (~45 yrs)	M70% / F30%
Intervention	160	81.9%	18.1%	18–70 (~42 yrs)	M68% / F32%
Sustainability	74	90.5%	9.5%	19–71 (~43 yrs)	M65% / F35%

Baseline attendance was below target due to high DNA rates. The intervention improved attendance and reduced DNAs, with sustained gains driven by repeat donors. Total plasma volume rose from 72,362 mL to 114,677 mL (+58.5%). Plasma volume collected per month was highest in the sustainability phase, representing a 23.7% increase over the baseline phase. Donor age remained stable; male predominance decreased slightly (70%→65%) with increased female participation (30%→35%). Attendance improved significantly across phases (χ^2 , $p=0.0013$), as did appointment utilisation, with a higher proportion of scheduled appointments being attended and fewer underfilled sessions ($p<0.0001$).

Conclusion:

The intervention resulted in a 16% increase in attendance and a 17% reduction in DNA rates compared with baseline. Improvements were sustained, demonstrating that targeted behavioural communication is an effective, scalable strategy to enhance donor attendance and operational efficiency in plasma collection services.

Bloodlines in transfusion, how ethnicity is reshaping Australia's ABO and D group distribution.

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Aim:

To evaluate the distribution of ABO and D within the Harmonising Age Pathology Parameters in (HAPPI) Kids study and correlate with ethnicity.

Methods:

HAPPI Kids is a prospective, cross-sectional study, that aimed to create paediatric laboratory reference intervals. Blood group was performed on a subgroup. Data was collected on birthplace and parental ethnicity (classified using Australian Standard Classification of Cultural and Ethnic Groups).

Chi-square test of independence was utilised to evaluate for significant associations between ethnicity and blood group.

Results:

2,459 participants had a blood group. Mostly group O (43.9%), then A (36.7%), B (14.6%) and AB (4.8%). Majority D positive (87%), D negative (13%). Only 5.7% were O negative. 151/2,459 (6.1%) were overseas born and there was an association between birthplace and ABO ($\chi^2 = 72.3$, $p < 0.001$). Oceanian born children were less frequently group B ($p < 0.001$). Only 51% of parents considered themselves Oceanian, highlighting diversity within the population. Parental ethnicity was associated with a child's ABO ($\chi^2 = 236.41$, $p < 0.001$) and D ($\chi^2 = 67.7$, $p < 0.001$). Children of Oceanian descent had higher expected frequencies of group A or O and less B (all $p < 0.05$). B was associated with parental ethnicity from Southern and central Asia, North-east Asia, South-east Asia and Sub-saharan Africa (all $p < 0.01$). AB frequency was higher in families of North Africa and Middle-eastern ethnicity ($p = 0.004$). D variability was driven by higher-than-expected rates of D negativity in Oceania or North-west European families (both $p < 0.05$) and higher D positivity in North-east Asia, South-east Asia and Southern and central Asia (all $p < 0.001$).

Conclusion:

Australia's ABO distribution, has a changing profile with increasing B, AB and D+ blood groups compared with historical data. Oceanian individuals were less frequently group B and more frequently D- than other ethnic groups, therefore ethnic diversity and variability in global

ABO distribution are key factors. Diminishing numbers of O negative individuals may impact future blood supply.

The blood group effect

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Developmental differences differ between neonates and adults with respect to ABO. ABO and RhD have not previously been considered in the establishment of paediatric laboratory reference intervals.

Aim:

To investigate the relationship and explore for any differences between ABO and RhD blood groups for common laboratory parameters in children.

Method:

The Harmonising Age Pathology Parameters in (HAPPI) Kids study is a prospective, cross-sectional study to develop age-appropriate reference intervals for laboratory parameters in well children. Blood group was performed on some individuals. Where tested, the FBC, coagulation profile, coagulation factors, coagulation inhibitors, large proteins and haemoglobins were analysed.

Statistical analysis was performed utilising SPSS to explore for between blood group differences. Data was assessed for normality. Normally distributed continuous variables were expressed as mean $\pm$ SD, otherwise medians were reported. One-way ANOVA, Kruskal Wallis tests and independent t test were used to assess for significance between categorical variables (i.e. ABO type or RhD type). A significant p value was considered <0.05 .

Results:

Blood group results were available for 2,103 children. Red cell count was higher in group B compared with group A or O individuals and Hb/HCT were higher in B compared with non-B individuals. APTT was prolonged in O compared with non-O individuals. Factor VIII, vWF levels were reduced in O individuals than A, AB or B.

RhD positive individuals protein S levels were reduced compared to RhD negative. Increased HbF and reduced HbA levels were noted RhD positive compared to RhD negative individuals.

Conclusion:

The B allele is an ancient polymorphism that persists, perhaps, due to balanced evolutionary processes and selective advantages. Consistent with other studies group B individuals appear to have better erythropoietic potential than other blood groups. Larger studies are needed to confirm the differences found between blood groups and better understand if ABO and RhD, impact paediatric disease pathogenesis.

Participation in the New Zealand blood service: the case of Filipino blood donors

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Aims:

New Zealand's demographic composition has become more diverse, resulting in a consequent need for blood donor strategies to be attuned to the diversity of motivations within different ethnic groups. This mixed methods comparative study investigated the motivations and experiences of Filipino donors in Aotearoa New Zealand. This exploratory research aimed to (1) gain a clear picture of blood donation amongst Filipinos in New Zealand; (2) analyse this group's interaction with blood donation institutions; and, given the first two points, (3) consider how the group's participation can be further strengthened to facilitate a blood supply which better matches our changing population's needs.

Methods:

Descriptive statistics on Filipino blood donor participation followed by an in-depth exploration of the motivations and experiences of 24 Filipino donors via a blood donor identity survey (France et al., 2014) and three focus groups.

Results:

Philippines-born individuals constituted 2.5% of NZBS donors compared with approximately 1.8% of the national population, indicating modest overrepresentation. Blood Donor Identity Survey results demonstrated strong internal motivation and low amotivation. Qualitative findings revealed that donation motivations were shaped by formative experiences within the Philippines blood system, where donation is often episodic and reciprocal. In New Zealand's voluntary, non-remunerative system, donation became routinised and institutionalised. Collection donation practices, particularly through religious and association networks, played a significant facilitating role. Gender disparities were evident, with male donors overrepresented relative to national patterns.

Conclusion:

Filipino donor participation reflects not only individual altruism but collective identity and institutional transition. Migration into a stable, voluntary system appears to enable sustained participation. Recruitment strategies that recognise collective engagement and address gender disparities may further strengthen participation. Findings contribute to broader discussions of how cultural context and health system structures shape blood donation culture.

Representation, inclusivity and behavioural messaging in blood sector social media

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Background and Aim:

Social media is increasingly used to promote blood and plasma donation; however, little research has examined representation, inclusivity and behavioural messaging within blood sector social media content. Identifying gaps in representation and messaging may help to broaden donor recruitment, particularly given an ageing donor population and potential shortfalls in donor numbers. This study aimed to characterise observable features of Australian blood donation social media posts and assess the extent to which content reflects known behavioural determinants.

Methods:

An exploratory mixed-methods content analysis was conducted across TikTok, Instagram and Facebook. Separate research-specific accounts were created to minimise algorithmic bias. Posts tagged #LifebloodAU from both organisational and individual creators were collected between 18–21 November 2025, with 50 posts sampled per platform (n=150). Firstly, quantitative coding of perceived observable characteristics including demographics, body representation and information characteristics was undertaken. Comparative analyses were conducted using chi-square tests ($P < 0.05$). Secondly, inductive thematic analysis of captions, transcripts and on-screen text was performed to identify broader behavioural themes and map findings to behavioural theory frameworks including COM-B, HAPA and Identity Theory.

Results:

Most posts featured human subjects (90%), predominantly aged 30–40 years (48.7%). Representation of older adults (>60 years; 8%), individuals with visible disability (3.3%), visible differences (2.7%), individuals who disclosed gender diversity ($\leq 2\%$) and larger body sizes (Pulvers categories 7–9; 0%) was limited. Racial or ethnic minority representation occurred in 26.7% of posts. Facebook content more frequently depicted the donation process and donation paraphernalia, while Instagram posts more commonly included instructional content, personal stories and references to research or data (all $p < 0.05$). Thematic analysis identified three overarching themes: (1) donation as meaningful and prosocial, (2) reducing barriers by framing donation as accessible and manageable, and (3) encouraging action through social influence and behavioural prompts.

Conclusion:

Australian blood donation social media content reflects several established behavioural determinants associated with donation behaviour; however, representation across age, body size, disability and gender diversity was limited. Greater inclusivity within donor-facing campaigns may improve relatability and support broader donor engagement strategies.

MMA under the microscope: reviewing methodological variation and clinical applications

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Background and Aim:

The monocyte monolayer assay (MMA) is an *in vitro* functional assay used to predict whether anti-red blood cell antibodies will induce destruction after binding to their concordant antigens. However, the MMA is technically demanding and lacks standardisation across the sector. This study aimed to review published MMA methods, and determine differences in methodology, interpretation and clinical use.

Method:

“Monocyte monolayer assay” was searched in four databases (Medline, Pubmed, Scopus, Web of Sciences). Duplicates and non-English articles were removed, and abstracts were screened to ensure the appropriate assay was mentioned. Full publications were examined, and those with detailed MMA methods, including incubation times, cell sources and calculation of readout indexes, were included in the final review.

Results:

After abstract screening, 315 papers remained. These were examined for the clinical uses of the MMA: haemolytic transfusion reactions (35.82%), haemolytic disease of the fetus and newborn (20.13%), autoimmune haemolytic anaemia (14.06%) or some combination of these (7.99%). Few papers contained methods sufficient for replication, with 64 remaining after screening full papers. These originated from 27 groups in 17 countries. There were several inconsistencies in MMA methods. Readout indexes were described ambiguously, with the same terms used to describe different indexes, or the same indexes described using different names. Several aspects of the method, including the use of controlled CO₂ culture conditions, the addition of complement, and incubation times varied considerably, although cutoff values (>5%) were mostly consistent between methods.

Conclusion:

Although cut-off values were mostly consistent, the methodologies applied to derive the assay results varied considerably. It is important to interpret results of any MMA in the context of methodology applied, which may vary between blood providers. There may be benefit to an external quality assurance scheme to assess the consistency of, and clinical relevance of MMA results.

Assessment of THP-1- driven inflammatory response as an alternative readout in the monocyte monolayer assay (MMA)

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Background and Aim:

The MMA is used to predict the clinical significance of anti-red blood cell (RBC) antibodies. One barrier to implementation of the MMA is the capacity to source fresh monocytes. THP-1 cells are a readily available monocyte alternative that have been used widely in functional immunoassays. We previously developed an MMA using THP-1 cells which was successful in determining clinical significance of antibodies but demonstrated enhanced monocyte binding and reduced phagocytic capacity (1). Further, we previously reported a chemokine driven response to clinically significant antibodies in a traditional MMA (2). Herein, we assessed the inflammatory mediators released by THP-1 cells during the MMA to assess the possibility of an alternative inflammation-based MMA readout.

Method:

Standard MMA and THP-1 modified MMA were run in parallel (n=4 each) using anti-D opsonised RBC and matched saline controls. Supernatants were retained following the co-incubation of RBC and monocytes or adherent THP-1 cells for 1 hour. Concentrations of inflammatory markers were determined by cytometric bead array (BD Biosciences). Paired t-tests were used to determine whether exposure to anti-D opsonised RBC induced an inflammatory profile in MMA using monocytes or THP-1 cells.

Results:

In the THP-1 MMA, IL-2, IL-4, IFN- α , IL-10, IL-1 α , IL-1 β and IFN- γ were below detection limits (<1pg/mL). While detected, HuCD54, IL-6, IL-8, IL-12, MIP-1 α , MCP-1 and TNF- α were not significantly different following exposure to anti-D opsonised RBC or the saline control. In contrast, inflammatory profiles of the standard MMA demonstrated the expected increases in MCP-1 (P=0.042) and IL-8 (P=0.027).

Conclusion:

Although the profile of inflammatory mediator concentrations were able to predict clinical significance of antibodies in a traditional MMA, the THP-1-driven MMA did not replicate these results, indicating that THP-1 driven inflammatory response is not a suitable alternative readout in the MMA.

References:

1. Lightbody et al, Vox Sanguinis, 2025 V120 (S1), p356
2. Lightbody et al, Vox Sanguinis, 2025 V120 (S2), p20

A case of discrepant RhD typing in a pregnant woman due to the Crawford antigen.

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Background

Antigenic variants encoded by the *RHCE* gene arise from single nucleotide variations (SNVs) or structural gene rearrangements. The low frequency Crawford antigen (RH43) encoded by the *RHCE*ceCF* allele (48G>C, 697C>, 733C>G) gives rise to a variant RhceCF polypeptide that expresses D-like epitopes recognised by some anti-D reagents. The classification of D-, Crawford+ red blood cells (RBCs) as D+ may have clinical implications. Here we describe an RhD phenotyping discrepancy in a pregnant woman due to the presence of a low frequency RhceCF antigen.

Case presentation

Whole blood samples from a 24-year-old female, gravida 2, para 1, were referred for RhD investigation due to discrepant routine D typing. The patient presented at 13 weeks gestation with a negative antibody screen. She had no known history of blood transfusion and no record of receiving RhD immunoglobulin (RhIg) prophylaxis during her first pregnancy.

Method

Phenotyping was performed by standard serological methods using two commercially available monoclonal anti-D reagents: Immulab Epiclone-2 (IgM RUM-1) and Immucor Gamma-clone blend (IgM/IgG GAMA401/F8D8). Genomic DNA extracted from EDTA-whole blood was genotyped using Immucor BioArray Solutions RHD and RHCE BeadChip Kits. Next generation DNA sequencing was performed using a custom targeted sequencing panel.

Results

The patient's RBCs were reactive in the immediate spin (IS) phase with anti-D clone RUM-1 and non-reactive at the indirect antiglobulin test (IAT) phase with anti-D GAMA401/F8D8 blend. Molecular typing confirmed an *RHD* deletion with a predicted phenotype of D-, C-, E-, c+, e+, VS+. Sequencing revealed heterozygosity for the *RHCE*01.20.06* (*RHCE*ceCF*) allele that encodes the low frequency RhceCF antigen, Crawford.

Conclusion

The low frequency *RHCE*ceCF* variant was responsible for the RhD typing discrepancy observed in this case. Molecular characterisation of the Crawford phenotype is particularly important for the clinical management of D- pregnant women at risk of Rh sensitisation.

Non-invasive monitoring of oxygen extraction using an optical sensor to guide transfusion decisions

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Aim:

Red blood cell (RBC) transfusions are guided by haemoglobin levels, which do not accurately represent real tissue oxygen demand. Oxygen extraction ratio (O_2ER) is a measure of demand which appears to accurately identify anaemic patients who will benefit from an RBC transfusion. While non-invasive measurement of arterial oxygen saturation ($SpaO_2$) by pulse oximetry is well established, current methods for measuring central venous saturation ($SpvO_2$) require invasive central venous catheters, which prevent broad clinical use. This study aimed to evaluate the feasibility of O_2ER estimation using a neck-worn reflectance photoplethysmography (PPG) sensor.

Method:

A prototype flexible reflectance sensor array was created by our investigators. The sensor was positioned on the skin over the anterior triangle of the neck in 20 healthy adults. PPG signals were recorded during normal breathing in both the sitting and supine positions. Signal processing was performed to isolate venous-dominant components, including internal jugular venous (IJV) pulsations and low-frequency respiratory modulations. Common carotid $SpaO_2$ and IJV $SpvO_2$ were estimated from AC/DC absorbance ratios using time-domain peak-and-trough detection and Fast Fourier Transforms (FFT).

Results:

$SpvO_2$ derived from internal jugular pulsations ranged from 65.7–80.9%, while respiration-derived $SpvO_2$ ranged from 68.6–76.5%. Pulse-derived estimates were less variable than respiration-derived estimates (SD 1.64% vs. 3.96%). Estimated O_2ER values ranged from 0.18–0.33 (SD 0.03), consistent with published literature. Sitting improved arterial pulse detection, while supine positioning enhanced internal jugular and respiratory modulation signals.

Conclusion:

Non-invasive O_2ER estimation using a neck-worn reflectance sensor is feasible and practical. Non-invasive measurement enables estimation of O_2ER without central catheters and provides a novel tool for transfusion research. A prospective cohort study is currently underway in ICU patients, which will calibrate our prototype device against gold-standard blood sampling to evaluate accuracy, clinical feasibility, and potential major impact on transfusion management.

Human platelet antigen prevalence in an Australian blood donor population

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Aim:

Alloantibodies against human platelet antigens (HPA) have been associated with thrombocytopenia, a condition that increases bleeding risk. HPA-matched platelets are important for effective platelet support. Previous Australian data on HPA prevalence, limited to HPA-1, HPA-3 and HPA-5, came from studies in South Australia (SA) (n=250, Chen; Pathology, 1997) and Western Australia (WA) (n=1,000, Verran; Pathology, 2000). This study aimed to determine HPA prevalence in the current Australian blood donor population and compare HPA profiles with other population groups (Curtis & McFarland, Vox Sang 2014).

Method:

Australian blood donors in the Platelet Panel (PP) (n=17,781, >99.9% male) generally selected based on physical factors (i.e. size and vein access), who donated from January 2023 to December 2024, were included in this study. Samples were phenotyped and/or genotyped for HPA-1, HPA-2, HPA-3, HPA-5, and HPA-15 using accredited methods. Using Pearson's chi-square test, HPA profiles for 2023–2024 blood donors were compared with those previously reported for: 1) SA and WA donors, and 2) those reported for Asian, African and Caucasian populations.

Results:

HPA profiles of the Australian blood donors (Table 1) did not differ significantly from those reported for SA (p=0.46) and WA (p=0.65) blood donors. HPA prevalence was more closely aligned with the profile reported for Caucasians than for Asians and Africans. HPA-3 and HPA-15 exhibited strong variations across population groups.

Conclusion:

This study determined the HPA profile in an Australian blood donor population and is the first to report on the prevalence of HPA-2 and HPA-15. As the PP blood donors are predominantly male, and Lifeblood actively retain HPA-1bb donors, the HPA profile may not fully represent the general population or even the broader blood donor population. Knowing the HPA prevalence in a blood donor population will guide management to meet transfusion needs for patients with antibodies against platelet antigens.

Table 1. Platelet antigen profile					
HPA	Australian blood donors PP (%) this study	Caucasian* (%)	HPA	African* (%)	Asian* (%)
HPA-1aa	74.6	72	HPA-1a	90	100
HPA-1ab	23.1	26	HPA-1b	10	0
HPA-1bb	2.3	2			
HPA-2aa	85.4	85	HPA-2a	71	95
HPA-2ab	13.9	14	HPA-2b	29	5
HPA-2bb	0.7	1			
HPA-3aa	39.3	37	HPA-3a	68	59.5
HPA-3ab	45.7	48	HPA-3b	32	40.5
HPA-3bb	15.0	15			

HPA-5aa	83.2	88	HPA-5a	82	98.6
HPA-5ab	16.0	20	HPA-5b	18	0.4
HPA-5bb	0.8	1			
HPA-15aa	26.6	35	HPA-15a	65	53
HPA-15ab	49.5	42	HPA-15b	35	47
HPA-15bb	24.0	23			
*Curtis & McFarland, Vox Sang 2014					

Unlucky 13: A tricky case of Anti-Lutheran 13 and a question of its significance.

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Case overview:

A 74-year-old female with metastatic breast cancer, receiving nab-paclitaxel, was referred for investigation of a pan-reactive antibody screen following transfusion of packed red cells 10 days prior. Investigations were suggestive of an antibody to a high-prevalence antigen. She had a distant history of prior transfusion without documented alloantibody formation. Reference laboratory testing demonstrated an alloantibody reactive with all panel cells and rare red cells. Red cell genotyping predicted a Lutheran 13 negative phenotype (*LU*02.-13/*02.-13*), with homozygosity for three defining variants (c.1340C>T, c.1671C>T, c.1742A>T). Targeted serological testing confirmed the presence of anti-Lutheran13 in our patient's serum.

Lutheran-13 was first described in 1983 in Lu(a-b+) individuals producing an antibody compatible only with Lu(a-b-) red cells¹. It is found on the fifth IgSF domain of the Lutheran glycoprotein close to the red blood cell surface¹. Lu13 is a high-prevalence antigen occurring in 99.9% of the population, with only a few Lu13 negative probands identified². Anti-Lu13 is an IgG antibody, and Lutheran alloantibodies are historically considered clinically insignificant, but this recommendation is limited by the few examples of Anti-Lu13¹⁻².

Prior to the results of the above investigations, the clinical need to manage symptomatic anaemia necessitated that three units of C-, K- red cells were transfused, with Lu status unknown. She remained clinically stable without an appropriate haemoglobin increment. However, post-transfusion biochemistry showed a peak total bilirubin of 51 µmol/L (reference 1–20) and a transient rise in lactate dehydrogenase (LDH) to 900 U/L (reference 120–250), noting elevated levels of LDH prior to transfusion.

Conclusion:

This case adds to the limited literature on the rare Lu13 negative phenotype and associated alloimmunisation. It raises interesting questions regarding the absence of antibody detection following earlier transfusions and whether the observed biochemical changes post transfusion reflect clinically relevant haemolysis.

References:

1. Reid ME, Lomas-Francis C, Olsson ML. The Blood Group Antigen FactsBook, 3rd edition. Oxford, UK: Academic Press/Elsevier; 2012.
2. Daniels, Geoff. (2013). Human Blood Groups, 3rd edition. 524-544. 10.1002/9781118493595.index.

Implementing B19 and HAV NAT testing: a structured, phased approach.

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Aim:

To implement Parvovirus B19 (B19) and Hepatitis A virus (HAV) nucleic acid testing (NAT) on all donations where plasma may be sent for fractionation, ensuring compliance with fractionation requirements while enabling the introduction of Individualised Donor Assessment (IDA) and maintaining operational continuity.

Method:

A national implementation was conducted across Donation Accreditation laboratories in Auckland and Christchurch. A structured, six-phase project approach was applied, comprising preparation; solution assessment and configuration; validation and regulatory approval; staged deployment of new middleware into existing NAT workflows; subsequent B19/HAV NAT deployment; and post-go-live monitoring. The selected solution utilised pooled testing (minipools of 16) on the existing Grifols Procleix Panther platform, supported by the Xpress pooler and Bloodstream middleware. Implementation included system configuration, interface development, standard operating procedure development, and end-to-end user acceptance testing. A comprehensive validation strategy was applied, including equipment qualification, method validation, interface validation, external quality control material evaluation, and system integration testing. Deployment followed a staged go-live model, with middleware introduced one site at a time prior to the new testing regime, supported by production verification testing, structured training, change management, and post-implementation monitoring.

Results:

The phased implementation approach enabled successful integration of B19/HAV NAT into existing NAT workflows without disruption to routine operations. Validation activities confirmed system performance, data integrity, and compliance with regulatory and quality requirements. The staged deployment reduced operational risk and supported user adoption. Critical success factors included strong governance, proactive risk management, vendor collaboration, and comprehensive project implementation, validation and training strategies.

Conclusion:

A structured, phased implementation approach provides a robust model for introducing new donor screening capabilities in regulated environments. This methodology supports safe adoption of new testing, maintains operational continuity, and facilitates future flexibility in testing strategy while enhancing plasma safety and supporting equitable donor eligibility policies.

Plasma to Port – Implementing sea freight at the New Zealand Blood and Organ Service

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Aim:

The New Zealand Blood and Organ Service (NZBS) sends frozen plasma to CSL Behring in Melbourne for fractionation. Increasing plasma volumes and operational demands highlighted the need for a more reliable, practical, cost-effective, and environmentally sustainable transport model than air freight. The aim was to implement sea freight for transporting frozen plasma from NZBS to CSL Behring.

Method:

Transporting pallets of plasma in reefer shipping containers, known as sea freight, was implemented in collaboration with CSL Behring. The project included updating plasma boxing processes and materials, developing a container loading procedure, and changes to transport scheduling. Temperature-loggers were required to ensure CSL Behring's frozen plasma temperature specifications were met. Performance qualification was undertaken on the initial shipments departing Christchurch to validate temperature control and process reliability.

Results:

While the performance qualifications on the first three containers were successful, temperature deviations were noted during loading of container four. This prompted an internal review of the procedure and container loading practice. In addition, representatives from CSL Behring observed the process and provided guidance. Several key improvements were made as a result. Sea freight resumed and the subsequent performance qualifications were successful. These learnings were applied when sea freight was implemented in Auckland.

An NZBS representative visited CSL Behring to observe the receipt and unloading of a container dispatched from Auckland, enabling an end-to-end understanding of the sea freight process.

Conclusion:

Sea freight has been successfully implemented, with over 60 containers of frozen plasma transported from Christchurch and Auckland. Early challenges were identified and resolved through collaborative engagement with CSL Behring, resulting in a robust and reliable transport process. The transition from air to sea freight has delivered operational, logistical, and sustainability benefits while maintaining product quality and compliance with temperature requirements.

Bridging the gap, taking therapy to the patient: Establishing a new apheresis service in the southern region of New Zealand

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Aim: Strategic Development and Implementation of a Comprehensive Therapeutic Apheresis Service for the Southern South Island of New Zealand through collaboration between New Zealand Blood Service and Health New Zealand.

Background: Therapeutic apheresis (TA) is a critical, often lifesaving, treatment for autoimmune, neurological, and haematological conditions. Despite its clinical value, access to specialised services remains limited in many regions, leading to treatment delays and patient transfers. The Southern region of the South Island of New Zealand provides care for 357,000 people over a geographical area of over 62,300 square kilometres. Previously, membrane filtration plasma exchange was available only via admission to the Dunedin Hospital Intensive Care Unit (ICU)—even for outpatients—or emergency transfer to Christchurch Hospital.

Methods: A multi-faceted approach undertaken to establish a regional TA unit, including identifying key stakeholders, securing capital investment, recruitment of specialised nursing staff, and developing clinical protocols aligned with American Society for Apheresis (ASFA) guidelines. Extensive consultation and strategic partnerships resolved operational challenges, resulting in development of a comprehensive governance framework, clearly defining roles, responsibilities, and risk stratification for after-hours care (7 am–10 pm), ensuring safe and efficient service delivery.

Results: Within 12 months, the service performed 57 apheresis procedures. Key milestones included establishing an on-call service, reducing patient transfers and saving over 100 ICU bed days. Notably, 26.3% of procedures were performed on the Medical Day Unit avoiding hospital admission altogether and improving patient experience. Implementation of standardised documentation and a TA registry enabled continuous monitoring and audit, demonstrating a very low rate of adverse events (1 mild in 57 procedures).

Conclusion: A structured, collaborative and multidisciplinary approach is essential for successful TA Service implementation. This initiative has significantly improved equitable access to specialised care in a geographically dispersed region, enhanced patient outcomes, and reduced reliance on critical care resources. The model provides a scalable framework for addressing regional disparities in access to complex treatments.

Trends in the use of immunoglobulin for neurological conditions in New Zealand

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Immunoglobulin (Ig) usage is growing in New Zealand at approx. 11% per annum, significantly exceeding population growth (0.7% in 2025). Almost 750 000g was issued to over 2000 patients from 01/01/2025 to 31/12/2025. The most common indication was chronic inflammatory demyelinating polyneuropathy (19.2% of total use).

Aim: To evaluate trends in Ig usage for neurological conditions in NZ over the last 5 years.

Method: Retrospective analysis of Ig usage for neurological conditions for the past 5 years was undertaken, using data collected from NZ Blood Service.

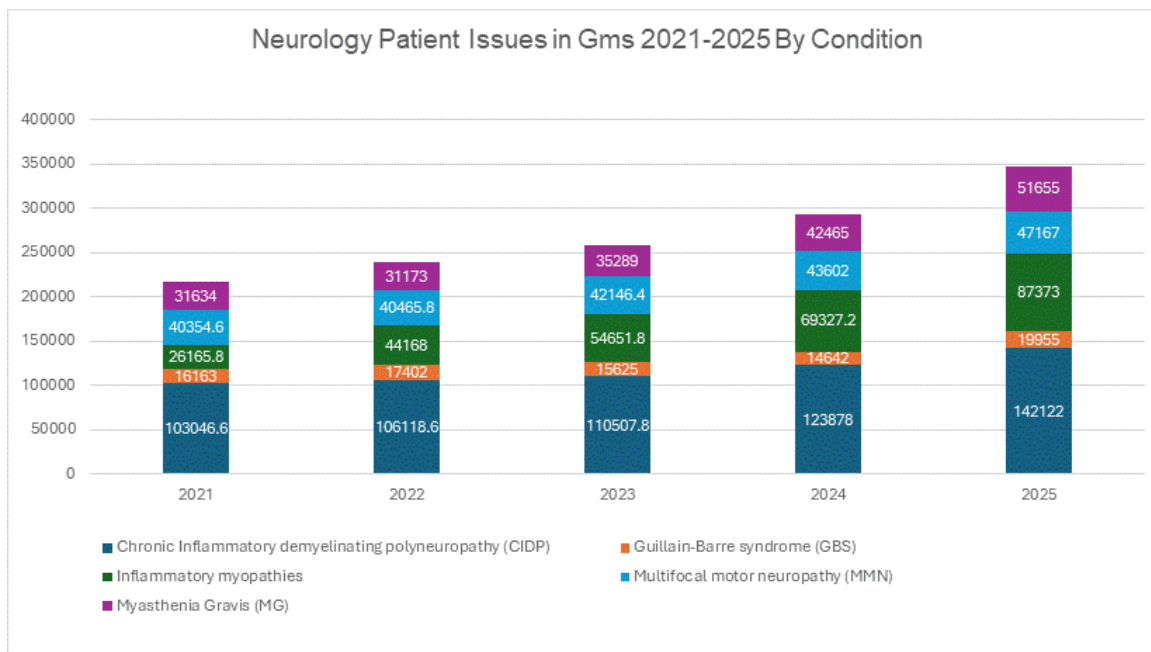
Results: In 2025, neurology patients accounted for approximately 46.7% of total Ig use for 558 patients (26.9% of recipients). The commonest neurological conditions are described in Table 1.

Table 1

New Zealand population – 5.3 million	CIDP:	GBS:	IM:	MMN:	MG:
Ig use (grams)	142 122	19 955	87 373	47 167	51 655
Ig use (g/1000 population)	26.82	3.77	16.49	8.90	9.75
% change in grams from 2021 to 2025	+37.9%	+23.5%	+333.9%	+16.9%	+63.3%
# patients treated with Ig	185	102	128	55	91
# treated patients/ 100 000 population	3.49	1.92	2.42	1.04	1.72
Ig use (g/patient)	768.23	195.64	682.60	857.58	567.64

Table 2: Ig issued for all neurological conditions 2021 – 2025

		Issue Date				
Condition Text		2021	2022	2023	2024	2025
Chronic Inflammatory demyelinating polyneur..	Distinct count of Patient ID	162	165	170	179	185
	Weight(gms)	103,047	106,119	110,508	123,878	142,122
Guillain-Barre syndrome (GBS)	Distinct count of Patient ID	86	98	92	80	102
	Weight(gms)	16,163	17,402	15,625	14,642	19,955
Inflammatory myopathies	Distinct count of Patient ID	60	88	92	116	128
	Weight(gms)	26,166	44,168	54,652	69,327	87,373
Multifocal motor neuropathy (MMN)	Distinct count of Patient ID	46	51	51	49	55
	Weight(gms)	40,355	40,466	42,146	43,602	47,167
Myasthenia Gravis (MG)	Distinct count of Patient ID	65	63	74	82	91
	Weight(gms)	31,634	31,173	35,289	42,465	51,655



Immunoglobulin utilisation increased across all neurological indications 2021 - 2025, with growth driven predominantly by chronic autoimmune conditions. While patient numbers rose modestly in CIDP, total Ig use increased disproportionately, suggesting escalation in dosing intensity or treatment duration. The most marked rise occurred in inflammatory myopathies, where both patient numbers and utilisation more than doubled; clinical practice shifted around 2023 toward broader use of Ig—particularly in dermatomyositis—along with treatment strategies increasing the number of treated patients and the average treatment intensity per patient. In contrast, acute conditions such as Guillain-Barré syndrome remained relatively stable, reflecting expected epidemiological variation.

Conclusion:

As the global demand for Ig increases, monitoring trends in usage is essential to ensure sustainability of plasma collections for Ig manufacture from NZ sourced-plasma. Further participation in clinical research will strengthen the evidence base and inform optimal, guideline-driven practice.

Trends in the use of immunoglobulin for haematological conditions in New Zealand

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Immunoglobulin (Ig) usage is growing in New Zealand at approx. 11% per annum, significantly exceeding population growth (0.7% in 2025). Almost 750 000g was issued to over 2000 patients from 01/01/2025 to 31/12/2025.

Aim: To evaluate trends in Ig usage for haematological conditions in NZ over the last 5 years.

Method: Retrospective analysis of Ig usage for haematological conditions for the past 5 years was undertaken, using data collected by NZ Blood Service.

Results: In 2025, haematology patients accounted for approximately 16.37% of total Ig use for 548 patients. The two commonest conditions are described in Table 1.

Table 1

New Zealand population – 5.3 million	Acquired Hypogammaglobulinaemia secondary to haematological malignancy (AHSHM):	Adult Immune Thrombocytopenic Purpura (ITP):
Ig use (grams)	99432	22030
Ig use (g/1000 population)	18.76	4.16
# patients treated with Ig	427	121
# treated patients/ 100 000 population	8.06	2.28
Ig use (g/patient)	232.86	182.07
% change in grams from 2021 to 2025	+39.1%	-18.8%

Ig use for AHSHM in NZ increased rapidly over the study period; however, international comparisons show substantially higher treatment rates in countries such as Australia—up to fourfold greater per 100,000 population. This difference may reflect broader access to novel therapies (e.g., daratumumab, CAR-T) and increased life expectancy.

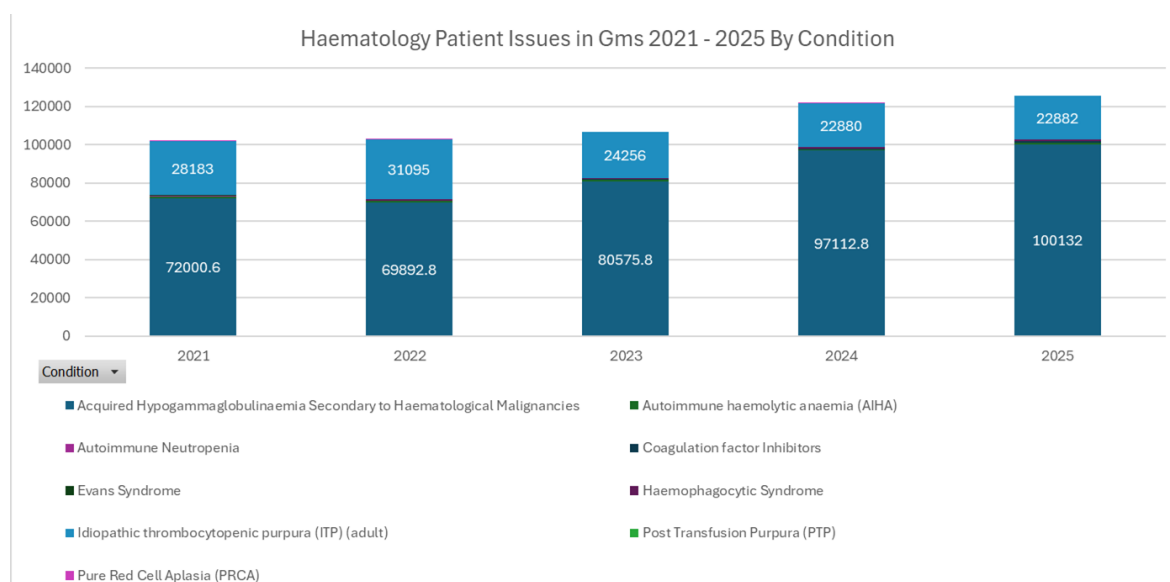
In contrast, Ig use for adult ITP has declined in recent years, likely due to alternative second-line treatments such as thrombopoietin receptor agonists (TPO-RAs) and anti-CD20 monoclonal antibodies. Governance criteria—an initial 1 g/kg dose with a second 1 g/kg only if response is inadequate—may also have reduced Ig utilisation for this indication.

Conclusion:

As the global demand for Ig increases, monitoring trends in usage is essential to ensure sustainability of plasma collections for Ig manufacture from NZ sourced-plasma. Further participation in clinical research will strengthen the evidence base and inform optimal, guideline-driven practice.

Table 2: Ig issued for all haematological conditions 2021 – 2025:

Condition		2021	2022	2023	2024	2025
Acquired Hypogammaglobulinaemia Secondary to Haematological Malignancies	Patient Count	278	289	321	370	430
	Weight(gms)	72,001	69,893	80,576	97,113	100,132
Autoimmune haemolytic anaemia (AIHA)	Patient Count	8	5	7	3	4
	Weight(gms)	997	777	1,128	130	755
Autoimmune Neutropenia	Patient Count	1				1
	Weight(gms)	130				140
Coagulation factor Inhibitors	Patient Count	1		2	2	3
	Weight(gms)	160		472	400	720
Evans Syndrome	Patient Count	3				1
	Weight(gms)	180				90
Haemophagocytic Syndrome	Patient Count	1	7	3	4	1
	Weight(gms)	200	902	92	955	650
Idiopathic thrombocytopenic purpura (ITP) (adult)	Patient Count	123	134	105	121	124
	Weight(gms)	28,183	31,095	24,256	22,975	22,882
Post Transfusion Purpura (PTP)	Patient Count				1	
	Weight(gms)				180	
Pure Red Cell Aplasia (PRCA)	Patient Count	2	3		2	
	Weight(gms)	200	418		268	



Evaluating digital morphology platforms in haematology: Impact on workflow and learning

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¹Ng Teng Fong General Hospital, Singapore, Singapore

Aim:

Digital morphology platforms such as CellaVision are increasingly integrated into clinical haematology laboratories to improve workflow efficiency, standardisation, and laboratory education. However, their effectiveness as a primary learning tool for morphology training remains uncertain. This study evaluated both the impact of digital morphology systems on laboratory workflow and medical laboratory technologists' (MLTs) perceptions and learning experiences using CellaVision compared with conventional manual microscopy.

Methods:

A combined operational and educational evaluation was conducted in the haematology laboratory at Ng Teng Fong General Hospital, Singapore. Peripheral blood smear samples analysed using the Sysmex DI-60 system were compared with manual differential counting to assess turnaround time, efficiency, and morphology reporting performance. For the educational evaluation, two questionnaire-based surveys were conducted among MLTs (n=18 and n=16) to evaluate perceptions, learning effectiveness, confidence, and engagement compared with manual microscopy. Likert-scale responses were analysed using medians, interquartile ranges, and the Wilcoxon signed-rank test.

Results:

The DI-60 system improved workflow efficiency, reducing average review time by approximately 48% compared with manual microscopy. Strong correlations ($r > 0.86$) between digital and manual differential counts supported comparable analytical performance. In the educational evaluation, 78% of respondents were likely or very likely to adopt CellaVision as a learning tool. However, manual microscopy received higher perceived scores for morphology learning effectiveness (median 4.20 vs 3.21) and learner engagement (median 4 vs 3). Manual microscopy was also perceived to provide greater confidence in identifying rare or abnormal cells. Wilcoxon signed-rank analysis demonstrated a statistically significant difference in engagement favouring manual microscopy ($p = 0.029$). Overall, most respondents (62.5%) preferred a blended learning model.

Conclusion:

Digital morphology systems enhance efficiency and support morphology training; however, manual microscopy remains essential for developing core morphological interpretation skills and confidence. A blended learning model integrating digital imaging with traditional microscopy may provide the most effective training strategy.

A case report of Matuhasi-Ogata phenomenon in a neonate

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Background:

The Mathuhasi-Ogata phenomenon is characterised by non-specific adsorption of antibodies to red cells pre-sensitised with a specific IgG antibody, in the absence of the corresponding antigen. This leads to the detection of both specific and non-specific antibodies in red cell eluates, complicating interpretation of serological results.

Aim:

We present a case report of Matuhasi-Ogata phenomenon in a neonate with a positive direct antiglobulin test (DAT) and unexpected detection of anti-K antibody in the eluate.

Method:

A 28-year-old antenatal patient, O Rh(D) positive, with known anti-K alloimmunisation presented at 16 weeks gestation. Anti-K antibody titres remained stable at 512 between 16-28 weeks gestation. Partner phenotyping determined a K- k+ phenotype and non-invasive prenatal analysis (NIPA) testing predicted a K- fetal phenotype.

Following delivery, a cord sample was tested for ABO/RhD, DAT, elution studies with antibody identification and phenotyping.

Results:

The neonate was A Rh(D) positive with a weakly positive (0.5+) DAT. Phenotyping confirmed the baby was K-, consistent with NIPA results. Review of the baby's history indicated no clinical or biochemical evidence of haemolytic disease of the newborn (haemoglobin 196 g/L; bilirubin 28 µmol/L). Elution studies identified anti-A, consistent with passively transferred maternal IgG anti-A bound to A antigens on baby's red cells, in addition to an unexpected anti-K antibody. The detection of anti-K in the eluate, in the absence of K antigens on the red cells, in combination with anti-A, supports non-specific adsorption rather than true antigen-antibody binding. This is consistent with Matuhasi-Ogata phenomenon.

Conclusion:

This case highlights the diagnostic complexity of non-specific antibody adsorption in eluates. Recognition of the Matuhasi-Ogata phenomenon is critical to prevent misinterpretation of non-specific antibodies as clinically significant alloantibodies, leading to unnecessary investigation and inappropriate clinical concern. Correlation of serological results with phenotype/genotype and a comprehensive transfusion history remain essential for accurate interpretation.

Impact of therapeutic blood donations - building the case for collaboration between national blood donation agencies and haemochromatosis patient organisations around the world.

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³Haemochromatosis International, , UK

Outline:

This review examines how strategic collaboration between Australian Red Cross Lifeblood and Haemochromatosis Australia has translated evidence into action, resulting in measurable improvements for therapeutic donors, the national blood supply, and the haemochromatosis community.

Background:

Despite accepting blood donations from people with haemochromatosis since 1998, it is only since 2013 that initiatives identified through regular communication between representatives of Lifeblood and Haemochromatosis Australia, have been proactively implemented to drive these improvements. Examples include the launch of the High Ferritin App; the inclusion of a therapeutic donor with haemochromatosis in Lifeblood's Donor Research Consultation Committee; the acceptance of plasma donations from people with haemochromatosis; translation of Lifeblood's research findings (Beyond the Iron Gate) into better donation experiences for haemochromatosis donors; improved messaging and appointment management for therapeutic donors; the introduction of a 'welcome' letter to therapeutic donors informing them about Haemochromatosis Australia and the Australian Haemochromatosis Registry; and targeted communication, via media releases and publications, to referring clinicians to encourage referral of eligible donors.

Conclusion

Therapeutic donors make a meaningful but often under recognised contribution to the national blood supply. Strengthened partnerships between blood services and haemochromatosis organisations can improve donor experience, reduce wastage and support global efforts to integrate therapeutic venesection into sustainable blood collection models.

Knowledge, Attitude, and Practices of Medical and Nursing Staff on HLA and Transplant at a Tertiary Care Centre in India

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¹AIIMS BHOPAL, Bhopal, India, ²AIIMS BHOPAL, Raisen, India, ³AIIMS BHOPAL, Bhopal, India

Aim:

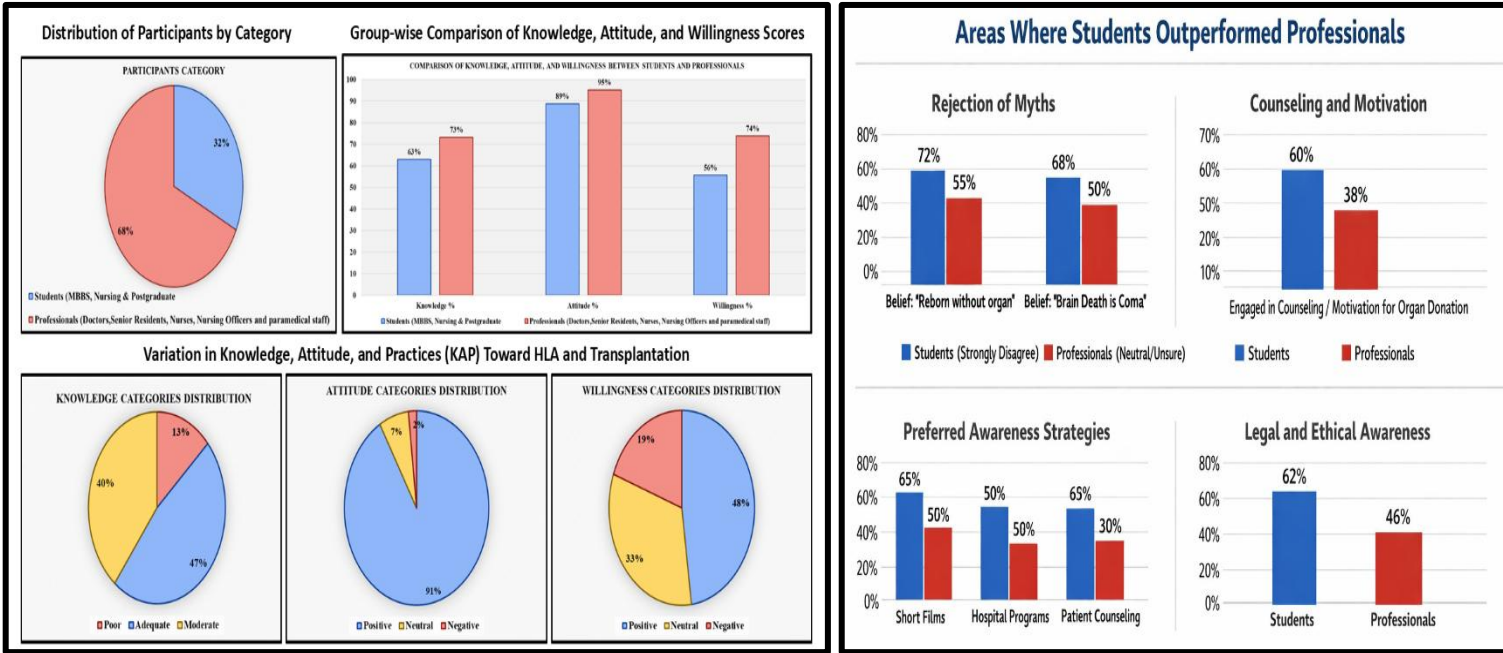
Transplantation is the most effective treatment for end-stage organ diseases, yet the gap between patients awaiting transplants and available donor organs remains significant. Healthcare professionals and students play a key role in influencing public perception and organ donation. This study aimed to assess Knowledge, attitude and practices of medical and nursing staff on HLA and transplant at a tertiary care centre in India and to identify gaps and barriers for guiding interventions.

Method:

An observational study was conducted at AIIMS Bhopal among 165 participants, including students and healthcare professionals. Data were collected using a structured, validated questionnaire assessing demographics, knowledge, attitudes, and willingness. It included 25 knowledge, 10 attitude, and 8 practice items. Knowledge was scored and converted to percentages. Attitude and willingness were measured on a Likert scale and converted to percentages. Data were analyzed using descriptive statistics and chi-square tests, with $p < 0.05$ considered significant.

Results:

Overall awareness was good, with professionals showing higher knowledge (73%) than students (63%), though gaps remained in registry, legal aspects, and myths. Attitude was highly positive in both groups (89% vs 95%), but family consent and emotional concerns limited impact. Willingness and practice were lowest (59% in students, 83% in professionals), reflecting poor participation in campaigns. Students excelled in rejecting myths, counselling peers, preferring grassroots strategies, and recognizing THOTA regulations and ethical safeguards.



Conclusion:

Despite strong awareness and positive attitudes, gaps persist in registry knowledge, legal understanding, and willingness, particularly among students. Targeted education, simplified registration processes, and tailored interventions addressing cultural and familial barriers are essential to improve organ donation rates in India.

Socio-ecological mapping of barriers and enablers for accessing immunoglobulin replacement therapy for patients with blood cancers

Ms India Read¹, Dr Catriona Parker¹, Associate Professor Leah Heiss¹, Dr Giannie Barsha¹, Dr Lauren Young¹, Prof Erica Wood¹

¹Monash University, Melbourne, Australia

Aim:

Identify factors influencing access to immunoglobulin (Ig) replacement therapy (IgRT) for patients with secondary immunodeficiency due to haematological malignancy, and to examine how these factors affect equitable access.

Method:

As part of the OPTIMAL Centre of Research Excellence in improving Ig use, people with lived experience of IgRT, haematologists, nurses (some representing consumer organisations), researchers, and those involved in Ig supply and policy were invited via the researchers’ networks to participate in an in-person co-design workshop in August 2025. Participants used evidence-informed patient personas to explore real-world barriers and enablers to IgRT access and delivery. Data were analysed using reflexive thematic analysis and themes were mapped to the socio-ecological model of healthcare.

Table 1. Participants

Participant type	Number of participants
Lived experience	4
Specialist medical practitioners	6
Nursing professionals/ consumer advocates	6
Ig supply	5
Policy officers	2
Researchers	6
Total	29

Results:

Twenty-nine mostly Victorian-based stakeholders participated in the workshop. Preliminary analysis indicates that IgRT delivery is shaped by interacting factors across multiple levels of the health system. At the:

- macro level: variation in funding models, policy settings, and geography contributes to inequitable access, particularly for patients in regional and remote areas.
- meso level; service delivery factors, including choice of infusion modality (intravenous vs subcutaneous), access to clinicians, patient education, and service navigation shape experiences of care.
- micro level; patient-specific factors including physical and cognitive status, health and digital literacy, language capabilities, financial constraints, and social support, further influence access and care.

These factors are interdependent and may act as either barriers or enablers depending on context.

Conclusion:

Access to IgRT in haematological malignancy is influenced by system, service, and patient-level factors beyond clinical indication alone. Addressing inequities in Ig access will require interventions at multiple levels that consider policy and funding models, service delivery and

care models, and individual patient resources and capabilities within the broader health system.

Engaging before enrolling: Reflections on a community-informed planning of a West Africa blood group genomics project

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¹Strategy and Research, Australian Red Cross Lifeblood, Brisbane, Australia, ²Strategy and Research, Australian Red Cross Lifeblood, Sydney, Australia, ³School of Health, University of the Sunshine Coast, Sunshine Coast, Australia, ⁴Faculty of Health, Queensland University of Technology, Brisbane, Australia

Aim:

We engaged with the Ghanaian community in Queensland as part of the planning phase for a new Australian Red Cross Lifeblood (Lifeblood)-led project, the West Africa blood group genomics project to share knowledge, seek feedback, and raise awareness of the proposed study.

Methods:

We undertook staged community engagement with African community groups. Initial consultation involved outreach to four organisations via email to seek early input into proposed study materials, recruitment approaches, and communication strategies. Two of four organisations—the Ghanaians in Queensland Association (GQA) and the Centre for Africa Research, Engagement and Partnerships (CARE-P) responded and provided detailed feedback.

A second engagement activity involved an in-person presentation to members of the Ghanaian community. Approximately 50 members participated in this session which included two presentations from Lifeblood: 1) an overview of blood groups and the role of Lifeblood in blood donation in Australia; and 2) the role of research in transfusion medicine, including findings from a previous blood group genomics studies from our team in a Kenyan cohort which informed the proposed project. Study aims, eligibility criteria, and planned activities of the proposed project were presented, followed by a Q&A session and an open discussion.

Results:

Feedback from GQA and CARE-P representatives directly informed revisions to participant information sheets, consent forms, and study protocols prior to ethics submission.

The engagement with members of the GQA was highly interactive. Participants asked insightful questions, offered constructive feedback, and expressed interest in the proposed study. The session also prompted interest in blood donation, with further enquiries about donor eligibility and donation processes.

Conclusion:

Early community engagement strengthened study design, ethics preparedness, trust-building and transfusion awareness. This approach will be extended to other West African diaspora communities. Conference attendees are invited to collaborate, join the project or assist with referral of eligible participants.

Advancing evidence-based immunoglobulin use and practice: The OPTIMAL NHMRC Centre of Research Excellence

Dr Lauren Young¹, Dr Giannie Barsha¹, Professor Dennis Petrie¹, Dr Laura Fanning¹, Prof David Burgner², Prof Jason Roberts³, A/Prof Anneke van der Walt¹, Associate Professor Leah Heiss¹, Dr James Daly⁴, Dr Sara Carrillo de Albornoz San Juan¹, Dr Adam Irving¹, Dr Khai Li Chai^{1,7}, Dr Thao Le¹, Assoc Prof Philip Crispin⁵, A/Prof Davinder Singh-Grewal⁶, Dr Catriona Parker¹, Ms India Read¹, Mr Jamie Jackson³, Mr Neil Waters¹, Professor Zoe McQuilten¹, Prof Erica Wood¹

¹Monash University, Melbourne, Australia, ²Murdoch Children's Research Institute, Melbourne, Australia, ³University of Queensland, Brisbane, Australia, ⁴Australian Red Cross Lifeblood, Brisbane, Australia, ⁵The Canberra Hospital, Canberra, Australia, ⁶University of Sydney, Sydney, Australia, ⁷St Vincent's Hospital, Melbourne, Australia

Aim:

OPTIMAL is an NHMRC Centre of Research Excellence (CRE) generating new knowledge and research capacity to inform policy; design, build & implement better systems for delivering immunoglobulin (Ig) therapy; and improve outcomes for patients. We present the structure, activities, and key achievements of the CRE to date.

Method and Results:

Governance & operations

- Stakeholder Advisory Committee: community, government & professional participation
- Steering Committee: investigators and PhD students, supported by operations team
- Stream-specific working groups for: (1) Ig replacement therapy for patients with blood cancers, and (2) immunomodulation in myasthenia gravis (MG) and Kawasaki disease (KD)

Research activities:

- Blood cancers: health systems design approaches to improve Ig delivery and patient experiences; dosing/pharmacokinetic and other observational studies; clinical practice guidelines (with European Hematology Association) and core outcome sets to guide and monitor practice
- New models of clinical demand (e.g. Ig vs novel therapies) using MGBase registry (for MG) and PAEDS (for KD) data
- Embedded health economic analyses to understand Australian costs, clinical outcomes and patient/practitioner preferences

Building research capacity:

- Supporting PhD scholarships, clinical fellowships and new early/mid-career researcher (EMCR) positions in health economics, health system design and pharmaceutical science, and funding EMCRC-led pilot studies
- EMCRC committee leads education/training opportunities, site visits, workshops with experts, and new research proposals

Communication & translation:

- National stakeholder/consumer engagement in project activities informs research priorities, enables project activities and will support translation
- Research is co-designed with stakeholders e.g. stakeholder workshop to map Ig service delivery (see companion abstract)
- Ideas, activities and progress shared via open meetings, educational webinars, and website

Conclusion:

OPTIMAL provides a dedicated 'home' for Ig clinical research in Australia, integrating research, education, capacity building and translation activities. Ongoing research is generating new clinical and health economic data to support policy, evidence-based guidelines and practice.

Emergency blood utilisation in the rural and regional aeromedical retrieval services in the Western New South Wales: A three-year retrospective review (2023-2025)

Miss Irene Chan¹

¹Nsw Pathology, Orange, Australia

Aim:

To evaluate the actual utilisation of emergency blood units issued to rural and regional helicopter retrieval services in Western New South Wales by comparing emergency unit issuance with subsequent transfusion usage over a three-year period (2023–2025).

Method:

A retrospective audit was conducted using laboratory information system data from Western NSW Health Pathology transfusion services. All emergency red cell units allocated for aeromedical retrieval missions between 1 January 2023 and 31 December 2025 were included. Allocation data were compared with transfusion, return, and discard records to determine actual clinical utilisation. Data collected included total emergency units issued, units transfused, units returned unused, and units wasted. Utilisation rates were calculated and analysed by year to identify trends and patterns in emergency blood use.

Results:

Across the three-year review period, a total of 448 emergency red blood cell units were allocated to support rural and regional aeromedical retrieval services across Western New South Wales. Preliminary analysis indicating clinical transfusion occurred in 46.2% (207) of allocated units, reflecting the requirement for immediate blood availability in time-critical scenarios. Wastage accounted for 3.3% (15) of total units, with remaining units returned unused. Despite a transfusion rate of 46%, wastage remained low at 3.3%, supporting the safety of current emergency blood provisioning while identifying opportunities to refine allocation strategies.

Conclusion:

This review highlights the importance of evaluating emergency blood unit utilisation within rural and regional helicopter retrieval services. Understanding the gap between emergency issue and actual transfusion supports evidence-based optimisation of emergency blood stock holdings, improves stewardship of a limited resource, and contributes to safer and more sustainable transfusion practices in geographically remote settings.

Implementation of low volume blood group and antibody (G&S) screening to reduce iatrogenic anaemia– a pilot project

Ms Pratima Chebrolu¹, Jess Cowley¹, Ms Kylie Rushford¹, Ms Amanda Ellison¹, Dr Joanna Loh^{1,2}, Ms Carolyn Greely¹, Dr Allison Mo^{1,2}

¹Monash Health, Melbourne, Australia, ²Monash University, Melbourne, Australia

AIM

Iatrogenic anemia can occur in hospitalised patients whom have impaired erythropoiesis and multiple blood draws. Haematology patients are amongst those most heavily transfused and frequently have blood group and antibody screens (G&S) samples taken. We studied the feasibility and effectiveness of changing from our 10mL EDTA tube to a new 6mL EDTA tube for G&S sampling.

METHODS

This prospective pilot study implemented 6mL G&S tubes for all patients admitted to the haematology ward over 15 days in January-February 2026, excluding patients with currently positive alloantibody screens. We compared a baseline '10mL' tube group over 12 days in July 2025 with the '6mL' tube pilot group. Successful implementation was defined as: 1) Reduction of at least 10% volume of blood collected in G&S tubes; 2) Less than 5% recollections needed.

RESULTS

The baseline '10mL' group had 78 samples from 38 patients and the '6mL' group had 88 samples from 47 patients. The average sample volume was less in the '6mL' vs '10mL' group (4.3mL vs 8.2mL, $p < 0.0001$), a 48% reduction. No samples in the '6mL' group required recollection. From the '6mL group', one patient had complex antibodies (two samples), one patient had a pan-reactive autoantibody (three samples) and two patients showed daratumumab interference (three samples). Notably, many G&S samples were not used to crossmatch for subsequent transfusion, but there was no difference between the two groups (72% from the '6mL' group and 67% from the '10mL' group, $p = 0.5$).

CONCLUSION

This pilot project demonstrated the successful implementation of smaller volume G&S tubes in haematology patients, without an increase in recollections and delay in blood product availability. Future work includes expanding to other wards, collecting more datapoints on anaemia and hospital blood usage rates. The high rates of samples not directly resulting in transfusion may be a potential target for reducing iatrogenic anaemia.

Enhancing haemovigilance data sharing through Power BI.

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¹New Zealand Blood Service, Auckland, New Zealand

Aim:

To make access to haemovigilance data timely, interactive, and engaging to support decision-making by key stakeholders.

Method:

Haemovigilance (HV) data are reported to the New Zealand Blood Service (NZBS) by hospitals across the country. These data are reviewed, cleaned, and published in the HV Annual Report. To improve access, up-to-date data were organised into two Power BI (Microsoft) reports: one focused on acute transfusion reactions (ATR), designed to support NZBS staff who liaise with hospital staff and patients, and another for donor adverse events (DAE), intended for use by blood collection staff.

The reports were designed to be easy to navigate with no specific training. The variables presented in the reports was selected iteratively based on user feedback.

Results:

Raw data from several different sources (including eProgesa, eTraceline, K2 Haemovigilance system) were transformed into interactive dashboards and reports.

The ATR report displays distribution of event types, quarterly progress of common events (allergic and febrile reactions), and grouping by sex at birth and age. Users can download data on individual hospitals. The DAE report presents donations by region, DAE types over time, grouping by sex at birth, fixed or mobile sites, and donation type.

The charts and tables are dynamic and interactive, enabling users to filter data and drill down to answer specific questions.

The reports were made widely available to authorised users on the organisational intranet. There has been a noticeable fall in the number of requests for bespoke data to the data analyst.

Conclusion:

Power BI has allowed patient-facing and donor-facing staff to explore data with the hope of reducing adverse events over time.

In the longer term, such access will enhance decision making, build confidence in the analysis of data, and greatly improve the speed at which new trends are detected.

Pregnancy and congenital dysfibrinogenemia: beating the odds

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¹Prince Of Wales Hospital, Randwick, Australia, ²University of New South Wales, Kensington, Australia, ³The Royal Hospital for Women, Randwick, Australia, ⁴NSW Health Pathology, ,

Background:

Fibrinogen is an essential plasma glycoprotein for clot formation. Congenital fibrinogen disorders are associated with increased risks of miscarriage, vaginal bleeding, placental abruption, post-partum haemorrhage, and thromboembolic events during pregnancy.

Aim:

To describe an individualised, safety focused management approach for pregnancy and birth in congenital dysfibrinogenemia, guided by limited formal recommendations.

Case Description:

A Polish-born woman two prior miscarriages at approximately ten weeks' gestation was found to have low fibrinogen levels and diagnosed with congenital dysfibrinogenemia, also present in her mother. No thrombotic history.

At 34 years old, she was referred from St Vincents Hospital at five weeks' gestation to the co-located Prince of Wales Hospital and Royal Hospital for Women for specialist monitoring and support. Care was coordinated through a multidisciplinary approach involving an Obstetric Haematologist and the Maternal Fetal Medicine team.

Antenatally, she received twice-weekly fibrinogen replacement, targeting a fibrinogen level ≥ 1.5 g/L in accordance with International Society on Thrombosis and Haemostasis guidance. She was iron replete.

Peripartum care included review of fibrinogen dosing, urgent fibrinogen measurement with twelve hourly monitoring, replacement to ensure fibrinogen level ≥ 1.5 g/L and intravenous tranexamic acid 1g prior to birth.

Postpartum management replacement aimed to maintain fibrinogen ≥ 1.5 g/L for three days following vaginal birth with oral tranexamic acid 1.5g three times daily for ten days and thromboprophylaxis until discharge.

A healthy boy was born at 39.9 weeks gestation, 3745 g, estimated blood loss 300 ml. She declined regional anaesthesia.

Discussion:

This case demonstrates that, despite significant obstetric risk, successful pregnancy outcomes in congenital dysfibrinogenemia are achievable through early referral, multidisciplinary care, and structured, individualised haemostatic management.

Epoetin alfa and beta dosing efficacy in patients declining blood products

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Aim: Epoetin alfa (EPO-a) and epoetin beta (EPO-b) are generally accepted by patients who decline blood products for the treatment of anaemia. However, limited literature exists regarding the optimal dosing of EPO for these non-subsidised indications. The Food and Drug Administration (FDA) recommends subcutaneous (SC) EPO-a 600 units/kg/week or 300 units/kg/day, depending on time pre-surgery. Some case reports describe intravenous EPO-b use. This study aims to describe the median haemoglobin (Hb) rise and EPO dosing used in patients declining blood products.

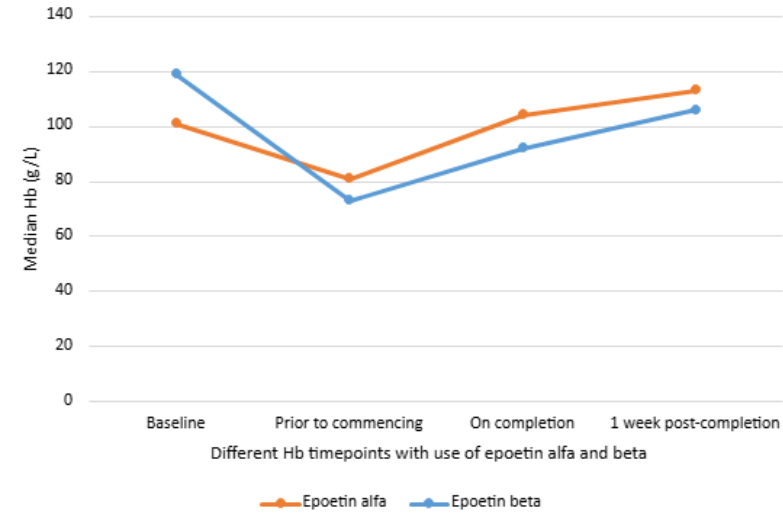
Method: In this retrospective study conducted at Victoria's largest public health service, pharmacy records identified adult patients treated with non-subsidised EPO-a and EPO-b from 1/1/2010 to 30/6/2025. Demographic data, Hb levels, EPO dosing and duration were extracted from hospital medical records.

Results: A total of 36 patients were identified; 4 received EPO-a and 32 received EPO-b. Median age was 65 years (IQR 63-70) for EPO-a and 74 years (IQR 61-81) for EPO-b. Most common indication for EPO-b was emergency treatment of severe anaemia (29/32, 90.6%) (Table 1). For EPO-a, patients received a median of 4 doses (IQR 3-5), with median 8 days (IQR 5-10) treatment. For EPO-b, patients received a median of 5 doses (IQR 2-6), with median 6 days (IQR 3-11) treatment. EPO-a dosing included 300 units/kg IV/SC alternate days (n=2, 50%) and 10,000 units SC 3 times a week (n=2, 50%). Most common EPO-b doses were 300 units/kg IV/SC daily (13/32, 40.6%) or alternate days (8/32, 25%). Median Hb increased by 20 g/L (IQR 16-27) with EPO-a and 16 g/L (IQR 12-24) with EPO-b following treatment (Figure 1).

Table 1. Indications used for epoetin alfa and beta

Indication of epoetin (n, %)	Epoetin alfa (n = 4)	Epoetin beta (n = 32)
Pre-surgery	0	2 (6.3%)
Emergency treatment of severe anaemia	2 (50%)	29 (90.6%)
Chemotherapy augmentation of haemoglobin	2 (50%)	1 (3.1%)

Figure 1. Median haemoglobin levels throughout epoetin alfa and beta treatment course



Conclusion: EPO-a dosing of 300 units/kg IV/SC alternate days or 10,000 units SC 3 times a week, and EPO-b dosing of 300 units/kg IV/SC daily or alternate days were effective in increasing the median Hb of patients treated for severe anaemia.

Assessment of albumin utilisation and prescribing practices: a five-year retrospective review

Miss Ruby Garland¹

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Aim:

Albumin is a blood product with evidence of benefit in selected patient cohorts; however, its use is less consistently monitored than other transfusion therapies. Baseline albumin prescribing practices at our institution were previously unknown. This study aimed to characterise albumin utilisation and identify areas for targeted assessment of compliance with evidence-based prescribing practices.

Methods:

A single-centre retrospective electronic audit was conducted of patients who received 4%, 5%, or 20% albumin between 1 January 2020 and 31 December 2025. Albumin used for extracorporeal circuits was excluded. For analysis, 4% and 5% albumin were combined into a single 5% category. Data was analysed using Microsoft Excel.

Results:

There were 28,952 prescriptions of 20% albumin administered to 4,147 patients across 6,960 admissions, equating to 2,952,149 mL. Albumin 5% accounted for 21,269 prescriptions administered to 8,012 patients across 8,804 admissions, totaling 8,760,781 mL. The most common volume of 20% albumin administered per admission was 101–200 mL (34.2%), while for 5% albumin it was 251–500 mL (41.4%). Median annual albumin volume per admission remained stable throughout the study period. Cardiothoracic surgery accounted for the highest number of 5% albumin prescriptions, while gastroenterology accounted for the highest number of 20% albumin prescriptions. Of all 5% albumin orders, 73.7% were prescribed in the intensive care unit (ICU). Indications were undocumented in 49,814 of 50,269 prescriptions. The most common pre-administration serum albumin level for 20% albumin was <25 g/L (31.7% of total volume administered), while for 5% albumin it was 35–49 g/L (24.6%).

Conclusion:

Albumin utilisation remained relatively stable over the study period, with most 5% albumin administered in ICU. The high rate of undocumented indications, substantial use of 20% albumin outside recommended thresholds and indications, and high utilisation in areas with limited supporting evidence highlight the need for targeted governance and optimisation of prescribing practices.

Implementation and outcomes of a nurse-led pre-operative anaemia optimisation pathway in a tertiary New Zealand hospital

Mrs Manpreet Gill¹

¹Health New Zealand | Te Whatu Ora - Counties Manukau, Manukau, New Zealand

Aim:

Pre-operative anaemia is associated with increased peri-operative transfusion, postoperative complications, and poorer surgical outcomes. A nurse-led patient blood management (PBM) pathway was implemented within a tertiary New Zealand hospital to improve identification and optimisation of anaemia prior to major elective surgery.

Method:

A retrospective review of patients referred to a nurse-led pre-operative anaemia optimisation service over a 12-month period was undertaken. Patients undergoing major elective surgery with suspected or confirmed anaemia and/or iron deficiency were referred through a dedicated PBM pathway. Data collected included referral specialty, anaemia prevalence, PBM intervention rates, iron therapy utilisation, haemoglobin (Hb) response following intervention, and peri-operative red blood cell (RBC) exposure.

Results:

A total of 331 patients were reviewed during the study period, of whom 220 (66%) were anaemic at referral. PBM involvement occurred in 181 patients, with 165/220 (75%) anaemic patients receiving iron replacement therapy. Intravenous iron was the predominant optimisation strategy. Clinically meaningful Hb improvement was observed following PBM intervention, with several patients demonstrating Hb increases greater than 30–50 g/L and multiple patients achieving pre-operative Hb ≥ 130 g/L. Referrals were received across multiple surgical specialties, predominantly general surgery and gynaecology. Despite a high burden of anaemia and complex surgical case mix, peri-operative RBC utilisation among PBM-managed patients remained low. Late referrals continued to limit opportunities for full pre-operative optimisation in some patients.

Conclusion:

A nurse-led PBM pathway enabled peri-operative anaemia optimisation across multiple surgical specialties within a tertiary hospital setting. The service demonstrated ongoing multidisciplinary engagement, high rates of anaemia intervention, meaningful haemoglobin improvement, and low peri-operative transfusion exposure. Earlier referral pathways may further improve opportunities for pre-operative optimisation and reduce avoidable transfusion exposure.

Audit out of hours packed red blood cell transfusion: documentation and guideline compliance at Cairns Hospital of medical and surgical patients.

Miss Kylie Grevell¹

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Aim:

To evaluate the clinical indications for out of hours packed red blood cell transfusions in medical and surgical patients at Cairns Hospital and assess the compliance with transfusion guidelines and documentation.

Method:

This retrospective clinical audit was conducted at a tertiary hospital in Far North Queensland. Medical records of patients who received out-of-hours PRBC transfusions between 2200 and 0600 hours over a six-month period from October 2025 to March 2026 were reviewed. A total of 139 patients from five medical wards and four surgical wards were included. Exclusion criteria included paediatric patients, intensive care unit (ICU), theatre and emergency department patients, day unit or outpatient transfusions, and patients managed under massive transfusion protocols or emergency haemorrhage scenarios.

Data collected included timing of transfusion, documented clinical indication, pre-transfusion haemoglobin (Hb) level, number of units transfused, and documented transfusion-related reactions. Principal analyses assessed compliance with institutional and national transfusion guidelines, appropriateness of pre-transfusion Hb thresholds, and completeness of clinical documentation.

Results:

A total of 139 out-of-hours PRBC transfusion episodes were identified. Common indications included active bleeding, symptomatic anaemia, peri-procedural support, gastrointestinal bleeding, post-operative bleeding and haematological malignancy-related anaemia. Most transfusions occurred at Hb levels below 70 g/L, consistent with restrictive transfusion practice; however, some transfusions were initiated above recommended thresholds. Single-unit transfusions were common, although multiple-unit transfusions occurred in patients with ongoing haemorrhage or significant blood loss. Documentation compliance varied across clinical areas. While most records included Hb level, timing and number of units transfused, incomplete documentation was identified in several cases, including unclear indications, limited symptom documentation and inconsistent recording of transfusion reactions or post-transfusion reassessment.

Conclusion:

This audit identified moderate compliance with institutional and national transfusion guidelines for out-of-hours PRBC transfusions at Cairns Hospital. While most transfusions were clinically appropriate and aligned with restrictive transfusion practices, variability was identified in pre-transfusion haemoglobin thresholds and completeness of clinical documentation. Inconsistent recording of clinical indications, symptom burden, and post-transfusion reassessment highlighted opportunities for improvement. Strengthening documentation practices and reinforcing adherence to evidence-based transfusion guidelines may improve patient safety, support appropriate utilisation of blood products, and reduce potentially avoidable out-of-hours transfusions.

Haemoglobin incrementation following red cell transfusion in patients with non-clinically significant cold-reactive allo-antibodies: a post hoc analysis

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Aim:

The presence of deemed non-clinically significant (NCS) cold allo-antibodies (Anti-Le^a, -Le^b, -Lua, -M, -N, and -P1) are frequently encountered during pretransfusion testing and although believed to have limited thermal amplitude and haemolytic potential, concerns remain regarding their impact on haemoglobin rise and whether blood warming should be used. We aimed to first determine whether transfusion of red cells, at room temperature, to recipients who have NCS alloantibodies results in lower-than-expected increments in the recipients' haemoglobin levels, for the volume of blood transfused, and whether there is evidence of haemolysis.

Method:

A retrospective analysis of 14 adult patients identified with NCS alloantibodies was conducted across a tertiary care centre between 2023 to 2025. 49 units of red cells were transfused in 33 transfusion events among the patients. In 6 transfusion events, active bleeding was present at the time of transfusion, so these events were excluded. The red cell alloantibodies identified were: 10 anti-M, 2 anti-Lua, 1 anti- Le^{a/b} and 1 anti-P1. The expected increment in haemoglobin (based on patient's weight) was compared to the actual haemoglobin increment with each unit transfused. Secondary outcomes included evidence of haemolysis.

Results:

Our results found, in 7 patients (26%), the increment met or exceeded the expected haemoglobin incrementation. In the remaining 20 (74%), the mean reduction in Hb incrementation was 4g/L, and 44% (range 2 – 100%) of the expected weight-based increment in haemoglobin per unit of red cells transfused. A rise in LDH (>250) occurred following 8 of the transfusions in which haemoglobin increments were inadequate (40%).

Conclusion:

Overall, these findings are suggestive that patients with NCS cold alloantibodies experienced a lower-than-expected haemoglobin incrementation. We propose a further prospective trial of transfusing red cells through blood warmers to patients with identified cold allo-antibodies.

Management of a Bombay phenotype (Oh) in pregnancy

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Background:

O_h phenotype is a rare blood type for which donor units may not be readily available. Antenatal management of O_h individuals remains complex in view of maternal and foetal considerations. There is also a lack of guidance on foetal monitoring in O_h pregnancies with case reports describing Haemolytic Disease of Foetus and Newborn (HDFN) of varying severity. Herein, we describe a case of O_h pregnancy with anaemia.

Case Description:

A 30-year-old Indian lady with a history of anaemia, immune thrombocytopenia and known O_h phenotype presented to the Obstetric Haematology clinic at 20 weeks gestation. Haemoglobin was 8.4g/dL with a ferritin of 4.3ug/L and B12 of 135pmol/L. Platelet counts was normal. Serologic testing demonstrated anti-H and warm reacting autoantibody. Anti-Le^b was also detected previously.

She received iron and B12 replacement both orally and parenterally. At 35+1 weeks, her haemoglobin improved to 11g/dL. As she required aggressive iron replacement for anaemia across pregnancy, decision was made to hold off autologous donation to avoid precipitating anaemia pre-delivery. 3 O_h donors were contacted for donation at term to ensure availability of liquid units in event of any unexpected bleeding.

Due to poor correlation with anti-H titres and HDFN risk, regular middle cerebral artery dopplers and growth monitoring ultrasounds were performed with normal readings.

Patient however had pre-term labour at 36+1 weeks undergoing emergency caesarean section with 800ml estimated blood loss. Haemoglobin fell to 7g/dL on post-op day 2. She received an O_h frozen washed unit and intravenous iron. She remained well postnatally with normalization of haemoglobin and ferritin. Baby was also well with no anaemia.

Conclusion:

Active patient blood management and close multidisciplinary coordination between various specialties and the bloodbank is key to minimise transfusion requirements and ensure successful outcomes in O_h pregnancies.

How many blood tests are too much in a small child? Can we reduce blood loss from frequent blood sampling?

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¹Perth Children's Hospital, Nedlands, Australia, ²PathWest Laboratories, Nedlands, Australia

Background:

Anaemia due to iatrogenic blood loss is well recognised; however, blood loss from frequent paediatric blood sampling is less well documented, particularly in patients weighing less than 10kg. The Oncology / Haematology inpatient ward introduced a guideline to help reduce blood loss from frequent blood sampling in this cohort.

Aim:

To assess compliance with the ward-based blood draw policy for patients less than 10kg and 20kg, including measuring blood transfusion requirements.

Method:

Patients weighing <10kg were identified, and blood sample volumes were monitored for two-weeks. Transfusion data were obtained from the Transfusion Medicine Unit (TMU). Patients weighing 10-20kg were audited for benchmarking purposes.

Results:

Ten patients were audited over two weeks: five <10kg and five 10-20kg. Diagnoses included Acute Lymphoblastic Leukaemia (ALL), Neuroblastoma, Severe Combine Immunodeficiency, and patients undergoing Haematopoietic Stem Cell Transplantation. 126 blood sampling days were reviewed.

< 10kg: weights ranged from 3.74-9.1kg (median 8.03kg) with 1-8 blood draws per day and total daily volumes of 3-78mL removed (median 3mL). 0.13-10.71% of patients blood volume (median 1.67%) were removed per day. Haemoglobin ranged from 24-129 g/L and platelet counts from 2-425 x10¹²/L. Patients received a total of 1669mL Red Blood Cells (RBC), 1805mL Platelets and 160mL FFP.

10-20kg: weights ranged from 11.6-19.35kg (median 17kg), with 1-5 daily blood draws and total volumes 9-80mL removed. 0.8%-6.4% patients' blood volume (median 2.06%) were removed per day. Haemoglobin ranged 37-153 g/L and platelets 2-203 x10¹²/L. Patients in this cohort received blood 2481mL RBC and 2915 Platelets.

Conclusion:

Blood sampling in patients weighing less than 10kg was largely compliant with the guideline. Despite compliance, some patients had up to 10% blood volume removed in one day. Medical and nursing staff need to consider frequency of blood tests, especially in those younger patients. Future initiatives will aim to review blood collections on other paediatric wards with aim to further minimise both discard volumes and frequency of blood draws.

Can we avoid pre-medications in paediatric patients having regular transfusions and allergic reactions?

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Background:

Blood transfusions are not without risks; however, literature shows mild allergic are often caused by donor proteins being seen as 'allergens' by the recipient's body. As such, future transfusions won't necessarily cause allergic reactions if these proteins are absent in subsequent donors.

At this tertiary paediatric hospital, current practice is to administer pre-medications to patients with previous mild allergic transfusion reactions, causing delayed discharges due to sedation.

There is a theoretical increased risk of infection and perhaps relapse with frequent use of steroids in these patients.

Aim:

To review and align current practice with evidence-based practices of not administering pre-medications to patients who have previously experienced a mild allergic transfusion reaction.

Method:

A six-month trial period was undertaken where no pre-medications were administered to patients who had experienced a previous mild allergic transfusion reaction.

Inclusion criteria:

- Red Blood Cell (RBC) and Platelet transfusions with or without a previously reported mild allergic transfusion reaction.

Exclusion criteria:

- Any other type of blood product transfusion
- Previously reported anaphylactic / anaphylactoid transfusion reactions
- IVIg
- Granulocytes transfusions

Results:

The trial ran for six months, across all wards and day treatment units of the hospital. During this time there were eleven reported transfusion reactions, with six being mild allergic reactions. All 6 allergic reactions were to platelets. Two different patients reported mild allergic transfusion reactions on two occasions, however no pre-medication was administered. Both patients received blood products after the reported reaction with no further reactions reported. No patient received a pre-medication prior to the reported reaction or for subsequent transfusions during the trial period.

Conclusion:

The trial was well received with no reported issues from departments during the trial. No risks to patient outcomes were identified from withholding pre-medications. This practice will now be embedded into routine policy and procedures.

In addition, both patients and parents preferred not to have drugs that induced drowsiness and caused longer time spent in the same day care clinic.

TRACE-PNG: A retrospective audit of high-risk transfusion burden and RBC utilization patterns in a tertiary hospital in Papua New Guinea

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Aim: To examine cumulative RBC exposure and patterns of repeat transfusion activity, and to identify potential target populations for transfusion surveillance and antibody screening strategies within a resource-limited transfusion service.

Method: TRACE-PNG (Transfusion Risk Assessment and Clinical Exposure - Papua New Guinea) is an ongoing three-year (2022-2024) retrospective transfusion audit conducted at PMGH. This analysis included all RBC-relevant transfusion requests received between January and December 2022. Requests were stratified according to cumulative RBC exposure into high-risk (≥ 3 units), increased-risk (2 units), low but real risk (1 unit), and unexposed (0 units) categories. Repeat-request patterns, RBC utilization burden, and ward-level clustering of RBC utilization were analysed descriptively at both request and patient levels.

Results: A total of 26,201 RBC-relevant transfusion requests involving 18,894 patients were analysed. Overall, 39.7% of requests resulted in RBC exposure, including 15.4% high-risk requests, 9.5% increased-risk requests, and 13.8% low but real risk requests.

Repeat-request recipients represented 18.1% of patients (3,419/18,894). A total of 9,025 RBC units were transfused during the study period, with repeat-request recipients accounting for 61.2% of total RBC utilization. Within the repeat-request subgroup, 1,599 recipients were classified as high-risk. High-risk repeat-request recipients accounted for 41.6% of total RBC utilization.

Ward-level clustering of RBC utilization among high-risk repeat-request recipients was greatest in surgical services, followed by medical and emergency services.

Conclusion: Transfusion burden was concentrated within a small subgroup of repeat-request recipients, predominantly among high-risk recipients in surgical, medical and emergency services. Ongoing repeat transfusion patterns in these patients warrant further investigation, especially in settings where routine antibody screening is not widely performed. These findings may help guide more targeted transfusion surveillance and risk-based antibody screening approaches within resource-limited transfusion services.

Evaluation of Patient Blood Management Practices and Transfusion Requirements in Patients Undergoing Elective Major Orthopaedic Surgery in Central India

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ABSTRACT

Aim:

The study aimed to evaluate patient blood management strategies and assess the requirement of blood transfusion in patients undergoing elective surgery in Orthopedics.

Method:

This study included medical records of patients undergoing elective major orthopaedic procedures. Patients with a history of previous surgeries, revision procedures, emergency hip, knee, or spine surgeries, and individuals below 18 years of age were excluded from the study. Ethical approval was obtained prior to commencement. Preoperative therapeutic measures were planned approximately 30 days before surgery. All eligible patients undergoing elective orthopaedic surgery, irrespective of anaemia status, were enrolled. Relevant clinical and laboratory data were collected and analyzed using SPSS version 20, and descriptive statistical methods were applied.

Results:

Out of 110 enrolled patients, 98 completed the planned treatment course. Male patients constituted 67.3% of the study population. Total Hip Replacement was the most frequently performed surgical procedure. Preoperative laboratory evaluation demonstrated improvement in baseline haemoglobin levels following preoperative optimization. A reduction in haemoglobin levels was observed in the postoperative period, consistent with expected perioperative physiological stress. Laboratory parameters, including serum iron and transferrin saturation, showed variable trends among patients. A proportion of patients adopted healthier dietary and lifestyle practices as part of preoperative preparation.

Conclusions:

Early identification of patients at risk of significant perioperative blood loss allows timely initiation of appropriate management strategies. Techniques such as intraoperative cell salvage may be considered in cases with anticipated blood loss exceeding 500 ml. The use of antifibrinolytic agents and targeted haemostatic therapies may contribute to effective bleeding control. Implementation of structured PBM strategies can improve utilization of healthcare resources, enhance patient outcomes, and reduce reliance on allogeneic blood transfusion.

Cryoprecipitate utilisation in Australian hospitals: a descriptive analysis from the National Transfusion Dataset

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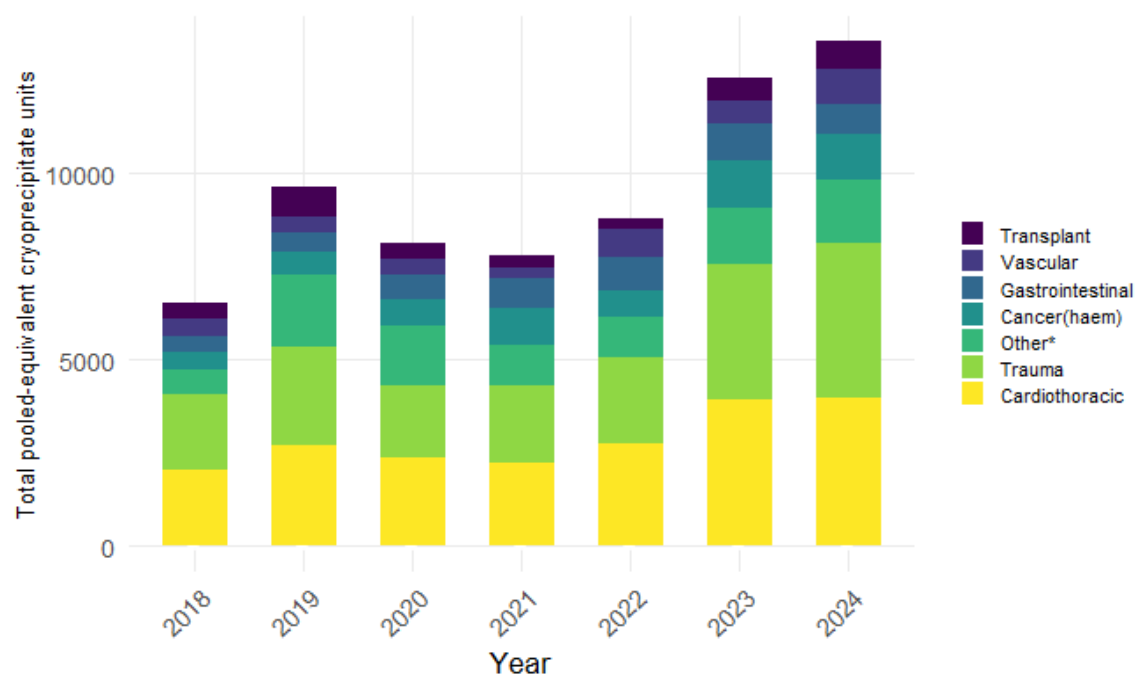
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Aim: Hospital demand for cryoprecipitate has increased in recent years but the reasons are poorly understood. The aim of this study was to characterise cryoprecipitate use across hospitals using National Transfusion Dataset (NTD) data.

Method: A retrospective analysis was conducted including 4,522 adult patients who received cryoprecipitate across seven Australian hospitals from 2018-2024. Data extracted included demographics, transfusion episodes, blood product use, hospital diagnostic and procedure codes, and laboratory results. Cryoprecipitate doses were standardised to pooled-equivalent units (units). Transfusion context categories were created using hospital admission diagnostic and procedure codes. Descriptive analyses were performed for all sites, and temporal trends assessed using regression analyses for three sites with complete annual data.

Results: Of 89,572 units of cryoprecipitate administered (4,822 transfusion episodes), 34% were used in massive transfusion. Median [IQR] patient age was 58 [40-70] years. 65% of patients were male. Median [IQR] units administered per episode was 15 [10-21]. Between 2018-2024 there was a significant increase in units administered (+983 units/year, 95%CI 212–1,753; $p=0.02$) (**Figure 1**) and transfusion episodes (+51 episodes/year, 95%CI 26–77; $p=0.003$). Number of units administered per episode increased by 2.4% per year (adjusted incidence rate ratio; aIRR 1.024, 95%CI 1.012–1.036; $p<0.001$). Greatest use overall was in cardiothoracic (30%), trauma (28%), haematological cancers (9%), gastrointestinal surgery (8%), vascular (6%) and transplant (5%). No single context drove temporal changes.

Conclusion: Cryoprecipitate use has increased due to both an increased number of transfusion episodes and the number of units transfused per episode. Further work is required to understand the drivers of these trends.



*Other includes: Orthopaedics, Cancer (non-haem), Gynaecology, Other general surgery, Neurosurgery, Obstetric, Urology, Non-malignant haem, Plastics, Critical Illness and ENT

Figure 1. Temporal trends in cryoprecipitate utilisation by transfusion context, 2018-2024

Pre-procedural transfusion practices in non-bleeding cirrhotic patients undergoing invasive procedures: a retrospective observational audit

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Aim:

To evaluate pre-procedural transfusion use in non-bleeding coagulopathic or thrombocytopenic patients with cirrhosis undergoing invasive procedures. Primary objective was to assess concordance with international transfusion guidelines. Secondary objectives included identify factors associated with transfusion use and post-procedural bleeding-related outcomes.

Method:

A single-centre retrospective observational audit was performed at an Australian tertiary hospital, including 345 adults with cirrhosis undergoing invasive procedures between 2018-2024 with abnormal pre-procedural coagulation or haematological parameters. Demographic, laboratory, procedural, transfusion, and outcome data were collected. Univariable analyses utilised Mann-Whitney U and Fisher exact testing, with parsimonious multivariable logistic regression used to identify independent predictors of pre-procedural transfusion and post-procedural transfusion outcomes.

Results:

Pre-procedural transfusion occurred in 21/345 patients (6.1%). Procedures were classified as low, intermediate, and high-risk in 13.6%, 36.8%, and 49.6% of cases, respectively. Overall guideline concordance was high (326/345 cases, 94.5%). On univariable analysis, transfused patients had lower haemoglobin, fibrinogen, platelet counts, and higher INR values. In multivariable analysis, only lower haemoglobin (OR 0.91, 95% CI 0.86–0.94, $p < 0.001$) and lower fibrinogen (OR 0.50, 95% CI 0.24–0.89, $p = 0.034$) remained independently associated with pre-procedural transfusion. Post-procedural transfusion was administered in 63/345 patients (18.3%). Transfused patients also had greater post-procedural transfusion requirements and longer hospital length of stay, which may reflect selection bias towards a more clinically unwell cohort. Early mortality events were rare ($< 1\%$), precluding meaningful analysis.

Conclusion:

Pre-procedural transfusion was uncommon despite a cohort enriched for intermediate- and high-risk procedures. Most cases were managed concordantly with guideline recommendations. The small number of transfusions outside guideline-based indications may reflect clinical complexities not captured in data collection. These findings will support development of local departmental transfusion protocols aimed at reducing unnecessary prophylactic transfusion in cirrhosis.

Coordinating albumin supply for cancer drug compounding: a pharmacy-pathology partnership in regional Australia

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Aim:

To describe a coordinated pharmacy-pathology supply model for human albumin to support third-party compounding of tebentafusp in a regional oncology setting, where infrastructure limitations and extended transport distances create logistical barriers not encountered in metropolitan cancer centres.

Method:

A retrospective review was conducted at Orange Health Service, a regional cancer centre in Orange, NSW, examining 13 tebentafusp compounding episodes requiring albumin as an excipient to prevent drug adsorption to infusion bag surfaces. As a regulated blood product, albumin was sourced through the hospital pathology department and transported via courier to an external compounding facility. The supply model was designed around the patient's existing 6-weekly medical review and pathology attendance cycle, with 6 vials dispatched per courier run — sufficient to cover one full treatment interval. Courier costs, ordering coordination, and albumin utilisation were reviewed.

Results:

Across 13 courier runs, albumin was successfully delivered to the compounding facility in all episodes with no supply failures or treatment delays. Aligning dispatch with the 6-weekly review cycle eliminated the need for ad hoc courier bookings and provided a predictable, auditable procurement schedule. A fixed courier cost of \$85.00 plus fuel levy and GST per run was incurred. No albumin wastage occurred, as the 6-vial quantity was matched precisely to the treatment interval and no patients ceased therapy during the review period.

Conclusion:

A formalised pharmacy-pathology collaboration, structured around existing patient review cycles, can reliably support tebentafusp compounding in a regional setting despite regulatory constraints on albumin as a blood product. Synchronising albumin procurement with 6-weekly clinical appointments eliminated wastage and reduced logistical complexity. This model demonstrates that equitable access to novel anticancer therapies in regional areas is achievable through structured inter-departmental coordination, and offers a reproducible framework for other regional and rural centres managing blood product-dependent compounding.

Progress, challenges and successes in building Australia's first vein-to-vein blood use registry: The National Transfusion Dataset

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Aim:

To highlight progress to date, along with successes and challenges in building the National Transfusion Dataset (NTD), the first integrated vein-to-vein dataset of when, where and why blood is used in Australia. The NTD links data from pre-hospital and hospital settings with clinical outcome registries.

Method:

The NTD builds on the success of the Australian & New Zealand (NZ) Massive Transfusion Registry, now expanded to capture all transfusions. The NTD is overseen by a national multidisciplinary Steering Committee. The dataset comprises all transfusion episodes for patients ≥ 18 years who received any blood product across participating hospital and pre-hospital sites in Australia. Variables collected include patient demographics, transfusion/laboratory data, and administrative diagnostic & procedure data. Clinical registries provide additional data on patient characteristics and other treatments that might influence blood use.

Results:

Progress to date includes ethics/governance approval at 43 Australian sites, with 19 sites having contributed data capturing over 220,000 transfusion episodes. Expansion to NZ is underway.

Successes include data linkages established with Australian Red Cross Lifeblood, Ambulance Victoria, and clinical outcomes registries including the Lymphoma & Related Diseases Registry, Aplastic Anaemia & Other Bone Marrow Failure Syndromes Registry, and the Australian & NZ Intensive Care Society Adult Patient Database. Hospital data reports and an interactive site level dashboard are in development, with a pilot dashboard available on the NTD website. Multiple analyses have been conducted using NTD data (see companion abstracts) and data have been shared with governments, clinicians, and at professional/scientific meetings.

Key challenges include:

- accessing and harmonising data across national research ethics/governance structures
- variability in dataset content and linkages across health service platforms
- staffing constraints within hospital teams, and
- long-term funding to support sustainability

Conclusion:

The NTD has demonstrated feasibility for site participation and data linkage and continues to expand. NTD data will support policy, haemovigilance, research and improving clinical transfusion practice.

Establishing a compliance-driven, risk-based internal audit programme in a multi-regulated organisation

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Background

The New Zealand Blood and Organ Service (NZBS) operates within a robust regulatory and accreditation environment to ensure safe, ethical, and high-quality delivery of blood, organ, tissue, and cellular therapy services. Alongside the external oversight, NZBS maintains an internal audit programme to support public trust and demonstrate continuous improvement. Historically, internal audit practices imposed a high audit burden, with activities often perceived as low-value, compliance-driven “tick-box” exercises.

Aim:

To review compliance requirements and develop a risk-based programme to improve internal audit efficiency and assurance, ensuring delivery of safe services offered by NZBS.

Method:

Regulatory and standards-based audit requirements were mapped and embedded as mandatory elements of the internal audit programme. For audit activities without prescribed audit frequency, a risk-based approach was applied, allowing audit frequency and scope to align with identified risk. Risk considerations are based on process or departmental complexity, compliance risks including historical audit performance, and organisational change. Internal audit scoping tools have been developed and introduced to support collaboration for internal audit assessments.

Results:

Implementation of the risk-based audit programme has improved prioritisation of audit resources and reduced overall audit burden. Auditor effort has been redirected towards high-risk areas, enabling audits to be conducted with greater depth and increased value to operational areas. The programme has improved sustainability, reduced audit rescheduling, and enhanced transparency in audit planning, while maintaining compliance with multiple regulatory obligations.

Conclusions:

A compliance-driven, risk-based audit programme enables more efficient and effective internal audit activity within a multi-regulated organisation. By focusing resources on higher-risk areas and value-adding activities, this approach strengthens assurance over processes that underpin product quality, patient and donor safety. Lessons learnt since the implementation of the on-going programme are being incorporated to continuously improve NZBS internal audit programme.

Transition of Albumex 4 to Alburex 5 in cellular therapy unit

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Aim:

To utilise process verification of controlled rate freezing (CRF) for cellular therapy (CT) products to both confirm equivalency of Albumex 4 with Alburex 5.

Method:

A process verification exercise was conducted following replacement of Albumex 4 with Alburex 5 as the human serum albumin component in the cryopreservative solution (CPS). Verification was performed using a controlled rate freezer with mock CT products representing worst-case conditions (90% albumin, 10% DMSO).

Freezing was performed under minimum and maximum load configurations, and critical process parameters including cooling rate, temperature attainment, and heat of fusion behaviour were assessed. Freeze profiles were reviewed to confirm process reproducibility and comparability between materials.

Results:

Process verification demonstrated comparable performance between Albumex®4 and Alburex®5, confirming suitability of the alternative albumin source within the CRF process. The freezing process was reproducible within defined operational limits.

Review of freeze profiles consistently demonstrated a temperature rise during crystallisation (heat of fusion), indicative of stochastic ice nucleation following supercooling. This observation highlights variability in nucleation behaviour and provides insight into process temperature trend. Literature indicates that increased supercooling is associated with variability in freezing profiles, increased intracellular ice formation, and reduced post-thaw viability [1]–[3].

Conclusion:

Process verification confirmed that the material change from Albumex®4 to Alburex®5 does not impact cryopreservation performance or process reproducibility. Importantly, integration of process verification with detailed freeze profile review enabled identification of variability associated with supercooling and spontaneous nucleation.

This highlights a key opportunity for process optimisation through improved control of ice nucleation. Controlled nucleation approaches, such as shock freezing or seeding strategies, enable initiation of ice formation at higher, defined temperatures, reducing supercooling and improving consistency of freezing behaviour.

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Evaluating the in vitro efficacy of pathogen reduction of platelets and plasma: First experience from Asia

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Aim:

To evaluate the in vitro efficacy of riboflavin and ultraviolet (UV) light–based pathogen reduction on platelets and plasma in an Indian blood banking setting and to assess the impact of preparation time on component quality.

Method:

This prospective in vitro experimental study was conducted in the Department of Transfusion Medicine and Department of Pathology at a tertiary-care center in India. Thirty-two pooled blood components were analyzed, including 16 pooled platelet units and 16 pooled fresh frozen plasma units. Platelet concentrates were prepared by pooling four random donor platelets, while plasma units were prepared by pooling two fresh frozen plasma units. Components prepared within 4 hours and 6 hours were evaluated. Platelet parameters assessed included platelet count, swirling, pH, blood gas analysis, biochemical markers, and aggregation. Plasma evaluation included prothrombin time (PT), activated partial thromboplastin time (APTT), factor VIII activity, fibrinogen, total protein, and serum albumin. All parameters were measured before and after pathogen reduction.

Results:

Pathogen reduction resulted in minimal changes in platelet counts, functional parameters, and biochemical markers, with most variations remaining within 10% of pre-treatment values. Platelet pH and swirling were preserved. Plasma showed mild prolongation of PT and APTT, along with a reduction in factor VIII and fibrinogen levels, which remained within clinically acceptable ranges. Components prepared within 4 hours demonstrated better preservation of in vitro parameters compared to those prepared at 6 hours.

Conclusion:

Riboflavin and UV light–based pathogen reduction of platelets and plasma is feasible and effective in the Indian blood banking setting, with acceptable preservation of in vitro quality. This study represents the first systematic evaluation of pathogen reduction of both platelets and plasma from Asia.

Improving good documentation practice in the workplace

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Aim:

Good Documentation Practices (GDocP) are essential in regulated industries to ensure data integrity, quality, and regulatory compliance. These principles are summarised by the ALCOA+ framework. While the principles are widely recognised, the “+” elements lack a mnemonic, contributing to reduced understanding and inconsistent application.

At New Zealand Blood Service (NZBS), poor adherence to GDocP is a significant contributor to documentation-related incidents, data integrity failures, and audit findings. Improving comprehension and practical application of these principles remains essential to reducing errors and strengthening data integrity with direct implications to compliance, product quality and patient safety.

Method:

ALCOA+ works poorly for operational staff.

The key problems are:

- The “+” is cognitively weak - no memory hook.
- Use of abstract or non-actionable terms such as “Contemporaneous” and “Enduring”.
- No behavioural cues - ALCOA+ tells people what good looks like, not what to do.

At NZBS, where acronyms dominate workplace language, if the acronym isn’t intuitive, it won’t be used. To reduce errors, a human-factors approach was used to redesign the framework which a simple action-oriented check, which can function as a single mental “stop check”.

Results:

This approach led to the development of **CLEAR DATA**, a plain-language mnemonic aligned to ALCOA+ principles:

C - Correct
L - Logged on time
E - Easy to Read
A - Accountable
R - Real

D - Don’t leave things out
A - Always the same
T - There when needed
A - Always safe

CLEAR DATA was designed for easy recall, clarity and useability under stress.

Conclusion:

CLEAR DATA translates ALCOA+ into a practical, staff-centred framework that supports accurate and reliable documentation practices. By focusing on behaviour rather than training, CLEAR DATA strengthens data integrity while supporting regulatory compliance, product quality and patient safety.

Using change management practices to scope an Environmental Monitoring System (EMS) tender at Australian Red Cross Lifeblood

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¹Australian Red Cross Lifeblood, Kelvin Grove, Australia

Aim:

To develop a supplier tender brief that translates internal user and technical needs into clear, testable requirements, demonstrating how change management practices can strengthen EMS tender scoping and support adoption readiness at Australian Red Cross Lifeblood.

Method:

Change management practices were applied during the tender scoping phase through early stakeholder engagement, role-based consultation and collaborative workshops. Stakeholders were selected using a change impact lens, prioritising roles most affected by alarm management, escalation pathways and after hours response expectations.

Five virtual workshops were conducted over a three-week period in August 2025 comprising three general user groups and two technical user groups. These sessions enabled participants to identify current challenges, future needs and perceived risks, while surfacing behavioural and operational impacts across sites prior to system selection.

Results:

Fifty contributed over 200 responses across general and technical user groups, representing a broad range of roles and locations

Clear differences emerged between general and technical cohorts particularly in priorities, risk perception and interaction with the system. These insights highlighted where role specific change impacts were likely to occur and identified areas requiring targeted engagement, communication and training during future implementation.

The insights informed the development of tender requirements grounded in real operational contexts and provided early visibility of adoption, usability and support considerations prior to system selection.

Conclusion:

Applying change management practices during tender scoping produced a supplier brief grounded in real operational needs and expectations. This collaborative approach strengthens adoption readiness, supports compliance and establishes a strong foundation for a modern, fit-for-purpose monitoring system. The approach aligns with Lifeblood's change management practice which emphasises early engagement, understanding impacts on people and roles and preparing the organisation for change alongside technical delivery.

Clinical and quality compliance audits driving collaborative quality improvement

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¹Nzbs, Auckland, New Zealand

Aim:

To demonstrate how long-standing clinical and quality compliance audits support complete vein-to-vein traceability of blood components and, recognising this as a shared responsibility, audit insights are now being used to foster collaboration and drive meaningful improvement in transfusion practice.

Method:

Clinical and quality compliance audits are conducted nationally by the New Zealand Blood and Organ Service (NZBS) as part of its Clinical Oversight Programme to support complete vein-to-vein traceability of blood components. Audits involve on-site review of a random sample of transfused patient records against standardised documentation criteria. Findings from repeated audit cycles are analysed to identify persistent risks and inform collaborative engagement with hospital partners. This work represents the initial phase of a shift from audit-driven assurance to collaborative quality improvement, including early engagement with a group of large hospitals within a single region and the establishment of an internal NZBS multidisciplinary working group to support ongoing collaboration.

Results:

Across audited hospitals, documentation required to demonstrate vein-to-vein traceability was frequently present but incomplete, resulting in ongoing gaps in evidence for key transfusion steps. Similar documentation risks have been consistently identified across multiple hospitals, clinical settings, and audit cycles, indicating system-level and process-related contributors rather than isolated individual performance issues. Aggregated audit findings have provided a strong evidence base for shifting from compliance-focused feedback toward collaborative quality improvement, directly informing the establishment of regional and internal structures aimed to support sustainable, system-level improvement.

Conclusion:

Ensuring vein-to-vein traceability is a shared responsibility across the transfusion system. This early-phase work shows how long-standing audit programmes can be repositioned to support collaboration, align priorities, and drive meaningful improvement. Establishing regional hospital partnerships and internal multidisciplinary working groups represents a critical first step toward sustained system-wide change in transfusion safety.

Introducing Gemba walks to strengthen a culture of shared Quality ownership at the New Zealand Blood and Organ Service

Mr Roger Jamieson¹

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Aim:

To strengthen quality culture at the New Zealand Blood Service (NZBS) by increasing the visibility and accessibility of the Quality and Regulatory Affairs team and supporting a shift toward shared ownership of quality, where quality is understood as everyone's responsibility, through the introduction of regular Gemba walks.

Method:

Principles underpinning Gemba walks were reviewed and adapted to suit the role of a quality function within NZBS. This included literature review, consultation with operational staff experienced in Gemba practices, learning from other services, and ongoing review and refinement through project discussions. Clear objectives were established to ensure Gemba walks promoted partnership, learning, and shared responsibility for quality, rather than functioning as inspections or informal audits. Consideration was also given to how the approach could be applied consistently across geographically dispersed and remote sites without a permanent quality presence. Practical guidance was developed to support quality staff to use Gemba walks as a routine mechanism for engagement, listening, and collaboration.

Results:

Quality specific Gemba walk guidance has been implemented, and Quality staff are encouraged to incorporate regular Gemba walks into their roles. Early observations suggest increased informal engagement between quality staff and frontline teams, improved mutual understanding of work and greater opportunity for staff to raise concerns and improvement ideas. This has supported early cultural signals that quality is a shared responsibility to be embedded in everyday practice, rather than a function owned solely by the quality team. Workload pressures remain a challenge to consistent uptake, highlighting the importance of leadership support and reinforcement.

Conclusion:

The introduction of Gemba walks has supported an early shift toward a "quality is my business" mindset at NZBS, by strengthening relationships between quality staff and frontline teams and embedding quality conversations at the point of work. While still in the early stages, this approach reinforces shared accountability for quality and provides a practical mechanism for supporting a collaborative, learning-focused quality culture.

When clinically significant antibodies go undetected: an EQA-based analysis of method sensitivity and antigen dosage

Mr Junho Kim¹

¹The Royal College of Pathologists of Australasia Quality Assurance Programs, Sydney, Australia

Introduction:

Accurate detection of clinically significant red cell antibodies is essential for safe transfusion practice. External quality assurance (EQA) programs continue to highlight inter-laboratory variability in antibody screening and identification, particularly for weak antibodies. This study examined false-negative antibody detection in Royal College of Pathologists of Australasia Quality Assurance Programs (RCPAQAP) Transfusion program samples, with emphasis on the influence of testing methodology and antigen dosage.

Methods:

A retrospective analysis was undertaken using data from the RCPAQAP's Transfusion programs. Survey samples containing weak but clinically significant antibodies were reviewed. Laboratory responses were grouped by testing methodology (tube, CAT-Gel, etc.) and by antigen expression in screening or identification cells (homozygous vs heterozygous). False-negative outcomes were defined as a non-reactive antibody screen or failure to identify the clinically significant antibody.

Results:

Variability in antibody detection (e.g., anti-S and anti-E) was observed across laboratories. False-negative results were more common when antigen expression was heterozygous rather than homozygous (e.g. anti-S). Differences between testing platforms were also noted, with reduced sensitivity for some weak antibodies in the CAT-Gel methods (e.g. anti-E). Antibodies showing dosage effects contributed most to variability and were responsible for a large proportion of missed detections.

Discussion:

The false-negative findings largely reflect potential interactions between antibody strength, antigen dosage, and the chosen testing method rather than random error. Although laboratories may achieve acceptable overall EQA performance, method-related limitations can still lead to the missed detection of clinically significant antibodies.

Conclusion:

EQA data provide valuable insight into systematic vulnerabilities in pre-transfusion testing and should be considered when reviewing improvements to enhance transfusion safety.

Enhancing transfusion communication in New Zealand: development and impact of a national hospital transfusion forum

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Introduction:

The Australian and New Zealand Society of Blood Transfusion (ANZSBT) recommends that health services providing transfusions endorse Hospital Transfusion Committees (HTCs) to oversee transfusion practices, including education and communication of changes to processes, components, and products. In New Zealand, the New Zealand Blood Service (NZBS) is the sole provider of blood components.

Method:

Transfusion Nurse Specialists (TNS) reviewed and redesigned their communication framework to improve the dissemination of evidence-based transfusion information to healthcare professionals across New Zealand. This work was informed by recent health system restructuring, evolving regulatory requirements, and the need to better highlight initiatives that support safe transfusion practice.

With support from the NZBS Chief Medical Officer, the national TNS group established the first National HTC ("NHTC") Meeting in March 2021. Invitations were extended to all HTCs across New Zealand, with attendance open to HTC nursing, medical, scientific, and quality members.

Results:

The NHTC Meeting successfully fostered collaboration between large tertiary centres and smaller regional services, providing a platform for shared learning and discussion of transfusion-related challenges within New Zealand. Since its inception, five national meetings have been delivered, averaging over 80 participants yearly and resulting in consistently strong engagement and with positive feedback from across the sector.

The initiative has continued to respond to participant feedback and emerging priorities. In 2024, the meeting expanded into a two-day event with the addition of a national Patient Blood Management seminar. In 2026, the NHTC programme further developed into a Clinical Transfusion Symposium open to all healthcare professionals working within transfusion.

Conclusion:

This transfusion focused forum has strengthened networking opportunities for attendees to increase communication pathways, provide supported collaboration across national healthcare settings, and best practice in transfusion medicine throughout New Zealand. This model demonstrates a sustainable and scalable approach to improving national transfusion education, clinical engagement, and governance.

Reference:

1. Australian and New Zealand Society of Blood Transfusion. *Guidelines for the Administration of Blood Products*, 3rd Edition, Revised 2024.

Statewide comparison of erythrocyte sedimentation rate measurements using glass and plastic tubes in New South Wales Health Pathology.

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Aim:

Following the cessation of manufacturing of plastic erythrocyte sedimentation rate (ESR) tubes, a statewide validation project was undertaken to evaluate the comparability of ESR measurements obtained using glass and plastic tubes across New South Wales Health Pathology, including patient samples and quality control material.

Method:

This statewide validation project was led by the Royal North Shore Hospital Haematology Laboratory and included participation from 10 laboratories across New South Wales using the Elitech Mixrate Mini analyser. Parallel ESR testing was performed on glass and plastic tubes for a minimum of 10 patient samples and one quality control sample per site. In total, 144 patient samples (ESR range 1–114 mm/hr) and 65 quality control samples at normal and abnormal levels were analysed. Statistical comparison was performed using correlation analysis and Bland-Altman analysis.

Results:

Bland–Altman analysis showed a mean bias of -0.076 mm/hr, with 95% limits of agreement from -6.13 to +5.98 mm/hr for ESR measurements using glass and plastic tubes. Results showed acceptable agreement across the analytical range, with increased variability observed at higher ESR values. Correlation between tube types was high ($r = 0.99$). In contrast, quality control material demonstrated consistent, tube-dependent differences at both normal and abnormal levels.

Conclusion:

ESR measurements obtained from patient samples using glass and plastic tubes demonstrated acceptable agreement, supporting continuity of patient result interpretation following tube substitution. However, the observed tube-dependent differences in quality control material highlight the need for tube-specific QC considerations during implementation.

High Cost, Low Clarity: Challenges in Auditing IVIg Use in Immune Thrombocytopenic Purpura

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Aim:

To assess the appropriateness of IVIg use in ITP at Te Toka Tumai Auckland and evaluate 7 day clinical outcomes.

Methods:

Intravenous immunoglobulin (IVIg) is a high-cost, plasma-based therapy used in immune thrombocytopenic purpura (ITP), typically reserved for patients at risk of life-threatening bleeding or refractory to first-line treatments. In New Zealand, IVIg prescribing is governed the NZBS Immunoglobulin Online (IgO) approval system. At our centre, IVIg use for ITP alone exceeds NZD \$600,000 annually. Despite the significant cost and oversight, auditing appropriateness of use remains challenging due to broadly defined guidelines and clinical documentation. A retrospective audit of 50 patients (85 IVIg episodes) between January 2023 and July 2025 was performed. IVIg requests and clinical records were reviewed. Appropriateness was assessed against operator-defined criteria reflecting local transfusion medicine specialist and haematologist practice, based on published Australian National Blood Authority (NBA) Ig Governance guidelines. A comparison was made with BloodSTAR's internal, more comprehensive criteria, derived from the same framework.

Results:

Compliance with indication criteria appeared high (92% using local criteria; 81% using BloodSTAR criteria). However, meaningful assessment was limited by several factors. Definitions of 'life-threatening bleeding' and 'potential for life-threatening bleeding' were imprecise and required subjective post hoc interpretation. Similarly, classification of 'refractory' disease lacked consistency, particularly in patients receiving multiple therapies. Although 76% of episodes demonstrated a platelet response at 7 days, interpretation of efficacy was confounded by concomitant treatments.

Conclusion:

Despite substantial cost and governance, assessment of IVIg appropriateness in practice remains difficult. Ambiguity in defining bleeding risk and refractoriness represents a key barrier to consistent prescribing and auditability. Standardised definitions, improved guideline transparency and documentation are required to allow for better stewardship of this high cost blood product.

Improving transfusion practice with the introduction of a clinical transfusion documentation competency, for nurses working in a regional hospital with satellite blood fridges

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¹Latrobe Regional Health, Traralgon, Australia

Aim:

Despite guidance being provided through various education formats for transfusion documentation, errors in: traceability, cold chain documentation and specimen labelling continue to occur. These errors contribute to delays and require significant resources from transfusion nurses to trace blood products to patients and follow up with the staff involved.

In 2024 a new transfusion documentation competency was implemented with the aim of improving documentation compliance and reducing errors.

Method:

Teaching resources were developed to enable several staff to complete the competency simultaneously, within a classroom style environment.

Staff were guided by the facilitator through the transfusion process with attendees completing the simulated documentation at each stage. This included specimen labelling and declaration, collection of blood from the blood fridge, blood arriving on ward, double independent checking, rate calculation and consideration of the 30minute/4hour rule.

Facilitators then reviewed each staff members work to ensure that the documentation met requirements, giving immediate feedback to staff.

Results:

Specimen labelling errors reduced from 80 in 2024 to 64 in 2025. In 2026, the reduction has continued, with only seven errors recorded to date.

Cold chain and traceability documentation errors reduced from 64 in 2024 to 42 in 2025. In 2026, the reduction has continued, with only eight errors recorded so far.

An overall reduction in transfusion errors was demonstrated, resulting in decreased need for transfusion nurses to trace blood products that were missing or recorded as “presumed transfused.”

Conclusion:

The training sessions allowed an opportunity for staff to ask additional questions to clarify transfusion knowledge. Feedback from the staff on the competency was positive, with staff finding it to be a valuable learning experience. The data demonstrated improved compliance with documentation requirements and a reduction in specimen labelling errors across the health service. As a result, it has been retained as a mandatory competency for nursing staff.

Integration of software and barcode scanners for risk mitigation during platelet collection

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Aim: Recent requirement changes for plasma collection resulted in citrate and ACDA fluid bags both having Correct Connect Leur adaptors. The similarity in connection ports increased the risk of using the incorrect fluid in platelet collections, should the citrate for plasma collection and the ACDA for platelet collections be accidentally switched.

To minimize this risk, barcode scanners were integrated with Trima Accel platelet collection devices. Barcode scanners were programmed with TOMEs (Terumo Operational Medical Equipment Software) to ensure that only barcodes for ACDA would be accepted for platelet collections. Additional enhancements aimed at improving compliance were also introduced. These enhancements included procedural alerts on the Trima screen reminding operators to check platelet swirl throughout the collection procedure.

Method: A retrospective review of Trima device records across 30 donor centres nationwide was completed. Incidence of adverse events and platelet aggregates were recorded to determine effectiveness of the barcode scanners and programmed procedural alerts.

Results: Implementation of barcode scanning prevented accidental switching of ACDA and citrate fluid connection ports, as the software program did not allow for operators to continue the collection if incorrect barcodes were scanned. Integrated alerts to check platelet swirl decreased the number of platelet aggregates from 0.06% of collections pre-implementation to 0.04% of collections post-implementation.

Conclusion: The introduction of barcode scanning on Trima Accel platelet collection devices enabled enhancements in donor safety by providing comprehensive traceability across products used during collection. Although rollout of the program was complex, the project successfully delivered a significant technology uplift to frontline teams and introduced user-friendly scanning functionality that reduced the risk of error during platelet donation procedures. The integrated alerts and alarms strengthened team member vigilance, ultimately ensuring optimal collection outcomes.

Real-world functional outcomes of multidisciplinary prehabilitation prior to autologous stem cell transplantation (AuSCT): a retrospective clinical audit

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¹Epworth HealthCare, Melbourne, Australia

Aim:

To evaluate patient engagement, attendance patterns, functional outcomes among patients participating in a multidisciplinary prehabilitation program prior to AuSCT.

Method:

A retrospective clinical audit was conducted of adult patients with haematological malignancies referred to a multidisciplinary allied health prehabilitation program prior to AuSCT at Epworth HealthCare between 2023 and 2024. The program included education, physiotherapy-led exercise prescription, dietetics-led nutritional assessment and intervention, and follow-up delivered via face-to-face and telephone consultations during the pre-transplant period as routine clinical care. Outcome measures included attendance and engagement, physiotherapy outcomes (6-minute walk test [6MWT], grip strength, Short Physical Performance Battery [SPPB], and patient satisfaction. Analysis was performed to evaluate engagement, attendance patterns, and changes in functional outcomes from initial review to transplant admission.

Results:

Approximately 23 patient episodes were included during the audit period. Attendance and engagement varied throughout the program and were influenced by treatment scheduling and symptom burden. Baseline physiotherapy assessments identified reduced physical function prior to conditioning therapy. Preliminary analysis of nine participants (39.1%) with paired physiotherapy assessments demonstrated improvements in functional outcomes between initial review and transplant admission. Mean 6-minute walk test (6MWT) distance increased from 479.2 ± 196.6 m to 535.0 ± 115.9 m, while mean Short Physical Performance Battery (SPPB) scores improved from 9.3 ± 3.9 to 11.8 ± 0.4 . Grip strength remained stable between assessments. Participants also demonstrated ongoing engagement in aerobic and strength-based exercise throughout the prehabilitation period. Patient satisfaction with the multidisciplinary program ranged from good to excellent. Data analysis is ongoing.

Conclusion:

This retrospective audit supports the feasibility of implementing multidisciplinary prehabilitation within routine AuSCT care, demonstrating favourable functional outcomes alongside high patient satisfaction. Findings will inform optimisation of the current service and the development of future prospective studies evaluating prehabilitation pathways in patients undergoing AuSCT.

Clinician-led, face-to-face scenario-based transfusion education improves requisite training completion and intern confidence in blood transfusion prescribing and management.

Mrs LEEANNE TURNER¹

¹Sunshine Coast Health, Britinya, Australia

Background:

Intern compliance with requisite blood management was below health service set targets, creating gaps in essential skills such as obtaining valid transfusion consent and recognising transfusion reactions.

Aim:

To improve intern completion of Blood Management training and enhance competence and self-reported confidence in transfusion consent and transfusion-reaction management.

Method:

Clinician-led, face-to-face transfusion workshops offer clear advantages over eLearning for early-career doctors by providing immediate feedback, real-time clarification, and interactive discussion of clinical scenarios, all of which enhance understanding, retention, and confidence. This format also promotes peer learning and strengthens professional relationships with senior clinicians. During the 2025 development phase, the program was internally piloted with small intern groups ($n=15 \times 4$) and refined prior to broader implementation. Pre- and post-session survey data from the subsequent delivery of face-to-face blood management training demonstrated increased knowledge and higher self-reported confidence in transfusion consent and reaction management, supporting the effectiveness of this educational approach.

Results & Discussion:

Sunshine Coast Health delivered the program to $n=73$ interns during the orientation period. Both quantitative and qualitative statistical and thematic evaluation was employed.

The face-to-face workshops delivered during the 2026 intern orientation program, allowed for active knowledge acquisition and maximal completion rates. Interest in this program approach by colleagues at another Hospital and Health Service, led to the sharing and concurrent implementation.

Pre/post surveys indicated improved knowledge and increased self-reported confidence in transfusion consent and transfusion-reaction management after the session, with completion rates of Blood Management training improving from 11% to 97%.

Conclusion:

Face-to-face scenario-based teaching enhanced intern confidence and completion rates. Increased confidence is likely to translate into improved clinical decision-making, earlier escalation to senior staff, and more effective communication in high-pressure situations. These findings reinforce the value of interactive, experiential learning in consolidating foundational knowledge and promoting patient safety and quality of care.

Improving transfusion safety through patient-held alert cards for irradiated blood product requirements in Western Australia.

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Aim:

Patients requiring irradiated blood products, including those who are immunocompromised or undergoing haematopoietic stem cell transplantation, are at ongoing risk of receiving inappropriate transfusions. This risk is amplified by fragmented care across multiple public and private healthcare facilities, where critical transfusion requirements may not be consistently communicated.

To design and implement a patient-held transfusion alert card to improve the communication of irradiated blood product requirements and enhance transfusion safety across Western Australia.

Method:

The West Australian Transfusion Education group (WAnTEd) co-designed a patient-held alert card incorporating key clinical information and a QR code linking to the Australian Red Cross Lifeblood irradiated blood products patient education resources. A pilot evaluation of 13 consumers was undertaken and included patients who require irradiated blood products (n= 9) and clinical staff (n= 4). A structured questionnaire assessed usability, clarity, and perceived safety impact. Feedback was used to refine the final design prior to governance review.

Results:

Three out of nine (33%) patient consumers who provided feedback were unaware they required irradiated blood products. 100% of consumers agreed the purpose of card was clear and the information easy to understand. 100% of the consumers who provided feedback stated they would use the card. Iterative refinements were made based on user feedback.

Conclusion:

A simple, low-cost patient-held alert card significantly strengthens transfusion safety by improving real-time communication of irradiated blood product requirements across healthcare settings. This initiative empowers patients, standardises critical information transfer, and has strong potential for scalable statewide implementation to reduce preventable transfusion risk.

Improving management of wrong blood in tube events at New Zealand Blood and Organ Service (NZBS).

Mrs Kelly Willoughby¹

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Aim:

To review and strengthen the process for recording, investigating and closing wrong blood in tube (WBIT) events detected by NZBS Blood Banks with the aim of improving patient safety and supporting effective haemovigilance.

Method:

A multidisciplinary process review was undertaken involving staff from NZBS blood banks, Transfusion Nurse Specialists (TNS), Haemovigilance, and Quality. The end-to-end process for logging, validation, investigation, record closure, work instructions and supporting training resources was reviewed. Participants identified process pain points, areas of ambiguity and factors contributing to delays in investigation and closure.

Results:

Completion of WBIT records was identified as a key bottleneck in the process. Investigation workflows rely on feedback from hospital staff to local Transfusion Nurse Specialists (TNS) regarding management of the event, which is frequently delayed, incomplete, or not received. This limits timely closure of records and reduces the quality of data available for haemovigilance learning.

As a result of the review, improvement opportunities were identified, including enabling hospitals to submit investigation summaries directly or documenting the level of engagement achieved by TNS's when follow-up is incomplete. Clarification and expansion of work instructions, particularly for validation and investigation of historical WBIT events, were also identified as necessary to support consistency and reduce variation in practice.

Conclusion:

Improving the WBIT investigation and documentation process is expected to support more timely and consistent event closure, enhance reporting to the NZBS Haemovigilance programme, and improve the quality of learning from WBIT events. Strengthening process clarity and data visibility provides an opportunity to better target and support hospitals, reduce the risk of future WBIT occurrences, and improve patient safety. Implementation is in progress and preliminary findings are expected to be available for poster presentation.

Altered s antigen expression due to c.152T>G on GYB in MNS system

Miss Emily Black¹, Dr Yew-Wah Liew¹, Ms Glenda Millard¹, Dr Emma Palfreyman¹, Mr Brett Wilson¹

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Background:

Australian Red Cross Lifeblood received customer feedback regarding a s antigen phenotype discrepancy. Phenotyping performed by the pathology provider found the red cell component was s positive using monoclonal anti-s but was labelled as s negative from phenotyping on a previous donation using human polyclonal anti-s on the Immucor NEO analyser. On a subsequent donation, Red Cell Reference investigated the discrepancy using serological and molecular techniques.

Results:

Phenotyping was performed by Red Cell Reference using a variety of monoclonal and polyclonal antisera (refer to table 1). The donation was Direct Antiglobulin Test negative.

Table 1. Serology performed by Red Cell Reference

Antisera	Clone	Score (0-12 scale)
Immulab monoclonal anti-s	P3BER	12
Immulab polyclonal anti-s	Human polyclonal	3
Ortho-clinical anti-s monoclonal	P3YAN3	Negative
Ortho-clinical anti-s polyclonal	Human polyclonal	1

The sample was genotyped using Immucor PreciseType™ HEA Molecular BeadChip, with results predicting a S+s+ phenotype. Next Generation Sequencing using Illumina technology also predicted a S+ phenotype but was unable to determine the s phenotype due to an additional heterozygous nucleotide substitution, c.152T>G on the s allele. This change affects the binding of some anti-s reagents resulting in the s phenotype discrepancy.

Conclusion:

Nucleotide substitution c.152T>G is not listed in ISBT tables. There is no association with a dbSNP reference or ClinVar. There is no known allele frequency suggesting this is a novel variant in the MNS system.

Validating a comprehensive B19 and HAV NAT testing solution, a multi-site approach

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Aim:

To design, execute, and verify a robust validation strategy for the introduction of Parvovirus B19 (B19) and Hepatitis A virus (HAV) nucleic acid testing (NAT), ensuring system performance, data integrity, and regulatory compliance across multiple sites.

Method:

A structured validation strategy was developed and implemented across Donation Accreditation laboratories in Auckland and Christchurch, aligned with GMP-principles. Validation activities were embedded within a broader multi-phase implementation plan and applied to all components of the solution, including the Grifols Procleix Xpress pooler, Procleix Parvo/HAV assay, Bloodstream middleware, system interfaces, and eProgesa configurations.

The approach incorporated installation, operational, and performance qualification where appropriate. Method validation was performed on the initial platform, with subsequent verification across remaining systems to confirm equivalence. Interface validation ensured accurate and secure data transfer, while external quality control materials were evaluated and integrated for ongoing monitoring. End-to-end user acceptance testing and system integration testing confirmed workflow integrity and fitness for purpose. Validation was executed sequentially across sites, with Christchurch as the primary implementation site, followed by Auckland. Regulatory compliance was achieved through Medsafe submission and approval, supported by validation documentation. Production verification testing and post-go-live monitoring confirmed system readiness and stability prior to operational release.

Results:

The validation approach confirmed that all components met predefined acceptance criteria, demonstrating accuracy, reliability, and data integrity of B19/HAV NAT across both sites. Method validation and verification established consistent assay performance, while interface and integration testing ensured seamless data flow. The phased approach enabled efficient validation without disruption to routine operations.

Conclusion:

A comprehensive validation strategy enabled the safe and compliant introduction of B19/HAV NAT. This approach provides a scalable model for validating complex, multi-component laboratory systems, supporting regulatory compliance, operational continuity, and sustained testing quality.

2 Cases of Matuhasi Ogata phenomenon – laboratory methods to bypass this interference

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Aim:

To identify method/s to bypass interference seen in elution's performed on patients presenting with Matuhasi Ogata Phenomenon.

Method:

2 patients presenting with Rh(D) negative blood groups and positive direct antiglobulin tests (DAT) where anti-D was eluted. The elution's also produced positive final wash results invalidating the test. The below methods were employed to assist in attempting to bypass this interference.

1. Increase in the number of times patient red cells were washed prior to performing the elution
2. Increasing wash solution concentration to packed red cell concentration ratio for washing of cells by decreasing volume of red cells washed prior to performing elution
3. Washing red cells with Phosphate Buffered Saline (PBS) only – substituting the wash solution in the manufactured eluate test kit for PBS
4. An EDTA tube of whole blood was warmed in the waterbath at 37°C for 30minutes prior to centrifuging sample to separate plasma and red cells for washing.
5. Performing antibody titres (anti-D) on each of the plasma samples using R2R2 cells

Results:

Anti-D titres ranged from 1:1024 to 1:256 000, titre did correlate with the strength of reactions in the final wash. Increased washing steps and wash solution to red cell ratio decreased reaction strengths in the final wash but failed to eliminate completely. Substituting the wash solution in the eluate kit for PBS didn't change the reaction scores in the final wash. Separating the EDTA whole blood at 37°C was able to yield a negative final wash and negative eluate result irrespective of the warm wash or room temp PBS washing.

Conclusions:

These results suggest Matuhasi Ogata Phenomenon is likely an in vitro phenomenon and separating the red cells from plasma at 37°C is able to bypass the interference seen in eluate testing.

Fetomaternal Haemorrhage (FMH) estimation by flow cytometry: anti-HbF or anti-RhD?

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¹Northern Pathology Victoria, Epping, Australia, ²Eastern Health Pathology, Box Hill, Australia, ³Roche Diagnostic, Melbourne, Australia, ⁴Pathology Queensland, Brisbane, Australia

Aim:

To evaluate the accuracy of Mollison's formula as published in the ANZSBT *Guidelines for the Laboratory Estimation of Fetomaternal Haemorrhage*, 2nd Edition, when calculating FMH volume using flow cytometry.

Methods:

Twenty-nine cord blood samples from Rh D positive neonates, all from Rh D negative mothers in a single metropolitan hospital, were analysed by flow cytometry (BD Lyric cytometer, BD FACSuite, FMH Quikquant Rapid Assay) using anti-D and anti-HbF antibodies to determine the percentage of foetal cells. HbA and HbF levels were quantified via capillary electrophoresis (Sebia Capillarys 2). Data were processed and analysed using Microsoft Excel.

Results:

Preliminary findings indicate a difference in foetal cell detection based on the antibody used. Using anti-HbF, an average of 4.26% of foetal cells (range 0.1–29.73%) were not detected, compared to 0.29% (range 0.02–1.32%) with anti-D. This discrepancy may contribute to underestimation of FMH and potential underdosing of RHlg prophylaxis. No correlation was observed between the proportion of undetected foetal cell population and HbA levels.

Conclusion:

Foetal cell detection by flow cytometry varies significantly depending on the antibody used. These results suggest that using anti-HbF alone may underestimate FMH. Our study is ongoing to assess if assumptions in Mollison's formula need to change according to the antibodies used to ensure accurate RHlg dosing.

From capillary passage to deformation dynamics: a framework for red blood cell assessment

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Aim: Failed or delayed red blood cell (RBC) deformation can lead to capillary trapping and microvascular obstruction. However, current capillary passage assays often measure transit alone, providing limited insight into deformation kinetics or post-stress recovery. We developed a time-resolved micropipette aspiration (MPA) framework to capture RBC deformation speed and recovery after unloading beyond deformation extent alone. We aimed to determine whether dynamic MPA parameters can identify mechanically vulnerable RBCs that deform slowly or fail to recover, suggesting increased capillary trapping risk.

Method: RBCs were assessed after hydrogen peroxide treatment (H_2O_2 ; 0 μM control to 1 mM) and in stored RBC components across five blood bag systems with different plasticiser and additive combinations. Individual RBCs were analysed by MPA using tongue length at 30 s as endpoint deformation (L_{30}). Tongue length ratio between early time point (1 s) and endpoint (30 s) L_1/L_{30} , and time to reach 80% of L_{30} (t_{80}) were used to quantify deformation kinetics. Recovery (post-stress mechanical resilience) was defined as return to original morphology after pressure release.

Results: Endpoint deformation L_{30} decreased by 18% at 1 mM H_2O_2 , with only limited endpoint change up to 500 μM H_2O_2 . By contrast, L_1/L_{30} decreased by 30% and t_{80} increased by 240%, with changes detectable from 250 μM H_2O_2 onward ($p < 0.05$). Cells with higher L_1/L_{30} and shorter t_{80} were more likely to recover, suggesting that post-aspiration recovery is more closely linked to deformation dynamics than endpoint deformation alone. In stored Lifeblood RBC samples, both L_1/L_{30} and t_{80} showed storage system dependent differences ($p < 0.05$), which were less evident from L_{30} alone.

Conclusion: Time resolved MPA identified RBC mechanical changes that were not captured by endpoint deformation alone. By linking deformation speed with post-stress recovery, this framework offers a more sensitive way to assess RBC mechanical resilience and identify RBCs at increased capillary trapping risk across stress and storage conditions.

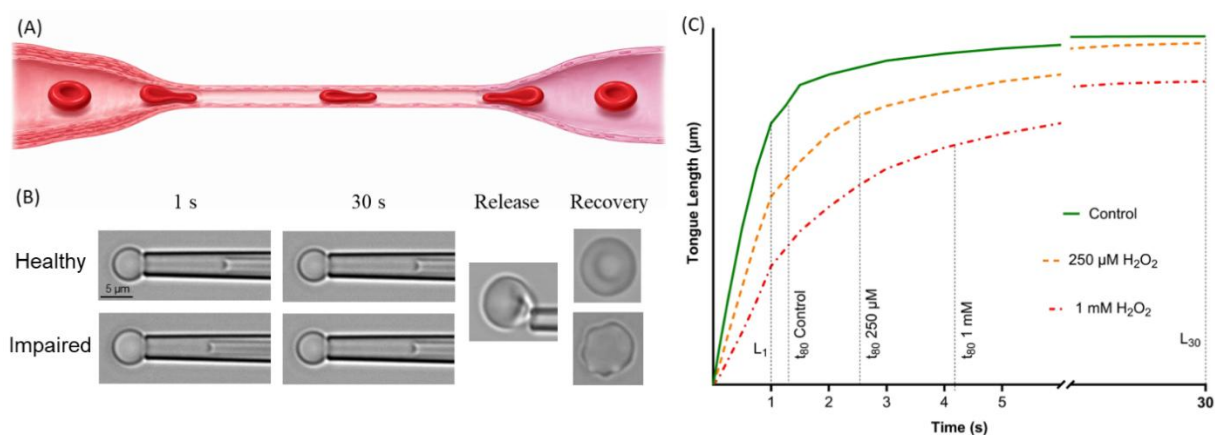


Figure. (A) Schematic of red blood cell microvascular transit, created with AI assistance. (B) Aspiration and recovery images. (C) Deformation curves under oxidative stress.

Investigation of anti-Hr and anti-hr^S in an antenatal patient with ceAR/ceAR genotype

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Aim:

To investigate an anti-e-like antibody in an antenatal patient phenotypically e⁺ and to determine whether the specificity represented anti-Hr, anti-hr^S or both.

Variant RHCE alleles such as *RHCE**ceAR encode partial e and c antigens and loss of high frequency antigens, Hr (RH18) and hr^S (RH19). Anti-Hr is clinically significant and associated with severe haemolytic transfusion reactions, whereas anti-hr^S is generally considered clinically insignificant. These phenotypes occur predominantly in individuals of African or Caribbean ancestry.

Method:

EDTA samples were referred to the Red Cell Reference Laboratory for confirmation of anti-e and classification of a weak D phenotype. Testing included routine blood grouping, phenotyping and antibody investigation by indirect antiglobulin techniques (IAT), papain treatment, allo-adsorption and elution using Immucor Gamma ELU-KIT II. Molecular testing was performed using Immucor BioArray HEA Precise, RHD and RHCE BeadChip™ kits.

Results:

The patient typed as A Rh(D) weak/variant and RHD genotyping identified the *DAR* allele, encoding partial D. Antibody identification demonstrated anti-e-like specificity despite an e⁺ phenotype with negative direct antiglobulin test (DAT) and auto control, excluding an autoantibody. Papain-IAT showed reactivity with all panel cells, including e- cells (R₂R₂ and r''r''), but not against Rh_{null} and -D- cells, suggesting an antibody to a high frequency Rh antigen. The patient's Fy(a-b-) phenotype suggested probable African ancestry. RHCE genotyping confirmed a *ceAR/ceAR* genotype, predicting loss of Hr and hr^S antigens. Given the predicted phenotype, allo-adsorptions were performed to exclude anti-D, -C and -E. Anti-hr^S was demonstrated in the R₂R₂ adsorbed plasma, while anti-Hr was detected by papain in eluates from R₂R₂ cells.

Conclusion:

This case demonstrates the complexity of antibody identification in patients with variant RHCE alleles. Systematic use of adsorption, elution and molecular testing enabled separation of anti-Hr from anti-hr^S, allowing identification of the clinically significant antibody. This approach was implemented for ongoing monitoring to detect additional allo-immunisation during pregnancy.

Variable M antigen typing associated with the MNS8 (Mc) variant

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Background:

The MNS blood group system M antigen, is routinely typed using monoclonal antisera, and anti-M antibodies are commonly detected in pre-transfusion testing. Monoclonal reagents are epitope-specific and may differ in their reactivity. This can lead to variable serologic phenotyping. Such variabilities may complicate antibody interpretation, particularly in patients with variant antigen expression. This case highlights clone-dependant variability in M antigen phenotyping observed during investigation of a patient with anti-M.

Case Summary:

A patient with anti-M demonstrated variable M antigen phenotyping. Antibody investigation showed a pan-reactive antibody with a positive direct antiglobulin test (IgG), strongest reactivity observed against M+ red cells. Allo-adsorption studies revealed an underlying anti-M, reacting with homozygous M+N- red cells.

Serological M phenotyping varied by reagent clone; positive with LM110/140, negative with BS57 and weakly reactive with a human source anti-M. Due to the variability, it was not possible to determine whether the antibody represented an auto-anti-M or an allo-anti-M in the setting of an M variant phenotype. The sample was referred for molecular investigation. Genotyping using the Immucor BioArray HEA Precise BeadChip™ Kit gave a predicted phenotype of M+N+. Next Gen Sequencing using the Illumina DNA Prep with Enrichment Kit along with a custom designed panel predicted the genotype: *GYPA*02/*08* & *GYPB*04/*04* consistent with the MNS8 (M^c) variant.

Conclusion:

Monoclonal antisera are designed to recognise specific antigenic epitopes and may demonstrate clone-dependant variability in reactivity, which can result in discrepant or variable serological phenotyping. In the setting of antigen variants, differences in epitope expression may further contribute to variable or absent reactivity with reagent clones. As the exact epitope targets of commercial antisera is not disclosed, caution should be exercised when interpreting phenotyping results. In this case, molecular testing suggests the presence of the MNS8 (M^c) variant, which raises the possibility of both a pan-agglutinating autoantibody and an anti-M.

Not all 3+ are equal: exploring “weak D” in pregnancy

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Aim:

RHD variants can result in reduced or altered D antigen expression. Accurate identification of clinically significant D variants is essential to guide clinical management. Pregnant women at risk of alloimmunisation should be managed as D-negative for transfusion and offered RhD immunoglobulin prophylaxis.

Currently ANZSBT guidelines recommend that weak D reactions ($\leq 2+$ [0-4+ scale]) in pregnancy be managed as D-negative, pending reference laboratory confirmation. However, with modern monoclonal anti-D reagents and changing population demographics, this threshold may miss clinically significant D variants. This study aimed to investigate the serological and molecular profile in samples with a strength of 3+ in routine D typing.

Method:

A study of 200 pregnant patients with 3+ RhD reactions identified during routine testing was undertaken. Samples were referred to the local Lifeblood Red Cell Reference laboratory for extended serological characterisation using column agglutination (CAT) and conventional tube techniques (CTT). A panel of commercially available human polyclonal and monoclonal anti-sera with a broad range of clones was used. The samples were then referred to Lifeblood's Brisbane laboratory for molecular analysis using the Immucor BioArray RHD BeadChip™ kit. Unresolved cases were further investigated with Next Gen Sequencing (Illumina).

Results:

Each sample showed variable agglutination reactions depending on testing platform and anti-D reagent used. Generally, agglutination reactions were stronger in CAT than CTT.

Molecular typing detected *RHD* variants in 88% (176/200) of samples while the remaining 12% carried the wild type *RHD* gene. Of 180, the most common D variants were DVII (n=37), weak D type 4.0 (n=27), weak D type 3 (n=27), weak D type 1 (n=16), DHMi (n=11), and DAR (n=9). The rest carried rarer known or novel *RHD* variants. For 76 patients, clinical management recommends that they should be treated as D-negative.

Conclusion:

Using a 3+ serological threshold identified a substantial number of *RHD* variants that would not be captured under current guidelines. This along with the high-than-expected prevalence

of DVII may support reconsideration of the significance of some *RHD* variants in alloimmunisation risk in this setting.

Type I anti-HNA-3a alloantibodies: potent activators of monolayer disruption

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Aim:

Human neutrophil antigen (HNA)-3a is expressed on choline transporter-like protein 2 (CTL2). Antibodies against HNA-3a have been associated with severe and fatal transfusion-related acute lung injury (TRALI). Epitope mapping suggests two types of HNA-3a antibodies exist: Type I antibodies can bind linearized antigens of HNA-3a, while type II antibodies require tertiary structure of CTL2 to bind. Evidence from laboratory and mouse studies demonstrate that antibody binding to HNA-3a expressed on pulmonary endothelial cells, rather than neutrophils, leads to disruption of intercellular junctions, fluid leakage and TRALI, without causing direct endothelial cell death. The aim of this study was to determine whether anti-HNA-3a antibody type impacts endothelial disruption.

Method:

Endothelial disruption was measured using transendothelial electrical resistance (TEER) (Applied biophysics). HNA3a/a positive human lung microvascular endothelial cells (HLMVECs) were grown to confluence and treated with lipopolysaccharide (2µg/mL) for 30mins. HLMVECs were then exposed to serum containing either type I or II anti-HNA-3a alloantibodies, antibody-negative control serum, or PBS (volume control). TEER (4000Hz) was measured for 60mins. Resistance was normalized at point of serum addition. Area under curve (AUC) analysis was done using trapezoidal rule with volume control as baseline. Significance determined using non-parametric ANOVA with Tukey's post hoc.

Results:

Only type I anti-HNA-3a sera (minimum normalised resistance: 0.658 ± 0.44 ; $P=0.0064$) caused significantly reduced TEER in comparison to control (minimum normalised resistance: 0.994 ± 0.066). AUC analysis indicated that treatment with type I sera (15.06 ± 2.427 negative AUC) significantly decreased resistance (and therefore increased permeability) of HLMVECs over the course of 60mins in comparison to type II (5.282 ± 4.868 negative AUC; $P=0.0218$) or control serum (0.707 ± 0.806 negative AUC; $P=0.0036$).

Conclusion:

Serum containing a type I anti-HNA-3a antibody induced greater HLMVEC permeability compared to serum containing type II anti-HNA-3a antibody. This suggests that epitope may be a factor in the severity of anti-HNA-3a mediated TRALI.

Chimera Transfusion Quick Guide

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Aim:

To investigate and resolve a mixed-field ABO discrepancy identified during routine blood group testing and determine appropriate transfusion management for a patient with suspected chimerism.

Method:

A 31-year-old female patient presented for routine fertility investigations. ABO and RhD blood grouping was performed on an EDTA whole blood sample using gel column agglutination technique. Mixed-field reactions were identified in the Anti-B columns of both the ABO/D and confirmation cards. Repeat testing was performed using a second analyser, alternate reagent manufacturer, tube methodology, and a second independently collected specimen. Patient clinical history was reviewed to exclude common causes of mixed-field reactions including transfusion, bone marrow transplant, pregnancy, IVF conception, and known twin relations. The sample was referred to Australian Red Cross Lifeblood for further investigation.

Results:

Repeat testing consistently demonstrated mixed-field reactivity in the Anti-B column across all methodologies and specimens. Common acquired causes of mixed-field reactions were excluded based on clinical history. Reference laboratory investigation confirmed the mixed-field reaction; however, a definitive blood group subtype could not be determined. Serological findings supported the presence of the B antigen with reverse grouping consistent with group B plasma characteristics.

Conclusion:

This case highlights the importance of investigating persistent mixed-field ABO discrepancies and recognising rare presentations of possible chimerism. In the absence of definitive subtype identification, conservative transfusion management was recommended, including group O red cell support and group B-compatible plasma products to minimise the risk of alloimmunisation and haemolytic transfusion reactions.

Probable para-bombay phenotype: A case study

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Case study:

A suspected rare para-Bombay phenotype was investigated at the New Zealand Blood Service National Reference Laboratory. A 56-year-old male presented with weak pan-reactivity during compatibility testing, normal ABO forward and reverse grouping, and a negative direct antiglobulin test.

Comprehensive serological investigations excluded the presence of multiple antibodies to high-incidence antigens. H typing of red cells was negative, and the patient's plasma was compatible with H-negative red cells, confirming the presence of anti-H. However, strong reactivity with anti-A,B antisera and weak incompatibility between the patient's red cells and plasma containing anti-H indicated residual A/B antigen expression, findings inconsistent with a true Bombay phenotype. Collectively, these results supported a para-Bombay phenotype. Definitive confirmation was not possible due to the unavailability of saliva secretor studies.

Conclusion:

This case highlights the importance of detailed serological investigation in the resolution of complex ABO phenotypes and underscores the role of reference laboratories in facilitating the provision of compatible blood when molecular or secretor testing is unavailable.

Liver transplant and transfusion – working together

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Background:

Royal Prince Alfred Hospital (RPAH) is the NSW state adult liver transplant centre. This audit aimed to review blood product usage in liver transplants at RPAH over the past 11 years, with the goal of identifying key patterns and trends to inform future practice.

Method:

This study will be a retrospective look back at 886 liver transplants that have occurred at RPAH between January 2014 and October 2025. Comparisons of disease aetiology, previous liver transplantation, total number of blood products as well as product by type breakdown will be examined for notable trends.

Results:

Between January 2014 and October 2025, a total of 886 liver transplants were performed at RPAH. The annual case numbers were stable (mean: 74 transplants/year), however, the total number of blood products used per procedure increased over time (Figure 1). Product utilisation patterns also shifted. Red cell usage remained relatively stable (mean 431 units per year), whereas cryoprecipitate usage increased (Figure 1). Additionally, although the number of patients requiring second or third liver transplants was low, these cases were associated with higher overall blood product utilisation.

Conclusion:

Royal Prince Alfred Hospital being the only adult liver transplant centre in NSW has given the RPAH Blood Bank staff a unique ability to audit trends in transfusion practice for liver transplants. Key trends identified such as product preference and potential load on the Transfusion laboratory will hopefully allow for better planning for product requirements from Lifeblood.

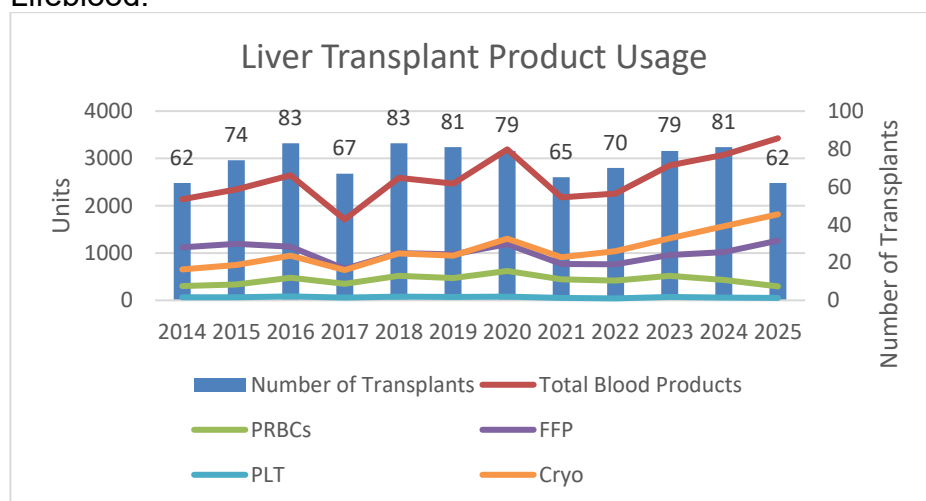


Figure 1. Total number of fresh blood products dispensed compared to number of liver transplants performed between January 2014 and October 2025.

Characterisation of umbilical cord blood T cells as a source for off-the-shelf allogeneic T-cell therapies

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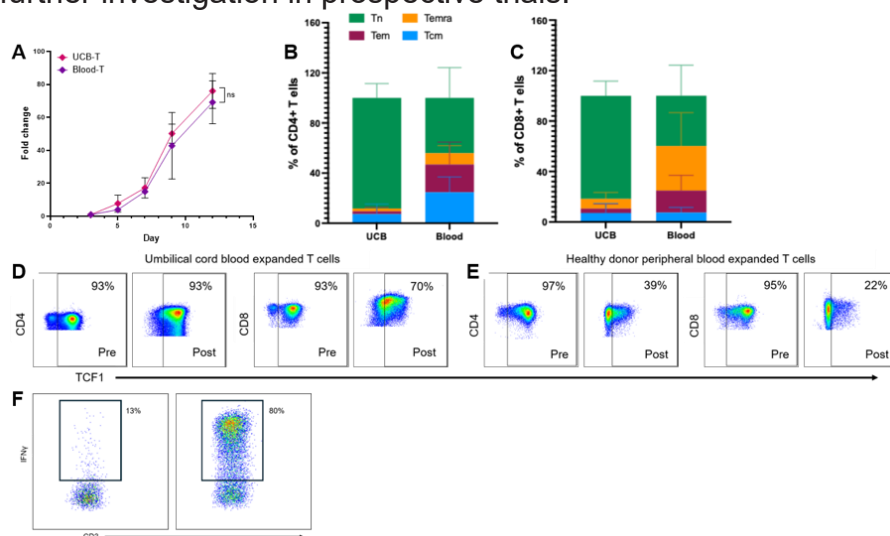
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Aim: Cellular therapies have demonstrated remarkable clinical responses in haematological malignancies; however, manufacturing delays, logistical barriers, and high costs remain important limitations. Third-party allogeneic strategies offer off-the-shelf production but graft-versus-host disease (GvHD) risk, and inferior T-cell persistence. This project aims to characterise UCB T cells as the basis for local development of off-the-shelf allogeneic cellular therapies to address these barriers.

Method: UCB mononuclear cells sourced from the Queensland Cord Blood Bank (QCBB; n=9) and peripheral blood mononuclear cells (PBMC) from healthy adult donors (n=6) were transduced separately with CD19 CAR (Miltényi) or NY-ESO-1-specific T-cell receptor (TCR) constructs using a lentiviral system. To expand, transduced cells were seeded at 1×10^6 cells/mL, activated with Transact in TexMACS supplemented with 2.5% human AB serum for 12–14 days using IL-12/IL-15. Expanded T cells were comprehensively immunophenotyped by 30-colour spectral flow (Cytex, Aurora).

Results: UCB T cells expanded comparably to healthy adult T cells at >40-fold (range 30–60-fold; Figure 1A), with similar transduction efficiency across constructs ($p = 0.4682$). UCB demonstrated a higher proportion of naïve T cells (Tn) in both CD4+ (88.2% vs 44.1%, $p=0.001$) and CD8+ subsets (81.7% vs 39.8%, $p=0.0027$) compared to healthy adult PBMC prior to expansion, with accordingly low proportions of Tem, Tcm, and Temra memory T-cell subsets (Figure 1B & C). Following expansion, TCF-1, a transcription factor associated with stem-like T-cell properties and improved adoptive T-cell persistence, remained highly enriched in UCB-derived T cells compared to adult PBMC (Figure 1D & E). TCR-transduced UCB T cells demonstrated robust cytokine response upon co-culture with target cells (Figure 1F).

Conclusion: UCB T cells can be efficiently expanded, engineered with CAR and TCR constructs and retain a stem-like phenotype that may confer persistence and efficacy advantages over existing allogeneic platforms. These findings support feasibility and warrant further investigation in prospective trials.



Detection and management of mixed field reactions in immunohaematology – an EQA review.

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Aim:

The RCPAQAP transfusion compatibility surveys consist of a simulated patient and donor unit samples designed to mimic various transfusion scenarios. The aim of this study was to evaluate laboratory performance in the detection and interpretation of mixed-field (MF) reactions in transfusion scenario-based proficiency testing, using RCPAQAP data to identify potential knowledge gaps and further educational opportunities.

Method:

Returned results from four RCPAQAP Transfusion compatibility survey cases, designed to replicate mixed field reactions, were reviewed. The detection rates and subsequent follow-up of transfusion decisions for the related donor units in the surveys were compared with methods and local policies.

Results:

Across four related scenarios, an average of 89% of participants correctly recognised and interpreted mixed field reactions. Method specific trends were noted with the CAT-gel platform demonstrating a statistically significant ($p < 0.05$) lower rate of misclassification compared to participants using CAT-glass beads and conventional tube methods. Variations in Laboratory Information Management System (LIMS) configuration and local policy-driven practices for indeterminate blood group results also contributed to apparent inconsistencies in decision making for donor unit transfusions.

Conclusion:

While limited, this review of EQA proficiency testing data provides further evidence of ongoing challenges with the management of mixed field reactions in the Transfusion testing space. While the analytical competence of recognising mixed field agglutinations has been demonstrated by most participants, variable testing practices and reporting protocols remain a consideration in the interpretation and management of patient cases with indeterminate blood groups. A combination of targeted education, and alignment with related reporting guidelines such as the ANZBT can all contribute to improved laboratory responses and support patient safety.

MRD-Seq: a flexible approach to residual disease monitoring in AML

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Aim:

Acute myeloid leukaemia (AML) is a genetically heterogeneous malignancy with poor prognosis and high relapse rates. While complete remission is achievable, many patients relapse due to persistent measurable residual disease (MRD). Sensitive MRD detection is critical for assessing treatment response and predicting relapse. Current quantitative PCR (qPCR)-based MRD assays are very labour-intensive to establish, and are thus only available for about one-third of AML patients. To address these limitations, we developed MRD-Seq, a next-generation sequencing (NGS)-based method for sensitive, broadly applicable MRD detection.

Method:

MRD-Seq involves amplification of genomic regions surrounding AML-associated somatic mutations, followed by next-generation sequencing of the amplified DNA and bioinformatics analysis. We applied MRD-Seq to *NPM1* Exon-12 mutations, assessing sensitivity using a dilution series of OCI-AML3 cells carrying the *NPM1* Type A mutation. We also evaluated MRD-Seq assay performance using genomic DNA (gDNA) versus complementary DNA (cDNA) as input material and directly compared both input types with the conventional RNA-based *NPM1* qPCR assay.

Results:

Both gDNA- and cDNA-based MRD-Seq assays achieved similar sensitivities of 1×10^{-4} to 10^{-5} , which were slightly lower than the sensitivity of 1×10^{-5} reached by the *NPM1* qPCR assay. Despite MRD-Seq having lower sensitivity, it provided robust detection across both gDNA and cDNA inputs, offering flexibility and applicability to a broader patient population.

Conclusion:

MRD-Seq is a practical and sensitive method for MRD monitoring that can be easily adapted to the majority of AML patients, addressing a critical unmet need in disease management. Its adaptability to virtually any somatic mutation makes it well-suited not only for AML but also for other malignancies where tumour-specific somatic mutations can be identified. This capability supports personalised disease monitoring, informs risk stratification, and facilitates timely treatment decisions, thereby improving identification of patients at risk of relapse and enhancing precision management in AML.

Lenalidomide-emergent B cell acute lymphoblastic leukaemia

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Aim:

Prolonged lenalidomide therapy in multiple myeloma (MM) is associated with second primary malignancies (SPMs), most commonly myelodysplastic syndrome and acute myeloid leukaemia. Lenalidomide-emergent acute lymphoblastic leukaemia (Len-ALL) is rare, with only 55 reported cases between 2013 and 2025. Here, we present four cases of Len-ALL.

Cases:

Patient 1: A 71-year-old man with IgGκ MM received lenalidomide maintenance for three years following VTD induction and tandem autologous stem cell transplantation (autoSCT). Investigation for severe thrombocytopenia, neutropenia, and rising paraprotein demonstrated 51% blasts on bone marrow aspirate and trephine (BMAT), consistent with Philadelphia chromosome-negative (Ph-) B-ALL with hypodiploid karyotype. He completed ALL-06 induction and commenced POMP maintenance but died from infection and progressive disease.

Patient 2: A 63-year-old man with IgD MM received lenalidomide maintenance for five years following VRD induction and autoSCT. He presented with fatigue and circulating blasts, with BMAT confirming Ph- B-ALL with hypodiploid karyotype. He is receiving an MDACC-style regimen with hyperCVAD and blinatumomab and is planned for allogeneic stem cell transplantation (alloSCT).

Patient 3: A 65-year-old man with IgA MM received lenalidomide maintenance for eight years following VCD induction and autoSCT. BMAT for mild cytopenias and macrocytosis confirmed Ph- B-ALL with del(20q). He is also receiving hyperCVAD and blinatumomab with planned alloSCT.

Patient 4: A 66-year-old woman with IgA MM presented with epistaxis, pancytopenia, and circulating blasts. She had ceased lenalidomide three months earlier after almost three years of therapy due to metastatic breast cancer. BMAT confirmed extensive Ph- B-ALL. Given comorbidities and patient preference, she is receiving conservative management.

Conclusion:

Len-ALL is a rare but genomically high-risk entity associated with prolonged lenalidomide exposure. Management is challenging due to older patient age and coexisting MM. Blinatumomab-containing induction may improve outcomes; however, the optimal consolidation strategy, including the role of alloSCT versus minimal residual disease-guided therapy, remains uncertain.

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Tetrandrine re-sensitises AML cells to HMA treatment after resistance induced by direct co-culture with bone marrow stromal cells in vitro

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Aim:

The bone marrow microenvironment is known to influence treatment response and can increase AML cell resistance to various anti-cancer therapies, including hypomethylating agents (HMA). Tetrandrine, derived from the Chinese herb *Stephania tetrandra*, is currently being explored as a clinical agent in HMA combination treatment. However, it is unknown how the bone marrow microenvironment may influence its efficacy. The aim of this study was to investigate the effects of tetrandrine treatment, alone and in combination with HMAs, on AML cells grown in mono-culture compared to those co-cultured with bone marrow stromal cells.

Method:

AML cell lines (SKM-1, THP-1, Kasumi-3, and BDCM) were cultured with and without HS-5 bone marrow stromal cells for at least 7 days prior to receiving a dose-response of tetrandrine, HMA (azacitidine or decitabine), or HMA sub-lethal pretreatment before tetrandrine combination treatment. Cell viability was measured using resazurin and then utilised for synergy combination estimation and area under the curve (AUC) calculation as a measure of resistance. AUC significance was calculated using a two-way ANOVA, with a Sidak post-hoc test.

Results:

Cell lines exhibited varying responses to single agent treatment, but all investigated lines revealed increased cell death when tetrandrine and HMA were combined, indicating synergistic interactions. While co-culturing significantly increased the resistance of AML cells to azacitidine ($p=0.0023$) and decitabine ($p=0.0077$) single agent treatment, it does not significantly increase resistance to tetrandrine single agent treatment ($p=0.8994$) nor HMA/tetrandrine combination ($p=>0.9999$). Additionally, co-cultured AML cells revealed increased synergy between tetrandrine/HMA when compared to mono-cultured cells.

Conclusion:

These results suggest that the increased resistance to anti-cancer agents, due to the bone marrow microenvironment, does not impact tetrandrine single agent and combination therapy allowing for a new combination to overcome HMA resistance.

Cutaneous pseudoprogression following Tisagenlecleucel (Kymriah) CAR-T Cell Therapy in relapsed/refractory B-Cell acute Lymphoblastic Leukaemia: A case report

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Background

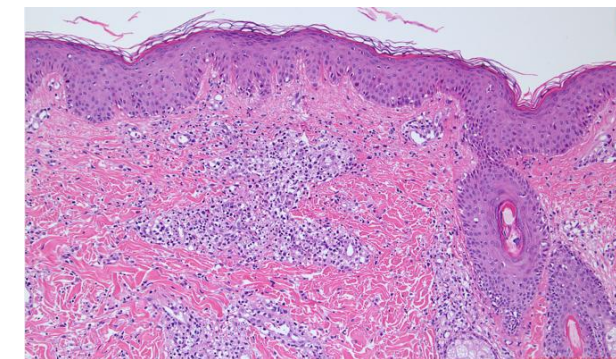
Chimeric antigen receptor T-cell (CAR-T) therapy with tisagenlecleucel has demonstrated efficacy in relapsed/refractory B-cell ALL. Pseudoprogression defined as a transient inflammatory response at disease sites driven by CAR-T cell infiltration rather than tumour proliferation is recognized in solid tumour immunotherapy but remains poorly characterized following CAR-T therapy. Distinguishing pseudoprogression from true disease progression has direct therapeutic implications, as misclassification may lead to unnecessary intervention or premature discontinuation of a potentially curative therapy.

Case Presentation

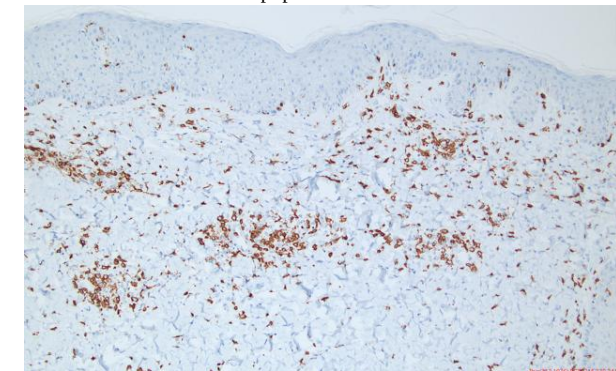
A 20-year-old male presented with relapsed Philadelphia chromosome-negative B-ALL (prior disease history summarized in Table 1) with extensive extramedullary disease, including testicular, nodal, and cutaneous involvement. Following orchidectomy and bridging therapy with vincristine/dexamethasone and inotuzumab-ozogamicin, he achieved MRD-negative remission with complete resolution of extramedullary disease on the PET imaging. After lymphodepletion, he received tisagenlecleucel. On D+3 he developed Grade 1 CRS, managed with tocilizumab/dexamethasone, and resolved at D+5. He did not experience any neurotoxicity. On D+6 , a nodular erythematous rash at the previous sites of disease appeared. Concurrently, ALC rose sharply from $0.26 \times 10^9/L$, reaching a peak of $8.82 \times 10^9/L$ on D+9, skin lesion burden was maximal at this time. ALC subsequently spontaneously declined over the following week to $1.32 \times 10^9/L$ by D+18, with parallel spontaneous regression of all cutaneous lesions by D+21. A punch biopsy of a chest lesion taken on D+7 demonstrated a lymphohistiocytic infiltrate composed of medium-sized CD8-positive T-cells with prominent apoptotic/leukocytoclastic debris. No B-cells were identified on immunohistochemistry. The findings were interpreted as consistent with CAR-T cell infiltration rather than progressive disease.

Table 1
Disease History and Treatment Pathway Prior to CAR-T Cell Therapy

Date	Event	Key details
2014	Diagnosis	Ph- B-ALL, CNS negative. Treated per COG AALL0932. Complete remission maintained through 2017.
July 2022	First relapse	Relapsed B-ALL with complex karyotype and clonal evolution, CNS negative. Treated per COG AALL1331.
Late 2022	Blinatumomab	MRD positive after re-induction; MRD negativity achieved after cycle 1 blinatumomab.
November 2022	Allogeneic SCT	Matched sibling donor SCT. Conditioning: TBI/cyclophosphamide. Complicated by mild chronic liver GvHD, which resolved by December 2023.



1. (HE 10x) Perivascular lymphohistiocytic infiltrate with prominent apoptotic debris.



2. (CD3 10x) CD3 immunohistochemistry.

Day +30 PET-imaging and bone marrow assessment confirmed MRD-negative complete remission.

Conclusion

This case illustrates the diagnostic challenge of pseudoprogression following CAR-T cell therapy. Recognition of the temporal concordance between peak ALC, lesion burden, and spontaneous regression is essential to distinguish pseudoprogression from true disease progression and to avoid unnecessary intervention that may compromise a potentially curative therapy.

Targeting leukaemia stem cells by inhibiting the aryl hydrocarbon receptor

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Aim:

Leukaemia stem cells (LSCs) not only drive and sustain acute myeloid leukaemia (AML), but frequently also survive chemotherapy and cause relapse. The aryl hydrocarbon receptor (AHR) was shown to be critical for the self-renewal properties of haematopoietic stem cells (HSCs). Here we investigate the effect of AHR inhibition on LSCs in mouse bone marrow transplantation models (MBMTM) of AML.

Methods:

Limiting dilution murine bone marrow transplantation assays were performed in order to measure LSC frequency in MBMTMs of AML. Competitive repopulation assays (CRAs) were employed to measure HSC frequency.

Results:

AHR inhibition eliminated LSC in our *CALM/AF10* AML model. None of the mice transplanted with leukaemia cells (n=9) that had been treated *ex vivo* with an AHR inhibitor developed leukaemia (Figure 1, red curve), whereas 8/9 mice developed leukaemia who had been transplanted with untreated leukemia cells (n=9).

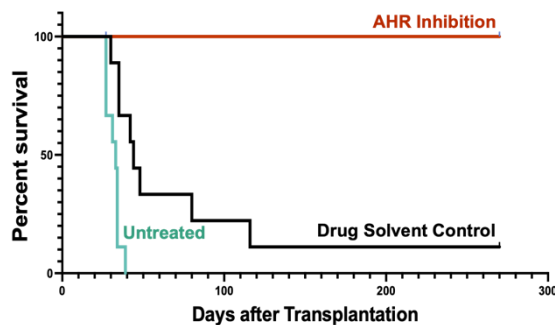


Figure 1. Survival of *CALM/AF10* AML model mice

In several CRAs we showed that AHR inhibition did not negatively affect healthy HSCs.

We then tested the effect of AHR inhibition on LSCs in two additional AML murine models: the *RUNX1/RUNX1T19a* and the *KMT2A/MLLT3* models. We also observed a similar deleterious effect of AHR inhibition on LSCs in these two models.

Conclusion

These results demonstrate that AHR inhibition specifically targets LSCs in different AML models, and at the same time does not negatively affect healthy HSCs. Thus, AHR inhibition shows promise as a new strategy to treat AML, hopefully with fewer side effects compared to conventional chemotherapy.

Characteristics, management and outcomes of adult Philadelphia-positive acute lymphoblastic leukaemia (Ph+ ALL) patients at Fiona Stanley Hospital

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Aim:

To present a case series that evaluates the characteristics, diagnosis, course, management, monitoring and outcomes of adult Ph+ ALL patients at Fiona Stanley Hospital (FSH) from 2015-present.

Method:

Our inclusion criteria included adult patients diagnosed with Ph+ ALL from January 2015 to April 2026 at FSH in Western Australia, with diagnosis established by both clinical and laboratory evaluation. We interrogated FSH medical records and laboratory results to evaluate patient characteristics, diagnosis, course, management, monitoring and outcomes.

Results:

Eight patients met the inclusion criteria, comprising four females and four males. The average age at diagnosis was 56.5 years (range =43–70 years). Common additional chromosomal abnormalities identified included der(22)t(9;22) abnormalities ($n=4$) and complete or partial deletion of chromosome 9 ($n=2$). Four patients had a minor breakpoint cluster region detected in isolation, and one patient had a major breakpoint cluster region detected in isolation. In one patient, both the minor and major breakpoint cluster regions were detected. All 8 patients received chemotherapy with Tyrosine kinase inhibitors (TKIs) as first-line therapy. Two patients had cytogenetic and CNS relapses following initial cytogenetic remission, requiring additional lines of therapy. Two patients received allogeneic hemopoietic stem cell transplants (allo-HSCT). Currently, only two patients are alive and in continued cytogenetic and molecular remission. Six patients died within 2 years of diagnosis: three due to treatment-related complications, and two due to disease relapse.

Conclusion:

Despite TKIs and selective use of transplantation, clinical outcomes were poor amongst our patient group, especially in relation to treatment-related complications, highlighting the need for more individualised therapeutic regimens considering baseline characteristics, tolerance of intensive therapies, and minimal residual disease monitoring. Further research exploring long-term data on adult Ph+ ALL patients in the TKI era is needed to inform therapeutic decision making.

Outcomes with tagraxofusp for the treatment of blastic plasmacytoid dendritic cell neoplasm in Australian patients

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Aim:

Since tagraxofusp was released for compassionate access in Australia in 2023 for the treatment of blastic plasmacytoid dendritic cell neoplasm (BPDCN), its effect on patient outcomes remains unknown. This study aimed to compare tagraxofusp outcomes in BPDCN patients with those achieved using conventional chemotherapeutic approaches such as hyperfractionated cyclophosphamide, vincristine, adriamycin, and dexamethasone (HCVAD).

Method:

Using a retrospective approach, adult Australian BPDCN patients treated at Sir Charles Gairdner Hospital in Perth, Western Australia, were divided into two groups: those who received first-line tagraxofusp (n = 2) and those who received first-line HCVAD-based therapy (n = 4). Baseline characteristics, median complete response (CR) rates, progression-free survival (PFS) and overall survival (OS) were analysed, and tagraxofusp-related adverse events were also evaluated.

Results:

All patients were male and median age at diagnosis was 71.5 years (tagraxofusp) and 63.5 years (HCVAD). All patients had skin lesions, 2/2 treated with tagraxofusp and 2/4 with HCVAD had leukaemic phase disease, and 1/2 tagraxofusp patients had CNS involvement at presentation. Preliminary results suggest tagraxofusp yielded a lower median CR rate (1/2 vs 4/4) and shorter CR duration (3.1 vs 107.4 months) compared to HCVAD regimens. Similarly, tagraxofusp was associated with shorter median PFS (2.8 vs 70.4 months) and median OS (6.0 vs 116.6 months). While 2/4 of the HCVAD group subsequently underwent autologous HSCT, none of the tagraxofusp patients received this treatment. Capillary leak syndrome was observed in all tagraxofusp patients and other adverse events reported in this group included cytopenias, ALT elevation and hyponatraemia.

Conclusion:

BPDCN is an uncommon diagnosis with no uniform approach to treatment. In this small series, durable disease control was achieved with chemotherapy +/- stem cell transplant, while tagraxofusp was associated with less favourable outcomes.

Functionally validating cooperating mutations in murine models of leukaemia

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Aim:

Acute Myeloid Leukaemia (AML) is driven by the acquisition of multiple genetic aberrations that cooperate. Our aim is to study which mutations cooperate with each other to drive AML.

Method:

CALM/AF10 (C/A) is a rare but recurring fusion gene detected in leukaemia and lymphoma. We have previously established two murine C/A-driven AML models and identified several additional acquired mutations, particularly in RAS pathway genes (e.g., *Flt3*, *Ptpn11* and *Cbl*). We thus hypothesised that the C/A fusion cooperates with RAS pathway mutations to drive AML.

To test this, bone marrow (BM) cells from C/A-expressing CD45.2⁺ mice were isolated prior to leukaemia onset and genetically modified using CRISPR/Cas9-mediated gene editing to introduce mutations in *Cbl*. Edited cells were transplanted into sub-lethally irradiated congenic (CD45.1⁺) recipient mice (*CA*⁺/*Cbl*^{mut}; n=3). Two control groups were included: one received unedited C/A-positive cells (*CA*⁺/*Cbl*^{WT}; n=3), and the other received C/A-negative cells with modified *Cbl* (*CA*⁻/*Cbl*^{mut}; n=5). Peripheral blood from the mice was analysed periodically for engraftment and editing efficiency.

Results:

Ten of the 11 transplanted mice engrafted successfully, with mean CD45.2⁺ engraftment of 82% at 8 weeks post-transplant and mean editing efficiency of 62.34% at the target site at 16 weeks post-transplant. One *CA*⁺/*Cbl*^{mut} mouse did not engraft and was excluded from analysis.

Strikingly, the remaining two *CA*⁺/*Cbl*^{mut} mice developed leukaemia with latencies of 72 and 86 days, whereas none of the control mice developed disease. The two leukaemias displayed different phenotypes: one myeloid, and the other biphenotypic, characterised by co-expression of myeloid and B-cell markers.

Conclusion:

Our results indicate that the C/A fusion cooperates with mutations in *Cbl*, to drive aggressive leukaemia, and highlight the role of mutational cooperativity in AML. This model provides a clinically relevant platform to study cooperating oncogenic mechanisms and develop more targeted therapeutic strategies in AML.

Lenalidomide-associated B-ALL: a single centre retrospective case series

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Aim:

Lenalidomide-associated B-cell acute lymphoblastic leukaemia (B-ALL) is an emerging but poorly characterised therapy-related neoplasm occurring in patients with multiple myeloma (MM). Although prior case series have suggested favourable initial response to standard ALL-directed therapy despite high-risk genomic features, the optimal management and long-term outcomes remain unclear. We aimed to describe the clinical characteristics and treatment outcomes of patients with lenalidomide-associated B-ALL at our centre.

Method:

We retrospectively reviewed patients who underwent autologous stem cell transplantation (ASCT) for MM at Auckland City Hospital (ACH) between September 2020 and March 2026 and subsequently developed B-ALL following lenalidomide maintenance therapy. Data collected included demographics, prior myeloma treatment lines including ASCT, duration of lenalidomide exposure, interval between MM and B-ALL diagnosis, cytogenetic and next-generation sequencing (NGS) findings where available, treatment regimens, and outcomes.

Results:

Among 246 patients who underwent ASCT, four developed B-ALL following lenalidomide maintenance therapy and met inclusion criteria. Cumulative lenalidomide exposure ranged from 2.9 to 4.3 years, with a median interval of 7.6 years between MM and B-ALL diagnosis. Cytogenetic and molecular analyses demonstrated hypodiploidy karyotype in one patient and complex karyotype in 3 patients. One patient had biallelic TP53. All patients were BCR::ABL1 negative. Patients received conventional adult ALL protocols, including UKALL60+ and CALGB >60 regimens. Outcomes were poor overall: one patient died during induction therapy, one had primary refractory disease, and two relapsed during consolidation or maintenance therapy within one year of diagnosis. Survival following B-ALL diagnosis ranged from 1 to 11 months.

Conclusion

Lenalidomide-associated B-ALL may represent a small but distinct high-risk therapy-related ALL-subtype with poor outcomes following conventional chemotherapy, contrasting with previously published studies. Further studies are needed to define optimal treatment strategies, identify patients at increased risk, and refine risk-adapted approaches to lenalidomide maintenance.

Real-world outcomes of frontline azacitidine-venetoclax in acute myeloid leukaemia: a single-centre retrospective analysis:

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¹Sir Charles Gairdner Hospital, Nedlands, Australia

Aim:

To evaluate real-world outcomes of frontline azacitidine-venetoclax in patients with acute myeloid leukaemia (AML) treated at a single tertiary centre.

Method:

We conducted a retrospective analysis of patients treated with frontline azacitidine-venetoclax between 2020 and 2025 using a local AML database in conjunction with pharmacy dispensing records. Baseline demographic, molecular and cytogenetic data were reviewed where available. Best documented response was determined from available bone marrow assessments. The primary endpoint was composite marrow response rate (CR/CRi/MLFS). Secondary endpoints included CR/CRi rate, 30-day mortality and relapse rate.

Results:

Forty-seven patients met inclusion criteria. Median age at diagnosis was 74 years (range 62–86). De novo AML accounted for 50% of cases, while 25% had secondary AML and 25% had therapy-related AML. Complex karyotype was present in 32% of patients. Median number of azacitidine-venetoclax cycles administered was 4 (range 1–31).

Response assessment was available in 43 patients, while four patients died prior to marrow reassessment. CR/CRi/MLFS was achieved in 30/43 evaluable patients (70%), while CR/CRi was achieved in 16/43 evaluable patients (37%), highlighting that a substantial proportion of responders achieved marrow clearance without full peripheral blood count recovery. Thirty-day mortality was 8.5%. Relapse was documented in 34% of patients during the available follow-up.

Exploratory subgroup analysis demonstrated CR/CRi/MLFS rates of 50% in TP53-mutated patients compared with 70% in TP53 wild-type patients.

Conclusion:

This retrospective analysis demonstrates response rates and early mortality consistent with published clinical trial data in an older AML population with diverse cytogenetic and molecular features.

Composite marrow response rates were broadly comparable to published clinical trials, although CR/CRi rates were lower when MLFS responses were excluded. Variation in practice regarding timing of marrow assessment and restarting treatment likely impacts documented response rates in the real world setting.

A phase 3 study of revumenib in combination with intensive chemotherapy in patients with newly diagnosed NPM1-mutated acute myeloid leukemia (REVEAL-ND NPM1): Trial in progress

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³The University of Texas MD Anderson Cancer Center, Houston, USA, ⁴University of São Paulo, São Paulo, Brazil, ⁵University of Osaka, Osaka, Japan, ⁶University Medical Center, Johannes Gutenberg-University, Mainz, Germany, ⁷Syndax Pharmaceuticals, Inc., New York, USA, ⁸University of Oxford, Oxford, UK

Aim:

To assess the safety and efficacy of revumenib in combination with intensive chemotherapy (IC) in patients with newly diagnosed (ND) nucleophosmin-1 mutation (*NPM1m*) acute myeloid leukemia (AML). There are currently no approved targeted therapies for ND AML harboring a *NPM1m*, which occurs in ~30% of ND adult AML cases. In *NPM1m* AML, the *NPM1m*/XPO1 protein complex binds to DNA to sustain the interaction of menin and wild-type KMT2A that drives upregulation of *HOX/MEIS* gene expression, resulting in hematopoietic differentiation arrest and leukemogenesis. Revumenib is a first-in-class, oral, potent, and selective inhibitor of the menin-KMT2A interaction. In the phase 1/2 AUGMENT-101 study (NCT04065399), revumenib monotherapy demonstrated clinically meaningful response rates and was generally well tolerated in relapsed/refractory *NPM1m* AML, leading to US Food and Drug Administration approval for that patient population in 2025. Standard AML treatment for younger, non-frail adults is based on IC regimens and hematopoietic stem cell transplant (HSCT). The addition of revumenib to standard IC may further improve treatment responses specifically in the ND setting.

Method:

REVEAL-ND NPM1 is a phase 3, multicenter, randomized, double-blind, placebo-controlled trial (NCT07211958). Eligible patients are aged ≥12 years with treatment-naïve ND *NPM1m* AML that weigh ≥40kg. Patients will be randomized 1:1 to revumenib or placebo in combination with IC. Induction consists of 1 to 2 cycles of revumenib or placebo (dosed orally) alongside IC with cytarabine and daunorubicin or idarubicin (dosed intravenously). Consolidation consists of 1 to 3 cycles of revumenib or placebo plus cytarabine. HSCT may be performed after initial induction or consolidation. Treatment with revumenib or placebo monotherapy will continue for up to 2 years, with long-term follow-up until death, withdrawal of consent, or study closure. See **Figure** for endpoints. Approximately 468 patients will be enrolled. Enrollment is ongoing as of January 27, 2026.

Results: N/A

Conclusions: N/A

Figure. Endpoints

Objectives	Endpoint(s)	Description
Primary	Event-Free Survival (EFS)	Time from treatment start to treatment failure, relapse, or death assessed by independent reviewers
	Measurable Residual Disease (MRD)-Negative Complete Remission (CR) in Bone Marrow	CR with no MRD assessed by independent reviewers
Key Secondary	Overall Survival (OS)	Time from treatment start to death from any cause
Additional Investigator-Assessed	Complete Remission Rate	Proportion of patients achieving complete remission
	Composite Complete Remission (CRc) Rate	Proportion of patients with CR or CR with incomplete hematologic recovery
	Overall Response Rate (ORR)	Proportion achieving any predefined response (CR, CRc, etc.)
	Duration of Response (DoR)	Length of time response is maintained (CR or CRc)
	Safety	Assessment of adverse events and tolerability
	Quality of Life (QoL)	Patient-reported outcomes related to well-being

CR, complete remission; CRc, composite complete remission; DoR, duration of response; EFS, event-free survival; MRD, minimal residual disease; OS, overall survival; QoL, quality of life.

Revumenib plus intensive chemotherapy for newly diagnosed acute myeloid leukemia harboring genetic alterations in KMT2A, NPM1, or NUP98: updated phase 1 results from SNDX-5613-0708

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Aim:

Evaluate revumenib plus intensive chemotherapy (IC) in SNDX-5613-0708 (NCT06226571), a phase 1 dose-escalation study in patients (18–75 years) with newly diagnosed acute myeloid leukemia (AML) with a *KMT2Ar*, *NPM1-mutated* (*NPM1m*), or *NUP98r*. Acute leukemias (AL) harboring *KMT2A* or *NUP98* rearrangements (*KMT2Ar* or *NUP98r*) and *NPM1m* AML exhibit poor outcomes. Revumenib is a first-in-class, oral, potent, and selective menin-*KMT2A* inhibitor used for the treatment of relapsed/refractory (R/R) *NPM1m* AML or R/R *KMT2Ar* AL.

Method:

Enrolled patients were administered either 110mg/220mg (dose level [DL] 1) or 160 mg/270mg (DL2) ± strong CYP3A4i with cytarabine and daunorubicin or idarubicin. Patients achieving complete remission (CR; ± hematologic recovery) received consolidation therapy with revumenib plus high-dose cytarabine, followed by optional hematopoietic stem cell transplant (HSCT) and revumenib maintenance. Primary endpoints were dose-limiting toxicities (DLTs) and safety; secondary endpoints included overall response rate (ORR), CR, composite CR (CRc), and measurable residual disease–negative (MRD–) CR.

Results:

As of 02Oct2025, 13 (DL1) and 18 (DL2) patients were treated. Median ages were 43.0 (DL1) and 57.5 (DL2) years. *KMT2Ar* was detected in 92% and 39% and *NPM1m* in 8% and 56%, respectively. Median treatment durations were 73.0 (DL1) and 34.0 (DL2) days. One DLT occurred (DL1). Adverse events are summarized in the **Figure**. No differentiation syndrome occurred. Any-grade QTcF prolongation occurred in 6% (DL1 only). ORR was 100% (DL1) and 92.9% (DL2); CRc, 100% and 85.7%; and CR, 91.7% and 78.6%, respectively. MRD– CR occurred in 100% (DL1) and 70.0% (DL2). Seven DL1 patients underwent HSCT (5 resumed revumenib). Median time to neutrophil and platelet recovery was 29.0 (both DL1/DL2) and 28.0/29.0 days (DL1/DL2), respectively.

Conclusion:

Revumenib plus IC demonstrated a manageable safety profile and promising deep responses with high MRD– CR rates, supporting evaluation of revumenib in the phase 3 REVEAL-ND *NPM1* trial (NCT07211958).

Figure. Summary of Treatment-Emergent Adverse Events.

Parameter, n (%)	DL1 (n=13)	DL2 (n=18)	Total (N=31)
Any TEAE	13 (100)	18 (100)	31 (100)
Revumenib-related	9 (69)	10 (56)	19 (61)
Grade ≥ 3 TEAEs^a	11 (85)	16 (89)	27 (87)
Febrile neutropenia	6 (46)	10 (56)	16 (52)
Platelet count decreased	5 (38)	4 (22)	9 (29)
Anemia	3 (23)	6 (33)	9 (29)
White blood cell <u>count</u> decreased	4 (31)	4 (22)	8 (26)
Neutrophil count decreased	4 (31)	3 (17)	7 (23)
Thrombocytopenia	1 (8)	5 (28)	6 (19)
Neutropenia	1 (8)	4 (22)	5 (16)
Grade ≥ 3 revumenib-related TEAEs^b	5 (38)	8 (44)	13 (42)
Anemia	3 (23)	3 (17)	6 (19)
Neutrophil count decreased	3 (23)	1 (6)	4 (13)
Serious TEAEs	6 (46)	8 (44)	14 (45)
TEAEs leading to dose modifications			
Reduction	2 (15)	0	2 (6)
Discontinuation	3 (23)	1 (6)	4 (13)
TEAEs leading to death	0	1 (6)	1 (3)

^aEvents that occurred in $\geq 15\%$ of total population. ^bEvents that occurred in $\geq 10\%$ of total population. DL1, dose level 1; DL2, dose level 2; TEAE, treatment-emergent adverse event.

Real-world use of IgPro10 (Privigen®): review of 10 years of post-marketing pharmacovigilance data

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Aim:

IgPro10 (Privigen®; CSL Behring) is an intravenous immunoglobulin (IVIG) first authorised in 2007 and approved worldwide for immunoglobulin replacement therapy (IgRT) in immunodeficiency diseases and immunomodulatory treatment of various autoimmune conditions. Here, we review post-marketing pharmacovigilance data received worldwide to characterise the real-world safety profile of IgPro10 over a 10-year period.

Method:

All post-marketing reports of adverse events (AEs) received worldwide between 01 January 2016 and 31 December 2025 were retrieved from the CSL Behring database. Patient population characteristics, indication, AE type, frequency, seriousness, and outcome were analysed in the context of an approximate total of 471,183,827 g of IgPro10 sold worldwide during this period. To optimally reflect the dosage regimens described within reference safety information and standard clinical practice, patient-years were estimated assuming 12 doses/year at 30 g per dose.

Results:

In total, 13,084 case reports were identified from an estimated exposure of 1,308,844 patient-years, with 46,122 AEs reported. Reported cases were predominantly in adult/elderly patients (79.4%; n=10,393), with most cases reported with immunomodulatory use (42.2%; n=5,516), followed by IgRT use for immunodeficiency conditions (33.6%; n=4,401). Of 46,122 AEs reported, the most common were headache, chills, and pyrexia, with a reporting rate of 0.17, 0.17, and 0.13 cases per 100 patient-years, respectively. Most AEs were non-serious (72.8%; n=33,602), with most patients reported as recovered/recovering (80.0%; n=6,278/7,852 [where patient-reported outcome information was provided]). Important risk adverse reactions, such as aseptic meningitis syndrome, thromboembolic events, haemolysis, and anaphylaxis were reported at rates of 0.04, 0.03, 0.02, and 0.02 cases per 100 patient-years, respectively.

Conclusion:

Over 10 years of global post-marketing use, reported AEs for IgPro10 were consistent with the known safety profile and current Product Information. These data reinforce the well-characterised and established positive risk-benefit profile of IVIG in real world clinical practice.

A case of T/Myeloid Mixed Phenotype Acute Leukemia

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BACKGROUND

Mixed phenotype acute leukaemia (MPAL) is a rare subtype of acute leukaemia, which is characterised by a blast population that displays evidence of two different lineages. Because of the ambiguous lineage and rarity of the subtype there is limited evidence and no consensus on how it should be treated.

CASE SUMMARY

Here we describe a case of T/ Myeloid MPAL in a 54 year old South Sea Islander male. He presented with flu like symptoms and general decline for six weeks with no significant medical history. The bone marrow aspirate showed a marked increase of pleiomorphic blasts. Flow cytometry demonstrated positive CD2, cytoplasmic CD3, CD7 , CD11b (dim) , DC 13, DC 15 (dim negative) CD 33, CD117. MPO was positive in a subset of the blast cells and overall the findings were suggestive of T/Myeloid MPAL. Molecular studies revealed FLT 3 ITD and TKD mutations, as well as a RUNX1 mutation. The patient was treated with Hyper- CVAD (Cyclophosphamide, Vincristine, Doxorubicin and Dexamethasone) chemotherapy and Midostaurin concurrently, and achieved complete remission after cycle 1A. He remains in complete remission following cycle 2B with negative FLT3 and flow cytometry MRD and is planned for an allogenic bone marrow transplant.

CONCLUSION

This case supports the use of Hyper CVAD and targeted therapy in MPAL. However, a more longitudinal assessment is needed to assess the durability of response and long-term outcome for this patient.

Identification of a novel NUP98 fusion partner in acute myeloid leukaemia: a case study.

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Case Study:

Chromosomal rearrangements involving the nucleoporin 98 (*NUP98*) are rare recurrent drivers of acute myeloid leukaemia (AML), accounting for 2-4% of adult cases, and are associated with adverse prognosis. Over 40 fusion partners have been characterised, typically placed at the C-terminal of the fusion gene, with the resultant oncoproteins thought to effect leukemogenesis through transcriptional and epigenetic dysregulation.

We describe the case of a 77 year-old man who presented with mild pancytopenia and 23% circulating myeloblasts ($0.6 \times 10^9/L$) on routine blood test monitoring. A diagnosis of AML was made, with a bone marrow morphology and flow cytometry demonstrating a heavy infiltrate of intermediate-large myeloblasts (50%), reduced trilineage haematopoiesis with no significant dysplasia and positive p53 immunohistochemistry. Myeloid next generation sequencing demonstrated a *TP53* R273H variant at a variant allele frequency (VAF) of 71.15%, and a *DMNT3A* L647H variant at a VAF of 36.83%.

Cytogenetics showed a complex karyotype, including 3-4 copies of an abnormal chromosome 11. *NUP98* interphase FISH probes revealed an atypical signal pattern. This was further interrogated with RNA gene fusion testing utilising the FusionPlex Heme v2 Panel which demonstrated a *NUP98::SNX29* fusion transcript. The chimeric protein is predicted to contain *NUP98* as the 5' fusion partner (NM_016320.5 [exon 11] chr11:3774546) and *SNX29* as the 3' fusion partner (NM_032167.5 [exon 12] chr16:12220490). *SNX29* encodes a member of the sorting nexin family with a proposed role in intracellular trafficking and signal transduction. It has not been previously described in association with myeloid malignancy.

Conclusion:

We thus report a novel non-HOX fusion partner with *NUP98*. This conferred a diagnosis of AML with *NUP98* rearrangement (WHO5) / AML with *NUP98* and other partners, with mutated *TP53* and complex karyotype (ICC). This contributes to the ever-expanding landscape of recurrent genetic abnormalities underpinning leukemogenesis in AML.

Case Report: Late onset ATRA induced pseudotumour cerebrii in an adult female patient receiving consolidation treatment for acute promyelocytic leukaemia

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Introduction:

Acute promyelocytic leukaemia (APL) can lead to severe coagulopathy and carries a high mortality risk in the acute phase. All-Trans Retinoic Acid (ATRA) and arsenic trioxide (ATO) (+/- anthracycline) remain the standard of care in treating APL. ATRA is known to have various mucocutaneous, gastrointestinal, and biochemical side effects. Pseudotumour cerebrii is a rare sequela of ATRA.

Case Summary:

A 28-year-old female presented with lethargy, generalized body aches and bruising. Full blood count revealed marked pancytopenia with blood film features concerning for APL. Cytogenetics identified t(15;17) abnormality, consistent with APL. The patient received induction therapy with ATRA and ATO (Lo Coco protocol). Complete remission was achieved post induction treatment. The patient received two further cycles of ATRA + ATO consolidation therapy without complication. Towards the end of her third consolidation treatment cycle, she presented with a severe headache, nausea and visual blurring with diplopia. No focal neurological deficits were isolated. However, fundoscopy revealed bilateral optic disc swelling (Figure 1). A CT-Brain and venogram showed bilateral symmetric thickening of the optic nerves (Figure 2). Lumbar puncture assessment revealed a high opening pressure (41cm H₂O), consistent with pseudotumour cerebrii. 20ml of CSF was drained and the patient was commenced on acetazolamide 250mg twice daily. ATRA was suspended. The patient's symptoms quickly resolved although her optic disc swelling persisted on fundoscopy for >1 month, thus ATRA was not recommenced and the patient continued single agent ATO. She remains in deep molecular remission from her APL.

Conclusion:

We report a case of pseudotumour cerebrii presenting after 3 treatment cycles of ATRA. This complication is predominantly described in younger patient populations during the early stage of induction treatment. This case highlights the importance of maintaining clinical suspicion even during later stages of consolidation treatment. If early intervention is initiated, long-term ophthalmic sequelae of raised intracranial pressure are avoided.



Figure 1. Colour Optos photography of the patient's left eye demonstrating optic disc swelling

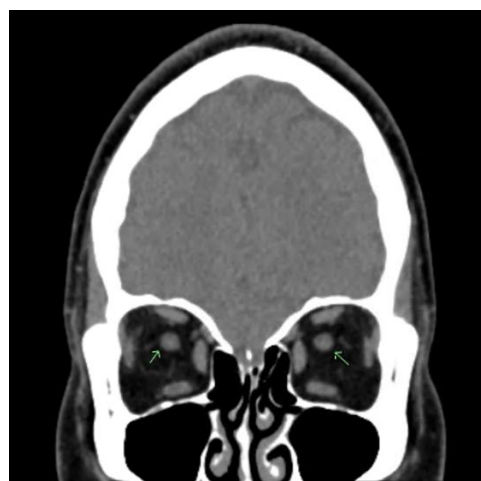


Figure 2. CT-Brain with IV contrast which demonstrates bilateral symmetric thickening of the optic nerves

Implementation of automated leukaemia measurable residual disease assays and impact on patient outcomes, laboratory workflow, and comparability with established methods

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Aim:

Validation of GeneXpert NPM1mut A/B/D, BCR::ABL p190 and PML::RARA BCR1/2/3 cartridge systems in real world settings.

Method:

To validate the Xpert NPM1mut cartridge 215 bone marrow (BM) and 68 peripheral blood (PB) post treatment samples were tested in parallel with Ipsogen RT-qPCR NPM1mut assay. Diagnostic samples (n=78), including 14 NPM1mut, 4 atypical NPM1mut and 60 wild-type were tested in parallel with High Resolution Melt assay for NPM1 mutations, and Sanger sequencing. To establish the optimal volume of BM sample loading volumes ranging from 5-50uL were tested. The comparability between extracted RNA input and whole lysate was determined by testing six samples.

The Xpert BCR::ABL p190 cartridge was tested with 376 samples (PB=264, BM=82, RNA= 30), including 60 diagnostic samples and compared with Ipsogen RT-PCR BCR::ABL p190 assay. To further test specificity nine samples with confirmed BCR::ABL p210 isoform were tested.

The Xpert PML::RARA cartridge was validated with 47 diagnostic samples (35 confirmed t(15;17) by FISH, 12 negative samples), and 308 MRD samples were tested (143 PB, 165 BM). These were compared with Ipsogen RT-qPCR PML::RARA assay (BCR1=182, BCR2=16, BCR3=83).

Results:

Xpert NPM1mut MRD results demonstrated higher NPM1mut/ABL1 ratios compared to Ipsogen (see figure 1A). RNA input samples demonstrated consistently lower NPM1mut/ABL1 % values when compared to whole BM/PB input.

Xpert PML::RARA demonstrated higher PML::RARA/ABL1 ratios compared to Ipsogen (figure 1B). Ten MRD samples were discordant. In three cases with atypical BCR2 breakpoints Xpert results were significantly higher than Ipsogen PML::RARA BCR2/3 assays.

The Xpert p190 cartridge demonstrated 100% sensitivity and 95.2% specificity in diagnostic samples, with low level BCR::ABL1/ABL1% (Below LoD;<0.0065%-0.026%) detected in p210 isoform confirmed samples.

Conclusion:

We demonstrate these assays remain comparable, however all three Xpert assays demonstrate a bias to higher target transcript/ABL1% compared to the associated Ipsogen RT-qPCR assay.

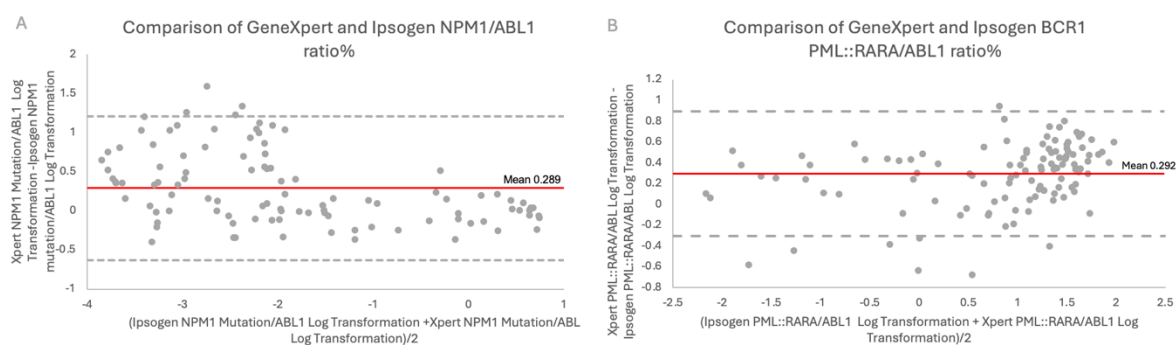


Figure 1: Bland-Altman plot A) Xpert NPM1mut in comparison to Ipsogen NPM1mut A & B assay results for MRD samples B) Xpert PML::RARA in comparison to Ipsogen PML::RARA BCR 1 assay results for MRD samples

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Establishing a Measurable Residual Disease (MRD) monitoring assay for FLT3 internal tandem duplication (FLT3-ITD)

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Aim:

Internal Tandem duplications of *FLT3* (FLT3-ITDs) are detected in approximately 30% of patients with AML. *FLT3*-ITDs are associated with poor treatment outcome and treatment resistance. Measurable residual disease (MRD) monitoring is an important tool to assess treatment response and detect relapse. The size of the *FLT3*-ITDs ranges between 3 to several hundred nucleotide bases, making them difficult to quantify using conventional methods such as qPCR. Considering the prognostic significance and prevalence of *FLT3*-ITDs in AML, we aimed to develop a Next Generation Sequencing-based MRD (MRDSeq) assay for *FLT3*-ITD, to offer improved AML disease management in Aotearoa New Zealand.

Method:

The MRDSeq method involves amplification of the genomic region of *FLT3*, flanking the site of ITDs, including the JM domain and part of the TKD (hg19, chr13:28608024-28608352), introduction of barcodes and adaptor sequences to enable sequencing on the Illumina NGS platform. The amplicons are sequenced to a depth of about 1 million, followed by data analysis employing the GetITD algorithm to identify reads containing ITDs or insertions.

Results:

We performed *FLT3*-ITD MRDSeq assays on a dilution series of the MV4-11 cell-line carrying a 30 bp ITD in the JM domain and on patient samples (n=10), and compared the results of the MRDSeq assay with the results of fragment analysis (FA) assay, the current diagnostic assay used to detect *FLT3*-ITDs. The *FLT3*-ITD MRDSeq analysis on the dilution series of MV4-11 cell line demonstrated that the sensitivity of *FLT3*-ITD MRDSeq assay is at least 10^{-3} . Comparison of the MRDSeq and FA results on the patient samples showed concordant findings in 8 out of 10 cases.

Conclusion:

The *FLT3*-ITD MRDSeq assay which we developed can be used for MRD assessment. Once our *FLT3*-ITD MRDSeq assay is validated on a bigger patient cohort, it can be routinely used to benefit *FLT3*-ITD positive AML patients.

NUP98 rearrangements in myeloid malignancies: cryptic but consequential

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Introduction:

Nucleoporin 98 gene rearrangements (*NUP98r*) are rare, adverse molecular lesions. WHO and ICC diagnostic classifications classify *NUP98r* as an AML-defining lesion, irrespective of blast count. *NUP98r* AML has poor induction response and high relapse risk. Allogeneic transplant (alloSCT) is recommended in first remission for transplant-eligible patients. The majority of *NUP98r* are cryptic on conventional cytogenetics and can be missed; dedicated FISH or RNA fusion panels are required for identification.

Here we describe two morphologically distinct myeloid neoplasms with normal karyotype, both harbouring cryptic *NUP98* rearrangements.

Case Summaries

Patient A is a 35-year-old female with a diagnosis of AML, with 64% myeloblasts on bone marrow (BM). Cytogenetics identified a normal karyotype. NGS identified a *FLT3*-ITD co-mutation. After the commencement of induction with 7+3 with Midostaurin, *NUP98r* was recognised on FISH, with RNA fusion studies revealing a *NUP98::NSD1* fusion (Figure 1). Patient A was referred for alloSCT.

Patient B is a 60-year-old female initially diagnosed with CMML-2 with 15% monoblasts on BM. Diagnostic chromosomal morphology was poor. As FISH for *NUP98* testing is not routine for CMML, the rearrangement was missed at diagnosis. NGS identified *FLT3* VUS, *RUNX1* and *WT1* mutations. Azacitidine was commenced with a plan for consolidative alloSCT. *NUP98r* was later identified on pre-alloSCT cytogenetic testing. RNA fusion panel was applied retrospectively to a diagnostic sample and identified a *NUP98::PRRX2* fusion (Figure 1), revising this patients' diagnosis to AML. Despite a favourable response to Azacitidine, delayed detection of *NUP98r* resulted in the patient receiving suboptimal AML-directed therapy. Patient B has since proceeded to alloSCT.

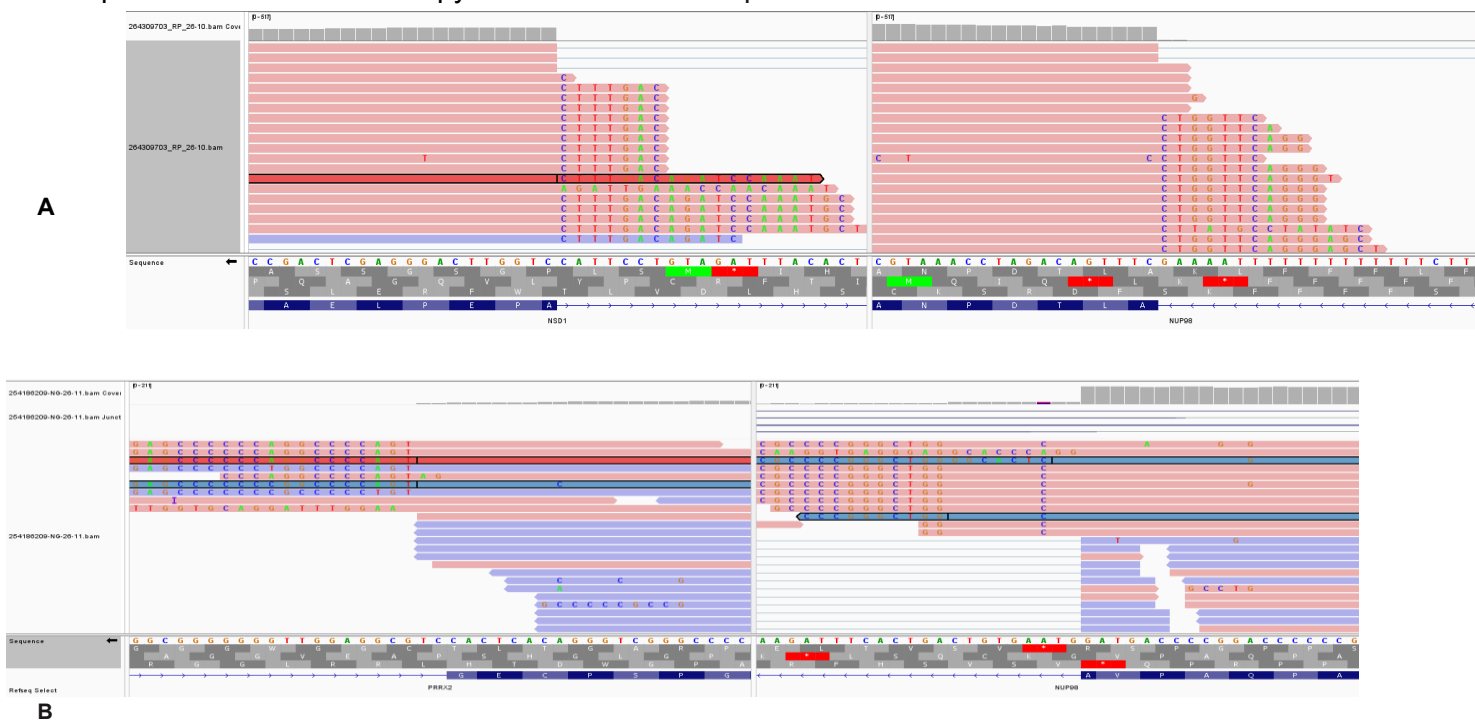


Figure 1. **A** *NUP98::NSD1* fusion, **B** *NUP98::PRRX2* fusion

Conclusion

These cases highlight the clinicopathologic heterogeneity and importance of FISH and/or RNA fusion

panels to identify cryptic *NUP98r* in myeloid malignancies with blasts > 10%. Identification of *NUP98r* has significant diagnostic, management, and prognostic implications and is an important part of the molecular work-up for this patient cohort

A phase 3 study of revumenib plus venetoclax/azacitidine in adults with newly diagnosed NPM1-mutated or KMT2A-rearranged acute myeloid leukemia ineligible for intensive chemotherapy (EVOLVE-2/HO177/AMLSG35-24/ACT-HOV-AML-002): Trial in progress

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Aim:

To evaluate whether revumenib plus venetoclax/azacitidine (VEN/AZA) improves overall survival (OS) and complete remission (CR) rates in patients with newly diagnosed (ND) *nucleophosmin-1 mutation* (*NPM1m*) or *lysine methyltransferase 2A* (*KMT2A*) acute myeloid leukemia (AML) ineligible for intensive chemotherapy (IC). Optimal treatment for patients with AML unfit for IC remains limited. In *NPM1m* or *KMT2A* rearrangement (*KMT2Ar*) AML, menin-KMT2A fusion proteins upregulate *HOX/MEIS* gene expression, resulting in hematopoietic differentiation arrest and leukemogenesis. Revumenib is a first-in-class, oral, potent, and selective inhibitor of the menin-KMT2A interaction that has shown clinically meaningful activity and favorable tolerability as a monotherapy in relapsed/refractory *NPM1m* AML or *KMT2Ar* acute leukemia. In the AUGMENT-101 study (NCT04065399). Combination regimens are being studied as front-line therapy for ND patients. In the phase 1b Beat AML study (NCT03013998), revumenib plus VEN/AZA produced deep responses in patients ≥60 years with ND *NPM1m* or *KMT2Ar* AML.

Method:

EVOLVE-2 is a phase 3, multicenter, randomized, double-blind, placebo-controlled trial (NCT06652438/EU-CT 2024-512733-32-00). Eligible patients are ≥75 years of age (18–74 years with comorbidities), have ND AML with centrally confirmed *NPM1m* or *KMT2Ar* (excluding *KMT2A* partial tandem duplications/deletions), are ineligible for IC, and are AML treatment-naïve. Patients will be randomized 1:1 to revumenib or placebo in combination with VEN/AZA and stratified by age (<75 vs ≥75 years), genotype (*NPM1m* vs *KMT2Ar*), and region (Europe vs Australia vs United States). In Cycle (C) 1, VEN is given daily on Days (D) 1–28 and AZA daily on D1–7, ± revumenib twice daily on D1–28. In C2+, responders (per 2022 European LeukemiaNet criteria) may adjust VEN based on remission status/count recovery. Treatment continues until disease progression, unacceptable toxicity, patient withdrawal, or death. Approximately, 448 patients will be enrolled. Enrollment is ongoing as of January 27, 2026.

Results:

N/A

Conclusion:

Figure. Endpoints		
Objectives	Endpoint(s)	Description
Primary	Overall Survival (OS)	Time from treatment initiation to death from any cause
	Complete Remission (CR) Rate	Proportion of patients achieving complete remission
Key Secondary	Event-Free Survival (EFS)	Time from treatment start to treatment failure, relapse, or death
	CR/CRh Rate	Proportion achieving CR or CR with partial hematologic recovery (CRh)
Other	CRh Rate	Proportion achieving CR with partial hematologic recovery
	CR/CRi Rate	Proportion achieving CR or CR with incomplete hematologic recovery (CRi)
	MRD Negativity	MRD-negative status among CR, CR/CRh, and CR/CRi
	Time to Response	Time from treatment initiation to first response
	Duration of Response (DoR)	Time from first response (CR, CRh, CRi) until disease progression or death
	Adverse Events	Incidence and severity of treatment-emergent adverse events
	Time to Hematopoietic Recovery	Time to recovery of blood counts (e.g., neutrophils, platelets)
	Transfusion Incidence	Incidence of platelet and red blood cell transfusions
CR, complete remission; CRh, complete remission with partial hematologic recovery; CRi, complete remission with incomplete hematologic recovery; DoR, duration of response; EFS, event-free survival; MRD, minimal residual disease; OS, overall survival.		

Integrating targeted RNA-sequencing with gene expression analysis to improve detection of MECOM (EVI1)-rearranged AML

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Aim:

MECOM (*EVI1* the oncogenic transcript) is a key driver of acute myeloid leukaemia (AML). Overexpression frequently arises from enhancer-hijacking via rearrangements (*MECOMr*) involving diverse, sometimes cytogenetically cryptic, partners that collectively confer dismal outcomes¹. Furthermore, *MECOM* overexpression is seen in subsets of *KMT2A*- and *NUP98*-rearranged AML with potential prognostic implications^{2,3}. Targeted RNA-sequencing (RNA-seq) is well-suited for detecting chimeric fusions but could fail to detect enhancer-hijacking and other regulatory events. Using the largest reported Australian AML cohort analysed by targeted RNA-seq, we assessed whether combining fusion calling with *MECOM* expression analysis improves *MECOMr* detection.

Methods:

We retrospectively reviewed 459 newly diagnosed or relapsed AML cases profiled by the Peter MacCallum Cancer Centre AllHaem 71-gene targeted RNA panel (11/2024–5/2026). Fusions were called independently by CLC Genomics Workbench (v.23) and Arriba (v.2.2.0); *MECOM* expression was quantified from the same data.

Results:

Fusion callers identified *MECOM* rearrangements with *RPN1* (3q21, n=5), *RUNX1* (21q22, n=4), *ETV6* (12p13, n=3), *TRA2B* (3q27.2, n=1), *THADA/ZFP36L2* (2p21, n=1) and 3p24 (n=1). Three were cytogenetically cryptic: *MECOM* insertion into 12p13, *TRA2B/MECOM* within a ring chromosome, and 3p24/*MECOM* [inv(3)(p24q26)] and were confirmed by FISH. Four cytogenetically detected *MECOMr* cases were undetected by both callers, prompting evaluation of expression as an alternative detection strategy. *MECOMr* cases showed substantially higher *MECOM* expression than other AML subclasses, although *RUNX1/MECOM* displayed lower expression than other *MECOMr* partners. (**Fig. 1**); *KMT2Ar* and *NUP98r* exhibited a bimodal distribution. Applying the lower IQR of *MECOMr* cases as an expression threshold (*MECOM*^{hi}) captured all four caller-undetected cases and identified another case cryptic to both cytogenetics and fusion calling (FISH: *MECOM* insertion near *NRIP1*). The biological and clinical relevance of FISH-negative *MECOM*^{hi} cases and bimodal *KMT2Ar* and *NUP98r* are undetermined and warrants further investigation.

Conclusion:

Integrating *MECOM* expression with fusion calling and cytogenetics improves detection of *MECOMr*-AML, and demonstrates a novel role for gene expression analysis in routine molecular diagnostics.

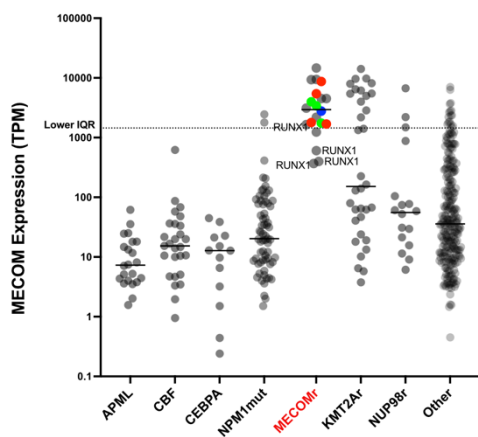


Figure 1. MECOM expression in newly diagnosed or relapsed AML shows differential expression amongst AML subtypes. Within the *MECOMr* group, green circles indicate cases detected by fusion caller only (cytogenetically cryptic), red circles: detected by cytogenetics but undetected by fusion callers, blue circle: FISH confirmed case that was cytogenetics cryptic and undetected by fusion callers, but had high *MECOM* expression. Abbreviations: APML acute promyelocytic leukaemia, CBF Core-binding factor AML, IQR interquartile range, TPM transcripts per million.

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Eno1 is variably expressed on the surface of AML/MDS patient samples ex vivo but not correlated with total ENO1 expression in AML cell lines in vitro

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Aim:

Alpha-enolase (ENO1) is a glycolytic enzyme that is highly expressed in AML, associated with poor prognosis, and has been identified as a potential therapeutic target. ENO1 is known to relocate to the cell surface in some cancers, suggesting its utility as a potential biomarker that could be easily detected by conventional flow cytometry. Thus, the aim of this study was to determine if ENO1 was expressed on the surface of AML cells and if this was correlated with overall expression.

Method:

ENO1 cell surface expression was measured by flow cytometry in 11 AML cell lines as well as 14 bone marrows and 14 peripheral bloods collected from 6 MDS and 13 AML patients at diagnosis. Blast cells were identified by viability, low side scatter and dim CD45 staining, with ENO1 positivity defined by MFI >1.3 and positive cells >10% relative to isotype controls. Western blotting was used to determine total ENO1 protein in AML cell lines and Pearson correlation tested associations between total and surface expression.

Results

ENO1 was expressed on the surface of 4 BM and 4 PB from 3/19 patients (1 MDS and 2 AML with inv(16)(p13.1q22)) with relative MFI=1.53 ± 0.21 and average positive blast cells of 25.2 ± 12.1%. There was perfect agreement between PB and BM results (kappa = 1.0, n=9). Cell lines expressed low but varying levels of surface ENO1, but these were not correlated to overall ENO1 expression (r=-0.14, p=0.68).

Conclusion:

This is the first study to identify the presence of ENO1 on the surface of AML and MDS cells and suggests that it may be unique to particular disease classifications. Although surface ENO1 did not correlate with total ENO1 expression in AML cell lines, these results provide evidence for independent regulation of distinct ENO1 functions.

Arsenic trioxide (ATO) and all-trans retinoic acid (ATRA) induction in a haemodialysis-dependent patient with acute promyelocytic leukaemia (APML): a case report

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Introduction:

ATO combined with ATRA is the current mainstay treatment of APML, however despite significant renal excretion use in severe renal impairment is not well studied, particularly during renal replacement therapies. One case series describes an APML patient on intermittent haemodialysis (HDx) used 10mg ATO three times a week post HDx to achieve comparable whole blood arsenic concentrations to those with normal renal function.

Case Summary:

A 29-year-old female with newly diagnosed standard-risk APML developed anuric renal failure due to disseminated intravascular coagulopathy, requiring intermittent haemodialysis throughout all APML treatment (APL0406 protocol).

Following consideration of recommendations from the Renal Drug Database, comprehensive literature review and multidisciplinary team discussion, the consensus was to reduce ATO to 40% (0.06mg/kg) daily post dialysis, on dialysis days only and ATRA to 25mg/m²/day. This was maintained throughout induction and four consolidation cycles. Therapeutic drug monitoring occurred three times a week with whole blood arsenic level taken immediately prior to HDx with a target of 0.8 - 2.2 μ M. Of 43 levels taken, 33 (77%) were within range. Seven levels (16%) below range were taken during the first week of each cycle, attributable to ATO reaching steady state; three (7%) were above range (2.39 - 2.94 μ M), taken on weekend days without HDx scheduled. No liver toxicity was observed and QTc was monitored regularly with only five instances (5%) more than 460msec; no doses of ATO were withheld.

Nine months from end of treatment, the patient remains in a molecular remission which was achieved after consolidation one and is currently awaiting renal transplant.

Conclusion:

This case report highlights that APML treatment can be safely and effectively delivered during renal replacement therapy with careful attention to dose reduction and serum whole blood arsenic level monitoring.

A challenging CD10+/cCD79a+/nTdT+, cMPO-negative acute myeloid leukaemia: The value of integrated and comprehensive molecular assessment for accurate disease classification.

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Background:

Acute myeloid leukaemia (AML) can show phenotypic heterogeneity, including rare expression of non-myeloid antigens (e.g. cCD79a, nTdT, CD10). When the cells lack morphological differentiation, this can raise suspicion of acute leukaemia of ambiguous lineage (ALAL). We report the case of an adult presenting with cytopenias and circulating blast cells that expressed both myeloid and lymphoid-associated antigens, thereby posing a diagnostic challenge.

Case Overview:

A 71-year-old Caucasian woman presented with several months of progressive macrocytic anaemia and neutropenia. Two years prior, she had received radiotherapy for breast cancer. Bone marrow examination showed 79% blast cells with minimal differentiation and reduced normal haemopoiesis. Flow cytometric and immunohistochemical analyses of the bone marrow trephine biopsy showed the blast cells to be CD34 and HLA-DR positive, express lymphoid-associated nuclear TdT, cytoplasmic CD79a, CD10 and CD7, as well as myeloid antigens (CD13, CD33, CD117); they lacked CD19, cytoplasmic CD22 and cytoplasmic myeloperoxidase. This ambiguous phenotypic profile precluded the ability to accurately define cell lineage assignment. Cytogenetics showed a normal karyotype and molecular studies for immunoglobulin and gene rearrangements were negative. A provisional diagnosis of ALAL was made, with AML with minimal differentiation a differential. Subsequent comprehensive NGS testing identified several myeloid specific mutations: DNMT3A 50%, TET2 45%, ASXL1 42%, RUNX1 35%, BCOR 31%, NF1 21% and NRAS 15%, supporting a final diagnosis of AML, myelodysplasia-related, post cytotoxic therapy (AML-MR, pCT).

Conclusions:

Primitive blast populations with atypical immunophenotypes may lead to misclassification of an acute leukaemia as ALAL. Rarely, AML with minimal differentiation can exhibit aberrant co-expression of non-myeloid (e.g. nTdT, cCD79a, CD10, CD7) antigens, complicating assignment of cell lineage. Integrated assessment by incorporating comprehensive genomic evaluation is central to the correct diagnostic classification of immunophenotypically challenging acute leukaemias.

An atypical aleukaemic presentation of B-lymphoblastic leukaemia manifesting with mild chronic neutropenia and thrombocytopenia.

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Background:

Aleukemic presentations of B-lymphoblastic leukaemia (B-ALL) are extremely rare. They predominantly affect children and typically manifest with extramedullary disease. Constitutional symptoms, transient anaemia and recurrent infections may precede the diagnosis of aleukemic B-ALL. Initial marrow examinations showing marrow hypoplasia, coupled with limited ancillary testing, may delay the recognition of B-ALL. We report the case of a young female with chronic neutropenia, thrombocytopenia and recurrent infections who presented with aleukemic B-ALL. We highlight the diagnostic process, and value of early and comprehensive ancillary testing, to confirm a diagnosis of B-ALL.

Case Overview:

A 25-year-old Caucasian female presented with eight months of mild neutropenia ($0.58-1.50 \times 10^9/L$) and thrombocytopenia ($96-123 \times 10^9/L$) in the setting of recurrent respiratory viral infections and fatigue. Comprehensive blood investigations revealed no attributable cause for her mild cytopenias. Routine marrow examination revealed a hypocellular marrow with an immature lymphoid infiltrate; flow cytometric and immunohistochemical analysis revealed the latter to be of B-lymphoblast origin. The differential diagnosis included B-ALL or expanded B-lymphoid haematogones arising from repeated viral infections. Her karyotype was normal. Immunoglobulin rearrangement analyses revealed monoclonal rearrangements involving IgH and IgK, whilst comprehensive genetic testing showed a ZNF384::SYRNG fusion and IKZF deletion, confirming a diagnosis of B-ALL.

Conclusions:

Prolonged, unexplained cytopenias without a clear secondary aetiology, in conjunction with recurrent infections in young adults, may rarely masquerade as an aleukemic presentation of B-ALL. Prompt marrow examination and the exclusion of extramedullary disease are recommended. The marrow is typically hypocellular in aleukemic B-ALL, complicating diagnostic certainty. Therefore, the early initiation of ancillary investigations (e.g. immunoglobulin rearrangement studies) are strongly recommended to confirm the presence of a clonal B-lymphoid malignancy.

PPM1D and TP53 mutations in patients with haematological diseases in Western Australia.

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Background & Aim(s):

PPM1D regulates cellular proliferation and apoptosis alongside TP53. *PPM1D* mutations are emerging as key players in haematological malignancies by inactivating TP53, conferring chemotherapeutic resistance and conferring inferior survival outcomes. We characterised the incidence and clinicopathological effects of *PPM1D* and *TP53* mutations in haematological malignancies in Western Australia.

Method:

Adult haematology patients (n=120) attending PathWest Laboratory Medicine between January 2024-April 2026 who had next generation sequencing (NGS) analyses performed through the Peter MacCallum Centre (ALLHAEM DNA panel; Illumina NovaSeq X Plus) were identified. Of those patients with *PPM1D* and *TP53* mutations, their demographic data, haematological diagnosis and presence of concurrent somatic variants were evaluated. Overall survival (OS) in *PPM1D* and *TP53*-mutated patients were also assessed.

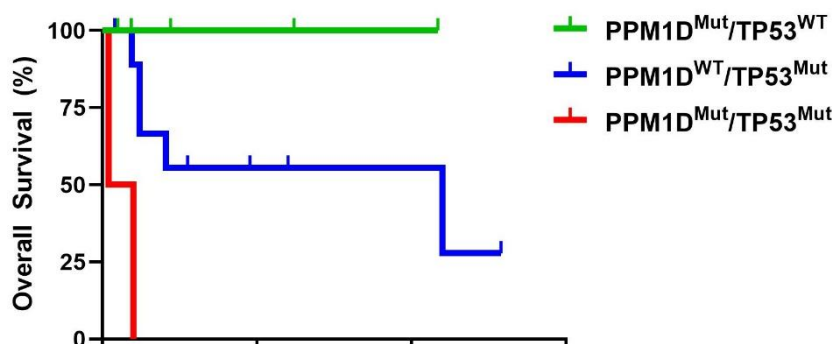
Results:

Seven patients (6%) had a *PPM1D* mutation (median age=67 years), whilst 12 patients (10%) had a *TP53* mutation (median age=48 years; n=6/12 with biallelic *TP53* inactivation); two patients co-harboured both mutations. Among *PPM1D* mutated cases, four patients had a myeloid disorder (MDS=3; AML=1), whilst three patients had a lymphoid malignancy (B-ALL=1; CLL=2). Five patients had acquired a *PPM1D* mutation post exposure to cytotoxic chemotherapy. *PPM1D* mutations included nonsense and frameshift mutations with VAFs ranging between 4-22% (mean=9%), all affecting the Degron domain of the PPM1D protein. With a median follow-up of 4.1 months, the median OS (figure 1) was poor among co-mutated *TP53* and *PPM1D* patients (1.2 months) and inferior to those with an isolated *TP53* (22 months) or *PPM1D* mutation (not reached).

Conclusion:

PPM1D mutations are rare but affect patients with both myeloid and lymphoid malignancies. In our cohort, the mutation is enriched among patients having previously received cytotoxic chemotherapy and MDS. Isolated *PPM1D* mutated patients had a better OS in comparison to those with exclusive and co-mutated *TP53*. Larger cohort studies are required to expand the clinicopathological insights of *PPM1D* mutations in patients with haematological malignancies.

Figure 1. Overall survival (OS) outcomes across adult haematology patients with isolated and co-mutated *PPM1D* and *TP53*.



Neutropenic enterocolitis: What we know in patients receiving myeloablative chemotherapy in acute myeloid leukaemia and autologous stem cell transplant conditioning.

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Aims:

Neutropenic enterocolitis (NEC) represents a potentially life-threatening complication in patients undergoing myeloablative chemotherapy for haematological malignancies. We characterised the incidence, management, and outcomes of patients undergoing myeloablative treatments for acute myeloid leukaemia (AML) and autologous stem cell transplant (AuSCT) who developed NEC.

Methods:

Patients receiving intensive induction chemotherapy for AML or myeloablative conditioning for AuSCT at Royal Perth Hospital from January 2025-March 2026 were screened for NEC. Data pertaining to basic demographics, neutrophil count, pre-existing bowel disease, onset and severity of NEC, treatment and clinical outcomes were obtained. Statistical analyses were performed using Mann-Whitney U-tests (GraphPad Prism).

Results:

8/15 (53%) AML and 7/19 (37%) AuSCT recipients developed NEC; their clinical characteristics are summarised in *Table 1*. Four patients (27%) had preceding bowel disease. Median neutrophil counts on admission were $1.4 \times 10^9/L$ (range: $0.05\text{--}21.3 \times 10^9/L$) and $2.7 \times 10^9/L$ (range: $1.3\text{--}5.6 \times 10^9/L$), respectively; all patients were neutropenic at colitis diagnosis. NEC developed at ~6 days (range: 3-8) post stem cell infusion in the AuSCT recipients, and at ~11 days (range: 7-25) post AML induction chemotherapy. Most patients developed abdominal pain and diarrhoea. Total parenteral nutrition and bowel rest were required in 67% of cases. Surgical intervention (n=1; 6%) and ICU admission (n=3; 20%) were infrequent, with one colitis-related death due to bowel perforation. Neutrophil recovery post treatment correlated with colitis resolution. Concurrent oral mucositis occurred in 53% of patients and was enriched among AuSCT recipients. Febrile neutropenia occurred in all patients, with common gut flora isolated in 8/9 (89%) positive blood cultures; four patients also had detectable *Clostridium difficile*. All patients required intravenous electrolyte replacement. Patients lost ~2.6kg (range: -6.5 to +1.5kg) despite intensive dietetics support.

Conclusions:

NEC is a common complication arising from myeloablative treatments in AML and AuSCT. Whilst most cases are managed conservatively, NEC-associated sepsis necessitating ICU support still affects ~20% of patients with significant morbidity.

Table 1. Study cohort diagnostic and treatment characteristics.

	AML (n=8)	AuSCT (n=7)
Median Age [years] (range)	56 (39-67)	55 (43-71)
Male	4	3
Diagnostic Subclassification	NPM1 ^{pos} /FLT3 ^{WT} = 2 NPM1 ^{pos} /FLT3 ^{pos} = 2 NPM1 ^{WT} /FLT3 ^{pos} = 1 AML-MR = 3	Multiple Myeloma = 3 High Grade B-cell Lymphoma = 4

Myeloablative Treatment	7+3 only = 3 7+3+Midostaurin = 3 7+3+GO = 1 CPX-351 = 1	Melphalan 200 mg/m ² = 3 BEAM = 3 Carmustine / Thiotepa = 1
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Abbreviations: AML – acute myeloid leukaemia; BEAM – carmustine + etoposide + cytarabine + melphalan; CPX-351 (liposomal cytarabine + daunorubicin) GO – gemtuzumab ozogamicin; MR – myelodysplasia-related; NPM1 – nucleophosomin 1; pos – positive; WT – wild type; 7+3 (cytarabine + idarubicin).

Challenges and clinical utility of RNA fusion testing in haematological malignancies

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Aim:

Gene fusions are the key drivers in haematological malignancies and play an important role in diagnosis, prognostication, therapeutic decision-making, and disease monitoring. Their increasing incorporation into the WHO Classification highlights the growing clinical importance of fusion detection in routine diagnostics. However, several challenges remain, including identification of cases with altered gene expression without formation of a chimeric fusion transcript due to “enhancer hijacking” events including *IGH*-related translocations, and variability in RNA fusion reporting and interpretation emphasising the need for standardised guidelines.

Our aim is to validate and establish an RNA fusion panel incorporating differential gene expression analysis for haematological malignancies in a NATA-accredited diagnostic laboratory.

Method:

The Illumina TruSight RNA Pan-Cancer Panel covering 1385 target genes was used for fusion detection in peripheral blood and bone marrow samples. Seventy-seven samples with previously characterised gene rearrangements, including commercial controls, were analysed for validation studies. Secondary and tertiary analyses were performed using the Illumina DRAGEN RNA and Dragen Differential Expression analysis pipelines and Ariba software.

Results:

All expected fusions were identified in both the commercial control and clinical samples, confirming the robustness of our secondary and tertiary pipelines in detecting fusions. Clinically significant fusions were detected across a range of haematological malignancies, assisting in diagnosis of clinically challenging cases and identification of molecular markers for disease monitoring in selected cases. Additionally, statistically significant oncogene upregulation was demonstrated in five of the six fusion transcript-negative samples, where enhancer hijacking was predicted, implicating dysregulated gene expression as the primary pathogenic mechanism in these cases. Further clinically relevant findings and interpretative challenges will be presented.

Conclusion:

Validation of the TruSight RNA Pan-Cancer Panel demonstrates reliable detection of clinically relevant fusion transcripts and gene expression alterations in haematological malignancies. Incorporation of this assay into routine diagnostics enables comprehensive and clinically meaningful identification of both known and novel gene fusions.

DUX4-rearranged acute lymphoblastic leukaemia exhibits selective vulnerability to GPCR-mediated calcium signalling disruption

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Aim:

DUX4-rearranged (DUX4r) B-cell acute lymphoblastic leukaemia (B-ALL) is driven by the transcriptional activity of the IGH::DUX4 fusion protein. To date, no targeted therapies exist. This study aimed to identify and characterise selective pharmacological vulnerabilities in DUX4r ALL using a patient transcriptomics-guided approach.

Method:

mRNA-sequencing data from DUX4r B-ALL patients (n=60) were analysed using DESeq2 to identify differentially expressed genes relative to other ALL subtypes (n=546 patients). Pathway enrichment analysis identified druggable targets. Drug efficacy was evaluated using cell lines representing distinct genomic profiles: NALM6 (DUX4r), REH (ETV6::RUNX1) and RS4:11 (KMT2Ar). Cellular responses to inhibitors were assessed through cytotoxicity (LD50) at 72 hours and calcium flux analysis. Three biological replicates and technical duplicates were used for in vitro analysis.

Results:

Gene set enrichment analysis (GSEA) utilising KEGG and Reactome databases identified several significantly upregulated ($p < 0.0001$) pathways in DUX4r patients, including PI3K-Akt signalling, calcium signalling and G-protein coupled receptor (GPCR) ligand binding. Dual PI3K-mTOR inhibition with dactolisib showed no significant difference between the cell line LD50 values ($p > 0.05$). Targeting the GPCR-calcium signalling pathway with KB-R7943, PH-064 and U73122 inhibitors demonstrated significantly lower LD50 values ($p < 0.001$) in NALM6 versus REH and RS4:11 lines. Calcium-flux assays demonstrated significantly enhanced calcium uptake in NALM6 cells compared to other cell lines, with each inhibitor significantly reducing NALM6 calcium uptake ($p < 0.05$). Published DUX4r ChIP-seq identified DUX4r neomorphic binding at the CXCR4 GPCR regulatory elements, absent in wild-type DUX4, directly linking the fusion protein to CXCR4 expression. Using the CXCR4 inhibitor, mavoxixafor, significantly reduced calcium entry into NALM6 cells but did not induce cell death.

Conclusion:

These findings implicate DUX4r-driven CXCR4-upregulation as a therapeutic vulnerability, dysregulating calcium signalling and promoting leukemic cell survival. CXCR4 inhibition with mavoxixafor represents a clinically actionable strategy, given its existing clinical development, warranting further investigation as a targeted therapy in combination with chemotherapy in DUX4r B-ALL.

Standardizing liquid biopsy for serial monitoring and prognostication in acute leukemia

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Aim:

To standardize liquid biopsy-based cfDNA assessment for serial monitoring and prognostication in patients with acute leukemia and to evaluate the predictive significance of cfDNA concentration ratios for treatment outcomes and minimal residual disease (MRD) positivity.

Method:

Twenty-five patients diagnosed with AML or ALL were enrolled and risk-stratified according to NCI criteria. Paired peripheral blood samples were collected at diagnosis and post-induction/follow-up. Plasma cfDNA was isolated using commercial extraction kits and quantified spectrophotometrically. Baseline cfDNA levels and cfDNA ratios (baseline/follow-up) were correlated with MRD status, relapse, resistant disease, and mortality outcomes. Statistical analysis included logistic regression and paired t-test analysis, with significance defined at $p < 0.05$.

Results:

Among the 25 patients, 80% belonged to the high-risk category. Elevated baseline cfDNA levels correlated with increased MRD positivity but did not independently predict relapse or mortality. In contrast, cfDNA concentration ratios demonstrated strong prognostic significance. Patients with cfDNA ratios ≥ 2.6 showed significantly higher rates of relapse, resistant disease, and mortality irrespective of MRD status ($p = 0.0017$). High cfDNA ratio scores outperformed conventional MRD assessment by flow cytometry in predicting adverse outcomes. Logistic regression analysis further validated cfDNA ratio > 2.6 as an independent predictor of poor prognosis ($p = 0.03$).

Conclusion:

Serial cfDNA monitoring using liquid biopsy represents a feasible and minimally invasive approach for prognostication in acute leukemia. A cfDNA ratio threshold of ≥ 2.6 may serve as a robust predictor of poor clinical outcome independent of MRD status. Standardization of cfDNA-based liquid biopsy could provide a cost-effective adjunct tool for serial monitoring and risk stratification in leukemia, particularly in resource-constrained settings.

The mutational analysis of the gene *DDX41* in Myelodysplastic syndromes and acute myeloid leukaemia

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Aim:

Co-occurrence of somatic and germline mutations in the DEAD-box RNA helicase-1 (*DDX41*) are associated with familial MDS and AML, and are found in about 4% of patients. In 12 out of 21 *DDX41*-mutated MDS/AML patients analysed in the BCRU, both germline and somatic *DDX41* variants were detected. However, in 7 patients, only germline *DDX41* mutations were detected, without somatic second-hit mutations. We aim to identify these missing second hit *DDX41* mutations, and also determine the spectrum of co-operating mutations in our *DDX41*-mutated MDS/AML cohort. Additionally, we established a loss-of-function *ddx41* leukemia zebrafish model to investigate the mechanisms of *DDX41* mutations in AML development.

Methods:

To identify undetected somatic mutations in the 7 patients mentioned above, we have developed a *DDX41*-focused next-generation sequencing (NGS) approach. This involves amplification of the *DDX41* locus from genomic DNA, followed by library preparation using the PCR product, NGS, and analysis, to detect larger genetic changes including deletions, inversions or translocations. We also used gene panel data to determine the mutational spectrum in the BCRU *DDX41*-mutated MDS/AML cohort.

Results:

The *DDX41*-focused NGS analysis was successfully established and optimized, yielding even coverage across *DDX41* exons and introns of the 5.5 kb *DDX41* genomic locus. Furthermore, we observed differences in the co-mutational spectrum between our *DDX41*-mutated and wild-type *DDX41* MDS/AML cohorts. While the most frequently-mutated genes in wild-type *DDX41* patients are *DNMT3*, *NMP1*, *FLT3* and *IDH2*, our *DDX41*-mutated patients most often carried co-mutations in *ASXL1*, *JAK2*, *SRSF2* and *EZH2*. This observation is consistent with the study by Makishima et al. in 2023.

Conclusion:

Our *DDX41*-focused approach can potentially identify larger rearrangements and pathogenic *DDX41* variants that have previously gone undetected. Moreover, the distinct co-mutational patterns in *DDX41*-mutated MDS/AML patients may help refine genetic screening strategies. Collectively, our findings can provide clinicians with crucial information in improving patient management.

Blastic plasmacytoid dendritic cell neoplasm (BPDCN): A single centre experience

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Introduction:

Blastic plasmacytoid dendritic cell neoplasm (BPDCN) is a rare malignancy that often presents with indolent cutaneous lesions followed by leukaemic dissemination to marrow, lymph nodes, and central nervous system. Prognosis is bleak, with a median survival of 12 - 24 months(1). While tagraxofusp is a FDA-approved CD123-directed therapy for BPDCN, most current therapy in Australia consists of adapted lymphoma regimens and allogenic stem cell transplantation.

Cases:

(1) An 84-year-old man with MDS presented with three weeks of characteristic "bruise-like" cutaneous chest lesions, fatigue and leukocytosis (blasts 52%). Bone marrow immunophenotyping confirmed BPDCN: CD4+(dim)/CD56+(dim)/CD123+/CD7+/CD33+/TdT+/HLA-DR+. He received tagraxofusp and triple intrathecal chemotherapy for CNS involvement. His course was complicated by recurrent *Bacteroides fragilis* septicaemia. He developed capillary leak syndrome, including generalized oedema, dyspnoea, and right-sided pleural effusion and died prior to cycle 3.

(2) A 73-year-old man presented with weeklong constitutional symptoms, atraumatic bruising, cytopaenias and elevated ferritin/LDH. He rapidly developed DIC and fulminant multiorgan dysfunction, including T1RF. Bone marrow biopsy confirmed extensive marrow infiltration of BPDCN: CD4+/CD56+/CD123+(strong)/CD13+/CD33+/cCD79a+/TdT+/HLA-DR-/CD15(mixed). High-dose cytarabine improved DIC before hyperCVAD and intrathecal methotrexate were commenced. Despite this, he developed worsening intracranial bleeding and pulmonary deterioration secondary to suspected opportunistic infection, dying 15 days after presentation.

(3) A 90-year-old man presented with three months of atraumatic, widespread, purple nodular lesions and pancytopenia. Cutaneous and bone marrow biopsy notably confirmed BPDCN. He commenced venetoclax/azacitidine but remained persistently pancytopenic and soon chose palliation.

Conclusion:

This case series highlights the marked clinical heterogeneity, diagnostic and therapeutic challenges of BPDCN in elderly patients, ranging from fulminant leukemic presentations to treatment-limiting toxicity. Australian BPDCN management also remains constrained by limited treatment access such as CD123-directed therapy.

Sources:

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Clinical characteristics and outcomes of cerebrospinal fluid-proven central nervous system involvement in acute myeloid leukaemia

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Aim:

Central nervous system (CNS) involvement in acute myeloid leukaemia (AML) is uncommon and poorly characterised. This study aimed to describe the clinical, molecular and treatment characteristics of patients with cerebrospinal fluid (CSF)-proven CNS disease in AML at a tertiary haematology centre.

Method:

A retrospective audit was performed of patients with AML who developed CSF-proven CNS disease between February 2005 and April 2026. Demographic, molecular and treatment-related variables were reviewed, including cytogenetics, next-generation sequencing (NGS), transplant status, extramedullary disease and relapse characteristics. Descriptive statistics were used, with continuous variables reported as median and interquartile range (IQR).

Results:

Twenty-three patients with symptomatic CSF-proven CNS involvement were identified. Median age at CNS disease was 51 years (IQR 35.5–61), with a slight female predominance. Median presenting white cell count at AML diagnosis was $41 \times 10^9/L$ (IQR 15.8–114.1) and median lactate dehydrogenase (LDH) was 946 U/L (IQR 501–1335). Monocytic morphology, *KMT2A* abnormalities (including both gene rearrangements and partial tandem duplications), *CBFB::MYH11* fusion and *FLT3-ITD* mutations were frequently observed. Most patients developed CNS disease following allogeneic stem cell transplantation. Four cases were identified within the final six months of the study period, including three with *KMT2A* abnormalities. Two patients developed isolated CNS disease whilst receiving menin inhibitor therapy. Outcomes were poor overall, with relapsed AML the predominant cause of death.

Conclusion:

CSF-proven CNS involvement in AML remains associated with poor survival. The recent clustering of cases with *KMT2A* aberrations and occurrence during menin inhibitor therapy raise important questions regarding CNS sanctuary site resistance. Increasing use of targeted and lower-intensity AML therapies with limited CNS penetration may warrant greater consideration of CNS assessment and CNS-directed therapeutic strategies in high-risk patients.

Beware the cytopenia: A single centre experience of acute promyelocytic leukaemia

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Aim:

Describe the presenting clinical and laboratory characteristics, molecular features, and outcomes in a cohort of patients with acute promyelocytic leukaemia (APL).

Method:

A single-centre retrospective cohort analysis was performed at an Australian tertiary hospital, including 102 patients diagnosed with APL between 2000-2026. Demographic, laboratory, and outcome data were collected and analysed using descriptive statistics.

Results:

The median age at diagnosis was 46.5 years (range 16-83), with a male predominance (60%). According to the Sanz risk stratification, 81% of patients were low/intermediate risk and 19% high risk. The majority (89%) presented with bicytopenia or pancytopenia. Three patients presented with isolated neutropenia (ANC 0.26-0.98x10⁹/L), while isolated anaemia (Hb 111g/L) and isolated thrombocytopenia (Plt 119x10⁹/L) were each observed in one patient. The median peripheral blood blast/blast equivalent was 0.44x10⁹/L (range 0.01-289.82). Sixteen patients (16%) presented without circulating disease; in two cases isolated neutropenia and in one case isolated anaemia were the only peripheral blood abnormalities. DIC occurred in 73.5% of patients and was most frequent in high-risk disease.

A bcr1 *PML::RARA* transcript was detected in 53% of cases. Conventional karyotype did not demonstrate a t(15;17) in five (5%) of the evaluable cases, whereas Fluorescence In Situ Hybridization detected a fusion signal in all. Of the evaluable patients, 38% achieved molecular MRD negativity post induction, 96% post consolidation cycle 1, and 100% by end of treatment. There were nine deaths during induction, most commonly due to infection (44%) and bleeding complications (33%). Two patients (2%) died following late disease relapse secondary to limited treatment per patient preference.

Conclusion:

This study demonstrates the known heterogenous presentation of APL and highlights the need for a high index of suspicion given the frequent paucity of circulating disease, occasional presentation with an isolated cytopenia and significant risk of early death.

Bone marrow necrosis complicating induction treatment of acute promyelocytic leukaemia

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Discussion:

Bone marrow necrosis (BMN) is a rare complication of induction treatment of acute promyelocytic leukaemia (APML). The onset, causative factors and management of BMN during APML treatment remains unclear and has been variably described in the literature¹⁻⁶. Here we present the case of a 36-year-old female who presents with standard risk APML. She had no DIC on presentation.

All-trans retinoic acid (ATRA) at 45mg/m²/day and arsenic trioxide (ATO) at 0.15mg/m²/day were promptly commenced, with oral prednisolone prophylaxis for differentiation syndrome (DS) at 0.5mg/kg/day. At day 9, hydroxyurea and dexamethasone were commenced due to leucocytosis (WCC 11.4 x 10⁹/L) and symptoms suggestive of DS.

At day 10 she developed severe, diffuse skeletal pains, with worsening leucocytosis (WCC 23 x 10⁹/L) and markedly elevated lactate dehydrogenase (LDH 2350 IU/L) prompting a clinical diagnosis of BMN.

ATRA/ATO were withheld, with symptomatic and biochemical resolution of BMN. ATRA was reintroduced on day 13 with a 50% dosage reduction, followed by ATO (at 50%) on day 14, followed by immediate re-occurrence of pain crisis (necessitating patient-controlled analgesia) and LDH elevation to 1160 IU/L.

ATRA/ATO were withheld, hydroxyurea ceased on day 17 and two doses of idarubicin (12mg/m²/day) were delivered on days 18 and 20. ATRA/ATO were re-introduced sequentially and gradually from day 23 and tolerated well. Day 34 bone marrow examination demonstrated complete morphologic remission. Standard consolidation with ATRA/ATO has been commenced and tolerated well to date.

Conclusion:

BMN complicating induction therapy in APML is poorly described in the literature and under recognised by clinicians. A high index of suspicion and timely initiation of supportive management is essential. Cases have been associated with ATRA, without ATO^{1,2}, as well as ATO, without ATRA^{3,4}. In our experience BMN was the result of the combination of both differentiation agents^{5,6}. BMN can be effectively managed with temporary cessation of ATRA/ATO and judicious re-introduction of both at a later timepoint.

Acute myeloid leukaemia presenting with extreme thrombocytosis in the absence of MECOM rearrangement: A case study

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Introduction:

Extreme thrombocytosis (platelets >1000x10⁹/L) is rare, with an incidence ~2-5.8%.¹ BCR::ABL-negative myeloproliferative neoplasms are the most common haematological cause, accounting for 49% in one case series.² Acute myeloid leukaemia (AML) is a rare cause which is frequently associated with MECOM rearrangements.³⁻⁵ Here we showcase a case of AML, presenting with platelets of >2000x10⁹/L without MECOM rearrangement.

Case Presentation:

A 67-year-old female was referred with an incidental finding of extreme thrombocytosis (counts at admission Table 1). The patient had a 6-month history of exertional dyspnoea, pruritus and weight loss. Physical examination was unremarkable. A presumed diagnosis of myeloproliferative neoplasm was made and hydroxycarbamide commenced empirically to control thrombocytosis. Marrow biopsy demonstrated increased blast population (~25% nucleated cells) with marked dysmegakaryopoiesis. Features were favoured to be suggestive of AML with megakaryocytic differentiation and atypia (Figure 1). Cytogenetics demonstrated normal female karyotype. Next-generation-sequencing results are shown in Table 2.

	Result	Unit	Reference Range
Haemoglobin	79	g/L	115-160
White Cell Count	2.88	X10 ⁹ /L	4.00-11.00
Platelet Count	2079	X10 ⁹ /L	150-400
Neutrophils	1.79	X10 ⁹ /L	2.00-7.50
No blasts seen on blood film			

Table 1. Presenting blood counts.

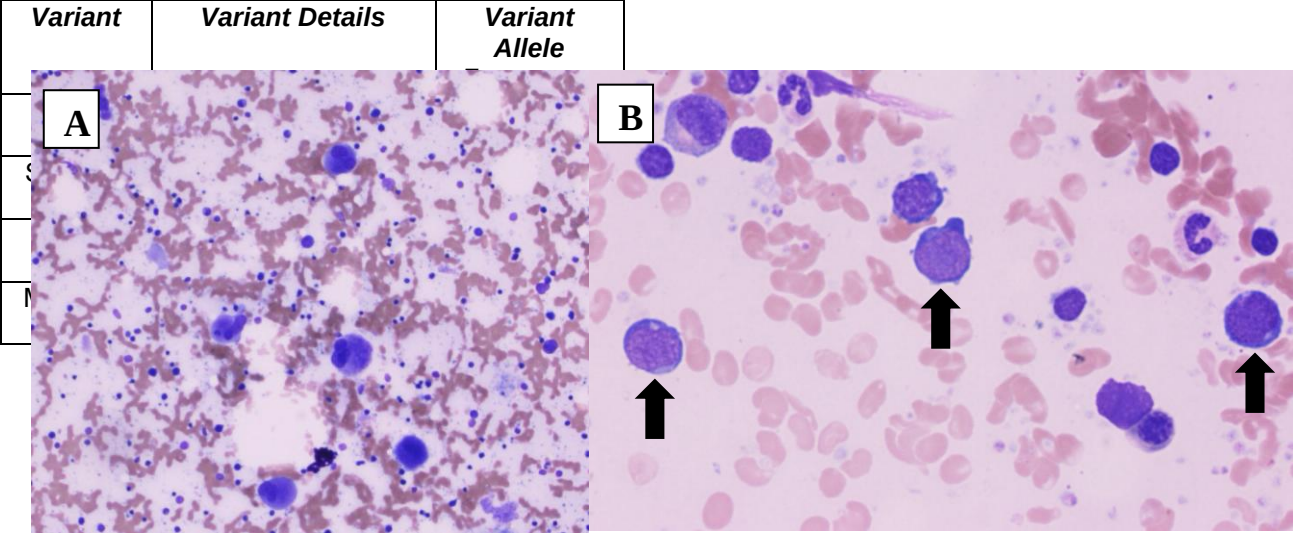


Figure 1. Bone marrow aspirate. A) 200x magnification demonstrating increased megakaryocytes with dysmegakaryopoiesis. B) 600x magnification demonstrating increased blasts with deeply basophilic cytoplasm, cytoplasmic budding and

The patient commenced on ‘7+3’ chemotherapy (cytarabine/idarubicin) which was complicated by neutropenic sepsis and bowel perforation, culminating in the patient’s passing 11 days into treatment.

Conclusion:

AML presenting with thrombocytosis is exceedingly rare. This case demonstrates the need for suspicion for alternate pathology when patients present with thrombocytosis in addition to cytopenias, highlighting the essential role of a marrow biopsy for diagnostic clarity.

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Real-world bridging therapy for relapsed/refractory B-acute lymphoblastic leukaemia prior to CD19 CAR T-cell therapy: a single-centre experience

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Aim: CD19 directed CAR T-cell therapy (tisagenlecleucel and brexucabtagene autoleucel) are approved for relapsed/refractory B-acute lymphoblastic leukaemia (R/R B-ALL). Bridging therapy (BT) options have expanded with inotuzumab ozogamicin (an anti-CD22 antibody-drug conjugate) and later generation tyrosine kinase inhibitors (TKI). We describe real-world bridging practice and outcomes.

Method: We retrospectively reviewed all R/R B-ALL patients infused with CD19-directed CAR-T at our centre between June 2020 and April 2026. Disease distribution and BT delivery location were recorded. Regimens were analysed by component (proportion containing each agent class); pre-infusion response was assessed by marrow morphology/flow cytometry, PET imaging, and/or CSF assessment for CNS disease.

Results: 16 patients underwent 19 infusions (tisa-cel n=8, brexu-cel n=11); 3 received repeat infusion at a separate timepoint. At apheresis, 15 (79%) had marrow involvement, 9 (47%) blood involvement by flow cytometry/morphology, 4 (21%) extramedullary disease, and 3 (16%) CNS disease. 17/19 (89%) received bridging. 47% (9/19) received chemotherapy, 42% (8/19) inotuzumab, 16% (3/19) a TKI, and 11% (2/19) radiotherapy (RT); regimens commonly combined modalities, including 2/19 (11%) inotuzumab + TKI combinations. Response was 8/8 (100%) for inotuzumab-containing regimens, 5/6 (83%) for chemotherapy without inotuzumab, and 2/2 each for TKI-containing and RT-containing regimens. Two patients (11%) proceeded directly to lymphodepletion without bridging and a further two received bridging without documented response assessment prior to LD; overall response to BT was therefore 14/15 (93%) among assessable bridged patients. 11/17 (65%) of bridging was delivered at referring sites rather than the CAR-T centre.

Conclusion: Inotuzumab was incorporated in nearly half of the bridging regimens for R/R B-ALL, with universal pre-infusion response. High response rates continue to be encouraging, with the growing use of targeted agents showing a shift away from cytotoxic bridging. As most bridging is delivered at referring sites, close coordination with the CAR-T centre remains key to optimal patient care.

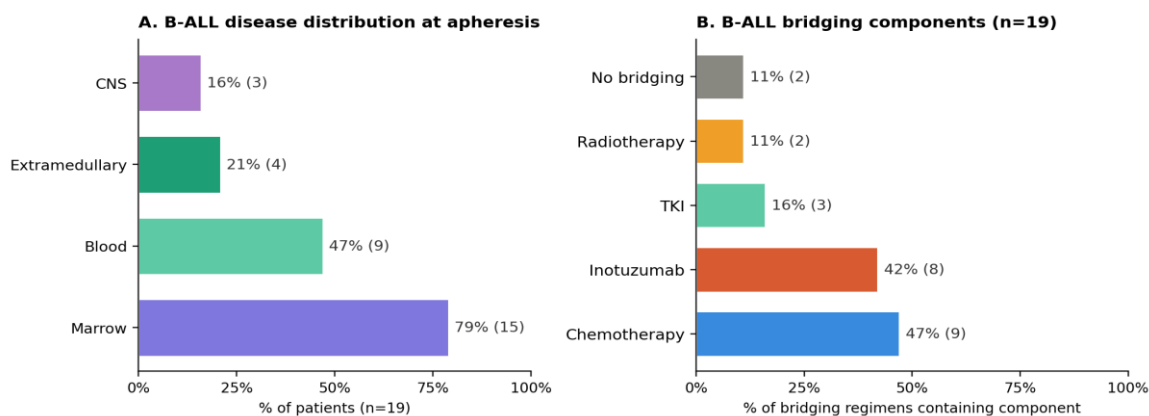


Figure. (A) Disease distribution at apheresis among the 19 patients (B) Bridging components — percentages reflect the proportion of the full cohort (n=19) containing each agent class. Regimens often combined multiple components

BCL2 expression via immunohistochemistry in acute myeloid leukaemia (AML) as a predictor of response to venetoclax-based therapy

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Aim:

We aimed to investigate the utility of assessing BCL-2 expression by immunohistochemistry (IHC) on bone marrow biopsy trephine as a prognostic marker for the response of AML to venetoclax therapy.

Method:

Archived pre-venetoclax therapy bone marrow trephine specimens from 61 patients at a single centre with newly diagnosed or relapsed AML were collected and assessed for BCL-2 expression via IHC. Data was retrospectively collected and analysed on the same patient cohort to determine clinical outcomes.

Multiple logistic regression was used to investigate the effect of age, venetoclax line of therapy, trilineage dysplasia, monocytic lineage, CD34 positivity, IDH, NPM1, FLT3 and TP53 mutation status and BCL-2 expression on response. The Kaplan-Meier method was used to calculate survival estimates and the log-rank test used to compare subgroups.

Results:

61 patients were identified in total over 4 years with a median age of 73 years (68-79), 63.9% with newly diagnosed AML and 36.1% with relapsed disease. BCL-2 expression greater than 20% was found in 68.9% of patients, which showed a higher likelihood of response to venetoclax therapy independent of other factors (odds ratio 2.4, 95% CI 1.7-6.7, $p = 0.04$). Advanced age and relapsed AML were associated with poor response. There was no observed difference in survival and degree of BCL-2 expression.

Conclusion:

BCL-2 expression via IHC of greater than 20% was predictive of response to venetoclax therapy in AML patients. This simple, rapid, low-cost test may be utilized to guide treatment decisions and potentially avoid unnecessary treatment toxicity.

Drug repurposing in transgenic zebrafish reveals active compounds against MLL-AF9 driven AML

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Aim:

KMT2A::MLLT3 (MLL-AF9)-driven acute myeloid leukaemia (AML) is an aggressive AML subtype associated with poor clinical outcomes. We previously established a transgenic zebrafish AML model, Runx1+23:MA9/lyz:EGFP, which is characterised by early myeloid expansion and enables visualization of lyz-positive myeloid cells *in vivo*. This study aimed to evaluate the utility of this model as a drug screening platform for the identification of therapeutically active compounds in MA9-driven AML.

Method:

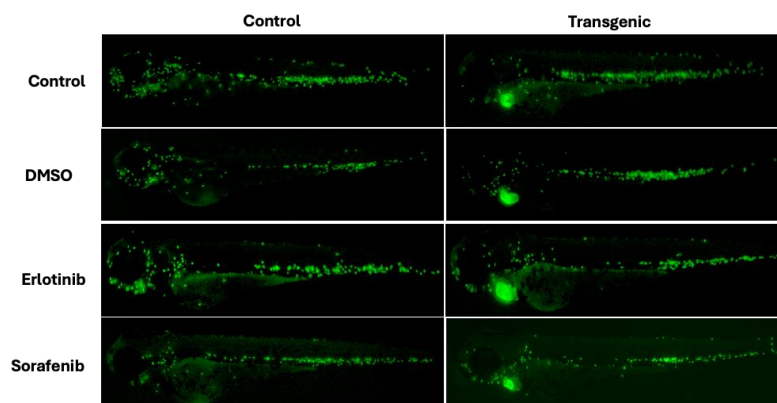
Runx1+23:MA9/lyz:EGFP transgenic embryos and control lyz:EGFP embryos were treated at 48 hours post fertilisation with 46 FDA-approved drugs and drug combinations. Following 24 hours of treatment, fluorescent microscopy was used to assess changes in the number of lyz:EGFP-positive myeloid cells. Flow cytometry was performed to quantify GFP-positive myeloid populations, and quantitative RT-qPCR was used to measure lyz expression, normalised to the housekeeping gene β -actin. Drug responses were evaluated based on efficacy, specificity, and reproducibility.

Results:

Nineteen individual compounds and three combination therapies reduced the number of lyz:EGFP-positive myeloid cells in MA9 transgenic embryos while showing minimal effects in control embryos. Fluorescence microscopy revealed a reduction in the myeloid population in transgenic embryos following treatment, compared with wild-type controls. These findings were further validated by flow cytometric quantification of GFP-positive cells and RT-qPCR analysis, which confirmed reduced lyz expression in treated transgenic embryos.

Conclusion:

Our findings demonstrate that the Runx1+23:MA9/lyz:EGFP zebrafish model is a robust and scalable *in vivo* platform for therapeutic screening in MA9-driven AML. The identification of 22 active treatments highlights the potential of zebrafish-based approaches to accelerate preclinical drug discovery and prioritisation of candidate therapies for MLL-AF9 rearranged AML.



A) Representative fluorescent microscopy images of zebrafish embryos from the control (lyz:EGFP) and transgenic (Runx1+23:MA9/lyz:EGFP) groups.

A single centre, retrospective review of CD19 targeted CAR-T cell therapy outcomes in adult B-ALL

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Aim:

CD19 directed chimeric antigen receptor (CAR) T-cell therapy is standard of care treatment for relapsed/refractory (r/r) B-ALL. We report a real-world analysis of patients treated with Brexucabtagene Autoleucel (Brexu-cel) and Tisagenlecleucel (Tisa-cel) in a single centre retrospective study.

Method:

We explored the outcomes in 13 adult patients who received CAR T-cell therapy for B-ALL at Royal Prince Alfred Hospital from January 2020 to March 2026 via electronic medical records analysis.

Results:

13 patients received either Tisa-cel(5) or Brexu-cel(8) with a combined median follow-up time of 27.5 months. Complete response (CR) was achieved in 11(85%) patients. Disease relapse occurred in 6(46%) patients with median progression-free survival (PFS) of 17.0 months and overall survival (OS) 45.7 months (5 deaths). Early CD19 B-cell recovery (<6 months) occurred in 46% of patients, with median recovery time of 4.7 months. 67% of all relapses were observed in patients with early CD19 B-cell recovery. 6 patients underwent further treatment for relapse (1/6 allogenic stem cell transplant [alloSCT], 4/6 blinatumomab, 2/6 second CAR T-cell, 2/6 donor lymphocyte infusion [DLI]). PFS post relapse was 17.1 months, as was OS. Cytokine release syndrome occurred in 85% of patients; 8% were grades ≥ 3 . Immune effector cell-associated neurotoxicity syndrome was reported in 31% of patients; 15% were grades ≥ 3 .

Conclusion:

Our data demonstrated high rates of initial complete remission with CAR T-cell therapy for r/r B-ALL in an Australian real world setting. We found comparable efficacy to the foundational ZUMA-3 and ELIANA clinical trials. Further salvage therapy was often required, and subsequently offered durable remission. Additionally, we demonstrated early CD19 B-cell recovery can be an important marker for pending relapse.

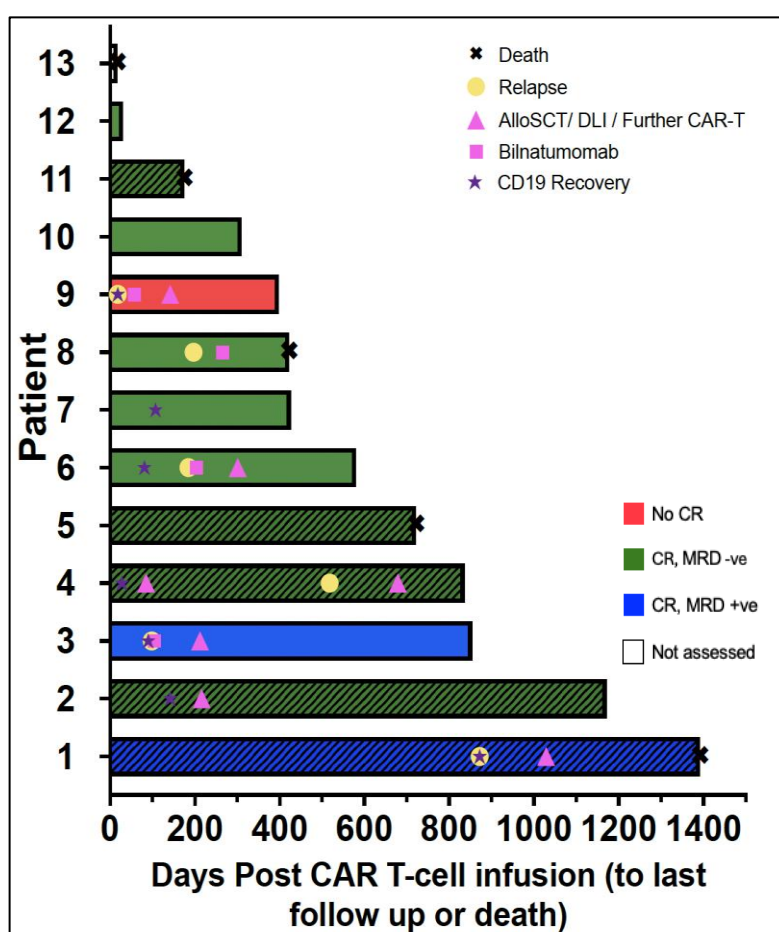


Figure 1. Swimmer plot of adult B-ALL CAR T-cell therapy outcomes

Note: shaded bars represent Tisa-cel; non-shaded represent Brexu-cel

Investigating metabolic and epigenetic modifiers of treatment response in acute myeloid leukaemia

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Aim:

Acute myeloid leukaemia (AML) remains difficult to treat, particularly in patients who are not suitable for intensive chemotherapy. AML is characterised by impaired differentiation, altered metabolism and frequent disruption of epigenetic regulation, creating interest in lower toxicity approaches that may enhance existing therapies. Ascorbate supports TET enzyme activity, while mitochondrial metabolism and quality control may influence treatment response. This study aimed to investigate whether modulation of these pathways alters AML cell phenotype and response to clinically relevant treatments.

Methods:

Human AML cell lines representing diverse molecular backgrounds were cultured in extended treatment systems with ascorbate and mitochondrial modulators, alone or in combination with subtype appropriate therapies including azacitidine, venetoclax azacitidine and ATRA. Cell growth and viability were monitored by serial cell counting with trypan blue exclusion, while differentiation was assessed by morphology and flow cytometric analysis of myeloid surface markers. Global 5-hydroxymethylcytosine (5-hmC) was measured using mass spectrometry, as a marker of TET activity, and mitochondrial phenotype was evaluated using flow-based mitochondrial probes. CRISPR/Cas9 edited models were generated to examine the contribution of TET2 to ascorbate response. Transcriptomic and pathway analyses are underway to provide broader insight into treatment associated cellular changes.

Results:

Preliminary data suggest that ascorbate can increase global 5-hmC across AML models, consistent with enhanced TET activity. Changes in proliferation and myeloid surface marker expression were observed in selected models, suggesting that response varies by AML context. Mitochondrial directed treatments also altered growth and mitochondrial phenotype in some cell lines. Ongoing analyses are investigating whether these changes modify response to established AML therapies.

Conclusion:

This work supports further investigation of metabolic and epigenetic modifiers as adjuncts to AML therapy. Defining which AML models respond to ascorbate or mitochondrial modulation may help identify rational treatment combinations and inform future genotype guided approaches.

Comparative evaluation of cytogenetic and genomic testing in myeloid disorders: A single-centre retrospective audit

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Aim:

Cytogenomic testing underpins diagnosis, prognostication and therapeutic decision-making in AML, MDS and/or MPN. Karyotyping and FISH have traditionally supported the detection of genetic abnormalities; however, FISH is hypothesised to be underutilised, even with the advent of next-generation sequencing (NGS).

This study aims to evaluate the diagnostic and prognostic utility of FISH in myeloid malignancies, and to determine its value in a contemporary setting where NGS is accessible.

Method:

A retrospective audit was conducted at The Canberra Hospital of patients diagnosed with a myeloid malignancy between November 2022 and January 2026. Cytogenetic and molecular data from 668 bone marrow and blood specimens from 535 patients were reviewed.

Karyotype, FISH, and external NGS tests were analysed, and turnaround time (TAT) for each of these tests were compared using the non-parametric Mann-Whitney test.

Results:

Among 158 diagnostic AML specimens, 61 harboured abnormalities detectable by FISH, however only 32.8% (n=20) were classified using FISH. In MDS and/or MPN, 45 out of 78 genetically defined entities were potentially detectable by FISH, yet only 6.7% (n=3) had a FISH test performed. Of all specimens in this study, 51 harboured a gene abnormality in the *TP53* region according to NGS, however only 11.8% (n=6) of these had a positive *TP53* FISH test performed.

In AML cases, there was a significantly ($p<0.001$) faster TAT for FISH (median 4 days) compared to DNA NGS panels (median 22 days) and RNA panels (median 19 days). The same trend was observed in cases of MDS and/or MPN.

Conclusion:

Even in the context of access to NGS, FISH provides significantly increased incremental diagnostic yield for routine genomic classification and prognostication in AML, MDS and MPN, due to faster TAT. These findings support continued role of FISH testing for faster TAT, at least until TAT for NGS can be improved.

Rapid integrated DNA/RNA panel testing for time-critical genomic classification of acute leukaemia: a regional centre experience

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Background:

Management of acute leukaemia increasingly relies on rapid identification of genomically defined disease subtypes that directly influence diagnosis, prognostic stratification, and selection of targeted or subtype-specific therapies. Patients with acute myeloid leukaemia (AML) and acute lymphoblastic leukaemia (ALL) commonly require urgent treatment decisions within days of presentation. Conventional diagnostic workflows typically combine multiple sequential assays including fluorescence in situ hybridisation (FISH), PCR-based testing, cytogenetics, and next-generation sequencing (NGS), resulting in workflow complexity, cost, and reporting delays. Expanding numbers of clinically relevant genomic alterations have further challenged the scalability of traditional rapid-turnaround approaches.

Aim:

To evaluate implementation of a rapid, low-throughput, automated DNA/RNA NGS panel workflow for upfront molecular classification of acute leukaemia in a regional tertiary centre.

Method:

An integrated DNA/RNA workflow incorporating RNA fusion panel reverse transcription and automated low-throughput capture-based library preparation was implemented for newly diagnosed acute leukaemia samples. The assay was designed to detect sequence variants, copy number alterations, tandem duplications, gene fusions, and gene expression abnormalities relevant to AML and ALL classification. Minimal batching was utilised to optimise turnaround time.

Results:

The integrated workflow enabled comprehensive genomic profiling from initial diagnostic specimens with actionable results available within approximately 2 –5 days of sample collection. The workflow showed high sensitivity for subtype defining genomic abnormalities, substantially reducing reliance on first-line FISH and targeted PCR screening. Rapid molecular subclassification supported timely therapeutic decision-making while simplifying laboratory workflows in a regional setting.

Conclusion:

Rapid integrated DNA/RNA panel testing is feasible and cost-effective in a regional centre and provides a scalable alternative to conventional tiered acute leukaemia diagnostic workflows, supporting contemporary genomically informed management.

A state-wide retrospective review of CNS diagnostic investigations in adults with acute lymphoblastic leukaemia

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¹Queensland Health, Royal Brisbane and Womens Hospital, Brisbane, Australia, ²Queensland health, Princess Alexandra Hospital, Brisbane, Australia

Aims:

To evaluate patterns of CNS assessment in adults with ALL across the state and describe the diagnostic yield and concordance of CSF cytomorphology and flow cytometry.

Methods:

We conducted a state-wide, multicentre, retrospective review of adults aged >16 years diagnosed with ALL, lymphoblastic lymphoma with marrow involvement, or lymphoid blast-phase myeloid neoplasms across public hospitals between January 2015 and February 2026. Diagnostic, laboratory and CSF assessment data was extracted from electronic medical records. CSF samples were classified according to cytomorphology, red cell count, white cell count, and flow cytometry results.

Results:

Data extraction is ongoing. In preliminary data from 438 patients, median age was 47.6 years (range 16.1-88.2). Of evaluable patients (242): 194 (80.2%) had B-lineage ALL/LBL, 44 (18.2%) T-lineage ALL/LBL and 3 (1.2%) CML in lymphoid blast phase. CNS testing status was available for 206 patients, of whom 184 (89.3%) underwent CSF assessment. CSF assessment occurred a median of 5 days after diagnostic marrow assessment (IQR 3-9; range 0-183). CNS involvement was identified in 10/190 evaluable patients (5.3%). Among tested patients, flow cytometry was performed in 98/184 (53.3%), cytomorphology in 155/184 (84.2%), and both in 85/184 (46.2%). Flow cytometry identified one case of CNS involvement not detected by cytomorphology/cell count and helped exclude involvement in seven cases with CSF WCC >5 but negative flow and no final CNS involvement.

Conclusion:

Preliminary data shows variability in the use of cytomorphology and flow cytometric assessment of diagnostic CSF samples. CNS involvement was uncommon. Flow cytometry showed complementary diagnostic value by identifying rare occult disease not detected by cytomorphology/cell count and by supporting exclusion of CNS involvement in selected high-WCC CSF samples.

A case of primary refractory acute T-cell lymphoblastic lymphoma with germline TET2 mutation

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¹Health New Zealand- Te Whatu Ora - Te Toka Tumai, Auckland, New Zealand

Abstract

A 48 year old male with distant history of early stage nodular lymphocyte-predominant Hodgkin lymphoma treated with radiotherapy, presented with right 3rd and 4th cranial nerve palsy, large mediastinal mass and multiple renal lesions. He was diagnosed with acute T-cell lymphoblastic lymphoma (T-LLy) with CNS and bone marrow involvement.

He was treated with UKALL14 protocol complicated by prolonged severe thrombocytopenia following phase 2 induction with significant delay in treatment. He has normal TPMT function and no cause for thrombocytopenia is identified. He had a repeat bone marrow biopsy which showed hypocellular bone marrow with ongoing morphological remission. The Allhaem NGS panel demonstrated a TET2 loss of function mutation with a high VAF which was later confirmed as a germline mutation on diagnostic bone marrow biopsy and hair follicle sample.

Interim PET CT scan demonstrated a very good partial response, with residual avidity in the mediastinal mass. He received IFRT to the mediastinal mass in conjunction with Daratumumab and achieved a CR after two cycles. The patient relapsed following four cycles of Daratumumab bridging and was treated with ALL06 re-induction with bortezomib followed by a MUD allogeneic stem cell transplant (alloSCT) in CR3. He has remained in remission 20-months post alloSCT.

This report describes the first documented case of T-lymphoblastic lymphoma harbouring a germline TET2 mutation complicated by profound haematological toxicity following intensive chemotherapy. This case underscores the importance of maintaining a broad differential diagnosis in patients with unexpected or disproportionate treatment-related cytopenias and highlights the potential role of novel therapeutic strategies as salvage therapy in this rare and aggressive lymphoid malignancy.

Application of machine learning in NPM1 mutated acute myeloid leukaemia in disease reclassification and prognostication

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¹Alfred Health, Melbourne, Australia, ²Monash University, Melbourne, Australia

Aim:

Nucleophosmin 1 (NPM1) mutated acute myeloid leukaemia (AML) is classified as favourable (with wildtype FLT3-ITD) in the WHO and ELN 2022 . Despite being a favourable marker, there are substantial number of disease relapses and mortality. We aim to utilise various unsupervised and supervised machine learning (ML) models to further subclassify and prognosticate NPM1 AML patients by integrating clinical, laboratory and genomic data.

Method:

210 NPM1 AML patients on the BEAT AML public database is trained with hierarchical clustering and k-means unsupervised models to uncover and discover whether NPM1 status (alone or with expression) carves patients into distinct groups. Subsequently; external validation with two different dataset- local AML data comprise 52 patients and the Austrian-German Acute Myeloid Leukaemia Study Group (AMLSG) public dataset with 436 patients.

After the clustering with unsupervised ML, a supervised classifier with logistic regression and nearest normal is utilised for prediction for survival prediction and prognostication. Similarly, the model will be trained with BEAT-AML where the AUC/calibration is quoted on AMLSG and the local cohort as external validation.

Results:

The unsupervised models are expected to stratify NPM1 AML patients into biologically and clinically meaningful subgroups, revealing heterogeneity not captured by current classification frameworks. Distinct clusters are anticipated to emerge with differing survival profiles, supporting the premise that NPM1 AML warrants further subclassification. The supervised classifiers are expected to demonstrate adequate discriminative performance, with AUC and calibration metrics indicating generalisability across external validation cohorts. Overall, findings are anticipated to support the utility of ML-based approaches in refining risk stratification and prognostication within this disease subtype. In further detail, results will be presented during the presentation.

Conclusion:

NPM1 AML ML models should be explored as a tool to refine classification and prognostication. Further studies is required to investigate and validate different ML algorithms applied to different AML subtypes and other myeloid neoplasms.

Review of rapid *PML::RARA* FISH testing for suspected acute promyelocytic leukemia

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¹NSW Health Pathology ICPMR, Westmead, Australia, ²University of Sydney, Sydney, Australia

Background:

Acute promyelocytic leukemia (APL) is a hematologic emergency requiring rapid diagnosis and prompt initiation of all-trans retinoic acid therapy to reduce early mortality. Detection of the *PML::RARA* fusion is critical for confirmation of diagnosis. Rapid fluorescence in situ hybridization (FISH) testing has become an important diagnostic modality in suspected APL cases.

Aims:

To review the utilization and diagnostic outcomes of urgent rapid *PML::RARA* FISH testing performed at the Institute of Clinical Pathology and Medical Research (ICPMR) NSWHP since implementation of onsite testing.

Methods:

A retrospective review was performed of all urgent requests for rapid *PML::RARA* FISH testing processed at ICPMR since implementation. Cases were assessed for diagnostic outcome and alternative recurrent cytogenetic abnormalities identified in *PML::RARA*-negative cases.

Results:

A total of 65 urgent requests for rapid *PML::RARA* FISH testing were identified during the study period. Of these, 24 cases (36.9%) were positive for a *PML::RARA* fusion confirming APL. Among the 41 negative cases, four were subsequently identified as having t(8;21)(q22;q22)/*RUNX1::RUNX1T1*-positive acute myeloid leukemia (AML). The remaining negative cases demonstrated a heterogeneous range of alternative diagnoses and cytogenetic findings. Rapid FISH testing enabled timely exclusion or confirmation of APL in critically unwell patients and facilitated appropriate early therapeutic decision-making.

Conclusions:

Rapid *PML::RARA* FISH testing remains a valuable frontline diagnostic assay in the assessment of suspected APL. While over one-third of urgent referrals were confirmed as APL, a subset of negative cases harboured other clinically significant recurrent AML-associated abnormalities, emphasizing the importance of comprehensive diagnostic assessment in suspected acute leukemia presentations.

Bloodless modified ALL06 protocol: T-cell acute Lymphoblastic leukaemia (ALL) in a patient who does not accept blood transfusion achieving remission

Dr. Matthew Wright¹, Dr Cherng Yih Hng¹, Dr Shane Gangatharan¹

¹Fiona Stanley Hospital, South Metropolitan Health Service, Murdoch, Australia

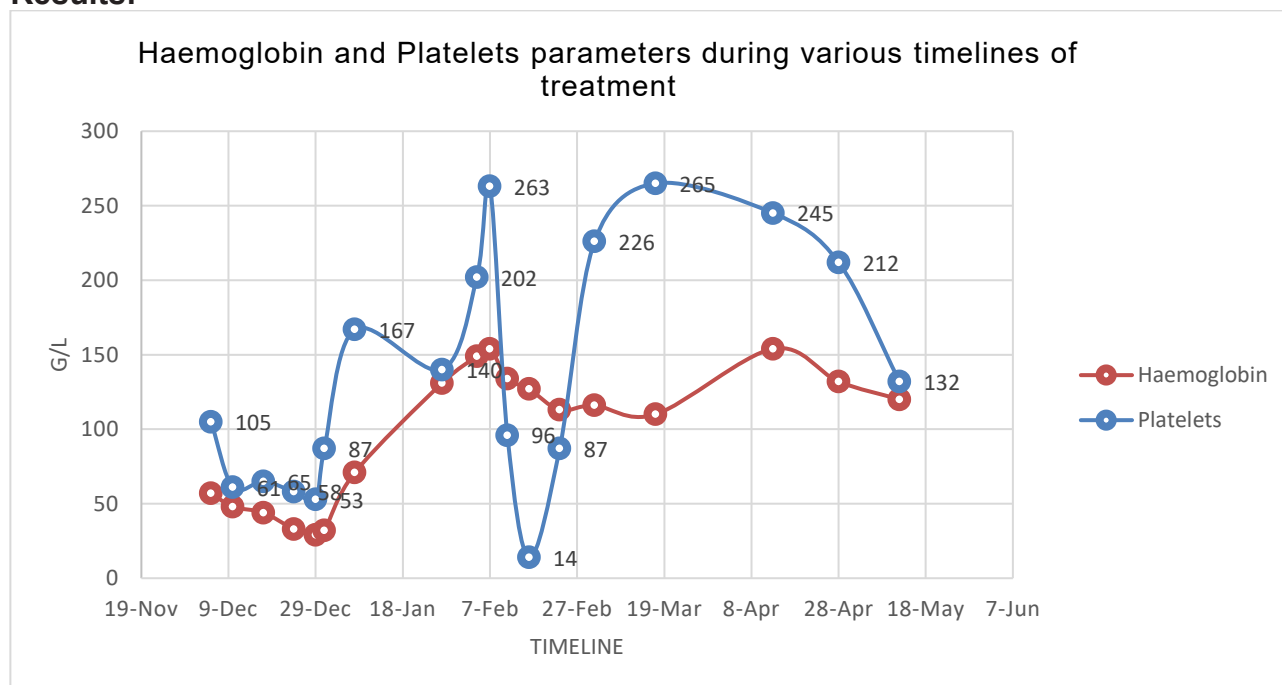
Aim:

The ALL06 protocol is standard of care for fit patients with T-ALL in Australia. Myelosuppression is a known adverse effect and therefore presents unique challenges for patients who do not accept blood transfusions. We present the considerations and adaptations of standard medical protocols whilst treating a Jehovah's witness with T-ALL to provide best possible care.

Method:

Sequential clinical and biochemical data were collected for a patient with T-ALL receiving ALL06 with modifications in accordance with expected tolerability of treatment.

Results:



Our patient is a 58-year-old female who presented with incidental severe pancytopenia. Flow cytometry of bone marrow aspirate was consistent with T-ALL. Being a Jehovah's witness, she elected not to receive most whole blood components, with exception of cryoprecipitate and Antithrombin III concentrate. Her supportive management included daily folic acid supplementation, erythropoietin and B12 injections.

Various strategies were implemented including blood conservation by minimizing venesections (three times a week), using paediatric tubes during collection and avoiding collection via PICC line to reduce blood volume wastage from discarding. She received the ALL06 protocol with the omission of daunorubin in Protocol I induction. Bone marrow biopsy confirmed remission. In Protocol I consolidation 6MP was omitted and extended recovery time was allowed in between cytarabine doses (up to one week) due to thrombocytopenia.

Haemoglobin at presentation was 54g/L and nadir was 29g/L (3 weeks after commencing weekly vincristine), followed by significant improvement to >80g/L two weeks later. She is now approaching the final week of her M block and remains in full haematological recovery.

Conclusion:

Our case report highlights the importance of individualizing leukaemia care. We show that Jehovah witness patient with T-ALL can be successfully treated with modified ALL06 protocol in conjunction with best supportive care.

FRALLE-93 in adults up to 65 years: a well-tolerated paediatric-inspired protocol with acceptable toxicity and durable outcomes

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¹Department of Haematology, Box Hill Hospital, Melbourne, Australia

Aim:

To characterise treatment-related toxicity and survival outcomes of FRALLE-93 protocol in adults up to 65 years, including the impact of incorporating immunotherapy.

Method:

A retrospective study of patients who underwent FRALLE93 between July 2006 and April 2026 was conducted at our centre. Treatment response was assessed with bone marrow aspirate and trephine in combination with Measurable Residual Disease (MRD).

Results:

A total of 47 patients aged ≥ 17 years treated with FRALLE-93 were included. Median age at diagnosis was 36.9 years (range 17.1–64.3), with 40% aged over 45 years. B-cell acute lymphoblastic leukemia (B-ALL) was the predominant subtype (27/47), followed by T lymphoblastic lymphoma(T-LL) (9/47) and T-cell acute lymphoblastic leukemia(T-ALL) (8/47). After a median follow-up of 7.2 years, 38(80.9%) patients remained alive; 9 deaths occurred (5 progressive disease, 3 transplant-related complications, and 1 from neutropenic sepsis). The 5-year overall survival for the entire cohort was 78.1% and was comparable in patients aged >45 years (77.8%). Allogeneic hematopoietic stem cell transplantation (Allo-HSCT) in first complete remission showed favourable outcomes, whereas outcomes beyond this were poor.

Infectious complications were the most common adverse events (34%). Significant L-asparaginase-related hepatotoxicity was observed in 8 patients (grade 3, n=5; grade 4, n=3). Hepatotoxicity resolved in all but two patients with persistent grade 1 biochemical derangement. No recurrent significant hepatotoxicity was observed following rechallenge. Two patients experienced uncomplicated pancreatitis that did not recur with subsequent L-asparaginase doses.

Rituximab was associated with a lower relapse rate (16.7% vs 27.8%). Blinatumomab demonstrated activity in high-risk disease states, including MRD-positivity post-induction and primary refractory disease, facilitating MRD clearance and improving post-relapse survival (214 vs 135 days), with two cases of ICANS resolved without long-term sequelae.

Conclusion:

FRALLE-93 has demonstrated durable survival and tolerability in adult patients, with the addition of immunotherapy improving outcomes and reducing reliance on allo-HSCT.

An analysis of autologous paediatric stem cell collection practice within New Zealand Blood Service (NZBS)

Ms Kriselvie Aboy¹

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Aim:

NZBS is the sole provider of Cellular Therapy collection in Aotearoa, New Zealand. The principles for apheresis are the same in adults and paediatrics, however, due to greater extracorporeal volumes for paediatric patient, important considerations are required. This study aims to review and summarize the operating parameters used by NZBS for paediatric stem cell collections.

Method:

A retrospective data collection was performed for paediatric patients 15 who underwent autologous stem cell collections in Starship Hospital in Auckland, NZ between January 2023 to December 2025 using the Spectra Optia Apheresis System. Descriptive analysis of variables such patient characteristics, procedure run values and summary was conducted and presented as numbers and frequencies.

Results:

26 procedures were analysed for patients from 6 months to 9 years old with all collections performed in the hospital setting. All patients had a central line, RBC custom prime and prophylactic IV calcium infusion. All patients were alert and awake during the procedures without sedation. The average procedure run time is 222 minutes, average blood volume processed is 2939mL and average flow rate is 15mL/ min. There is a strong positive correlation between patient weight and inlet flow rate ($r= 0.90$) which indicates that flow rate is adjusted based on patient weight. Two cases reported irritability and headache coinciding with low ionized calcium however, procedures were not aborted and was managed effectively by adjusting the rate of calcium infusion. 61% of patients achieved target cell dose with an average collection efficiency of 61%. Multiple collection days is attributed to a lower pre harvest CD34 count.

Conclusion:

Paediatric stem cell collection presents challenges requiring special considerations. Balancing efficient procedures to meet targets with safety is essential. Despite conservative flow rates, targets were achieved without complications. Reviewing target volumes to prevent unnecessary prolonged procedures is recommended.

Brachial neuritis following autologous stem cell transplantation for diffuse large B-cell lymphoma: a case report

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Background:

Brachial neuritis is a rare, likely immune-mediated peripheral nerve disorder that affects the brachial plexus. It classically presents with severe shoulder and upper limb pain which later evolves into profound muscle weakness. Although autologous stem cell transplant (ASCT) is associated with autoimmune neurological phenomena, brachial neuritis in the post-transplant setting is rarely reported and may be under-recognised within haematology practice.

Case:

We describe a man in his sixties who developed severe bilateral shoulder and upper limb pain three weeks after ASCT for diffuse large B cell lymphoma. Examination demonstrated painful bilateral restriction of shoulder movements with left greater than right shoulder weakness. Initial brain and spine MRI and electrophysiological studies were non-diagnostic. Three weeks after symptom onset, new left-sided focal neurological deficits emerged, including wrist drop, elbow flexion and finger extension weakness. Repeat electrophysiological studies of the left upper limb confirmed brachial plexopathy with predominant posterior cord involvement. The patient was treated with intravenous methylprednisolone followed by a slow prednisolone wean and was transferred to a regional hospital for rehabilitation. At three-month follow-up, additional right-sided deficits, including sensory loss in the axillary nerve distribution and unilateral scapular winging, became apparent. Repeat electrophysiological studies were consistent with a diagnosis of bilateral brachial neuritis.

Discussion/Conclusion:

Brachial neuritis can be challenging to diagnose; severe pain often precedes objective neurological deficits and early investigations can be falsely reassuring. ASCT may act as an immune trigger for brachial neuritis, potentially through immune perturbations that occur during immune reconstitution. Timely recognition can optimise pain management, facilitate earlier allied health involvement and consideration of immunosuppressive treatment. Brachial neuritis should be considered in patients with severe upper limb pain post-ASCT, although further research is needed to clarify causality.

Gilteritinib resumption after hematopoietic stem cell transplantation versus best supportive care in relapsed/refractory FLT3-mutated acute myeloid leukemia: a landmark and propensity-matched cohort study

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Aim:

Patients with relapsed/refractory (R/R) *FMS*-like tyrosine kinase 3-mutated (*FLT3*^{mut+}) acute myeloid leukemia (AML) typically experience poor outcomes and need effective post-hematopoietic stem cell transplantation (HSCT) maintenance options. We evaluated efficacy outcomes in patients with R/R *FLT3*^{mut+} AML who resumed gilteritinib or received best supportive care (BSC) post-HSCT.

Method:

This noninterventional retrospective analysis compared patients from the ADMIRAL and COMMODORE trials who resumed gilteritinib post-HSCT, and an external comparator group of real-world patients who received BSC between 2015-2022. Adults with R/R *FLT3*^{mut+} AML who underwent HSCT, were alive 90 days post-HSCT, achieved engraftment and any complete response, and had grade ≤2 graft-versus-host disease were included. Baseline confounding variables between the treatment groups were adjusted by 1:1 propensity score matching in the per-protocol population (PPP; patients meeting all protocol-specified criteria) based on prespecified covariates. Primary and secondary outcomes were relapse-free survival (RFS) and overall survival (OS), respectively.

Results:

The PPP comprised 45 and 90 patients in the gilteritinib and BSC groups, respectively, and 45 and 38 patients, respectively, had confirmed *FLT3*^{mut+} status at R/R diagnosis. Propensity score matching yielded 40 patients per group. Univariate analyses of the PPP (RFS hazard ratio [HR] 0.55 [95% CI: 0.32-0.96]; OS HR 0.71 [95% CI: 0.41-1.25]) and multivariable analyses of the matched-analysis population (RFS HR 0.28 [95% CI: 0.13-0.62]; OS HR 0.53 [95% CI: 0.23-1.25]) showed that gilteritinib was associated with lower risk of relapse and death versus BSC. Similar results were observed in univariate analyses (RFS HR 0.38 [95% CI: 0.21-0.71]; OS HR 0.50 [95% CI: 0.27-0.95]) and multivariable analyses (RFS HR 0.36 [95% CI: 0.18-0.74]; OS HR 0.52 [95% CI: 0.25-1.08]) of the confirmed *FLT3*^{mut+} status at R/R diagnosis subgroup.

Conclusion:

In patients with R/R *FLT3*^{mut+} AML undergoing HSCT, resumption of gilteritinib was associated with lower relapse risk and a trend toward improved survival versus BSC post-HSCT.

Peri-transplant Ruxolitinib use in Myelofibrosis allogeneic stem cell transplantation: Real-world outcomes from a single-centre Australian cohort

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Background:

Allogeneic stem cell transplantation (allo-SCT) remains the only curative therapy for myelofibrosis (MF), but is associated with substantial transplant-related morbidity and mortality. Ruxolitinib is increasingly used pre-transplant as bridging therapy, and emerging prospective data suggest peri-transplant continuation may reduce inflammatory toxicity and GVHD. However, real-world data remain limited.

Methods:

We performed a retrospective single-centre cohort study of consecutive adult MF patients undergoing first allo-SCT at Fiona Stanley Hospital between 2016–2026. Patients were grouped according to ruxolitinib exposure strategy: no JAK inhibitor (No JAKi; n=4), pre-transplant ruxolitinib discontinued before stem cell infusion (Pre-Tx Rux; n=26), and peri-/post-transplant ruxolitinib continuation (Peri/Post-Tx Rux; n=13). Outcomes included engraftment, acute and chronic GVHD, overall survival (OS), CMV reactivation, and NRM.

Results:

Forty-three patients were included with median age 61 years (IQR 53–65); 56% received unrelated donor grafts. Median neutrophil and platelet engraftment were 22 and 32 days, respectively, with no significant differences between groups. Primary graft failure occurred in 2/43 patients (4.7%), both outside the peri/post-transplant ruxolitinib group.

Grade II–IV acute GVHD occurred in 35% overall and was numerically lower with peri/post-transplant ruxolitinib continuation compared with pre-transplant-only exposure (23% vs 38%, p=0.48). Moderate chronic GVHD occurred in 15% versus 8%, respectively, with no cases of severe chronic GVHD observed.

At last follow-up, overall survival was 74% overall and appeared favourable with peri/post-transplant ruxolitinib continuation compared with pre-transplant-only exposure (100% vs 58%, p=0.007), although follow-up remained shorter in the peri/post-transplant cohort (median 12.6 vs 56.6 months). CMV reactivation occurred in 29% overall and was numerically higher with peri/post-transplant ruxolitinib continuation (42% vs 23%, p=0.27).

Conclusions:

Peri/Post-transplant ruxolitinib continuation was feasible and associated with preserved engraftment, absence of graft failure in this real-world MF allo-SCT cohort. Prospective multicentre studies with longer follow-up are required to validate the potential GVHD and NRM benefits of peri-transplant ruxolitinib strategies.

Beyond one-size-fits-all: Pharmacogenomic and Pharmacokinetic determinants of PTCy outcomes in allogeneic transplantation: The Cy-PGx study

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Background: Post-transplant cyclophosphamide (PTCy) has transformed graft-versus-host disease (GVHD) prophylaxis in allogeneic haematopoietic stem cell transplantation (allo-HSCT) and following the practice-changing ALLG-CAST and BMTCTN1703 trials, is now standard of care across donor types at our centre. However, marked inter-patient variability persists in both efficacy and toxicity, including GVHD. Cyclophosphamide metabolism is influenced by polymorphic enzymes and transporters, yet pharmacogenomic (PGx) determinants of exposure and outcomes have not been systematically evaluated in the modern PTCy allo-HSCT setting.

Aims: (1) characterize the prevalence of actionable PGx variants in cyclophosphamide metabolic, transport and detoxification pathways in allo-HSCT recipients; (2) define associations between these variants and individual cyclophosphamide pharmacokinetic exposure; and (3) determine the impact of PGx-PK profiles on clinically meaningful outcomes, transplant-related toxicity, engraftment kinetics, and transplant-related mortality.

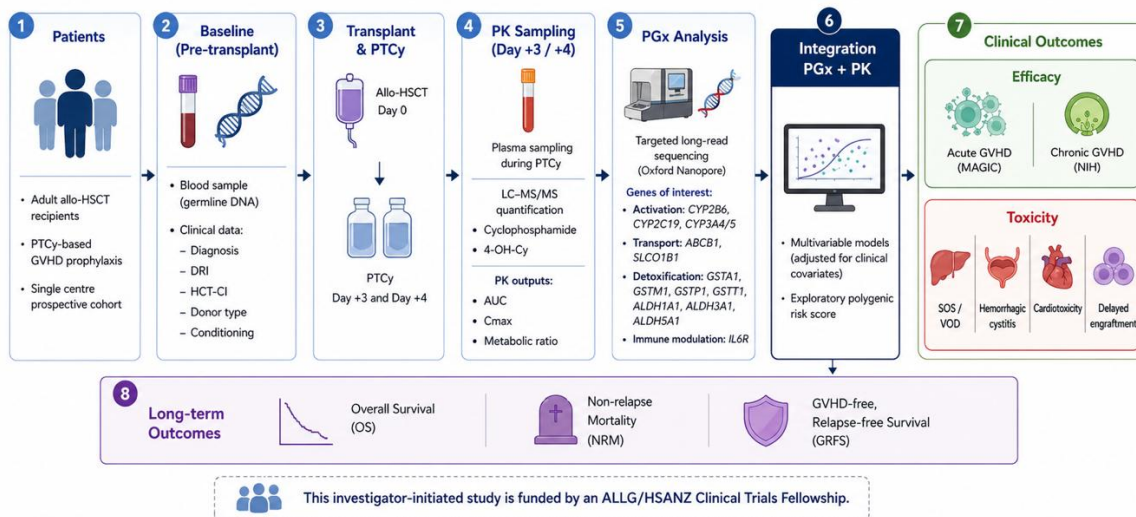
Study Design and Methods: Cy-PGx is a prospective, single-centre observational study enrolling adult SoC allo-HSCT recipients receiving PTCy-based GVHD prophylaxis at Fiona Stanley Hospital . Germline DNA is collected pre-transplant and analysed using targeted long-read sequencing (Oxford Nanopore) of variants in pathways of activation(CYP2B6, CYP2C19, CYP3A4/5), transport(ABCB1, SLCO1B1), detoxification(GSTA1, GSTM1, GSTP1, GSTT1, ALDH1A1, ALDH3A1, ALDH5A1) implicated in the Cyclophosphamide metabolism.

Pharmacokinetic sampling is performed during conditioning, D0 and during PTCy(days+3 and +4), with quantification of cyclophosphamide using LC–MS/MS. Clinical outcomes are prospectively captured using standardised criteria (MAGIC, NIH, CTCAEv5.0). Multivariable models will be used to examine the relationship between pharmacogenomic variants, cyclophosphamide exposure, and clinical outcomes.

Conclusion: Cy-PGx represents the first prospective integration of pharmacogenomics and pharmacokinetics to define drivers of variability in PTCy response across the full spectrum of allo-HSCT donor types. This study aims to generate mechanistic and clinically relevant data to support future precision dosing and risk-adapted GVHD prophylaxis strategies. This investigator-initiated study is funded by an ALLG/HSANZ Clinical Trials Fellowship and the authors acknowledge the support of the ALLG network.

Cy-PGx Study Design

Prospective integration of pharmacogenomics and pharmacokinetics to predict cyclophosphamide-related outcomes in allo-HSCT



Vedolizumab for steroid-refractory Ruxolitinib-exposed lower gastrointestinal acute graft-versus-host disease: Real-world outcomes from a single-centre cohort

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Background

Steroid-refractory (SR) lower gastrointestinal (LGI) acute graft-versus-host disease (aGVHD) remains associated with high morbidity and mortality, with limited real-world data on ruxolitinib-exposed patients. This study aims to describe response rates and survival outcomes in a real-world population of such patients treated with vedolizumab.

Methods

We retrospectively analysed 12 adult allogeneic stem cell transplant recipients treated with VDZ for SR-LGI-aGVHD at a single tertiary centre between 2018 and 2026. The primary endpoint was day-28 LGI overall response rate (ORR). Secondary endpoints included ORR at days 14 and 56, overall survival (OS), steroid tapering, infectious complications, and prognostic factors.

Results:

Patients received a median of 2 VDZ infusions (IQR 1–3; range 1–6). At VDZ initiation, 91.7% (11/12) had grade III–IV LGI-aGVHD, and 66.7% (8/12) received VDZ as fourth-line or later therapy. Median time from LGI-aGVHD diagnosis to VDZ initiation was 32 days (IQR 8–43), and from meeting SR criteria to VDZ was 21 days (IQR 5–34). Ten patients (83.3%) had prior ruxolitinib exposure, with 8 continuing concurrent ruxolitinib during VDZ treatment. In the intention-to-treat population, ORR at days 14, 28, and 56 were 33.3% (4/12; CR 8.3%), 41.7% (5/12; CR 25.0%), and 50.0% (6/12; CR 50.0%), respectively. Among evaluable patients, ORR at day 28 and 56 reached 71.4% (5/7; CR 42.9%) and 85.7% (6/7; CR 85.7%), respectively. Steroid reduction by day 28 occurred in 63.6% (7/11), with ≥50% reduction achieved in 45.5% (5/11).

Six-month and 12-month OS were 50.0% and 33.3%, respectively. Day-28 responders demonstrated superior survival compared with non-responders/non-evaluable patients (6-month OS 100% vs 14%; log-rank $p=0.004$). Infectious complications occurred in 83.3% (10/12) of patients, predominantly bacteraemia.

Conclusion:

VDZ-containing salvage therapy demonstrated clinically meaningful activity in heavily pre-treated, predominantly ruxolitinib-exposed SR-LGI-aGVHD. Outcomes remained limited by early non-relapse mortality. Early steroid tapering and day-28 response strongly correlated with survival and may represent clinically useful prognostic landmarks. Prospective studies are needed to define optimal timing, combination strategies, and patient selection for gut-directed therapy in SR-LGI-aGVHD.

Table 1. Baseline patient, transplant, and GVHD characteristics at vedolizumab start

Characteristic	N (%) or Median (IQR)
PATIENT & TRANSPLANT CHARACTERISTICS	
N	12
Age at alloSCT, median (IQR)	48 years (38–58)
Sex — Male, n (%)	10/12 (83%)
—	—
Underlying diagnosis	—
AML / secondary AML	5 (42%)
MDS / MPN-MDS	4 (33%)
Lymphoma (FL/DLBCL, cHL)	2 (17%)
T-ALL	1 (8%)
—	—
Donor type	—
HLA-matched related (MRD)	3 (25%)
Matched unrelated (MUD)	6 (50%)
Mismatched unrelated (MMUD)	3 (25%)
Graft source — PBSC	11/12 (92%)
Conditioning intensity — RIC	8/12 (67%)
DLI preceding GVHD	2/12 (17%)

Lenalidomide and donor lymphocyte infusion for late relapse of del(5q) myelodysplastic syndrome following allogeneic stem cell transplantation: a case report

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Background

Relapse following allogeneic stem cell transplantation for myelodysplastic syndrome remains a significant therapeutic challenge. Lenalidomide has established efficacy in del(5q) myelodysplastic syndrome; however, its post-transplant use is limited by concerns regarding graft-versus-host disease. Emerging evidence suggests low-dose lenalidomide may augment graft-versus-leukaemia effects, in addition to its direct activity against the malignant clone, and also improve donor chimerism in selected patients.^{1,2}

Case presentation

A male patient with del(5q) myelodysplastic syndrome underwent matched unrelated donor allogeneic stem cell transplantation in May 2022 at the age of 54, following conditioning with fludarabine, melphalan and anti-thymocyte globulin, GVHD prophylaxis with Methotrexate and Cyclosporine. He had previously demonstrated prolonged response to lenalidomide achieving transfusion independence for 20 months prior to declining counts. Post-transplant complications included limited cutaneous graft-versus-host disease which resolved, allowing cessation of immunosuppression.

Almost 3 years post-transplant, he developed progressive mixed donor chimerism with worsening pancytopenia. Initial decline in donor chimerism responded to donor lymphocyte infusion; however, 9 months later, he again had declining counts and subsequent marrow studies demonstrated recurrent del(5q) cytogenetic abnormalities with low-level excess blasts consistent with early relapse. Donor chimerism was 79% in both marrow and peripheral blood.

Given the low disease burden, prior lenalidomide responsiveness, late relapse and prior donor lymphocyte infusion tolerance, a combined immune-directed strategy was pursued. The patient received repeat donor lymphocyte infusion followed by recommencement of lenalidomide at 5 mg alternate daily dosing, rising to 5mg alternating with 10mg daily. Subsequent donor chimerism improving to 92% with modest platelet recovery and minor skin acute graft-versus-host disease responding to topical steroid during early follow-up.

Conclusion

This case highlights the potential role of low-dose lenalidomide combined with donor lymphocyte infusion as an immune-directed salvage strategy in late post-transplant relapse of del(5q) myelodysplastic syndrome. Careful patient selection and close monitoring for graft-versus-host disease remain essential.

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Cytomegalovirus reactivation associated with secondary graft dysfunction following autologous and allogeneic hematopoietic stem cell transplantation: A three-case series

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Background

Cytomegalovirus (CMV) reactivation following hematopoietic stem cell transplantation (HSCT) and associated marrow suppression and secondary graft dysfunction appears underreported in autologous transplantation and secondary graft failure.

Cases

Case 1

A 56-year-old man with Mantle Cell Lymphoma received R-HyperCVAD prior to BEAM autograft. Initial engraftment occurred; however, progressive cytopenias developed from D+18. CMV activation was identified and Valganciclovir therapy was commenced. Following CMV clearance, infusion of stored PBSCs at Day +56 resulted in full engraftment. The patient died 14 years post autograft in remission.

Case 2

A 56-year-old man underwent BEAM autograft for Mantle Cell Lymphoma following R-CHOP/R-DHAP. Primary graft failure occurred CMV activation was identified of 42,700 IU/ml on qPCR. Antiviral therapy with Valganciclovir was initiated, together with G-CSF, Eltrombopag and with platelets and RBCs; however, the patient developed ongoing complications including infections and progressive clinical deterioration, and he remained dependent on transfusions. Consideration was given to allogeneic transplantation. There was no evidence of lymphoma relapse, but the patient died from infectious complications ten months post autologous transplant.

Case 3

A 68-year-old man received haploidentical related donor allogeneic HSCT for AML, but at Day +155 he developed fever and abrupt marked CMV activation from 0 to 29,400 IU/ml, received Valganciclovir then severe pancytopenia followed. He was changed to Maribovir pancytopenia persisted but declining donor chimerism to 52%, with very hypocellular marrow. A second allograft is being considered.

Discussion

Recognition and management of CMV reactivation and graft dysfunction following autologous as well as allogeneic HSCT remains clinically important, including with cytopenias and no alternative aetiology. Potential mechanisms include direct CMV-mediated marrow suppression, immune dysregulation, inflammatory marrow microenvironment injury, and antiviral-associated hematopoietic toxicity.

Conclusion

Early recognition, serial viral surveillance, and consideration of CMV-associated marrow suppression are important in patients with unexplained post-transplant cytopenias or secondary graft dysfunction.

Dissecting cellular therapy harvesting in Aotearoa New Zealand: Insights from the New Zealand National Therapeutic Apheresis Registry

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Aims:

The New Zealand Blood Service (NZBS) is the primary provider of cellular therapy collections via apheresis in Aotearoa New Zealand. In 2025, NZBS established the National Therapeutic Apheresis Registry (TAR) to systematically capture nationwide data on apheresis procedures, supporting clinical decision-making, procedure standardisation, adverse event surveillance, and research. This study summarises national cellular therapy harvesting activity and describes current practice patterns.

Methods:

We conducted a retrospective descriptive analysis of non-identifiable TAR data for all cellular product collections performed by NZBS across five centres between April 2025 and March 2026. Variables analysed included patient demographics, procedure characteristics, and harvested product parameters.

Results:

A total of 562 cellular therapy collections were performed, including 529 haematopoietic progenitor cell (HPC) collections: 65 allogeneic donor and 464 autologous patient collections. Among autologous HPC collections, the most common indications were multiple myeloma (67%) and non-Hodgkin lymphoma (21.6%). Collection efficacy was good, with high collections per mobilisation, collection efficiency, and CD34⁺ cell yield. The overall safety profile was also favourable, with a very low incidence of serious adverse events. However, substantial inter-centre variability was observed, with more than a two-fold difference in cell yield and up to a six-fold difference in adverse event rates. In the allogeneic donor setting, citrate-related toxicity accounted for a consistently high rate of adverse events across centres. Lymphocyte collections for advanced cellular therapy manufacturing remain relatively rare in New Zealand.

Conclusions:

Cellular therapy harvesting activity is increasing in New Zealand. National registry data reveal significant regional variability and provide a robust platform to support quality improvement, standardisation of practice, and collection optimisation while safeguarding patient safety

	HPC Autologous		HPC Allogeneic		Lymphocyte Auto and Allo
	National	Regional	National	Regional	National
Collections per mobilisation	1.6	1.4 - 1.9	1.0	1.0 -1.1	1.0
Collection Efficiency (%)	59.6%	59.8 - 73.5%	63.5%	61.0 – 74.0%	-
CD34 collection yield (x10 ⁶ /kg)	3.5	2.3 - 5.2	6.8	5.5 – 6.9	-
Adverse events	20.8%	5.5 - 33%	37.5%	33 - 50%	16%
Citrate toxicity	68.2%	47 - 75%	86%	81 -100%	100%
Severe	0.3%	-	0%	-	0%
Post-thaw CD34 recovery	62.0%	55.0 – 67.0%	-	-	-

Table 1. Cellular therapy products collection and product characteristics. National = national average; Regional= range of regional averages; Collection Efficiency = Collection Efficiency 2.

Donor-only metaphase karyotypes after sex-mismatched HSCT: a diagnostic pitfall in post-transplant relapse assessment

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Abstract

Aim: In sex-mismatched haematopoietic stem cell transplantation (HSCT), donor-only metaphase karyotypes may be interpreted as evidence of successful engraftment. However, in clinically suspected relapse, the presence of only donor-sex metaphases should not be immediately regarded as donor-derived leukaemia, because recipient leukaemic cells may be underrepresented in metaphase culture. We aimed to define cytogenetic pitfalls in distinguishing engraftment, recipient relapse, and true donor-derived malignancy.

Method: We retrospectively reviewed bone marrow chromosome studies performed from February 2018 to April 2026 at a single institution. Among 2,010 patients, 63 had undergone sex-mismatched HSCT. Four clinically discordant cases were selected in which relapse or post-transplant malignancy was not adequately explained by metaphase cytogenetics alone. Conventional karyotypes were compared with X/Y interphase FISH, disease-specific FISH or short tandem repeat chimerism, and marrow findings.

Result: Three cases represented recipient-derived relapse or persistent disease despite donor-only metaphase results. In two B-lymphoblastic leukaemia cases, metaphase cytogenetics showed donor karyotypes, including //46,XX[20] or //46,XY[20], whereas X/Y FISH detected residual recipient cells and disease-specific assays demonstrated persistent BCR::ABL1 rearrangement, even when PB STR showed near-complete chimerism (99.7% donor). One AML case repeatedly showed donor-only //46,XY metaphases during morphologic relapse or persistence, with recipient cells detectable by X/Y FISH in a later specimen. In contrast, one aplastic anaemia patient developed true donor-derived MDS, supported by donor-sex abnormal metaphases with monosomy 7 and absence of recipient cells by X/Y FISH.

Conclusion: Donor-only metaphase cytogenetics after sex-mismatched HSCT should not be equated with complete engraftment or absence of relapse. Conversely, donor-sex metaphases in clinically suspected relapse should not be automatically labelled donor-derived leukaemia without confirmatory cell-origin studies. Integrated interpretation with X/Y FISH, disease-specific FISH, STR chimerism, and marrow findings is essential to avoid both false reassurance and diagnostic misclassification.

Table. Four discordant cases showing interpretive pitfalls of donor-sex metaphase karyotypes after sex-mismatched HSCT

Abbreviations: HSCT, haematopoietic stem cell transplantation; PB, peripheral blood; STR, short tandem repeat; NA, not available .

Item	Case 1	Case 2	Case 3	Case 4
Diagnosis / transplant setting	B-ALL with BCR::ABL1, 27/M; sex-mismatched HSCT 6 months after diagnosis	AML, 58/F; 1st HSCT from brother, 2nd HSCT from son	B-ALL with BCR::ABL1, 56/F; 2nd HSCT was sex-mismatched	Aplastic anaemia, 15/M; haploidentical HSCT from sister
Post-HSCT clinical status	1 year post-HSCT relapse with 82% blasts; later persistent disease with 96% blasts	Relapse/persistent disease after HSCT; blasts 9.4%, 11%, and later 18%	Relapse 5 months after 2nd sex-mismatched HSCT; blasts 87%	MDS 5 years post HSCT; Donor-derived origin confirmed
Metaphase cytogenetics at discordance	//46,XX[20] at relapse; later recipient leukaemic clone reappeared	Repeated donor-only karyotypes: //46,XY[30], //46,XY[20], //46,XY[20]	//46,XY[20] despite relapse	//45,XX,t(5;13),-7[8]/46,XX[12]
X/Y interphase FISH	XY recipient cells 21%; XX donor cells 79%	XX recipient cells 8%; XY donor cells 92%	XX recipient cells 32%; XY donor cells 68%	XY recipient cells 0%; XX donor cells 99%; X-only 1%
Disease-specific Interphase FISH	BCR::ABL1 6%; later BCR::ABL1 92%	NA	BCR::ABL1 77% at relapse	Monosomy 7 in 52%
STR chimerism	PB STR: 99.7% donor	NA	NA	NA

Allogeneic stem cell transplantation in TP53-mutated myeloid neoplasms: outcomes from a NSW tertiary centre

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Aim:

Patients with TP53-mutated acute myeloid leukaemia (AML) and myelodysplastic syndrome (MDS) have a dismal prognosis and the role of allogeneic haematopoietic stem cell transplantation (HSCT) remains unclear.¹ This study aimed to evaluate outcomes of allogeneic HSCT in TP53-mutated myeloid neoplasms from a NSW tertiary transplant centre. Primary outcome was overall survival (OS) and secondary outcomes included progression free survival (PFS) and non-relapse mortality (NRM).

Method:

Adult patients that underwent allogeneic HSCT for TP53-mutated myeloid neoplasms at St Vincent's Hospital Sydney from 2016 to February 2026 were included. De-identified data was retrospectively collected from electronic databases. Kaplan-Meier analysis was performed for OS and PFS, measured from HSC infusion until date of first event, using Cox regression/log-rank test comparisons. NRM and relapse incidence were analysed using competing risks analysis.

Results:

In total, 23 patients were identified (AML=12, MDS=9, myelofibrosis=2). Fifteen (65.2%) patients had biallelic/multi-hit TP53 mutations with a variant allelic frequency $\geq 50\%$ at diagnosis in 34.8%. Complex karyotype was present in 12/20 (60%). Median age at transplant was 58 (range, 24-71) and in CR1 in 78%. Donor type was matched related in 9%, matched unrelated 48% and haplo-identical 30%. Conditioning was myeloablative in 13% and reduced-intensity 83%. At a median follow up of 30 months, median OS and PFS were 13.2 months and 4 months respectively (**Figure 1A,B**). Estimated 1-year and 3-year OS was 55% (95%CI:34.2-75.8) and 35.7% (95%CI:13.4-58.0). Estimated 1-year and 3-year PFS was 34.2% (95%CI:14.6-53.8) and 23.5% (95%CI:5.1-41.9). Complex karyotype was significantly associated with inferior PFS (HR 3.31, 95%CI:1.05-10.39, $p=0.041$) with a trend towards inferior OS seen (HR 3.33, 95%CI:0.88-12.6, $p=0.076$). Cumulative incidence of NRM at 3 years was 26.1% and relapse incidence 50.4%.

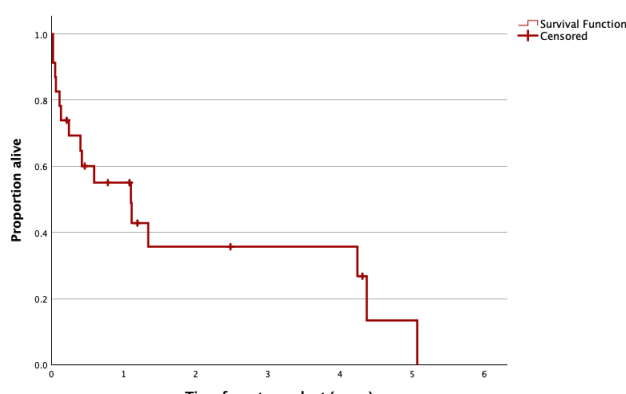


Figure 1A. Overall Survival

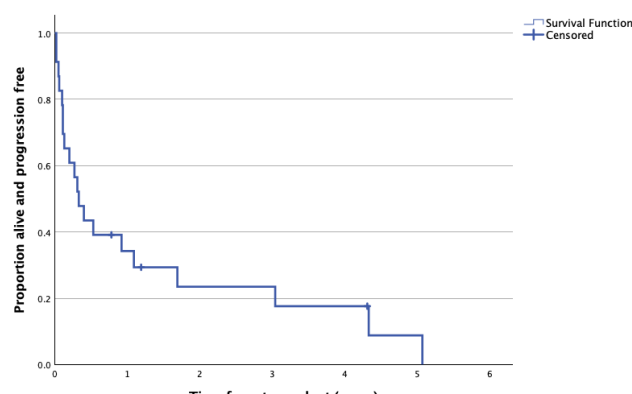


Figure 1B. Overall Progression Free Survival

Conclusion:

Patients with TP53-mutated myeloid neoplasms continue to have poor survival despite allogeneic HSCT. Clinical trials and novel strategies are urgently needed to improve outcomes.

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CAR-T experience from a regional Haematology centre: Retrospective review of the first 20 patients treated at Townsville University Hospital (TUH).

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Aim:

Retrospective review of the first 20 patients treated with CAR-T cell therapy-was conducted as an opportunity for internal quality improvement and to demonstrate feasibility of a regional CAR-T Cell treatment centre.

Method:

Electronic medical records were reviewed for 20 patients treated with CAR-T cell therapy at TUH between 2024 and 2026. Informed consent was obtained. Measured outcomes and data points included indication, toxicity (CRS, ICANS), response (OS/PFS) and location of referral.

Results:

Treatments included 16 Yescarta (axicabtagene ciloleucel) and 4 Tecartus (brexucabtagene autoleucel) infusions. The primary indication for patients treated with Yescarta included 11 relapsed DLBCL (7 treated in 2nd line, 4 in 3rd line), 1 PMBCL, 2 HGBCL-NOS and 2 transformed follicular lymphoma. The primary indication for patients treated with Tecartus included 3 MCL and 1 B-ALL. All 20 patients who underwent apheresis proceeded to re-infusion. The median age was 63. Patients were from a wide range of locations, with average distance to treatment centre of 357km. CRS occurred in 80% of patients; grade 3 CRS occurred in one patient, with no grade 4/5 events. ICANS occurred in 40% of patients, with 2 grade 3 events and 1 grade 4 event. ICU admission occurred in 20% of cases, median stay was 4 days. 75% of patients are alive and in ongoing follow up. 3/5 deaths were within 30 days, due to progressive disease, sepsis and cardiac event. 2 later deaths were due to progressive disease. CR rates at D+30 and D+100 were 10/17 58% and 11/16 68% respectively.

Conclusion:

Our analysis confirms comparable efficacy and toxicity to other published real-world data. This highlights the feasibility of operating a regional CAR-T cell treatment centre in Australia, including those with large geographical catchments.

Donor full blood count parameters at assessment and their impact on engraftment outcomes in related allogeneic stem cell transplantation: a single-centre audit

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Aim:

In related allogeneic stem cell transplant, ANZTCT guidelines specify minimum thresholds for platelet count, haemoglobin (Hb), and neutrophil count (ANC).^[1] These thresholds screen for occult haematological disease in the donor^[1,2] and maintain donor safety during G-CSF mobilisation and apheresis, which causes platelet decline in approximately 25% of donors.^[3,4] Whether these parameters influence recipient engraftment outcomes has not been well characterised. This audit evaluated compliance of donor FBC parameters with ANZTCT guidelines and determined whether platelet count, Hb, WCC, and ANC at the time of donor assessment predicted time to engraftment.

Method:

We reviewed data from 87 consecutive related allo-SCT recipients (107 collections) at a single centre between February 2020 and December 2025. Donors were haploidentical (n=46) or matched sibling (n=41). FBC parameters were assessed against ANZTCT thresholds^[1] and linear regression models examined their association with engraftment outcomes. The association between ANC $<2.0 \times 10^9/L$ and engraftment was assessed using an independent samples t-test.

Results:

The most common diagnoses were AML (41%) and ALL (18%). Anaemia was present in 4.6% of donors, thrombocytopenia in 2.3%, and neutropenia in 3.4%. All donors met ANZTCT neutrophil, platelet and haemoglobin thresholds. Median days to neutrophil and platelet engraftment were 20 (range 12-33) and 25 (range 14-128) days respectively. Primary graft failure occurred in 2.3%. Donor FBC parameters did not meaningfully predict engraftment outcomes. The only borderline significant association was donor platelet count and neutrophil engraftment ($p=.049$, $R^2=4.3\%$), with negligible clinical magnitude. All other associations were non-significant ($p=0.105-0.881$, $R^2<3.1\%$). Only 3 donors had ANC $<2.0 \times 10^9/L$, precluding meaningful group comparison.

Conclusion:

This audit confirms strong compliance with ANZTCT donor FBC guidelines, supporting robust donor safety practices. Donor FBC parameters at assessment did not meaningfully predict recipient engraftment outcomes. These thresholds serve as safety screens rather than engraftment predictors.

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Autologous graft-versus-host disease after autologous stem cell transplantation for multiple myeloma: an under-recognised rare complication with diagnostic and management challenges

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Aim:

Autologous graft-versus-host disease (AGVHD) is a rare and under-recognised complication of autologous stem cell transplantation (ASCT). In contrast to classical graft-versus-host disease seen in allogeneic stem cell transplantation, current knowledge of AGVHD is limited to case reports and small retrospective studies. Here, we report the first documented case of AGVHD in the Australian and New Zealand literature and review its diagnostic challenges, management strategies and clinical outcomes.

Method:

We describe a single-patient case of AGVHD with detailed clinical, microbiological, radiological, and histopathological correlation. Extensive investigations, including endoscopy with biopsy, dermatological assessment, infectious screening, and chimerism studies, were undertaken to exclude alternative diagnoses and confirm AGVHD.

Results:

A 56-year-old man with IgG kappa multiple myeloma underwent ASCT following melphalan conditioning. Thirteen weeks post-transplant, he developed persistent diarrhoea, vomiting, anorexia, renal impairment, thrombocytopenia and a maculopapular rash. Extensive infectious workup was negative. Transfusion-associated GVHD and mixed chimerism were excluded. Endoscopic biopsy demonstrated apoptotic colopathy consistent with GVHD, whilst skin biopsies supported cutaneous involvement. AGVHD was diagnosed based on clinicopathological correlation. The patient's cutaneous manifestations were corticosteroid-responsive whilst his gastrointestinal disease was not. Ruxolitinib was therefore initiated alongside total parenteral nutrition and octreotide, resulting in clinical improvement. Despite this, he was later readmitted with septic shock and suspected colonic perforation, ultimately dying two months after his diagnosis of AGVHD.

Conclusion:

This case highlights the diagnostic complexity and therapeutic challenges of AGVHD and its potential for poor outcomes. Diagnosis is hindered by the nonspecific clinical and histopathological findings associated with the condition, while evidence to guide its management remains limited. Although corticosteroids are the mainstay of treatment, clinical responses are variable, and optimal second-line therapies have not been clearly defined. Greater clinical awareness, diagnostic vigilance and analytical studies are essential to elucidate the pathophysiology, risk factors and diagnostic and management strategies for AGVHD.

Interim results from RESELECT2: A clinical trial evaluating eltrombopag and ruxolitinib for the treatment of poor graft function following allogeneic stem cell transplantation and relapsed/refractory aplastic anaemia

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Aim:

To evaluate the safety and efficacy of combination ruxolitinib and eltrombopag for the treatment of poor graft function (PGF) following allogeneic stem cell transplantation, and relapsed/refractory severe aplastic anaemia (SAA).

Method:

RESELECT2 is an ongoing prospective single-arm clinical trial, enrolling patients with PGF or relapsed/refractory SAA. Study treatment involves 12 weeks of combination ruxolitinib and eltrombopag. Primary endpoints include rate of complete haematological response (CR), and incidence of adverse events on trial. A total of 20 patients will be recruited, and outcomes will be compared with a historical control cohort.

Results:

Over 15 months, 10 patients with PGF and 1 patient with SAA have been recruited to RESELECT2 across two Australian centres. 8 patients with PGF have reached trial end, including 7 who have completed 12 weeks of treatment and are evaluable for response and 1 patient who died of infection on trial. 5/7 PGF patients have achieved CR (median time to CR: 24 weeks), and 2/7 remain transfusion dependent. The patient with SAA completed 12 weeks of treatment, and no response or adverse events were observed.

Transfusion support was compared for all patients (N=7) with available complete transfusion data between trial day 1 and the most recent follow-up timepoint (Figure 1). At a median follow-up of 24 weeks (range:4-48 weeks) mean units of packed red blood cells transfused per 28 days reduced from 6.9 to 1.6. Similarly, in the four patients requiring platelet transfusion, the mean platelet transfusion requirement per 28 days reduced from 5.7 to 2.3.

Dose modification of ruxolitinib due to cytopenias was required in only 3/11 patients. Non-haematological adverse events included two episodes of grade 3 CMV reactivation, and an atraumatic osteoporotic fracture.

Conclusion:

Interim results of RESELECT2 demonstrate patients receiving combination eltrombopag and ruxolitinib for PGF experienced a reduction in transfusion burden, with a favourable safety profile.

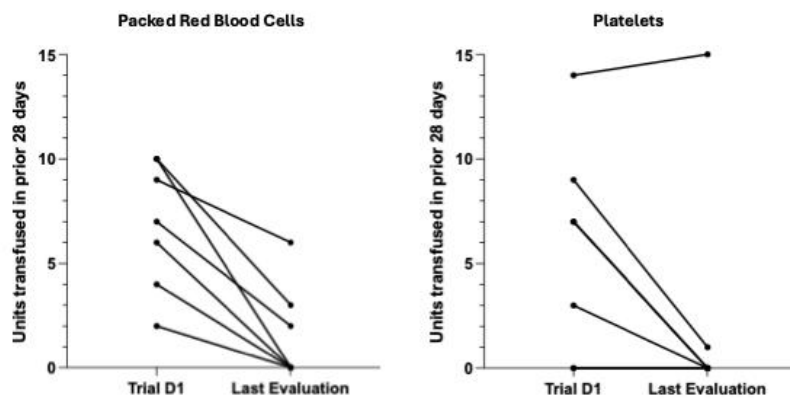


Figure 1: Units of packed red blood cells and platelets transfused to each trial participant within a 28-day period. Comparison is performed between the 28 days prior to trial day 1, and the 28 days prior to the most recent evaluation for all participants with available complete transfusion records (N=7).

Food-Triggered Gastrointestinal Reactions Resembling FPIES After Allogeneic Stem Cell Transplantation: an Under-Recognised Mimic of Gastrointestinal GvHD

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Aim:

To describe a Gastrointestinal symptoms after allogeneic stem cell transplantation (AlloSCT) are commonly attributed to graft-versus-host disease (GvHD), infection, medication toxicity or functional bowel disorders, while immune-mediated food reactions are rarely considered. We describe a series of post-AlloSCT patients with reproducible food-triggered gastrointestinal episodes resembling food protein-induced enterocolitis syndrome (FPIES), a rare non-IgE-mediated food allergy.

Method:

We conducted a retrospective case series at a single Australian tertiary transplant centre. Post-AlloSCT patients reporting reproducible acute gastrointestinal reactions to specific foods were identified through clinical review and structured patient interviews using a modified, standardised FPIES survey. Demographic, transplant, graft-versus-host disease (GvHD), donor, conditioning, and symptom data were collated descriptively.

Results:

Eleven patients aged 26–72 years developed new, reproducible acute reactions to specific foods 11–18 months post-transplant. Symptoms occurred several hours after ingestion and included severe abdominal cramping, nausea, vomiting, and diarrhoea, most commonly triggered by seafood or fish. All patients reported prior tolerance to the implicated foods. Eight patients had prior GvHD, including one with gastrointestinal GvHD. No clear sex predominance was observed. Reactions showed protein selectivity, with some patients tolerating certain fish species or processed forms while reacting to others, supporting food-specific immune reactivity rather than nonspecific intolerance. Serum IgE levels, tested in two patients, were low. Available sibling donor histories did not identify corresponding food allergy.

Conclusion:

Identification of 11 patients with reproducible, food-specific FPIES-like gastrointestinal reactions at a single transplant centre suggests that this phenotype may be under-recognised in AlloSCT survivors. Recognition is important, as these episodes may prompt unnecessary investigations or escalation of immunosuppression if misattributed to transplant-related complications. Haematologists should consider FPIES-like reactions when gastrointestinal symptoms are reproducibly linked to specific foods. Prospective studies incorporating formal allergy assessment and, where safe, supervised oral food challenge are warranted to confirm diagnosis and define biomarkers and pathogenesis.

Time to transplant stratified by donor type and delivery location in South Western Sydney

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Background: The SWSLHD allogeneic transplant program is funded to perform transplantation using family derived donors (i.e. HLA matched or haploidentical). Recipients of matched unrelated donor (MUD) allografts are referred to external institutions. 70% of patients from South Western Sydney self-report an ethno-cultural background other than European. In this setting, procuring matched unrelated grafts for timely transplantation is challenging, necessitating preferential use of haploidentical donors. Thus time to transplant is a vital metric for both disease outcome, and health access equity in this socio-economically disadvantaged community.

Aim: To evaluate time to transplant (time from unrelated donor search to transplant day 0), comparing locally performed haploidentical and matched sibling allografts with externally referred MUD allografts.

Method: All transplants in our program between 2020 and 2025 was retrospectively audited and stratified between haploidentical, matched sibling and MUD transplants. Unrelated donor search dates and transplant infusion dates were then identified and linked with ANZTCT and CIBMTR registry data to provide baseline characteristics. Ethnicity was self-reported in the medical record. Statistical analysis was then carried out.

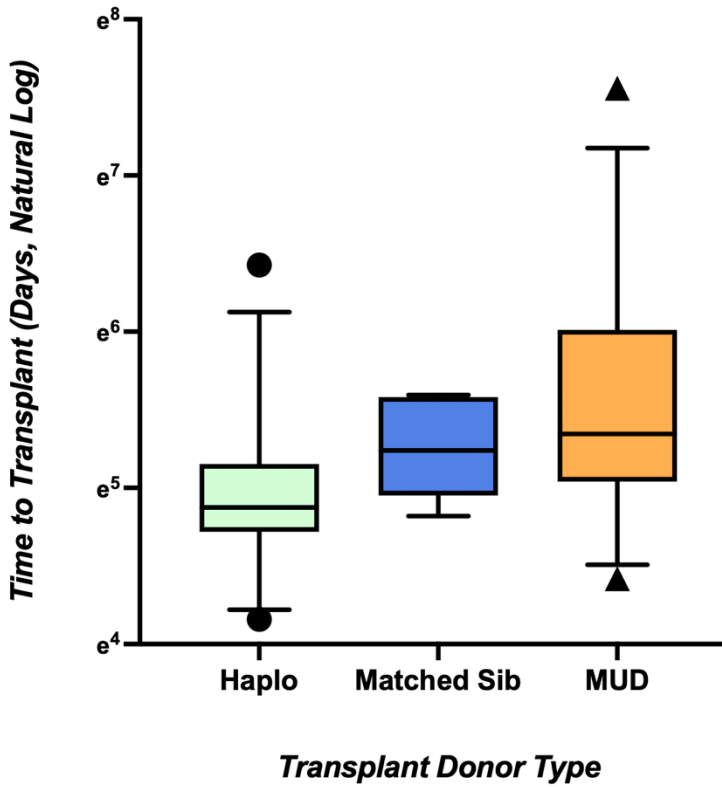
Results: In the study period, 57 haploidentical and 38 matched sibling allogeneic stem cell transplants were performed in our facility. 31 MUD transplants were performed at two other referral transplant units in Sydney. Baseline characteristics of recipients are summarised below. 70 patients also underwent an unrelated donor search who did not reach transplant. The median time to transplant was 135 days for the haploidentical group, 188 days for the matched sibling group, and 209 days for the MUD group. While the difference was not significant for the matched sibling cohort, the difference between the haploidentical and MUD transplant cohorts was significantly different (p=0.0002.)

Conclusion: Haploidentical allografts were delivered with a significantly faster time to transplant than referred MUD allografts. Initiatives to optimise transplant access and delivery in South Western Sydney need to be further investigated.

	Haplo	Sib	MUD
N	57	38	31
Disease	60% AML 18% other myeloid 16% ALL 6% other lymphoid	39% AML 29% other myeloid 16% ALL 16% other lymphoid	53% AML 24% other myeloid 17% ALL 6% other lymphoid
Gender	66% male 34% female	64% male 36% female	53% male 47% female
Median Age	55	51	56
Ethnicity	27% Euro 30% Middle East 26% Asian	27% Euro 27% Middle East 27% Asian	35% Euro 22% Middle East 25% Asian

Time to Transplant
Stratified by Donor Type

	17% Other	19% Other	18% Other
Median	5	5	5
4 dose			
base	22%	23%	21%
pse			
s to	22	19	12
trophil			
raftment			
/	64%	32%	41%
activation			
HD	28%	27%	24%



Incidence of cytomegalovirus (CMV) infection and Valganciclovir treatment efficacy in a cohort of patients undergoing Allogeneic Haematopoietic Stem Cell Transplants at Liverpool Hospital from 2022-2024

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Aim:

This audit aimed to assess the incidence of CMV infection and clearance rates on Valganciclovir therapy in patients who underwent allogeneic haematopoietic stem cell transplant (Allo-HSCT) at Liverpool Hospital (Sydney, Australia) from 2022 to 2024.

Method:

A single site retrospective medical records audit of Liverpool Hospital's Allo-HSCT database from 2022-24 was performed. CMV surveillance was performed twice weekly, on Monday and Thursday, using quantitative nucleic acid amplification testing (QNAT) on plasma specimens. Plasma assays were reported as either not detected, low positive (IU/ml < 500 – no quantification), or detected with quantification (IU/ml > 500). Any seropositive result was considered evidence of CMV infection, and two consecutive negative results to indicate successful CMV clearance. 44 patients were identified who received Allo-HSCT over 2022-2024. No patients were excluded. Descriptive statistical analysis was performed, and graphs were generated using GraphPad.

Results:

The median age at time of transplant was 46 years (range 22- 69), with 34% being female. All patients received CMV prophylaxis during conditioning with intravenous Ganciclovir as per protocol. No patients received Letermovir. CMV infection occurred in 24 patients (55%), median time to CMV infection was 31 days (range 8- 63). Of those with infection, three (12.5%) had a low positive result, and cleared CMV DNAemia without antiviral treatment. Where first line therapy was initiated (n=21), oral Valganciclovir was used in 86% (18/21 patients). Six patients (25%) required second line treatment with intravenous Ganciclovir, and three patients (12.5%) required third line treatment with Foscarnet and/or Cidofovir. CMV DNAemia clearance with first line Valganciclovir was achieved in 83% (15/18). Two patients (8.3%) deceased during their third line treatment course.

Conclusion:

Incidence of CMV infection was 55%, CMV clearance was high with first line oral Valganciclovir which is similar to published prospective studies.

Table 1: Description of patient cohort and Donor cohort demographics

Characteristics	Number (n=44)	Percentage
Patient Demographics		
Median age (years)	46	-
Sex		
Male	29	66%
Female	15	34%
Type of Malignancy		
Acute Myeloid Leukaemia	17	38.6%
Acute Lymphoblastic Leukaemia	11	25%
Other	8	18.2%
Non-Hodgkin Lymphoma	4	9.1%
MDS	2	4.5%
Chronic Lymphocytic Leukaemia	1	2.3%
Hodgkin Lymphoma	1	2.3%
Donor Demographics		
Median age (years)	37.5	-
Sex		
Male	27	61.3%
Female	17	38.6%
Donor Type		
HAPLO identical	23	52.3%
NON-HAPLO identical	21	47.7%
Donor / Recipient CMV IgG serostatus		
Donor + / Recipient +	27	61.3%
Donor - / Recipient +	8	18.2%
Donor - / Recipient -	5	11.4%
Donor + / Recipient -	4	9.1%

Early ST2 and REG3 α kinetics predict adverse outcomes following myeloablative allogeneic stem cell transplantation

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Aims:

To evaluate whether early fold changes in ST2 and REG3 α predict adverse outcomes following allogeneic haematopoietic cell transplantation (HCT), and to assess differences according to conditioning intensity.

Methods:

We performed a retrospective analysis of patients enrolled in a prospective institutional biomarker study with serial blood sampling following informed consent. Serum ST2 and REG3 α levels were measured pre-conditioning, on day 0, and on day 14 post-HCT using ELISA, and fold change was calculated.

Patients were stratified by conditioning intensity into myeloablative conditioning (MAC) and reduced-toxicity conditioning (FluMel). The MAC cohort uniformly received busulfan–cyclophosphamide (BuCy)-based conditioning, with anti-thymocyte globulin added for unrelated donor transplants.

The primary endpoint was adverse outcome, defined as a composite of grade 3–4 acute GVHD, ICU admission, or multi-organ failure. Receiver operating characteristic (ROC) analysis assessed predictive performance. A combined biomarker model classified patients as low risk (no biomarker elevation) or high risk (≥ 1 biomarker elevated). ST2 elevation thresholds were derived from ROC analysis, while REG3 α elevation was defined using the cohort median. Categorical outcomes between groups were compared using Fisher's exact test.

Results:

In the MAC cohort (n=28), day 0 ST2 fold change over pre-conditioning predicted adverse outcomes (AUC 0.72) and grade 3–4 GVHD (AUC 0.77). Using the combined biomarker model, low-risk patients had fewer adverse outcomes than high-risk patients (14% vs 47%, p=0.18). REG3 α demonstrated a similar directional trend and contributed to risk stratification.

In the FluMel cohort (n=61), ROC analysis showed limited predictive discrimination. However, exploratory analysis demonstrated a higher incidence of adverse outcomes in high-risk compared with low-risk patients (42.5% vs 21%, p=0.21).

Conclusion:

Early post-transplant increases in ST2 are associated with adverse outcomes following myeloablative transplantation. A combined ST2 and REG3 α biomarker model identifies a low-risk population and may enable earlier intervention prior to clinical deterioration. Prospective validation in larger cohorts is warranted.

Impact of post-transplant cyclophosphamide as graft versus host disease prophylaxis on platelet engraftment after allogeneic bone marrow transplantation

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Aim

To analyse the impact of post-transplant cyclophosphamide (PTCy) on platelet engraftment following allogeneic bone marrow transplantation compared with historical cyclosporin A (CSA) + methotrexate (MTX) graft versus host disease (GvHD) prophylaxis.

Method

After the publication of the CAST (Curtis et al, NEJM 2025)¹ and CTN1703 studies, our centre changed routine GvHD prophylaxis from CSA+MTX to PTCy in both matched sibling and matched unrelated donor transplants from July 2025 (see Table 1). Some studies report delayed platelet engraftment following PTCy-based regimens^{2,3}. This single-centre retrospective study analysed all patients undergoing allogeneic bone marrow transplantation at The Royal Melbourne Hospital in 2025, comparing platelet engraftment data in the pre- and post-PTCy period. Time to platelet engraftment was analysed and compared between cohorts. Platelet engraftment was defined as the first of 3 consecutive days with a platelet count $\geq 20 \times 10^9/L$ without platelet transfusion in the preceding 7 days. Exclusions from the analysis included second allograft, failure to achieve platelet engraftment or death prior to platelet engraftment.

Results

A total of 77 adult patients were analysed, including 34 receiving PTCy. Time to platelet engraftment was longer in the PTCy group (39 vs 30 days; $p=0.045$; see Figure 1).

Conclusion

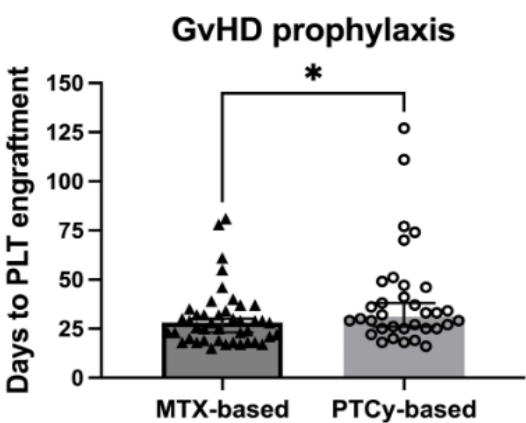
The implementation of a PTCy-based GvHD prophylaxis regimen at our centre increased mean time to platelet engraftment. Additional analysis is ongoing, including analysis of transfusion requirements, day centre utilisation and bleeding complications and incorporation of accruing data from patients undergoing transplantation in Jan-June 2026.

Table 1

	January 2025 to June 2025	From July 2025
Sibling Donor	CSA 3mg/kg/day from D-1 MTX 15mg/m ² D+1, 10mg/m ² D+3/+6/+11	PTCy 50mg/kg D+3/+4 CSA 3mg/kg/day from D+5
Unrelated Donor	CSA 3mg/kg/day from D-1 MTX 15mg/m ² D+1, 10mg/m ² D+3/+6/+11 rATG 0.5mg/kg D-3, 2mg/kg D-2 /-1	PTCy 50mg/kg D+3/+4 TAC 0.03mg/kg/day from D+5 MMF 15mg/kg TDS from D+5 to D+35

Abbreviations: Cyclosporin (CSA), Methotrexate (MTX), Rabbit Anti-thymocyte globulin (rATG), Post transplant cyclophosphamide (PTCy), Tacrolimus (TAC), Mycophenolate (MMF)

Figure 1



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Evaluation of busulfan dosing: impact of initial AUC, BMI, and the role of alternative dosing strategies in myeloablative allogeneic haemopoietic cell transplantation (HPCT)

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Aim: Busulfan remains central to myeloablative conditioning for allogeneic HPCT. Concerns regarding toxicity and substantial pharmacokinetic (PK) variability have driven the adoption of therapeutic drug monitoring.^{1,2} After observing an unexpectedly low initial AUC (2335mmol.min/L) in a patient with BMI of 53 kg/m², we reviewed first dose IV busulfan exposure in our centre. We aimed to: (1) evaluate initial AUC following ABW25-based dosing; (2) assess the relationship between BMI and AUC; (3) compare alternative dosing weights for correlation with clearance; and (4) identify weight-based formulae that better predict PK behaviour.

Method: From June 2018 to August 2025, 100 matched-donor HPCT recipients received IV busulfan ×4 (3.2mg/kg dosing was as per the institutional guidelines based on ABW25) with cyclophosphamide per eviQ protocols.³ Where post-transplant cyclophosphamide (PTCy) was used, conditioning cyclophosphamide was reduced to 50mg/kg. AUC was calculated from concentrations taken 0 and 15 minutes post completion and 4,5,6 and 8 hours post start of initial infusion. Subsequent doses targeted an AUC of 5000mmol.min/L. PK modelling used a one-compartment model with first-order elimination.

Results: Median initial AUC was 4,261mmol.min/L (range 2,335–7,187), with a median dose increase of 17%. Increasing BMI was associated with lower initial AUC, indicating dosing utilised underestimated clearance with higher BMI (Figure 1). Comparative regression demonstrated that ABW40 correlated better than ABW25 with clearance, outperforming most other size measures (Table 1). Extrapolated dose simulations showed ABW40 based dosing reduced AUC variability across BMI, with less outliers at BMI extremes.

Conclusion: Higher BMI was associated with increased busulfan clearance and lower initial AUC. ABW40 provided the more accurate allometric scaling than ABW25, reducing PK variability across the cohort. These findings prompted a practice change to ABW40 based dosing at our centre and support consideration of second-day AUC monitoring in patients with extreme BMI.

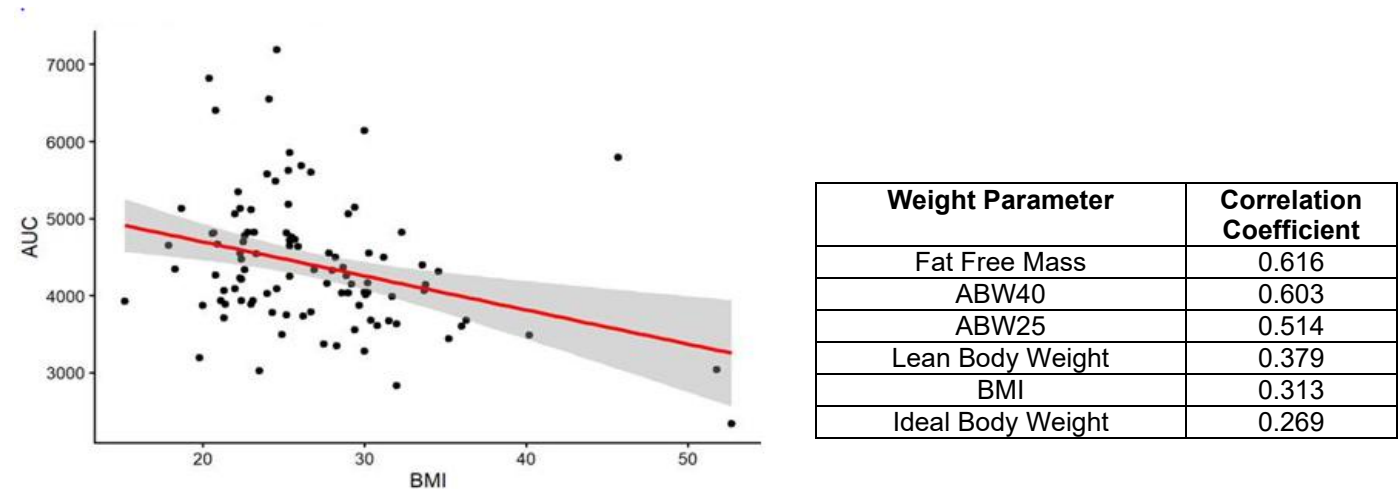


Fig 1: Initial Busulfan AUC versus BMI

Table 1: Correlation coefficient versus weight parameter

Assessing the role of Montelukast in minimising infusion related reactions to Obinituzumab in chronic lymphocytic leukaemia patients

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Introduction:

Obinituzumab (O) is a CD20 monoclonal antibody known for relatively high rates of infusion related reactions. IRRs are driven by mast cell & basophil activation, releasing histamine, leukotrienes & cytokines resulting in amplified inflammatory signalling & rapid B-cell lysis. Routine pre-medication includes paracetamol, corticosteroids & antihistamines. However, IRRs remain a relatively common occurrence and can be a barrier to administration of O. Montelukast is a cysteinyl-leukotriene receptor antagonist. Blockade of this receptor prevents leukotriene driven events such as bronchoconstriction, vascular permeability & reduces mast-cell mediated inflammatory amplification, complementing antihistamines & steroids.

Aim:

To demonstrate the efficacy & safety of adding montelukast as a pre-medication to the standard Venetoclax / Obinituzumab (VenO) regime.

Method:

A retrospective, single centre analysis of patients - from 2023 to 2026 - to assess the relationship between routine montelukast pre-medication & IRR incidence.

Results:

17 patients received VenO. 12 patients received VenO with standard premedication. 58% of patients who received standard premedication had infusion reactions. Of the 5 patients who reacted on D1 and received Montelukast on D2 none had an infusion reaction. Reduction in infusion reactions on D2 has led to Montelukast being incorporated as standard of care for CLL patients. Since this modification 5 patients received Montelukast in addition to standard of care pre-medication. 40% who received Montelukast in addition to standard of care pre-medication had infusion reactions; this is a reduction from the reported rates acknowledging the patient numbers are too small to determine statistical significance.

Conclusion:

Overall, rates of infusion reactions were reduced although numbers are too small to determine statistical significance. Further data analysis will be performed using larger patient numbers to confirm statistical significance.

Rituximab monotherapy for CLL with CNS involvement

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Presentation:

A 73-year-old female with known CLL presented in October 2023 with multiple cranial nerve palsies (right VII, left VI, left superior division CN III). FBC: Hb 138g/L, platelets $111 \times 10^9/L$, WCC $17.2 \times 10^9/L$, lymphocytes $13.9 \times 10^9/L$. The patient was extensively investigated for broad differential diagnoses including autoimmune, demyelination, infection, vasculitis, paraneoplastic, and CLL. CSF showed very small monoclonal B cell population, other screening tests negative. An MR brain showed multifocal T2 and FLAIR hyperintense lesions in cortex, subcortical and deep white matter. A brain biopsy was performed; histology was reviewed locally and referred externally for CNS pathologist expert opinion; a diagnosis of CLL involvement in CNS was made.

Background:

The patient was diagnosed with Binet A CLL in 2010. She required treatment with BR in 2018 to nodal PR. Other comorbidities include atrial fibrillation on rivaroxaban and a chronic rectal fistula.

Treatment & Outcome:

She received 4 doses of IV rituximab ($375 \text{mg}/\text{m}^2$) weekly, with BTKi planned if there was no response. The cranial nerve palsies responded rapidly, with improvement following the first dose. Complete resolution of the palsies by end of treatment course. Lymphocyte count also normalised ($4 \times 10^9/L$).

Post rituximab treatment, the patient was monitored closely. Six months later, she met standard iwCLL criteria for re-treatment. Zanubrutinib 160mg BD was commenced.

Discussion:

CLL with CNS involvement is rare. There was limited evidence available at the time of presentation and no standardised approach for therapy. A recent publication supports the use of BTKi in this setting. We elected to use a sequential approach as the patient's clinical status was not rapidly progressing, which allowed us to establish effectiveness of individual agents. Although traditionally not thought to penetrate the CNS adequately, this case highlights that intravenous rituximab monotherapy may be effective and well tolerated for CLL with CNS involvement.

Cutaneous Richter's transformation in a patient with chronic lymphocytic leukemia with translocation (2;14)

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Aim:

Richter's transformation of chronic lymphocytic leukemia (CLL) to cutaneous diffuse large B-cell lymphoma (DLBCL) is rare.

Method:

We report a case of CLL with Richter transformation to cutaneous DLBCL and the treatment outcome.

Results:

A 68-year-old gentleman was diagnosed with Binet Stage A CLL in 2009 with incidental finding of lymphocytosis. Fluorescence in situ hybridization (FISH) analysis did not reveal TP53 mutation. He remained asymptomatic and was on active surveillance. He presented with multiple subcutaneous nodules in 2022. Clinical examination revealed multiple subcutaneous firm nodules with overlying violaceous rash over four limbs and back.

Blood results showed hemoglobin 11.4g/dL; WBC 23.1x10⁹/L with 89% lymphocyte; platelet 109x10⁹/L and LDH 233 U/L. Skin biopsy demonstrated medium to large size atypical lymphoid infiltrate in dermis. Immunophenotyping was positive for CD20, CD10 and c-MYC and negative for CD3, CD5, CD23, CD56, BCL2, BCL6 and CD30. Ki67 was estimated to be about 80-90%. FISH was negative for MYC translocation. Bone marrow exam showed CLL without large cell transformation. A complex cytogenetics abnormality was detected: 42~46,XY,t(2;14)(p16;q32)[4],-13[4],-17[4]+mar1[4],+mar2[3][cp4]/46,XY [16].

The diagnosis of diffuse large B-cell Richter transformation of CLL was established. He underwent treatment with rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone (R-CHOP). All skin nodules resolved clinically after 6 cycles of R-CHOP.

Translocation (2;14)(p16;q32) is a rare but recurrent chromosomal aberration in CLL. This translocation juxtaposes the BCL11A (B-cell lymphoma/leukemia 11A) gene at 2p16 with the IgH gene at 14q32. Over-expression of BCL11A, resulting from fusion to the IgH locus, blocks cell differentiation, inhibits cell apoptosis and promotes cell proliferation which leads to development of B cell lymphoma.

Conclusion:

We showed a rare case of cutaneous Richter syndrome harbouring t(2;14)(p16;q32). He responded well to R-CHOP therapy. How would the acquisition of t(2;14)(p16;q32) alter the disease prognosis in cutaneous Richter syndrome remains to be studied.

Infusion-Related Reactions Following First-Dose Obinutuzumab in Chronic Lymphocytic Leukaemia Patients at Sir Charles Gairdner Hospital

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Aim:

To evaluate the incidence and severity of infusion-related reactions in patients with CLL receiving first-dose obinutuzumab.

Method:

Patients with CLL who received their first dose of obinutuzumab at Sir Charles Gairdner Hospital between December 2003, and February 2026 were included. Data were collected through retrospective chart review. Patient and disease characteristics, including lymphocyte count, splenomegaly, and comorbidities, were recorded. Clinical outcomes analysed included IRR incidence and grade, management strategies, and associated hospital resource utilisation.

Results:

A total of 52 patients received obinutuzumab during the study period. The median age was 76.5 years (range 54–93). Patients received treatment across three regimens: chlorambucil–obinutuzumab (38.5%), venetoclax–obinutuzumab (59.6%), and Zanubrutinib–obinutuzumab (2%). The median lymphocyte count at infusion was 32 (range 0.84–432). IRRs occurred in 33 patients during day 1 or 2. Reactions were graded as follows: grade 1 (9%), grade 2 (45%), grade 3 (42%), and grade 4 (3%). Of the 30 patients whose infusions were interrupted, 17 were re-trialled the same day, while 13 were not (rechallenged the next day [n=7], abandoned during that admission [n=4], or ceased indefinitely [n=2]); 3 patients had already received the full dose. Forty-four patients required inpatient admission, with a median length of stay of 4 days.

Conclusion:

First-dose obinutuzumab is associated with a high rate of IRRs in patients with CLL, resulting in significant morbidity and healthcare resource utilisation. These findings highlight the importance of patient and staff education and standardised management protocols. Further research is needed to identify strategies to mitigate obinutuzumab-related IRRs.

Anti DPPX encephalitis associated with chronic lymphocytic leukaemia: a New Zealand case

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Aim:

To describe the first reported New Zealand case of anti-DPPX encephalitis occurring in association with newly diagnosed chronic lymphocytic leukaemia (CLL), and to highlight therapeutic considerations in this rare condition.

Method:

A single-centre case review was undertaken. Clinical records, neuroimaging, cerebrospinal fluid (CSF) studies, immunological testing, and haematological investigations were analysed descriptively.

Results:

A 55-year-old man presented with four months of diarrhoea and 12 kg weight loss, followed by neuropsychiatric symptoms and generalised seizures. Investigations demonstrated previously undiagnosed CLL and encephalitic changes on brain MRI. CSF analysis showed elevated protein and was positive for anti-DPPX antibodies. Initial treatment with intravenous methylprednisolone and IVIg, followed by rituximab, resulted in partial improvement. At three months, the patient demonstrated marked cognitive and physical recovery with resolution of MRI abnormalities and reduction in lymphadenopathy and splenomegaly, although CSF anti-DPPX antibodies persisted. Given relapse risk and limited therapeutic guidance, ibrutinib therapy was initiated via Named Patient Pharmaceutical Assessment approval.

Conclusion:

This case underscores the importance of clinical vigilance and interdisciplinary management in anti-DPPX encephalitis and represents the first reported use of ibrutinib in this setting.

Real-world outcomes of BTKis in treating patients with relapsed/refractory chronic lymphocytic leukaemia (CLL): a retrospective analysis using the Australian Pharmaceutical Benefits Scheme (PBS) dataset

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Aim:

Three covalent Bruton tyrosine kinase inhibitors (BTKis), ibrutinib, acalabrutinib, and zanubrutinib, are approved in Australia for relapsed/refractory (R/R) CLL. Given limited long-term real-world evidence, we evaluated treatment persistence (TP), time to next treatment (TTNT), and overall survival (OS) for each BTKi in clinical practice.

Method:

This retrospective cohort study used data from 10% of patients who began BTKi treatment for CLL, listed on the PBS, between 1 March 2018 and 31 December 2025. Inclusion required ≥1 BTKi monotherapy prescription and an authority code for R/R CLL. Eligibility was limited to individuals who began therapy ≥3 months post-BTKi approval, to exclude those enrolled in access programmes before reimbursement. TP, TTNT, and OS were analysed using the Kaplan-Meier method.

Results:

Among 387 patients with R/R CLL with a median follow-up of 14 months, 232 (60%) received ibrutinib, 105 (27%) acalabrutinib, and 50 (13%) zanubrutinib; the median age was 76 years, and 62% were male. TP at 12 months was highest for zanubrutinib (72%; 95% CI: 65-87), followed by ibrutinib (66%; 95% CI: 61-71) and acalabrutinib (61%; 95% CI: 52-70). For all BTKis, both median TTNT and OS were not reached; at 12 months, the percentage of patients who had not received subsequent treatment was highest for ibrutinib (88%; 95% CI: 84-91), followed by acalabrutinib (87%; 95% CI: 80-93) and zanubrutinib (80%; 95% CI: 70-91). OS at 12 months was highest for zanubrutinib (95%; 95% CI: 89-100), followed by ibrutinib (87%; 95% CI: 84-91) and acalabrutinib (86%; 95% CI: 79-92).

Conclusion:

In naïve treatment comparison, zanubrutinib had numerically higher TP and 12-month OS. All BTKis showed similar durability, with median TTNT and OS not reached, and most patients remained on initial therapy.

Real-World Impact of Atrial Fibrillation (AFib) on Cardiovascular (CV) Outcomes and Healthcare Resource Utilization (HCRU) in Patients With Chronic Lymphocytic Leukemia (CLL)

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Aim:

This study evaluated the real-world impact of AFib on CV outcomes and HCRU in patients with CLL overall, by age, and by Bruton tyrosine kinase inhibitor (BTKi) therapy.

Method:

Using the US Symphony database, we identified adults newly diagnosed with CLL (2014-2024) and followed for 1 year post-diagnosis to assess incidence of AFib. Subsequent CV outcomes and HCRU were captured. Exploratory analyses compared outcomes among first-line (1L) BTKi (ibrutinib, acalabrutinib, zanubrutinib).

Results:

In 233,362 CLL patients, 13.1% had AFib within 1 year of diagnosis. A significantly greater proportion of CLL patients with AFib had ≥ 1 inpatient visit within 1 year of diagnosis vs without AFib (54.9% vs 23.2%, $P < .0001$), and higher likelihood to incur inpatient service (OR: 2.28, 95%CI [2.21, 2.35], $P < .0001$). Significantly higher proportions of CLL patients with AFib had subsequent stroke (14.3% vs 8.9%), bleeding (27.9% vs 19.1%), and heart failure (54.5% vs 18.9%) vs without AFib ($P < .0001$). Age ≥ 65 , male, non-white, and AFib were associated with subsequent stroke, bleeding, or heart failure ($P < .01$). Results were consistent in patients aged ≥ 65 years. In patients initiating 1L BTKi, AFib rate within 1 year of treatment was 11% (zanubrutinib), 13% (acalabrutinib), and 16% (ibrutinib) ($P < .0001$). Compared with ibrutinib and acalabrutinib, a lower proportion of CLL patients with AFib receiving zanubrutinib had subsequent stroke (12.2% vs 9.4% vs 4.8%, respectively), bleeding (27.4% vs 21.5% vs 17.4%), and heart failure (50.9% vs 45.6% vs 39.6%) ($P < .002$). Compared with zanubrutinib, acalabrutinib (OR 1.29, 95% CI 1.12–1.50; $P = .0005$) and ibrutinib (OR 1.69, 95% CI 1.48–1.93; $P < .0001$) were associated with higher odds of inpatient service use within 1 year of initiation.

Conclusions:

CLL patients with AFib experience substantial real-world CV and HCRU burden. Exploratory analyses suggested 1L zanubrutinib may offer potentially favorable outcomes over other BTKi in lessening AFib-related clinical and HCRU complications.

Subsequent therapies and time to second progression-free survival events (PFS2) in treatment-naïve chronic lymphocytic leukemia/small lymphocytic lymphoma (TN CLL/SLL) previously treated with zanubrutinib or bendamustine-rituximab (BR) in SEQUOIA

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Aim:

In SEQUOIA, progression-free survival (PFS) and time to next treatment (TTNT) significantly favored zanubrutinib vs BR in TN CLL/SLL without del(17p). Outcomes on subsequent treatment after progressive disease (PD) on zanubrutinib are presented.

Method:

Patients (pts) were randomized to receive continuous zanubrutinib or six cycles of BR (crossover to zanubrutinib was allowed after PD) and followed post-PD for subsequent treatment. This analysis evaluated PFS, TTNT, TTNT or death (TTNT-D), and PFS2. *P*-values are descriptive.

Results:

As of October 31, 2025, 479 pts were randomized (241 zanubrutinib, 238 BR); median follow-up (FU) was 78.7 months (range, 0.0-96.0). Baseline demographics and disease characteristics were well balanced between the arms. PFS favored zanubrutinib vs BR (HR, 0.28; 95% CI, 0.21-0.38; *P*<.0001); 78-month PFS rates were 70.9% (95% CI, 64.2-76.6) vs 28.6% (21.7-35.8; COVID-adjusted: 73.7% vs 29.0%). Most zanubrutinib-treated pts (211 of 241; 87.6%) had no subsequent treatment; 34 pts died without subsequent treatment. TTNT (HR, 0.23; 95% CI, 0.15-0.35; *P*<.0001) and TTNT-D (HR, 0.37; 95% CI, 0.27-0.50; *P*<.0001) favored zanubrutinib vs BR. Overall, 24 (10.0%) pts receiving zanubrutinib and 82 (34.5%) receiving BR had PD and subsequent treatment (zanubrutinib: BCL2 inhibitor [BCL2i]-based treatment [54.2%], chemoimmunotherapy [33.3%], or BTK inhibitor [BTKi] [12.5%]; BR: BTKi, [93.9%; 71 crossover pts], BCL2i-based treatment [3.7%], or chemoimmunotherapy [2.4%]). Median time from PD to next treatment was 2.1 vs 7.4 months, respectively. Of zanubrutinib pts who received BCL2i-based treatment (median FU, 33.5 months), 10 remain alive without PD, two died, and one had PD. PFS2 significantly favored zanubrutinib vs BR (HR, 0.66; 95% CI, 0.45-0.98; *P*<.05); 78-month PFS2 rates were 81.3% (95% CI, 75.6-85.8) vs 73.8% (67.2-79.3).

Conclusion:

Initial zanubrutinib provides durable benefit with favorable PFS2 vs BR. BCL2i-based salvage after zanubrutinib achieved high PFS rates at almost 3 years of FU.

A case of necrotising herpes simplex virus lymphadenitis: a rare but important mimic of Richter's transformation of chronic lymphocytic leukaemia

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Background

Herpes simplex virus lymphadenitis (HSV-L) is a rare complication of HSV reactivation that may occur in immunosuppressed patients, including those with chronic lymphocytic leukaemia (CLL). HSV-L may closely resemble Richter's transformation (RT) clinically and radiologically, creating diagnostic uncertainty.

Case presentation

We report a case of necrotising HSV-2 lymphadenitis in a patient with relapsed CLL presenting with rapidly progressive lymphadenopathy, autoimmune haemolytic anaemia, and widespread adenopathy with necrotic lymph nodes on CT imaging. FDG-PET/CT demonstrated intensely FDG-avid necrotic lymph nodes with central photopenia and an SUVmax of 8.1, which was atypical for CLL. Core biopsy revealed extensive nodal necrosis with viral cytopathic changes. HSV-2 infection was confirmed by immunohistochemistry and polymerase chain reaction, with no evidence of large-cell transformation. The patient was treated with intravenous aciclovir followed by oral therapeutic valaciclovir and has commenced long-term valaciclovir prophylaxis, with resultant clinical, haematological and biochemical improvement. Zanubrutinib was concurrently commenced for relapsed CLL.

Conclusion

This case highlights HSV-L as an important infectious mimic of RT in patients with CLL and demonstrates the limited specificity of FDG-PET/CT in distinguishing aggressive lymphoma from infectious or inflammatory processes. Histopathological confirmation remains essential to establish the correct diagnosis, guide appropriate management, and avoid inappropriate escalation to lymphoma-directed therapy in immunocompromised patients.

Updated safety and efficacy of all-oral sonrotoclax + zanubrutinib in relapsed/refractory (R/R) chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL), including patients with del(17p)/TP53

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Aim:

BGB-11417-101 (NCT04277637) is a phase 1/1b global study. Updated safety/efficacy with sonrotoclax + zanubrutinib (SZ) in patients with R/R CLL/SLL are described.

Method:

Eligible patients (≥1 prior treatment; no progressive disease [PD] on prior BTK inhibitor) received zanubrutinib (320mg QD or 160mg BID) for 8-12 weeks, then added sonrotoclax by ramp-up (40/80/160/320/640mg QD). Endpoints included safety/tolerability, overall response rate (ORR per iwCLL 2018), and undetectable minimal residual disease (uMRD4) in blood by flow cytometry.

Results:

As of 06Dec2025, 47 patients (sonrotoclax 320mg, n=22) were enrolled (TP53 mutation or del[17p], 37%; unmutated IGHV, 77%). Patients had a median of 1 prior treatment (range, 1-3). Seven patients were last treated with a BTK inhibitor. Median study follow-up was 37.8mo (range, 10.2-57.8). Of 47 patients, 66% discontinued SZ, most due to protocol-defined elective discontinuation (51%); 3 (6%) discontinued due to PD.

TEAEs led to SZ discontinuation in 4 patients (8%; arthralgia, myelodysplastic syndromes, meningococcal sepsis, multiple myeloma) and zanubrutinib alone in 1 (2%; intracranial hemorrhage). Most common grade ≥3 TEAE was neutropenia (28%). No TLS occurred; no TEAEs led to death.

In 46 efficacy-evaluable patients, ORR was 98% (complete response [CR], 54%; median time to response [TTR], 2.6mo). In the sonrotoclax 320-mg cohort (n=21), ORR was 100%

(CR, 52%; median TTR, 2.5mo). All 3 evaluable BTK inhibitor–pretreated patients achieved PR. PD occurred in 1 patient with *TP53* mutation/del(17p)/mutated IGHV. With sonrotoclax 320mg, the best blood uMRD4 rate was 86% (median time to uMRD4, 5.3mo [range, 2.5-16.3]). Best uMRD4 rates at weeks 24/48/96 were 52%, 81%, 82%, respectively.

Conclusion:

In patients with R/R CLL/SLL, sonrotoclax 320mg + zanubrutinib was well tolerated, with low rates of treatment discontinuation due to TEAEs, and continued to demonstrate substantial antitumor activity (ORR, 100%; uMRD4, 86%), including in BTK inhibitor–pretreated patients.

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BGB-16673, a Bruton tyrosine kinase (BTK) degrader, in BTK inhibitor (BTKi)-naive patients with chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL) and other B-cell malignancies in the CaDAnCe-101 study

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Aim:

BGB-16673 is a BTK degrader that blocks signaling by tagging BTK for degradation through the cell's proteasome pathway, leading to tumor regression. We report phase 1 results of BGB-16673 in BTKi-naive patients with B-cell malignancies from the phase 1/2 CaDAnCe-101 study (BGB-16673-101; NCT05006716).

Method:

BTKi-naive patients with CLL/SLL, mantle cell lymphoma (MCL), marginal zone lymphoma (MZL), Waldenström macroglobulinemia (WM), or Richter transformation (RT) received BGB-16673 200 mg orally QD.

Results:

As of December 15, 2025, 54 patients (CLL/SLL, n=29; MCL, n=8; MZL, n=10; RT, n=2; WM, n=5) received BGB-16673 (median age, 68 years; median number of prior therapies, 2 [range, 0-9]). Median follow-up was 8.3 months; 43 patients (79.6%) remained on treatment.

Any-grade treatment-emergent adverse events (TEAEs) occurred in 83.3%, including contusion (27.8%) and petechiae (18.5%). Grade ≥ 3 TEAEs occurred in 33.3%, including neutropenia (14.8%), anemia, hypertension, lower respiratory tract infection, pneumonia, and thrombocytopenia (each 3.7%). No major hemorrhage, opportunistic infections, or febrile neutropenia occurred. TEAEs led to two discontinuations (3.7%; metastatic brain neoplasm, n=1; back pain, n=1) and one death (1.9%; metastatic brain neoplasm); all had CLL/SLL. In CLL/SLL (n=29), the most common grade ≥ 3 TEAE was neutropenia (20.7%).

In 22 evaluable patients with CLL/SLL, overall response rate was 86.4% (partial response [PR], n=15; PR with lymphocytosis, n=4; median follow-up, 8.2 months). All responses were ongoing (n=19). Median time to first response was 2.8 months. Responses occurred in 4/4 patients with unmutated IGHV and 4/6 with del(17p) and/or TP53 mutation. At 6 months, no PFS events occurred. Efficacy in other cohorts is not reported due to small sample sizes. All

44 patients with available data showed complete steady-state BTK degradation in peripheral blood.

Conclusion:

BGB-16673 is well tolerated, with no reported opportunistic infections or major hemorrhage, and shows promising antitumor activity in BTKi-naïve patients with CLL/SLL. ©EHA2026.

Pegylated asparaginase related VTE in adults with acute lymphoblastic leukaemia: a single centre retrospective audit

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Aim

Venous thromboembolism (VTE) is a significant complication of pegylated asparaginase (PegA) therapy in acute lymphoblastic leukaemia (ALL). Increasing use of paediatric-inspired ALL regimens incorporating higher cumulative PegA exposure in adults has heightened concern regarding thrombosis risk. Existing recommendations regarding thromboprophylaxis and antithrombin (AT) replacement remain inconsistent, resulting in variable international practice. At our centre, routine thromboprophylaxis with low molecular weight heparin and AT monitoring are not routinely used in patients considered low risk for thrombosis or bleeding. We aimed to determine the incidence of VTE in adults receiving PegA-containing induction therapy for ALL and assess associations with PegA exposure, corticosteroid dosing, platelet count, and body mass index (BMI).

Methods

We retrospectively reviewed patients aged ≥ 18 years with newly diagnosed Philadelphia-negative B-ALL or T-ALL/T-lymphoblastic lymphoma treated with PegA-containing induction chemotherapy between January 2019 and February 2026. Patients with presenting platelet counts of < 50 were excluded. Clinical data collected included demographics, history of VTE, cumulative PegA and corticosteroid exposure during induction, platelet count, BMI, and VTE events. Univariate logistic regression analysis assessed associations between clinical variables and VTE risk during induction.

Results

Forty-six patients were included. Five patients developed VTE during induction therapy (10.8%), including one deep vein thrombosis, one PICC-associated thrombosis (which developed while on prophylactic enoxaparin), and three cerebral venous sinus thromboses (CVST). All patients received anticoagulation without major treatment-related complications. There were no VTE-related deaths. No significant associations were identified between VTE risk and cumulative PegA exposure, BMI, or presenting platelet count. Increasing corticosteroid exposure demonstrated a non-significant trend towards increased VTE risk. Analyses were underpowered due to limited event numbers.

Conclusion

VTE occurred in 10.8% of adults receiving PegA-containing induction therapy for ALL, with CVST comprising most thrombotic events. These findings support further evaluation of risk-adapted thromboprophylaxis strategies during induction therapy.

Role of mutational analysis and chemotherapy sparing regimens in palliative management of blast phase CML.

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Background:

With the advent of TKI therapy, the incidence of Ph+ CML in blast phase has dramatically reduced. Nonetheless, some patients lose response and are either ineligible / do not wish for intensive chemotherapy based treatment.

Case presentation:

We present a 64-year-old male who was diagnosed with CML in chronic phase, treated initially with dasatinib (best response CCyR) but switched to nilotinib after seven months, due to developing of grade 4 pleural effusions. On nilotinib he progressed rapidly into blast phase CML and mutational studies showed E255K mutation. Opting for quality of life and declining intensive chemotherapy he was treated with dasatinib, prednisolone and prophylactic intrathecal methotrexate (GIMEMA LAL1205 protocol). He cleared his Ph+ blast phase and got to MR4 molecular response. Unfortunately, after 23 months he lost response and mutational analysis was again performed. This predicted response to asciminib, and he again achieved MR4 but relapsed after 8 months. Subsequent mutation profile showed A337T mutation with resistance to asciminib. With 33% blasts appearing in peripheral blood he commenced Ponatinib, Prednisolone and IT Methotrexate, clearing his blasts in <4 weeks and his BCR-ABL at 4 months had reduced from 52.72% to 0.40%

Conclusion:

This case highlights the importance of repeating mutational analysis in CML when there is a loss of response, as it can impact treatment management. It also demonstrates the utility of chemotherapy sparing regimens such as GIMEMA LAL1205 protocol in the palliative setting to induce remission and maintain quality of life.

Is a bone marrow biopsy required to diagnose chronic myeloid leukaemia? The Western Australian experience.

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Background & Aims:

Chronic myeloid leukaemia (CML) is defined by the *BCR::ABL1* fusion. Peripheral blood (PB) film and bone marrow (BM) biopsy assessments determine the blast burden, whereby <20% blasts defines chronic phase (CML-CP). Rarely, blast phase (CML-BP) occurs with ≥20% myeloblasts or ≥10% lymphoblasts. We correlated the blast burden of newly diagnosed adult CML on PB and BM to determine if discrepancies between these diagnostic methods resulted in disease reclassification of CML-CP vs. CML-BP.

Method:

We retrospectively identified newly diagnosed CML patients through PathWest Laboratory Medicine from 1-September-2019 to 1-April-2026. Demographic data, baseline full blood count (FBC) parameters and LDH were obtained. The blast burden was quantified on PB and aspirate by manual enumeration and flow cytometry, and correlated with CML-CP vs. CML-BP classifications, *BCR::ABL1* breakpoint, additional cytogenetic abnormalities (ACA), marrow reticulin fibrosis and ELTS score.

Results:

117 CML patients (male=81) were diagnosed during the study period with a median age of 55 years (range: 15-87). Median diagnostic FBC parameters showed haemoglobin 114g/L (59-166g/L), WCC $91.72 \times 10^9/L$ (4.42 - $592 \times 10^9/L$), basophils $2.59 \times 10^9/L$ (0 - $41.53 \times 10^9/L$), platelets $331 \times 10^9/L$ (20 - $1,821 \times 10^9/L$) and LDH 760IU/L (210-3780IU/L). 116/117 patients had a major p210 *BCR::ABL1* breakpoint. Sixteen patients (14%) had ACA. Most patients had an intermediate (27%) or high (32%) ELTS score. 112 patients (96%) had CML-CP with concordant blast burden across all diagnostic methods. Five patients presented with CML-BP (myeloid=2, lymphoid=3) with a median blast burden varying between the PB 15% (0-54%), BM 40% (10-98%) and flow cytometric 42% (6-47%) methods. Two lymphoid CML-BP patients had <5% blasts on the PB, but showed increased blasts on the BM (15-20%) without increased reticulin marrow fibrosis or ACA.

Conclusion:

CML typically presents in chronic phase with a concordant blast burden across both the PB and BM. Although rare, lymphoid CML-BP may not be detected on the PB alone. Therefore, marrow assessment in any suspected CML case is recommended to exclude CML-BP.

The invisible burden of chronic myeloid leukaemia: hidden quality of life and long-term care challenges in Australian patients

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Background and Aim

Although tyrosine kinase inhibitor (TKI) therapy provides disease control for most patients with chronic myeloid leukemia (CML), chronic toxicities and psychological burden continue to impair quality of life (QoL). Treatment-free remission (TFR) offers potential functional recovery, yet access and prioritisation of long-term outcomes remain inconsistent in Australian practice. This study characterises QoL burden, unmet needs, and TFR access, establishing a patient reported outcome (PRO)-driven framework in CML care.

Method

We conducted a qualitative Australian CML Patient Council to capture lived experience beyond molecular outcomes. Seven adults with CML across Australia were sampled by treatment and TFR experience; two were leaders of CML patient support communities (>900 members). Semi-structured discussions explored long-term symptom burden, psychological outcomes, and healthcare interactions. Data were analysed thematically using persona-based segmentation.

Result

Participants included five women and two men (median age 60 years, range 40–80) with a median disease duration of 15 years. 6/7 had attempted TFR, and four were in sustained TFR (3–13 years). Despite disease control, all participants reported multi-domain TKI toxicities including fatigue, musculoskeletal pain, cognitive impairment, oedema, dermatologic changes, and metabolic or menstrual effects, described as cumulative and under-recognised. Symptoms were frequently deprioritised in favour of molecular response. Diagnostic gaps were common, with delayed recognition of abnormal results in 3/7. Four experienced emotional distress at diagnosis, yet only 1/7 received structured psychological support. Access to TFR varied, with peer influence shaping decision making in 5/7 and clinician reluctance reported in 1/7. Structural gaps were identified in special populations, including pregnancy related uncertainty and adult only admission for adolescent presentation. Participants uniformly rejected the framing of CML as a “good cancer.”

Conclusion

Durable molecular responses have transformed CML survival but not lived experience. These findings highlight the need for systematic integration of PROs to align long-term CML care with outcomes that matter to patients.

Dasatinib-induced chylothorax: a case report

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Aim :

Dasatinib is a second-generation BCR-ABL tyrosine kinase inhibitor used in chronic myeloid leukaemia (CML) and Philadelphia chromosome-positive acute lymphoblastic leukaemia. Pleural effusion is a well-recognised adverse effect; however, chylothorax is a rare and mechanistically distinct complication, with proposed pathophysiology including lymphatic injury via PDGFR- β inhibition. We report a case of dasatinib-induced chylothorax in a patient with complex, heavily pre-treated CML.

Method:

A 31-year-old female was diagnosed with CML in 2017 and sequentially treated with imatinib then nilotinib following rising BCR-ABL transcripts. In 2020, blast crisis with myeloid sarcoma and a Y263H kinase domain mutation, conferring resistance to both prior agents, was identified. Molecular complete remission was achieved with cytarabine-based induction. Allogeneic stem cell transplantation was deferred due to financial constraints, and dasatinib 140mg daily commenced as maintenance. In 2023 the dose was reduced to 100mg then subsequently to 70mg daily in 2025 due to symptomatic bilateral pleural effusions and diarrhoea. The patient subsequently re-presented with progressive exertional dyspnoea.

Results:

Chest radiograph confirmed moderate bilateral pleural effusions. Thoracentesis of the right hemithorax drained 1.8L of milky fluid; triglyceride level of 6.96mmol/L confirmed chylothorax. Dasatinib was ceased, with significant radiographic improvement at two weeks. Given the Y263H mutation, imatinib and nilotinib were not viable options. Asciminib was precluded by financial constraints. Following multidisciplinary review, bosutinib was selected as subsequent therapy.

Conclusion:

Chylothorax is a rare but important dasatinib complication that can occur at any dose or time point. It is biochemically distinguishable from more common dasatinib-associated effusions and requires prompt recognition, as cessation is typically necessary. In patients with complex mutation profiles and limited therapeutic alternatives, this poses significant management challenges. A high index of suspicion should be maintained in patients on dasatinib presenting with pleural effusion.

Allogeneic haematopoietic cell transplantation for Hodgkin's lymphoma: real-world outcomes from a single-centre cohort

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Aim

Hodgkin's lymphoma (HL) is a B-cell malignancy with a high overall cure rate using first-line chemoradiotherapy.¹ However, approximately 10–30% of patients develop relapsed or refractory (R/R) disease.² Salvage therapy followed by auto-HCT achieves long-term remission in approximately 50% of patients.¹

In patients with multiply R/R HL after auto-HCT, allogeneic haematopoietic cell transplantation (allo-HCT) offers a potentially curative treatment.³ Reduced-intensity conditioning (RIC) are favoured over myeloablative approaches, preserving the graft versus lymphoma effect while reducing early transplant-related mortality.⁴ The implementation of post-transplant cyclophosphamide (PTCy) and pre-treatment with immune checkpoint inhibitors (ICI) has significantly improved the outcomes of allo-HCT, with large retrospective cohort studies showing progression free survival (PFS) and overall survival (OS) from 70-90%, and 80-95% respectively.^{4,5,6,7,8} While allo-HCT following treatment with ICI may be associated with increased risk of GVHD, PTCy appears to minimise this.⁹

Method

We conducted retrospective analysis of consecutive adult patients with Hodgkin's lymphoma who underwent allo-HCT at our institution from 2004 to 2025 (N=19). Kaplan-Meier methodology was used to calculate OS and PFS from the date of alloHCT. Secondary endpoints included non-relapse mortality (NRM) and relapse incidence.

Result

At time of analysis, with a median follow up of 4.5 years, overall mortality was low, with 4 deaths recorded, 3 (16%) of which were in the absence of relapse. Relapse or disease progression was documented in two patients (11%), of whom one died from disease. The estimated PFS and OS at 4.5 years were 87.7% and 73.9% respectively. Most patients (53%) underwent a haploidentical transplant. Amongst patients who received PTCy (10) there were no cases of relapses or death.

Conclusion

In this real-world single-centre cohort, alloHCT is shown to be a potentially curative strategy for selected patients with multiply R/R Hodgkin's lymphoma, particularly those who have failed autologous transplantation. The predominance of haploidentical donors supports the feasibility of alternative donor alloHCT. Furthermore, targeted therapies have transformed the relapsed/refractory HL landscape, making contemporary real-world alloHCT outcome data increasingly important to improve outcomes.

Allogeneic haematopoietic cell transplantation for peripheral T-cell lymphoma: Real-world outcomes from a single-centre cohort.

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Aim:

Peripheral T cell lymphoma (PTCL) represents a rare, heterogenous group of non-Hodgkin lymphomas (NHL) that account for 10% of all malignant lymphomas.¹ PTCL is characterized by a highly aggressive clinical course and historically poor outcomes, with 5-year overall survival (OS) rates as low as 30–40% across most subtypes, and 5-year progression free survival (PFS) of 20–30%.² Key histological variants include angioimmunoblastic T cell lymphoma (AILD), anaplastic large cell lymphoma (ALCL) and peripheral T cell lymphoma not otherwise specified (PTCL-NOS), each with distinct biological and clinical features.

Although novel targeted agents continue to emerge, durable disease control, particularly in the relapsed and refractory setting remains an unmet clinical need. First-line therapy, typically anthracycline-based chemotherapy such as CHOP, is associated with high relapse rates, with addition of etoposide only marginally improving overall response rate.³ Consolidation with autologous haematopoietic cell transplantation (auto-HCT) has long been utilised in patients achieving remission, however the OS and PFS remains poor (40–50%)^{4,5}. Allogeneic haematopoietic cell transplant (allo-HCT), while often reserved for relapsed or refractory PTCL, offers a potentially curative treatment, utilising the allogeneic graft-versus-lymphoma effect, and could be considered first line for consolidation therapy.

Method:

We performed a retrospective analysis of adult patients with PTCL (n=21) who underwent allo-HCT at our institution. Kaplan-Meier methodology was used to calculate progression-free survival (PFS) and overall survival (OS).

Results:

In the PTCL cohort, with a median follow-up of 4.7 years, the estimated PFS and OS plateaued at 75.0% and 77.7% respectively. Overall mortality was low, in 4 of 21 patients (19%). The convergence of PFS and OS curves indicates the majority of events occur early, with survivors maintaining sustained remission.

Conclusion:

Allo-HCT achieves durable long-term disease control in patients with PTCL and suggests a favourable mortality profile. It is an effective therapeutic strategy in patients with PTCL and warrants further prospective evaluation.

IRF4 (MUM1) and SERBP1 expression are associated with resistance to guadecitabine (SGI-110) in peripheral T-cell lymphoma

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Aim:

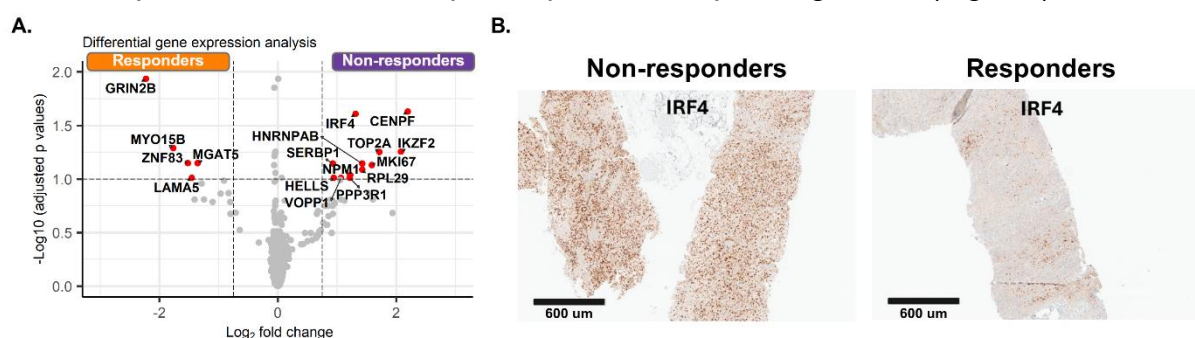
Peripheral T cell lymphomas (PTCL) are aggressive non-Hodgkin lymphomas with a 5-year survival < 50%, and limited effective salvage therapies. Hypomethylating agents (HMA) including guadecitabine (SGI-110) represent a novel treatment approach, however, less than half of patients respond to therapy^{1,2}. Therefore, there is a need to identify predictive biomarkers to guide patient selection for HMA therapy in PTCL.

Methods:

Whole transcriptome sequencing was performed on Formalin Fixed Paraffin Embedded (FFPE) tumour samples (n=11) from PTCL patients before guadecitabine treatment in a single arm phase II study (ACTRN12618000028202)¹. To address technical variation associated with small sample size and RNA degradation in FFPE samples, we designed and implemented a specialised bioinformatic workflow to identify the reliable set of candidate genes and pathways associated with therapeutic response. Protein expression of candidate genes was also assessed by immunohistochemistry (IHC).

Results:

Our analysis revealed *IRF4* (*MUM1*) and *SERBP1* as the most reliable genes that were differentially expressed in non-responders compared to responders (Fig 1.A). Gene set enrichment analysis (GSEA) demonstrated the enrichment of pathways associated with DNA methylation and cell cycle progression in non-responders. Importantly, IHC analysis confirmed elevated protein levels of *IRF4* (*MUM1*) in non-responding cases (Fig 1.B).



Figure

1. A. Differentially expressed genes (adjusted p value<0.1 and log2foldchange >0.75). **B.** Representative IHC images of *IRF4* (*MUM1*) on FFPE samples.

Conclusion:

We identified *IRF4* (*MUM1*) and *SERBP1* as candidate genes that are associated with resistance to guadecitabine in PTCL. Our IHC analysis further suggests *IRF4* (*MUM1*) as a clinically translatable biomarker that is strongly correlated with higher enrichment of gene set related to DNA methylation and cell cycle progression. However, these findings require further validation in larger independent cohorts and functional studies to assess the predictive

potential of *IRF4* (*MUM1*) for HMA resistance and its mechanistic contribution to PTCL pathogenesis.

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Intrathecal Methotrexate for high-grade ICANS after CAR-T cell therapy: A single-centre real-world case series from Western Australia

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Introduction:

Immune effector cell-associated neurotoxicity syndrome (ICANS) remains a major complication of chimeric antigen receptor T-cell (CAR-T) therapy. While corticosteroids are the standard treatment, outcomes remain poor in steroid-refractory cases. Intrathecal methotrexate (IT MTX) therapy emerged as a potential rescue strategy, although evidence remains limited to small retrospective series. We evaluated the real-world use of IT MTX for high-grade ICANS at a single Australian centre.

Methods:

A retrospective single-centre case series of patients who received IT MTX for grade 3/4 ICANS following commercial CAR-T therapy at Fiona Stanley Hospital (March 2025-May 2026). ICANS was graded according to ASTCT criteria. The primary endpoint was early neurological response, defined as improvement to below grade 3 within 48 hours of IT administration.

Results:

Six patients received IT MTX (12 mg). All were steroid and anakinra refractory. Median age was 71 years (range, 49–79). CAR-T products were axicabtagene-ciloleucel (n=4) and brexucabtagene-autoleucel (n=2). Diagnoses included DLBCL (n=4), MCL (n=1), B-ALL (n=1).

Median ICANS onset was D+3 (range, 1–4), ICANS peaked at grade 4 in 5/6 patients. IT MTX was administered at a median of 2.5 days (range, 1–22) after High-grade ICANS onset. Three patients (50%) achieved rapid neurological improvement to below grade 3 within 48 hours of IT MTX; all responders received IT within 4 days of grade 3/4 ICANS onset. We documented four non-relapse deaths: two from ICANS, one from ICANS with bacterial pneumonia, and one from a fungal infection post-ICANS resolution. No procedure-related complications occurred.

At D+30, three patients achieved complete metabolic remission, including two long-term survivors who remain in remission at M+12 and M+3, respectively.

Conclusion:

In this real-world cohort, early IT MTX administration for high-grade ICANS was associated with rapid neurological improvement in selected patients whereas delayed administration appeared less effective. These findings support a potential time-sensitive therapeutic window. Prospective multicentre studies are needed to validate efficacy and optimal timing.

HCT-CI fails to predict outcomes or toxicity in a large real-world LBCL cohort treated with Axicabtagene Ciloleucel: The Australian Car-T world consortium (AusCART) experience

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Background:

The Hematopoietic Cell Transplantation-Comorbidity Index (HCT-CI) is a validated risk assessment tool for allogeneic stem cell transplantation, but its utility in predicting outcomes following Chimeric Antigen Receptor (CAR) T-cell therapy remains uncertain. We assessed the prognostic value of HCT-CI in relapsed/refractory large B-cell lymphoma (LBCL) patients treated with axicabtagene ciloleucel (axi-cel) in a contemporary Australian real-world cohort.

Methods:

We performed a retrospective multicentre analysis of LBCL patients undergoing leukapheresis for axi-cel between January 2020 and November 2025 across Australian CAR-T Real World Consortium (AusCART) sites. HCT-CI was calculated at leukapheresis and stratified as Low (0), Intermediate (1–2), or High (≥ 3). Endpoints included progression-free survival (PFS), overall survival (OS), response, toxicities (CRS, ICANS, ICAHT), and healthcare utilisation.

Results:

Among 555 apheresed patients, 519 (94%) proceeded to infusion, with similar infusion rates across HCT-CI groups (Low 94.6%, Intermediate 91.4%, High 94.3%; $p=0.383$).

Among infused patients, 245 (47%) were classified as Low HCT-CI, 159 (31%) Intermediate, and 115 (22%) High. Baseline characteristics were broadly balanced across groups. Median age was 65 years, 53% were primary refractory.

Complete response (CR) rates comparable across groups (Low 71%, Intermediate 73%, High 73%). With a median follow-up of 12.3 months, 12-month PFS for the infused cohort was 51% (Low 50.2%, Intermediate 50.7%, High 53.1%; $p=0.881$), while 12-month OS was 69.9% (Low 70.4%, Intermediate 71.0%, High 67.3%; $p=0.409$). The incidence and severity of toxicities were also similar across categories, grade ≥ 3 CRS (5%; $p=0.418$), grade ≥ 3 ICANS (21%; $p=0.469$), ICU admission (24%; $p=0.812$), and grade ≥ 3 ICAHT (26%; $p=0.948$). Tocilizumab (81%), corticosteroid (70%), and anakinra use (20%), as well as hospital length of stay ($p=0.830$), did not differ between groups.

Conclusions:

HCT-CI did not meaningfully stratify efficacy, toxicity, or survival outcomes following axi-cel in this large Australian real-world LBCL cohort, suggesting transplant-era comorbidity indices may have limited discriminatory value for contemporary CAR-T eligibility assessment.

Australian real-world outcomes of second-line Axicabtagene Ciloleucel for large B-cell lymphoma: an AusCART Consortium analysis

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Background:

Second-line (2L) CD19-directed CAR T-cell therapy has become a standard-of-care option for early relapsed or refractory large B-cell lymphoma (LBCL), but real-world outcomes in the Australian population have not been described.

Methods:

We performed a retrospective analysis of Australian patients apheresed for 2L axi-cel in 2025 at six Australian centres that participate in the AusCART consortium. Baseline characteristics, bridging therapy, response, progression-free survival (PFS), overall survival (OS) and toxicities were summarised. Efficacy endpoints included best overall response rate (ORR), complete response (CR), PFS and OS from infusion. Toxicities were graded using ASTCT criteria for cytokine release syndrome (CRS) and immune effector cell-associated neurotoxicity syndrome (ICANS).

Results:

Among 196 patients apheresed for 2L axi-cel, 186 were infused. Median age was 65 years (range, 21–83), 67% were male, and histologies included DLBCL (55%), transformed follicular lymphoma (17%) and high-grade B-cell lymphoma (13%). Primary refractory disease was present in 66%, and 63% were refractory to their most recent therapy. Bridging included systemic therapy alone in 33%, radiotherapy alone in 29%, combined modality treatment in 13% and 4% had no bridging. 34% had progressive disease following bridging. With median follow-up of 6 months, best ORR was 84% and CR rate was 72%. Estimated PFS at 3, 6 and 12 months was 79%, 69% and 59%, respectively; corresponding OS was 90%, 85% and 66%. Acute toxicity was clinically significant but consistent with the axi-cel toxicity profile: grade ≥ 3 CRS occurred in 14 patients (8%) and grade ≥ 3 ICANS in 48 (26%), with no grade 5 CRS or ICANS. ICU admission by day 28 occurred in 69 patients (37%).

Conclusions:

In this Australian real-world cohort, 2L axi-cel delivered high early response rates and encouraging 12-month disease control despite a predominantly refractory population. Longer follow-up is required to define durability and late toxicity.

Rare cutaneous malignancies following CAR T-cell therapy: A case series

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Case Study:

Secondary primary malignancies (SPMs) following CAR T-cell therapy occur in approximately 6-8.5% of long-term follow-up cohorts, with skin cancers the most common solid tumour SPMs.^{1,2} We describe three cases of rare, aggressive cutaneous malignancies arising in patients who had achieved complete remission (CR) following standard-of-care axicabtagene ciloleucel CAR-T therapy for DLBCL: two cases of Merkel cell carcinoma (MCC) and one case of poorly differentiated metastatic dermal sarcoma.

MCC is a rare, aggressive neuroendocrine skin tumour, accounting for less than 1% of cutaneous malignancies globally. Australia has the world's highest MCC incidence (1.3/100,000), likely due to intense UV exposure.³ Australian MCC is predominantly Merkel cell polyomavirus (MCPyV)-negative, in contrast to the MCPyV-positive tumours predominating in Northern hemisphere populations. Post-CAR-T immune dysregulation - including B-cell aplasia, hypogammaglobulinaemia, and persistent lymphopenia - closely resembles the immunosuppressive environment known to predispose to MCC development. Immunosuppression is also a recognised adverse prognostic factor; three-year MCC-specific survival is nearly half that of immunocompetent individuals.⁴ This is particularly relevant in CAR-T recipients, in whom T-cell reconstitution is profoundly impaired: intratumoral T-cell infiltration is associated with favourable MCC survival.⁵

Three cases are summarised in Table 1. No prior cases of MCC or dermal sarcoma as SPMs following CAR-T therapy were identified on literature review.

Conclusions:

Profound and prolonged post CAR-T immunosuppression combined with Australia's high UV environment increases the risk of rare, aggressive cutaneous SPMs. These cases underscore the need for structured post-CAR-T surveillance protocols at Australian centres.

Table 1 – Patient characteristics and outcomes

Feature	MCC #1	MCC #2	Dermal sarcoma
Age at CAR-T	62	81	70
Prior lines of therapy	3	2	5
Prior malignancies	None	SCC right cheek (resected)	CRC 2009; multiple SCCs; smouldering (asymptomatic) myeloma
Response to CAR-T	CR	CR	CR
Time to diagnosis post CAR-T (months)	5	11	6
Site	R posterior calf (non-exposed)	L eyelid (sun-exposed)	Scalp (sun-exposed)
Stage at diagnosis	I	I	IV
MCPyV status	Not tested	Weak/equivocal	N/A – sarcoma (extensive IHC exclusion panel; subtype undetermined)
CD4/CD8 count at SPM dx (x10 ⁹ /L)	0.02/0.02	0.23/0.22	Not collected
B-cell aplasia	Yes	No	Not collected
IVIg post CAR-T	Yes	No	Yes
Treatment	RT	WLE + SLNB	RT → WLE → PD-1i + Ipilimumab
Outcome	Relapse → Further RT → Avelumab → Carbo/Etop Died 11.5 months from diagnosis	Follow-up ongoing	Died 6 months from diagnosis

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Real-world bridging strategies for relapsed/refractory mantle cell lymphoma for brexucabtagene autoleucel: a single-centre experience

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Aim: Brexucabtagene autoleucel (brexu-cel) is approved for relapsed/refractory mantle cell lymphoma (R/R MCL). Bridging therapy (BT) is administered to most patients awaiting infusion but optimal regimen composition is poorly defined, as this population is typically refractory to chemoimmunotherapy and BTK inhibitor (BTKi) therapy. We describe real-world bridging practice and outcomes.

Method: We retrospectively reviewed all R/R MCL patients infused with brexu-cel at our centre between February 2024 and May 2026. Disease distribution and BT delivery location were recorded. Given the heterogeneous and often individualised nature of bridging regimens, these were analysed by component (proportion of full cohort containing each class). Response was any pre-infusion response on PET and/or clearance of disease at previously involved sites.

Results: 19 patients were infused. All had nodal disease; 11 (58%) had marrow involvement, 12 (63%) blood involvement by flow cytometry/morphology, and 9 (47%) had concurrent marrow, blood, and nodal disease. All received bridging (19/19, 100%) and regimens commonly combined modalities. 84% (16/19) contained rituximab, 68% (13/19) chemotherapy, 58% (11/19) a BTKi (predominantly zanubrutinib), 21% (4/19) radiotherapy, and 16% (3/19) venetoclax. Cytarabine was the most common chemotherapy agent (9/13, 69%), either as the sole cytotoxic agent (combined with rituximab and zanubrutinib) or as part of multi-agent chemotherapy regimens such as R-DHAC. Chemotherapy-containing regimens responded in 10/13 cases (77%); BCL2i 2/3 (67%); radiotherapy 2/4 (50%). In most cases, zanubrutinib was continued post-progression through to lymphodepletion rather than introduced as new bridging. Overall response to BT was 14/19 (74%). 16/19 (84%) of bridging was delivered at referring sites rather than the CAR-T centre.

Conclusion: Real-world bridging for R/R MCL is multimodal, with BTKi continuation often combined with chemoimmunotherapy. High response rates support continued use of such composite regimens. With most bridging delivered at referring sites, close collaboration with the CAR-T centre remains essential for safe, timely delivery.

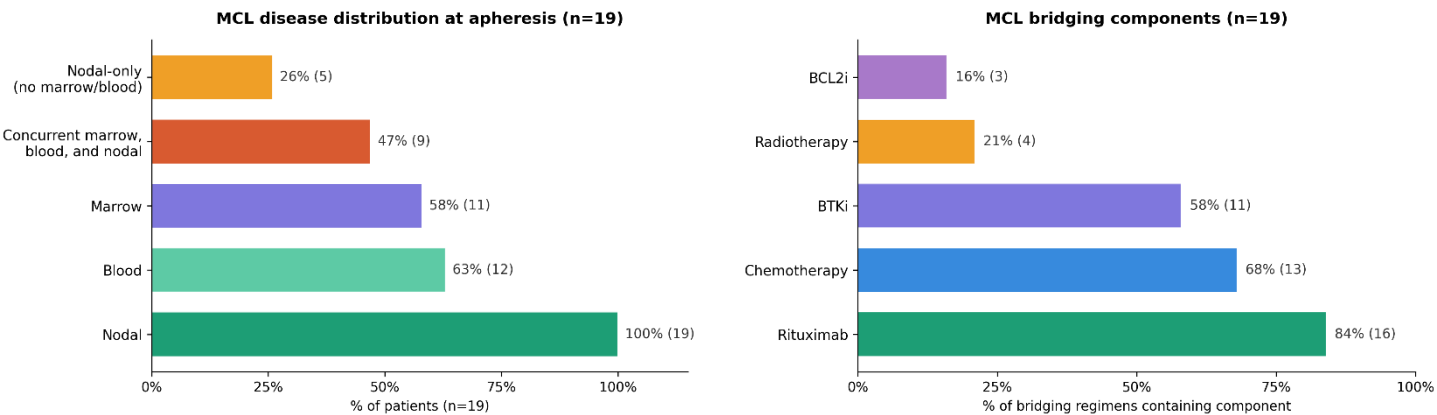


Figure. (A) Disease distribution at apheresis among the 19 patients. (B) Bridging components — percentages reflect the proportion of all bridging regimens (n=19) containing each agent class; many regimens contained multiple components.

Exploring outcomes of Culturally and Linguistically Diverse (CALD) patients with Diffuse Large B Cell Lymphoma: a retrospective study from 2017-2021

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Aim:

DLBCL is an aggressive lymphoma with varying outcomes due to social and biological factors(1–3). CALD patients have known barriers and inequity in cancer care, however, there have been no Australasian studies examining their outcomes in DLBCL(4). This study investigates differences in clinical outcomes between CALD English-speaking (CALD-ENG), CALD non-English speaking (CALD-OTHER) and non-CALD patients with DLBCL, within South-Western Sydney Local Health District (SWSLHD).

Method:

A retrospective study of 267 patients with DLBCL in SWSLHD, diagnosed between 2017-2021. Overall survival(OS), Progression free survival(PFS), baseline demographic characteristics and clinical characteristics were collected. CALD population was defined as people born in non-English speaking countries, and/or who do not speak English(5).

Baseline characteristics were compared using Kruskal-Wallis, or Chi-squared tests as appropriate. OS and PFS were assessed using univariable and multivariable cox regressions, with Kaplan–Meier survival curves used for visual representation.

Results:

CALD-ENG patients were younger with median age of 63 compared to 70 for CALD-OTHER, and 66 for non-CALD. Both CALD groups had lower socioeconomic status, with 56.9% of CALD-ENG and 75.7% of CALD-OTHER having index of relative socioeconomic disadvantage of 1, compared to 40.2% of non-CALD ($p < 0.0001$).

At 5 years there were significant differences in OS between the groups (log-rank=7.12, $p=0.03$), with CALD-ENG group highest at 76%, versus CALD-OTHER and non-CALD (58-59%). Multivariable regression over the full period found hazard ratios of 2.07(CI:1.1-3.9) & 2.1(CI:1.2-3.9) for CALD-OTHER and non-CALD respectively. Similarly, the CALD-ENG group had better 5-year-PFS compared to other groups(73% vs 52-53%), and a lower HR over the study period(CALD-OTHER: HR = 1.87, non-CALD: HR = 2.12).

Conclusion:

CALD-ENG population had improved OS and PFS outcomes in DLBCL, compared to non-CALD and CALD-OTHER. CALD and English-language status are therefore determinants for clinical outcomes in DLBCL within this population. This novel finding requires further studies to investigate the underlying mechanism and potential sequelae.

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Progressive multifocal leukoencephalopathy presenting as subacute cerebellar syndrome following anti-CD19 CAR-T cell therapy

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Case Study:

A woman in her late eighties with primary refractory diffuse large B-cell lymphoma (DLBCL) received R-mini-CHOP and consolidative radiotherapy. For residual disease, she received allogeneic anti-CD19 CAR-T therapy with cyclophosphamide and fludarabine lymphodepletion. Her post-infusion course was uncomplicated and PET-CT demonstrated metabolic remission. She presented 14 months post-infusion with subacute functional decline and falls, progressing to a pancerebellar syndrome. MRI demonstrating confluent FLAIR/T2 hyperintensity in the bilateral cerebellar white matter and peridentate regions without enhancement or diffusion restriction, extending into the middle cerebellar peduncles. Immunological assessment at 16 months found an inverted CD4:CD8 ratio of 0.48, CD4 percentage of 20% and moderate hypogammaglobulinaemia (IgG 4.9 g/L) with an elevated CD19 count, indicating a functionally naïve B cell lymphocyte population.

CNS lymphoma recurrence and paraneoplastic cerebellar degeneration were investigated with sequential MRI, PET, CSF cytology, flow cytometry and a paraneoplastic antibody panel. Empirical dexamethasone produced no response. Positive JCV PCR on CSF confirmed PML at 16 months post-infusion. Pembrolizumab was decided against given patient's frailty and rapidly progressive course. The patient died shortly after diagnosis.

Conclusion:

Progressive multifocal leukoencephalopathy (PML) is a demyelinating disease resulting from JCV reactivation with impaired cellular immunity. CD19-directed CAR-T therapy carries a reported PML incidence of 0.9 per 1,000 recipients, arising 6–31 months post-infusion (Blood 2023;141:673). This susceptibility reflects the prolonged immune dysregulation following CAR-T therapy, encompassing hypogammaglobulinaemia, CD4 lymphopenia and impaired T-cell reconstitution, which may sustain vulnerability to opportunistic infection well beyond the period of acute toxicity.

Following CD19-directed CAR-T therapy numerical recovery of lymphocytes does not signal functional immune reconstitution and hypogammaglobulinaemia and CD4:CD8 ratio inversion may persist. Immunological monitoring and active surveillance for opportunistic infection should be considered. Subacute neurological decline should prompt investigation for PML and CSF JCV PCR testing should be prioritised regardless of interval from infusion.

10 years of the Australian and New Zealand Lymphoma & Related Diseases Registry (LaRDR)

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Aim:

LaRDR is a clinical quality registry that analyses and reports data on participants with lymphoma or a related disease to monitor and benchmark care, and support research. In January 2026, the 10,000th participant was registered. Here we describe recruitment at participating hospitals in metropolitan & non-metropolitan locations in Australia, and New Zealand (NZ).

Method:

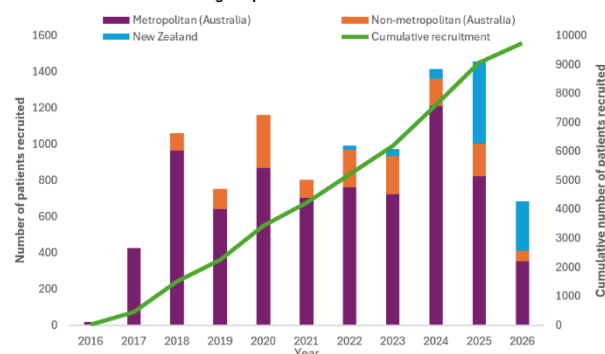
Data collection commenced with a pilot at Australian metropolitan hospitals in 2016, then non-metropolitan hospitals from 2018, and NZ hospitals from 2022. Eligible patients enrolled between January 2016 and April 2026 were included in this analysis. Australian hospitals were

categorised into metropolitan or non-metropolitan locations based on their representations in LaRDR's Regional/Rural Reference Group. Frequencies with percentages, and medians with interquartile range, were used to report on categorical and continuous variables, respectively. Missing data were managed by complete case analysis.

Results:

Data on 9748 patients with available recruitment date were included from 39 hospitals: Australian metropolitan (59%), non-metropolitan (31%) and NZ (10%). See Figure 1. Of 9186 patients with complete data diagnosed from January 2016, 78% patients were from Australian metropolitan sites, 13% non-metropolitan, and 9% from NZ (Table 1). Median age at diagnosis, sex distribution, and patterns of diagnoses across participating hospitals were similar.

Figure 1. The number of patients recruited to the Lymphoma and Related Diseases Registry by year and locations of their treating hospitals.



Conclusion:

LaRDR provides vital real-world data from hospitals across Australia and NZ, with NZ patients now representing 10% of registrations. LaRDR's Regional/Rural Reference Group plays an important role in supporting recruitment at non-metropolitan hospitals. LaRDR has already supported 41 research projects, published 16 peer-reviewed papers and is coordinating the Global Lymphoma Registry Alliance. LaRDR thanks all patients, participating sites, investigators, staff and supporters, and welcomes new sites, project ideas and data requests. More info: lardr.org

Table 1. Demographics of patients diagnosed from 2016-2026, by locations of their treating hospitals. LaRDR: Lymphoma and Related Diseases Registry; HL, TCL, DLBCL, FL, MCL: Hodgkin, T-cell, diffuse large B-cell, follicular and mantle cell lymphomas; PTL: post-transplant lymphoproliferative disorder; CLL: chronic lymphocytic leukaemia.

Characteristics	Locations of the LaRDR participating hospitals			
	All (N=9186)	Metropolitan (Australia) (n=7004)	Non-metropolitan (Australia) (n=1337)	New Zealand (n=845)
Median age at diagnosis (IQR)	66 (54-74), n=9182	65 (53-74), n=7001	67 (56-75), n=1336	66 (53-74), n=845
Male sex (%)	5379/9182 (59)	4096/7000 (59)	774/1337 (58)	509/845 (60)
Diseases (%)				
DLBCL	3295/9183 (36)	2549/7002 (36)	439/1336 (33)	307/845 (36)
Other BCL	1609/9183 (18)	1260/7002 (18)	189/1336 (14)	160/845 (19)
FL	1471/9183 (16)	1100/7002 (16)	241/1336 (18)	130/845 (15)
HL	1128/9183 (12)	837/7002 (12)	160/1336 (12)	131/845 (16)
CLL	685/9183 (8)	494/7002 (7)	163/1336 (12)	28/845 (3)
TCL	540/9183 (6)	431/7002 (6)	66/1336 (5)	43/845 (5)
MCL	393/9183 (4)	275/7002 (4)	76/1336 (6)	42/845 (5)
PTLD	56/9183 (<1)	52/7002 (<1)	2/1336 (<1)	2/845 (<1)
Other lymphomas/related diseases	6/9183 (<1)	4/7002 (<1)	0 (0)	2/845 (<1)
Median follow-up duration (months)	24	24	29	21

Attributes mapping of global lymphoma registries in a Lymphoma Registry Alliance (LyRA)

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Aim:

The Global LyRA unites stakeholders from 48 real-world lymphoma registries, including institutional databases and research consortia. Understanding their diversity is fundamental to streamlining collaborations and enhancing data interoperability for international benchmarking and research. We aim to identify and report the characteristics of the LyRA members.

Method:

All LyRA member organisations were invited to provide information from Jun 2025 to Jan 2026. Member type, established year, leading jurisdiction, mode of consent and data entry, patient accrual, availability of clinical quality indicators (CQIs) and capacity for data sharing were collected and descriptively analysed. Interviews were conducted to clarify on responses.

Results:

Twenty-one members (44%) from 16 jurisdictions across Europe, Asia & Oceania provided information, including population-based cancer registries (33%), disease registries (33%), research consortia (14%), institutional databases (10%) and cohort studies (10%). 80% of organisations waived consent, 56% captured all lymphomas, 67% collected data manually (Table 1). 14 members collected follow-up data semi-annually (n=4), or on a rolling basis (n=10) (e.g. upon clinical reviews). 7 members also linked with government datasets (n=5) or imported data extracts (n=2).

Seven organisations were established as clinical quality registries (CQRs), with six capturing CQIs defined by expert consensus or national guidelines. CQIs include stage reporting, wait times to treatment decisions, inclusion on clinical trials, and survival rate. The remaining CQR report on clinical outcomes.

Sharing data at various sensitivity levels is permitted by regulatory requirements. Visualisations (33%) or aggregated data (38%) are publicly available. Anonymised datasets with registry governance or ethics approval could be provided (20%), accessed in a secure portal (52%), or by file transfer (95%). Requests of identifiable data were only available in 15% upon similar approval.

Conclusions:

This mapped information present opportunities for members to share knowledge, align practice models, and encourage large-scale collaborative research in lymphoma care.

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LyRA

and

Table 1. Characteristics of LyRA members.

Member type	Number of pts (range)	Established year (range)	Consent (%)		Disease (%)		Mode of data collection (%)		Collection of clinical quality indicators (%)	
			Waived*	Opt-in	All lymphomas	Subtypes	Manual entry	Multi-modal	No	Yes
N=21	N=973899		17 (80)	4 (20)	12 (56)	9 (45)	14 (67)	7 (33)	15 (72)	6 (28)
Population-based cancer registry (n=7)	1451-703715	1953-2025	6 (28)	1 (5)	6 (28)	1 (5)	2 (10)	5 (23)	2 (10)	5 (23)
Disease registry* (n=7)	0-9071	2015-2024	5 (23)	2 (10)	5 (23)	2 (10)	7 (32)	0 (0)	6 (28)	1 (5)
Consortium (n=3)	121-3000	2016-2025	3 (14)	0 (0)	1 (5)	2 (10)	2 (10)	1 (5)	3 (14)	0 (0)
Institutional database (n=2)	135-158	2023	2 (10)	0 (0)	0 (0)	2 (10)	1 (5)	1 (5)	2 (10)	0 (0)
Cohort study (n=2)	600-6000	2018-2023	1 (5)	1 (5)	0 (0)	2 (10)	2 (10)	0 (0)	2 (10)	0 (0)

*Including one planned registry not yet in operation.
*Waived consent includes opt-out approach and compulsory registration abide by the law.

Transformation to classical Hodgkin Lymphoma following Bruton Tyrosine Kinase inhibitor therapy for low grade B-NHL: a case series

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Background

Histologic transformation of indolent B-cell lymphoma (B-NHL) to high-grade lymphoma is an uncommon but recognized phenomenon. Limited data exists regarding Hodgkin transformation occurring while being treated with Brutons tyrosine kinase inhibitors (BTKi).

Aim

To describe histological confirmed transformation to Hodgkin lymphoma in after BTKi therapy.

Method

Retrospective case series.

Results

We identified 3 cases with the last 2 years at our centre with biopsy confirmed cHL/Hodgkin-like phenotype after prior BTKi therapy.

Case 1: 57-year-old female diagnosed with Stage III marginal zone lymphoma (MZL) in 2020. First line therapy (R-CHOP/GDP) achieved CMR for 2 years. Second line therapy with Zanubrutinib for symptomatic skin/soft tissue disease (biopsy confirmed MZL). PET-scan re-staging at 12 months due to non-specific abdominal pain, fatigue/ nausea. New abdominal LNs on biopsy confirmed Hodgkin transformation (cHL). Treated with 6xA(B)VD achieving PET-scan CMR. 6 months later, progressive cervical lymphadenopathy was biopsied confirming MZL relapse. Current therapy with R² chemo-immunotherapy.

Case 2: 68-year-old male diagnosed with Stage IV EBV associated large cell lymphoma in 2020. First line therapy 8xHyperCVAD. In remission for 3 years with low-level EBV viremia detected. Gastroscopy performed due to progressive nausea, loss of appetite/weight. Duodenal biopsy demonstrated malignant ulcers (Lymphoplasmacytic lymphoma, LPL). Second line therapy with Zanubrutinib. 6-month PET-scan showed mixed response, and imaging-directed sacral biopsy revealed Hodgkin-like transformation. Subsequent therapy 3 x R-GDP and autologous stem cell transplant (March 2026).

Case 3: 74-year-old female diagnosed with chronic lymphocytic leukaemia in 2020. First line therapy with 6x Chlorambucil/obinutuzumab. Second line therapy with acalabrutinib (2023), after 2 years noted to have large retroperitoneal mass. Biopsy confirmed Richter transformation to cHL. Current therapy R-mini-CHOP.

Conclusion

The transformation of indolent B-cell lymphoma to cHL during BTKi therapy is rarely reported. This case series should prompt a larger multi center review.

Secondary histiocytic sarcoma masquerading as abscess: A case report

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Introduction

Histiocytic sarcoma (HS) is an extremely rare, aggressive myeloid neoplasm derived from non-Langerhans histiocytic cells that can present in a variety of ways.

Case presentation

A 60 year old man undergoing R-CHOP chemotherapy for transformed follicular lymphoma had a routine progress PET scan post cycle 4 that demonstrated a new destructive, FDG avid mid-thoracic paraspinal mass suspicious for disease progression, with complete metabolic response elsewhere. He had recent onset of back and right chest pain. The initial core biopsy favoured a suppurative inflammatory process with a heavy neutrophilic infiltrate consistent with an abscess, with negative microbiology and immunostaining negative for lymphoma. Conservative management was trialled with antibiotics, however progress imaging demonstrated no response. A second core biopsy reported similar findings to the first biopsy. A surgical incisional biopsy was performed and histology demonstrated a poorly cohesive histiocytic population with significant atypia strongly positive for CD163 and CD68 consistent with HS, which was somewhat obscured by the unusually heavy tumour-associated neutrophil inflammatory infiltrate. Identification of IGH clonality, molecular variants in *CREBBP*, *TNFRSF14*, *CD79b*, *MAP2K1* and aberrant somatic hypermutation in *BCL2* and *CXCR4* on formalin-fixed paraffin-embedded (FFPE) tissue were consistent with a direct molecular link to the patient's underlying follicular lymphoma (i.e. secondary HS).

Conclusion

Histiocytic sarcoma is a challenging diagnosis due to its rarity and variety of clinical presentations. This case highlights that HS can arise from histiocytic transdifferentiation of lymphoma, and should be considered as a possibility, albeit rare, when identifying new, suspicious lesions during the course of lymphoma treatment. This diagnosis can be supported by molecular testing demonstrating the co-existence of abnormalities typical of B-cell lymphomas (clonal IG rearrangements, aberrant somatic hypermutation, *CREBBP* mutations) alongside *MAPK* mutations typical of HS.

Trial in progress : Early clinical data from “PLATYPS”, a first-in-human clinical trial of an Australian-developed and manufactured CD19-targeting CAR-T cell product (PMCC-COE19)

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Background: Chimeric antigen receptor (CAR) T-cell therapies have revolutionised treatment paradigms for many haematological malignancies, however the majority of CAR T-cell products administered to Australian patients are developed and manufactured internationally. The “PLATYPS” study was designed to assess safety and feasibility of an Australian-developed and manufactured CD19-targeting CAR-T cell product (PMCC-COE19) in a first-in-human study.

Methods: PMCC-COE19 is a 2nd generation TCRζ-41BB co-stimulated CD19-targeting (FMC63) autologous CAR T-cell product, featuring shortened manufacture with cytokine fortification. PMCC-COE19 was designed and developed at the Peter MacCallum Cancer Centre (PMCC). Approval was granted by the Therapeutic Goods Administration (TGA) to evaluate PMCC-COE19 under the Clinical Trial Approval (CTA) scheme in the first-in-human “PLATYPS” study, which opened at PMCC in October 2025. Adult patients with relapsed/refractory CD19-expressing B-cell malignancies and no superior treatment options are potentially eligible, including central nervous system (CNS) disease. Patients receive standard lymphodepleting chemotherapy followed by a single infusion of PMCC-COE19, using an accelerated single patient dose escalation schema.

Results: Three patients have been enrolled to date, with median age of 53 years (range 53-65) and 4 prior lines of therapy (range 4-6); see Table 1. The target dose was successfully manufactured in all patients, however one infusion didn’t proceed due to clinical and radiological progression of CNS disease despite bridging radiotherapy. No dose limiting toxicity has been observed, nor cytokine release syndrome (CRS) greater than Grade 1; see Table 1. CAR T-cell engraftment was demonstrated by detection of PMCC-COE19 in peripheral blood. The best response to date is a partial response (Dose Level 1), and ongoing assessments are awaited.

Conclusions: Preliminary data from “PLATYPS” indicates feasibility and safety of onshore manufacturing of an Australian-designed autologous CAR T-cell product, representing an important advancement of sovereign capability and capacity in the cellular therapy space. Patient accrual and dose escalation are ongoing.

Table 1

Patient ID	Age/sex	Histology	Prior lines of therapy	Infused (Y/N)	Dose Level	CRS / ICANS	Best response
PLATYPS-001	65M	FL	6	Y	1	Possible Gr 1 CRS [#]	PR
PLATYPS-002	53M	PCNSL	4	N*	n/a	n/a	n/a
PLATYPS-003	53M	FL	4	Y	2	Possible Gr 1 CRS [#]	<i>awaited</i>
[#] likely disease related fevers; *not infused due to CNS progression despite bridging radiotherapy							

PLATYPS A **P**hase I, Open-**L**abel, Single **A**rm **T**rial to Assess the Efficacy and Safety of PMCC-COE19 in **P**atients with CD19-Expressing B-Cell Malignancies; FL follicular lymphoma; PCNSL primary central nervous system lymphoma; CRS cytokine release syndrome; ICANS immune effector cell-associated neurotoxicity syndrome; CNS central nervous system; PR partial response; n/a not applicable

Hypertension treatment for patients receiving covalent Bruton tyrosine kinase inhibitors (BTKis) in routine clinical practice in Australia: A retrospective pharmacy-linkage study

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Aim:

Hypertension (HTN) is a recognized class effect of BTKis, attributed to on- and off-target activity, increasing with treatment duration, and contributing to cardiovascular risk. While second-generation BTKis are safer than ibrutinib, HTN remains a clinically relevant concern, needing monitoring and management. Given limited real-world evidence, this analysis explores use of anti-HTN medications in patients before and after starting BTKi treatment.

Method:

In this retrospective, observational study, we analyzed data from the NostraData Prescription longitudinal database, including all patients aged ≥ 18 years with B-cell malignancies initiating treatment with a covalent BTKi (ibrutinib, acalabrutinib, zanubrutinib) between September 2023-August 2024. Two cohorts were studied: Cohort 1 included patients on anti-HTN treatment within 3 months of BTKi-initiation; Cohort 2 included patients who were not. Patients with heart failure were excluded. Anti-HTN treatment initiation and escalation (addition of new a new drug, change of drug class, or increase in dose) were also assessed.

Results:

In Cohort 1, 237/259 patients (91.5%) had unchanged anti-HTN treatment within 3 months of BTKi initiation. Of these, 32.5% escalated anti-HTN treatment after initiation of a BTKi (n/%): zanubrutinib (55/33.1%), acalabrutinib (17/29.8%), or ibrutinib (5/35.7%). Of 22 (8.5%) patients who escalated anti-HTN treatment within 3 months prior to BTKi-initiation, 17 (77.3%) further escalated anti-HTN treatment after. This included 10 (71.4%) zanubrutinib, 4 (80%) acalabrutinib and 3 (100%) ibrutinib patients. In Cohort 2 (n=371), 56 (15.1%) started anti-HTN treatment after initiating a BTKi, with similar rates (n/%) observed in patients on zanubrutinib (40/15.1%) and acalabrutinib (13/15.1%); of 21 patients in the ibrutinib group, 3 (14.3%) started anti-HTN treatment.

Conclusion:

BTKi therapy was associated with a meaningful need for HTN management, with $\sim 1/3$ of patients with pre-existing HTN requiring treatment intensification and $\sim 15\%$ of previously untreated patients initiating therapy, broadly consistent across BTKis. Comparable rates were seen with zanubrutinib and acalabrutinib.

Prognostic impact of baseline bone marrow involvement in nodal peripheral T-cell lymphoma: An Australasian-Canadian collaborative study

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Aim: Baseline bone marrow involvement (BM+) is a marker of advanced-stage lymphoma; however, its prognostic significance in nodal peripheral T-cell lymphomas (nPTCL) remains unclear. We assessed whether biopsy-confirmed BM+ at diagnosis is associated with survival outcomes and/or provides independent prognostic value beyond established clinical risk factors.

Method: Retrospective analysis was conducted using the Australasian Lymphoma and Related Diseases Registry (LaRDR; Jan 2016–Dec 2023) and the Princess Margaret Cancer Centre lymphoma database (PMH; Nov 2011–Mar 2024). Adults (≥ 18 years) with a baseline bone marrow biopsy who received frontline therapy for nPTCL were included, comprising PTCL-not otherwise specified, T follicular helper (TFH)-type lymphomas (angioimmunoblastic T-cell lymphoma, PTCL with TFH phenotype, follicular T-helper lymphoma), and anaplastic large cell lymphoma. PFS and OS were estimated using the Kaplan-Meier method and compared between patients with and without BM+ at diagnosis (log-rank test). Multivariable Cox proportional hazards regression (MVA) assessed the independent association between BM+ and OS.

Results: A total of 436 patients were included (LaRDR n=351; PMH n=85), of whom 85 patients (19.5%) had BM+ at diagnosis. Patients with BM+ were more likely to have poorer ECOG performance status (PS) and B-symptoms, with no difference in median age or sex.

There was no significant difference in PFS between patients with and without BM+ ($p=0.055$). OS was inferior in BM+ cases ($p=0.012$) (Figure 1); however, BM+ was not independently associated with OS on MVA adjusting for age, ECOG-PS, nodal subtype and the presence of B-symptoms (HR 1.28, 95%CI 0.89-1.83; $p=0.18$).

Figure 1

Figure 1A: PFS from commencement of frontline therapy

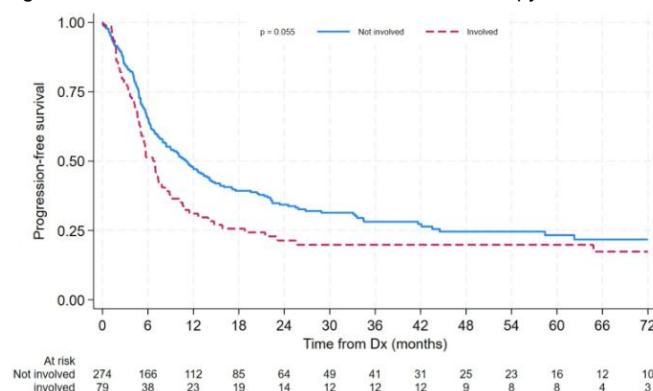
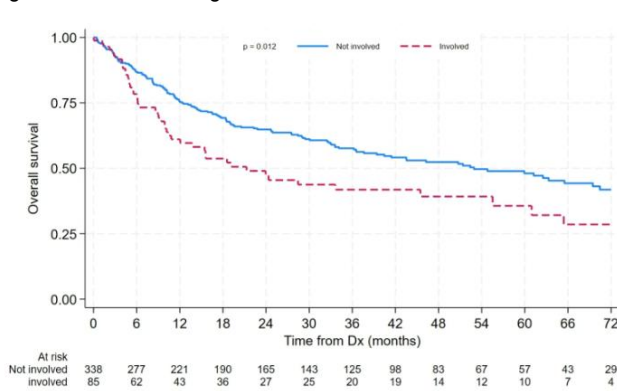


Figure 1B: OS from diagnosis



Conclusion: While BM+ is associated with inferior OS in nPTCL, our analysis demonstrated it does not retain independent prognostic significance after adjustment for clinical risk factors; this may be limited by sample size. BM+ is associated with higher ECOG-PS, potentially impacting therapy delivery. Further research is needed to clarify the role of BM+ within modern risk stratification frameworks.

Phase 1 study to evaluate safety, tolerability, pharmacokinetics (PK), and clinical activity of the antibody-drug conjugate (ADC) ARC-02 as monotherapy and in combination with rituximab in adults with B-cell non-Hodgkins lymphoma (NHL)

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Background: In individuals with B-cell NHL, up to 50% experience refractory/relapsed (R/R) disease, with limited treatment options. The anti-CD79b ADC polatuzumab-vedotin is indicated for treatment of aggressive high-grade lymphomas but not other B-cell NHLs. ARC-02 is a novel anti-CD79b ADC developed using proprietary AraLinQ™ technology, which enhances ADC homogeneity and stability, offering improved on-target activity and enhanced safety. Preclinical studies of ARC-02 noted a 16-fold higher therapeutic index over polatuzumab-vedotin. This was based on an up to 8-fold improvement in safety margin and potent cytotoxicity in NHL cell lines and xenograft models, with ARC-02 achieving comparable efficacy at 2-fold lower payload delivery (Schlereth, 2022; Kallenberger, 2024).

Study rationale: Polatuzumab-vedotin use is limited to a subset of aggressive lymphomas, with toxicities restricting treatment duration. Improved ARC-02 characteristics supports its evaluation in a range of B-cell lymphomas as monotherapy or in combination with rituximab. The latter is further supported by preclinical evidence of potential synergy between CD79b-targeted therapy and rituximab (Kawasaki, 2022).

Methods: ARC-02-101 is a first-in-human open-label, dose-finding phase 1 study designed to evaluate the safety, tolerability, PK, and preliminary clinical activity of ARC-02 in adults with R/R B-cell NHL. Eligible participants must have received ≥2 prior systemic therapies. Part A will evaluate ARC-02 monotherapy and Part B will evaluate combination with rituximab. Both parts include dose escalation and expansion phases, with commencement of Part B informed by findings from Part A dose escalation. Dose escalation follows accelerated titration design with single-participant cohorts used for the first 2 dose levels, before transitioning to a Bayesian Optimal Interval design. The primary endpoint is safety for the dose escalation part and investigator-assessed objective response rate for dose expansion. Secondary endpoints include additional response determinants and PK. These data will inform the recommended phase 2 dose of ARC-02 monotherapy or in combination with rituximab.

Initial results from LOTIS 7: A phase 1b study of Loncastuximab Tesirine plus Glofitamab in patients with relapsed or refractory diffuse large B cell lymphoma

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Aim:

Loncastuximab tesirine (lonca) is a CD19-directed antibody–drug conjugate, and glofitamab is a CD20×CD3 bispecific T-cell engager; both are approved in the EU and USA for later-line relapsed/refractory (R/R) diffuse large B-cell lymphoma (DLBCL). The phase 1b LOTIS-7 study evaluates the combination of lonca plus glofitamab in patients with R/R aggressive B-cell non-Hodgkin lymphoma (B-NHL).

Method:

LOTIS-7 (NCT04970901) enrolled patients with histologically confirmed R/R B-NHL after ≥1 prior systemic therapy. Lonca was administered intravenously every 3 weeks (Q3W) at escalating doses of 90, 120, or 150 µg/kg, followed by dose expansion at 120 or 150 µg/kg for a fixed duration (≤8 cycles), with dose reduction to 75 µg/kg for cycles ≥3 per label. Glofitamab was given using step-up dosing followed by 30 mg Q3W for ≤12 cycles. Primary objectives were safety, tolerability, and identification of the recommended expansion dose; secondary endpoints included efficacy, pharmacokinetics (PK), immunogenicity, and immune-cell dynamics

Results:

As of 17 January 2025, 31 patients received ≥1 dose of lonca (median age 73 years; 61.3% with ≥2 prior therapies; 19.4% prior CAR-T therapy; 45.2% primary-refractory disease). The most common grade ≥3 treatment-emergent adverse event was neutropenia (32.3%). Cytokine release syndrome (CRS) and immune effector cell–associated neurotoxicity syndrome (ICANS) were limited to grade 1–2 (CRS: 38.7%; ICANS: 6.5%), with no grade ≥3 events. In the efficacy-evaluable population (n=22), the objective response rate was 95.5%, with a complete response rate of 90.9%; median duration of response was not reached. Among responders, 20 of 21 remained in complete response at data cut-off. PK analyses demonstrated comparable lonca exposure versus historical monotherapy, with lower C_{max}. Immune profiling showed T-cell margination, increased activated CD4⁺ and CD8⁺ T cells, and evidence of immune activation with modest IL-6 induction.

Conclusion:

Loncastuximab tesirine combined with glofitamab demonstrated a manageable safety profile and encouraging antitumor activity in heavily pretreated patients with R/R aggressive B-cell lymphoma, supporting continued clinical evaluation of this combination.

Lymphoma incidence and prevalence projections, Australia, 1982–2045: a statistical modelling study

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Aim:

The Australian Institute of Health and Welfare (AIHW) publishes prevalence projections for aggregate non-Hodgkin lymphoma (NHL) and Hodgkin lymphoma (HL) but not by NHL subtype, despite marked clinical heterogeneity. We projected incidence and prevalence to 2045 for HL and three NHL subtypes — diffuse large B-cell lymphoma (DLBCL), follicular lymphoma (FL), and mantle cell lymphoma (MCL) — in Australia, by sex.

Method:

Age–period–cohort models were fitted to AIHW incidence data (1982–2021 for HL/NHL; 2003–2021 for subtypes) using natural cubic splines, with damping of future period and cohort effects. Counts were obtained by applying modelled rates to ABS Series B population projections. Prevalence at 2-, 3-, 5-, 10-, and 40-year durations was computed by a modified counting method incorporating projected survival. 95% credible intervals were derived from 1,000 Monte Carlo draws.

Results:

Between 2021 and 2045, projected annual cases rose substantially: HL +34% (females) / +68% (males); aggregate NHL +65% / +69%; DLBCL +45% / +50%; FL +13% / +35%; MCL +169% / +141%. Age-standardised rates declined for most subtypes — MCL was the exception — indicating that incidence growth is driven by population ageing rather than rising age-specific risk. 5-year prevalence across the four modelled subtypes rose from approximately 18,300 (2021) to 27,200 (+48%) and 40-year prevalence from 58,500 to 112,000 (+92%); sensitivity analyses with no continued survival improvement reduced 40-year prevalence by only ~7%, indicating ageing was the dominant driver of prevalence growth. Aggregate NHL and HL incidence projections agreed within 2–5% of AIHW (2026–2035).

Conclusion:

Both case counts and prevalence will rise substantially to 2045, driven primarily by Australia's population ageing. Subtype-specific projections fill a gap in AIHW publications and can inform health technology assessment and haematology workforce planning.

Successful use of etoposide base formulation following severe immediate hypersensitivity reaction to etoposide phosphate in a patient with Burkitt lymphoma

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Introduction:

Hypersensitivity reactions occur in approximately 1-3% of patients treated with etoposide and are characterised by hypotension, bronchospasm, urticaria, and respiratory distress.

Hypersensitivity reactions to etoposide base are well documented and thought to be largely due to the polysorbate 80 solvent, rather than the drug itself. In contrast, such reactions to etoposide phosphate are rarely reported and often thought to be reactions to the drug itself, rather than a solvent.

We describe a case in which etoposide phosphate treatment was discontinued following an immediate hypersensitivity reaction, with subsequently well-tolerated etoposide base treatment.

Case Summary:

A 33-year-old male with Stage IV Burkitt lymphoma received R-CODOX-M alternating with R-IVAC chemotherapy. During the first cycle of R-IVAC, rituximab had been administered 4 hours prior without complication. Three minutes into the first etoposide phosphate infusion, he developed a severe reaction with hypotension (BP 80/57mmHg), tachycardia (HR 137bpm), bronchospasm and reduced alertness.

ICU admission and treatment with adrenaline was required. Thirty minutes after the etoposide reaction, serum tryptase level was 10.3microg/L. It peaked to 11.5microg/L ~3 hours after the infusion commenced and decreased to 4.5microg/L ~24 hours later. This first-dose reaction was suggestive of a non-IgE anaphylactoid chemotherapeutic sensitivity, with the modest rise tryptase attributed to hypotension.

Chemotherapy restarted four days later without etoposide phosphate. Etoposide base formulation was introduced on day 5 with a slower infusion over 60 minutes. Pre-medications included oral loratadine, paracetamol, IV promethazine, IV hydrocortisone and oral/IV dexamethasone. These were gradually tapered and all pre-medications were ceased by the final day of treatment without recurrence of hypersensitivity.

Conclusion:

Severe immediate non-IgE mediated hypersensitivity reactions to etoposide phosphate may not always represent a reaction to etoposide itself. Thus, there is a role for re-challenge with etoposide base. This supports alternative formulations in managing etoposide hypersensitivity. One further cycle of R-IVAC is planned using etoposide base.

ALK-positive ALCL: first described adult case of synchronous CNS and systemic involvement at presentation: a case report and review of the literature

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Aim:

Anaplastic large cell lymphoma (ALCL) represents a group of heterogenous CD30+ mature T Cell lymphomas, which vary in their clinical, histological, and molecular characteristics. A majority of ALCL are ALK positive, which is characterised by translocation t(2;5) leading to the fusion of the ALK gene to the nucleophosmin gene. CNS presentations of ALCL are rare and restricted to case reports. A synchronous CNS and systemic presentation in an adult has never been reported. This paper aims to report this novel presentation and to present a viable treatment strategy for this condition.

Methods:

A 31-year-old woman presented with headache and tonic-clonic seizures. MRI revealed a 15-mm enhancing left frontal convexity lesion with broad dural contact. A left frontal craniotomy was performed, and pathological analysis was conducted. Initially the diagnosis was unclear, with the most likely diagnosis being thought to be ALK-positive histiocytosis, with a differential of ALK-positive ALCL. The patient was treated with a modified MARIETTA protocol (without rituximab) and consolidated with a carmustine-based autologous stem cell transplant. End of treatment PET-CT and MRI brain showed a complete metabolic response. shows complete metabolic response on PET-CT and MRI brain.

Results:

A modified MARIETTA protocol (without rituximab) and consolidation with carmustine-based autologous stem cell transplant, has been demonstrated to be a viable treatment strategy for adult synchronous CNS and systemic presentation ALK-Positive ALCL.

Conclusions:

This case presents the first successful treatment of a synchronous presentation of CNS and systemic ALK-positive ALCL, and the importance of a multidisciplinary approach for diagnosis.

Performance status the dominant reason for patients not proceeding to CAR-T in relapsed/refractory DLBCL: a single centre real world Australian experience

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Aim:

CAR-T cell therapy has demonstrated superior outcomes compared to salvage chemotherapy in relapsed/refractory (R/R) DLBCL/tFL, however not all patients receive this treatment. To assess factors that limit CAR-T use, a review of all patients with R/R DLBCL/tFL is required, including those not formally referred for CAR-T.

Method:

We performed a retrospective audit of all patients diagnosed with R/R DLBCL at Princess Alexandra Hospital (PAH) since CAR-T cell therapy program commencement in May 2025. Patients referred from external centres were not included.

Results:

From March 2025 to April 2026, 19 patients within PAH were diagnosed with R/R DLBCL/tFL. Eight patients were assessed as eligible for CAR-T, with one patient declining CAR-T. All 7 consenting patients proceeded, with none failing collection, manufacture, nor failing to reach infusion. Median time from relapse to apheresis was 25 days, and median vein-to-vein time was 28 days. Holding radiotherapy was required for one patient. Patients were bridged with radiation (n=4), R-GemOx (n=1), continued epcoritamab (n=1) or observed (n=1). Three patients were not eligible due to late relapsing disease. Of the remaining eight patients considered not suitable for CAR-T, 6 patients (75%) had ECOG ≥ 2 , one patient did not have adequate histology, and one patient had disease trajectory considered unbridgeable. One patient initially deemed not suitable was re-assessed after progression on epcoritamab and proceeded to CAR-T.

Conclusion:

In this patient population, less than 50% of patients diagnosed with R/R DLBCL/tFL received CAR-T cell therapy despite rapid access to apheresis and limited requirement for holding therapy. Of those not proceeding, performance status was the most significant barrier, accounting for >50% of patients not receiving CAR-T. This study may still underestimate rates of R/R DLBCL patients not proceeding to CAR-T as well as other patient barriers, as only data from within a CAR-T treatment centre was available.

A retrospective single centre study describing frailty in elderly diffuse large B cell lymphoma (DLBCL) using the Clinical Frailty Score (CFS) and its association with adverse outcomes

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Aim: Frailty has been associated with adverse outcomes such as mortality and treatment related side effects in elderly DLBCL patients. The Clinical Frailty Score (CFS) is a quick effective tool in characterising a patient's underlying frailty and has been validated for retrospective use in research studies. There is not much known on the use of CFS in DLBCL patients and its potential correlation with adverse outcomes.

Method: A retrospective study was conducted by reviewing existing medical records of new diagnosis DLBCL in patients aged 65 years and over, from January 2019 – December 2023, treated at Western Health. CFS scores were retrospectively allocated to each patient based on documented functional status. Statistics was done using Excel and SPSS. Chi-square analysis was done for comparing outcomes between fit (CFS 1-4) and frail (CFS 5-9) groups for categorical variables.

Results: A total of 81 patients were included in the study, with the median age being 74 years. The overall median stage of disease was III with a predominance of GCB subtype (n = 34, 41.9%). 25 patients (30.8%) died within 24 months of their lymphoma diagnosis, most commonly from lymphoma, followed by infections. 16 of the 81 (19.8%) relapsed within 24 months of diagnosis with median time to relapse 6.4 months. The median CFS was 4. There was no statistically significant difference between the fit and frail groups for relapse, death, Grade 3-4 adverse events, end of treatment PET CMR results and non-completion of treatment. There was statistical significance for chemotherapy dose reduction (p = 0.043) in the frail group compared to the fit group. Statistical analysis is ongoing for Kaplan-Meier curves for PFS and OS between the two groups.

Conclusion: CFS of 5 or more was associated with dose reduction during DLBCL treatment in patients aged 65 years and older.

Managing early-stage unfavourable Hodgkin Lymphoma in Pregnancy: A case of successful treatment with BEACOPDac escalated dose and ABVD

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Aim:

To describe a case of Hodgkin Lymphoma (HL) in pregnancy successfully treated with the “2+2” regimen: 2 cycles of escalated dose bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, dacarbazine, prednisolone (BEACOPDac escalated dose) followed by 2 cycles of doxorubicin, bleomycin, vinblastine, dacarbazine (ABVD).

Background:

HL is the most common lymphoma in pregnancy. The recent position statement by Mills et al., stated that patients with aggressive lymphomas in pregnancy should receive standard of care haematological treatment where possible, aiming to optimise maternal survival.¹

Case:

A 40-year-old woman, G4P1M2, presented in 2025 at 10 weeks gestation in an IVF pregnancy with painless lymphadenopathy. Core biopsy was performed, followed by a staging PET at 12 weeks demonstrating adenopathy above the diaphragm in >3 nodal regions, diagnosing early-stage unfavourable classic HL.²

ABVD is the traditional pregnancy regimen for HL with the most maternal and fetal/neonatal outcome data. However, outside pregnancy, the standard is now the 2+2 regimen, which improved progression free survival compared to ABVD with reduced long-term toxicities.^{3, 4, 5} Individually, these agents have been used safely in 2nd and 3rd trimesters of pregnancy.

Multidisciplinary counselling, discussing maternal and fetal risks of treatment was undertaken with haematology, obstetrics, and Mothersafe (teratology).

She received 2 cycles of BEACOPDac escalated dose commencing at 13 weeks gestation followed by 2 cycles of ABVD without dose reduction, complicated by one admission with febrile neutropenia. Elective Caesarean-section occurred at 37 weeks after preterm prelabour rupture of membranes. Birthweight was 2270g, (5-10th centile) requiring an 18-day admission for feeding, with no congenital abnormalities. The placental was small and histopathology showed patchy low grade chronic villitis and maternal vascular malperfusion. Fetal growth and placenta most likely reflected in-utero cytotoxic exposure.⁶ Maternal end of treatment PET postpartum demonstrated a complete metabolic response (Deauville 3).

Conclusion:

This case report represents the first reported successful use of BEACOPDac escalated dose followed by ABVD, for early-stage unfavourable HL during pregnancy.

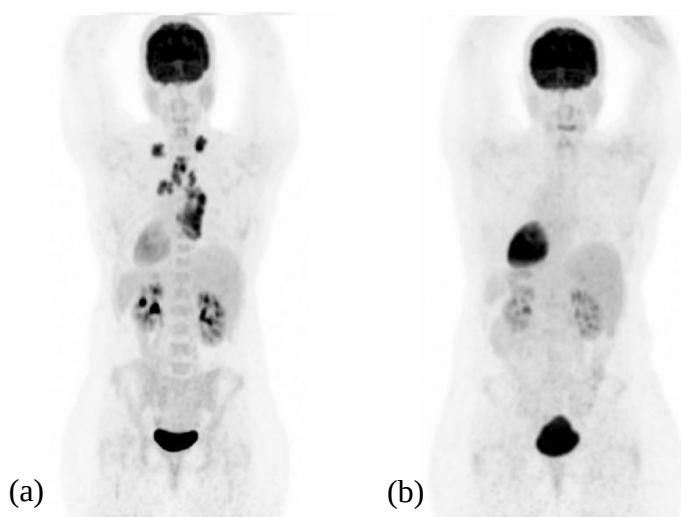


Figure 1: Comparison of pre-treatment PET (a) with post-treatment PET (b) demonstrating complete metabolic response

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Outcomes of pirtobrutinib in second-line (2L) chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL) after first-line (1L) cBTKi therapy: BRUIN phase 1/2 and BRUIN CLL-321 studies pooled analysis

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Aim:

Pirtobrutinib, a highly selective, non-covalent BTKi, was safe and effective in the BRUIN Phase-1/2, which was confirmed in the phase-3 BRUIN CLL-321 study. Both studies were conducted in a broad population of patients with R/R CLL/SLL, including those pre-treated with a cBTKi. We report the safety/efficacy of pirtobrutinib for patients with 2L CLL/SLL, using pooled data from the BRUIN Phase-1/2 and CLL-321 studies.

Method:

This pooled analysis on BCL2i-naïve patients with CLL/SLL, treated with 2L pirtobrutinib after 1L cBTKi therapy with/without an anti-CD20 antibody evaluated investigator-assessed PFS/iwCLL 2018 criteria, OS, time-to-next-treatment (TTNT), and safety.

Results:

37 eligible patients (BRUIN Phase-1/2:n=17; CLL-321:n=20) received pirtobrutinib 200mg daily and received prior cBTKi treatment with ibrutinib (76%), acalabrutinib (14%), zanubrutinib (8%), or other cBTKi (3%), and CD20 antibody (11%). 22/26(85%) had unmutated IGHV gene, 13/30(43%) had mutated *TP53*, and 15/31(48%) had del(17p). Patients discontinued prior cBTKi therapy due to disease progression (57%), toxicity (35%). Median follow-up was 30.3-months, median PFS was 19.5-months(95%CI:11.7-44.7). Median PFS for patients who discontinued their previous cBTKi due to disease progression:13.9-months(95%CI:7.4-19.5) and toxicity:44.7-months(95%CI:10.6-not estimable). Median TTNT for all patients:32.5-months(95%CI:16.6-47.4). Median OS was not reached; the 24-month OS rate was 81.1%(95%CI:61.9-91.3). Median time-on-treatment was 17.6-months(range:0.9-57.2), and 35% remained on pirtobrutinib at data-cutoff. 97% experienced ≥1 tx-emergent adverse event (TEAE), most-commonly anemia (27%), neutropenia (24%), hemorrhage (22%), and pneumonia (22%). Grade≥3 TEAEs occurred in 68%. TEAEs of atrial fibrillation/flutter occurred in 1 patient, hypertension in 5, and hemorrhage in 8 patients. Treatment-related AEs led to pirtobrutinib dose reductions in 3 patients.

Conclusion:

Pirtobrutinib demonstrated clinical benefit and tolerability in 2L CLL/SLL pre-treated with a cBTKi, including those with high-risk genetic features. Pirtobrutinib is a 2L option after 1L cBTKi use and may help inform future treatment sequencing strategies.

Clinical outcomes of Loncastuximab Tesirine in relapsed/refractory DLBCL in routine practice from a Regional Australian Centre

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Title (in sentence case):

Aim:

Loncastuximab tesirine (loncastuximab) is a CD19-directed antibody–drug conjugate used in relapsed or refractory diffuse large B-cell lymphoma (R/R DLBCL). This study aimed to evaluate the efficacy, tolerability, and feasibility of loncastuximab in routine clinical practice.

Methods:

We retrospectively reviewed patients with R/R DLBCL treated with loncastuximab at Cairns Hospital in 2025. Clinical characteristics, treatment outcomes, and adverse events were analysed.

Results:

Five patients were included. The age at treatment initiation ranged from 71–79 years, with two males and three females. Diagnoses included three de novo DLBCL, one high-grade B-cell lymphoma, and one transformed DLBCL. Three patients had received four prior lines of systemic therapy, while the remaining patients had received three and two prior lines, respectively. None had undergone stem cell transplantation, and one patient had prior chimeric antigen receptor T-cell (CAR-T) therapy. Three patients had refractory disease to their most recent treatment, while two had relapsed disease. Four patients received more than six cycles of loncastuximab (range, 2–12 cycles). Best response assessment showed partial response (PR) in four patients, while one patient developed progressive disease (PD) after cycle 2. The patient with PD had an overall survival (OS) of 70 days, whereas patients achieving PR had OS approaching 300 days or longer.

The most common adverse events were rash and fluid retention. Notably, four patients discontinued treatment because of fluid retention.

Conclusion:

Loncastuximab appears to be an effective treatment option for heavily pretreated patients with R/R DLBCL in real-world practice. However, fluid retention is a significant toxicity that requires close monitoring and proactive management.

Autologous stem cell transplant in Peripheral T-cell lymphoma, single centre experience

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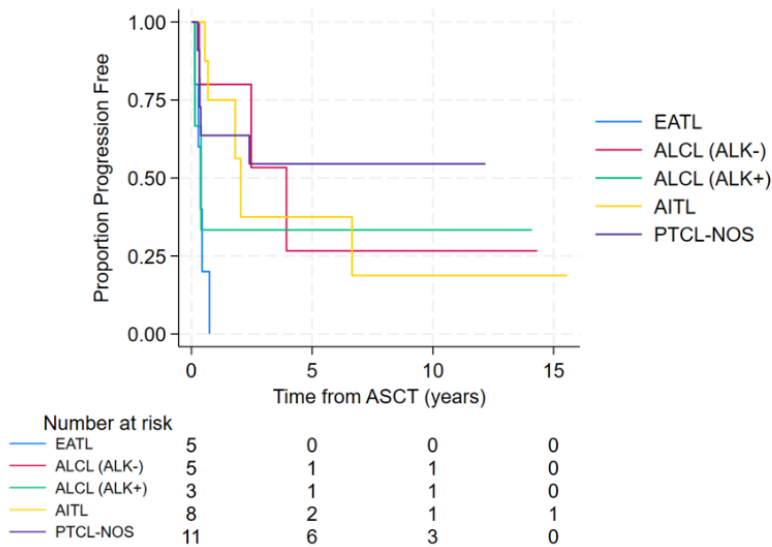
Aim: Peripheral T-cell lymphomas (PTCL) are a rare group of lymphoid malignancies with a heterogenous, but overall poor prognosis. This study aimed to determine the outcome of patients with PTCL undergoing autologous stem cell transplant (ASCT) at the Royal Brisbane and Women's Hospital (RBWH).

Method: Patients who underwent ASCT for PTCL at RBWH between September 2006 and November 2025 were evaluated. Baseline disease characteristics, prior treatment and pre-transplant disease status were assessed. Kaplan-Meier method was used to determine progression-free survival (PFS) and overall survival (OS). Cox proportional hazards modelling was used to assess impact of prognostic factors.

Results: Thirty-two patients were identified for analysis; 11 PTCL-NOS, 8 AITL, 5 EATL, 5 ALK+ ALCL, 3 ALK- ALCL. Patients were predominantly male (21/32) with a median age of 53 (26-72) and median prior lines of therapy (PLOT) of 1 (1-3). Pre-transplant disease status was complete remission (CR) in 26 patients (22 CR1, 4 CR2) and partial response (PR) in 6. At a median follow-up of 10.6 years, the median OS was not met. 19/32 (59%) patients relapsed; 8 (25%) survived, including 3 (9%) with follow-up <6 months and 5 (16%) who underwent allogeneic stem cell transplant. Mortality occurred in 13/32 (41%) patients, predominantly of PD (38%) with only 1 transplant-related mortality (3%). Median PFS was 2.04 years (range 0.14-15.56). Relapse occurred in all five patients with EATL, 5/6 patients in PR and 5/7 patients with >1 PLOT (Figure 1). Two-year OS was lower in patients with PR vs. CR (21% vs. 71%, HR 2.39 [0.73-7.9], p=0.18).

Conclusion: ASCT can achieve long-term disease control in patients with PTCL. Outcomes are heavily dictated by histology and pre-transplant disease status. Patients with EATL, best response of PR and relapse after chemotherapy should be prioritised for non-ASCT approaches.

Figure 1: Progression Free survival post ASCT by disease histology



Real-world outcomes of BTKis in patients with relapsed/refractory mantle cell lymphoma (MCL) in Australia: a retrospective analysis using the Australian Pharmaceutical Benefits Scheme (PBS) dataset

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Aim:

In Australia, three covalent Bruton tyrosine kinase inhibitors (BTKis), ibrutinib, acalabrutinib, and zanubrutinib, are approved and reimbursed for treating relapsed/refractory (R/R) MCL. This study evaluated treatment persistence (TP), time to next treatment (TTNT), and overall survival (OS) in patients with R/R MCL.

Method:

This retrospective cohort study used data from 10% of patients who began BTKi treatment for MCL, listed on the PBS, between 1 August 2018 and 31 December 2025. The analysis included only those who began therapy ≥3 months post-PBS listing, excluding those in access programmes before reimbursement. Outcomes by BTKi were 12-month TTNT, OS (both analysed using Kaplan-Meier method), and TP.

Results:

Among 114 patients with R/R MCL, the median age was 76 years, and 74% were male. Treatment distribution was 60% (n=68) ibrutinib, 31% zanubrutinib (n=35), and 10% (n=11) acalabrutinib. Overall median follow-up was 36 months. TP (95% CI) was highest with zanubrutinib at 85% (73-97), versus 42% for both acalabrutinib (14-70) and ibrutinib (32-53). Median TTNT was not reached (NR) for all BTKis; at 12 months, the percentage of patients who had not received subsequent treatment was highest with zanubrutinib (94%; 95% CI: 87-100) and lowest with ibrutinib (82%; 95% CI: 74-90). Median OS was 23 months for ibrutinib, 17 months for acalabrutinib, and NR for zanubrutinib. Twelve-month OS was highest with zanubrutinib (86%; 95% CI: 74-97), compared with ibrutinib (72%; 95% CI: 63-82) and acalabrutinib (50%; 95% CI: 22-78). This trend continued at 24 months: zanubrutinib (78%; 95% CI: 64-93), ibrutinib (56%; 95% CI: 46-67), and acalabrutinib (19%; 95% CI: 0-49).

Conclusion:

Zanubrutinib was associated with improved outcomes (higher TP, delayed TTNT, improved OS) compared with ibrutinib and acalabrutinib in R/R CLL. Results should be interpreted with caution because of potential confounding by treatment era and access to subsequent therapies, including CAR-T.

Combination Bendamustine/Rituximab & Acalabrutinib for first line transplant ineligible mantle cell lymphoma: two case reports

Dr Roohi Mohammed¹

¹Cairns Hospital, Cairns North, Australia

Introduction:

Mantle Cell lymphoma (MCL) is a heterogenous and often aggressive type of non-Hodgkin lymphoma affecting older adults with a median age at diagnosis of 65 years. Treatment of Mantle Cell lymphoma in older, frail, transplant ineligible patients remains a challenge. Current regimens include Bendamustine-Rituximab (BR) or single agent Bruton Tyrosine Kinase (BTK) inhibitors such as Acalabrutinib. We present two transplant ineligible patients with aggressive MCL treated with combination therapy BR + Acalabrutinib accessed compassionately in the first line

Case Presentation:

Case 1 regards a 77-year-old male with stage IV MCL, blastoid variant (splenic and peripheral blood involvement); MIPI 8.3, Ki67 80%. Deemed transplant ineligible due to age and history of heart failure with reduced ejection fraction. Completed 5 cycles of Acalabrutinib + BR with notable side effects being rash and cytopenias.

Case 2 regards a 75-year-old male with Stage IV MCL pleomorphic subtype (osseous, hepatic, splenic and peripheral blood involvement); MIPI 9.5, Ki67 90%, P53 >90%. Deemed transplant ineligible due to age and chronic kidney disease (CKD) stage 3. Completed one cycle of Acalabrutinib + BR. Major side effects include cytopenias requiring transfusion support.

Discussion:

The cases discussed demonstrates the potential efficacy and safety of implementing Acalabrutinib upfront in combination with BR for older, frail, transplant ineligible patients in Australia. Case 1 demonstrated clinical remission after 5 cycles with minimal adverse events while Case 2 showed a reduction in peripheral blasts and LDH with tolerable side effects to date. Longitudinal data and larger cohorts are needed to assess overall and progression free survival in this subgroup. However, these cases shed light into how chemotherapy-free combination strategies could improve outcomes for older, high-risk patients.

An inherited curse: A case of T-PLL with germline ATM gene mutation and concurrent thyroid malignancy

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Introduction

T-PLL is a rare LPD and has poor prognosis. We describe a case of T-PLL with germline ATM mutation.

Case report

A 69-year-old man presented with Platelets $38 \times 10^9/L$, Hb105 g/L, ALC $13.7 \times 10^9/L$, ANC $1.8 \times 10^9/L$. 12 months prior he was found to be a heterozygous carrier of pathogenic ATM variant; c.7271T>G p.(Val2424Gly). Flow on blood showed an expanded T-lymphocyte population expressing CD2/CD3/CD4/CD5/ CD7/TCR alpha/beta and negative for CD1a/CD8/CD56/CD57/CD16. Bone marrow aspirate was dry. Trephine showed a T-cell infiltrate with the same immunophenotype as in the peripheral blood. FISH on blood confirmed loss of one copy of ATM and TCRA/D rearrangement. Molecular studies showed mutations in p. (Val2424Gly) VAF68% p.(Ala573Val) VAF29% and STAT5B p.(Asn642His) VAF4%. Two clones were detected on TCR clonality testing. PET/CT showed disease confined to the marrow, an incidental finding of FDG-avid thyroid nodule was subsequently found to be a papillary carcinoma.

The patient received 12 weeks of Alemtuzumab 30mg IV three times weekly. At completion his Hb 95g/L ANC $1.1 \times 10^9/L$ Platelets $115 \times 10^9/L$ and ALC $0.7 \times 10^9/L$. Marrow showed residual T-lymphocytes with marked fibrosis and osteosclerosis. No secondary cause was found to explain the desmoplastic reaction and sclerosis. MRD testing done on blood using NGS (LymphoTrack) was positive at 7.15×10^{-5} with emergence of a new TCR clone at 4.04×10^{-3} . PET/CT showed new FDG-avidity in cervical and inguinal lymph nodes. This is consistent with a partial response to therapy. He was consolidated with a reduced intensity allograft.

Conclusion

Germline ATM mutations are associated with T-PLL. The other molecular findings in this case are typical of T-PLL. Activating variants in JAK/STAT pathway are common subclonal mutations. The unusual feature of this case was the marked marrow sclerosis and fibrosis which are rarely described in T-PLL.

Time to first fever is strongly associated with subsequent severe ICANS in r/r LBCL treated with axi-cel

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Aim: Axicabtagene ciloleucel (axi-cel) is now standard-of-care treatment for relapsed/refractory large B-cell lymphoma (r/r LBCL) in second line (2L) and beyond. However, immune effector cell associated neurotoxicity syndrome (ICANS) is a serious adverse event that can result in significant morbidity and mortality. Pre-infusion patient and disease characteristics were analysed to identify factors associated with time of onset of sequential grades of cytokine release syndrome (CRS) and ICANS and the temporal relationship between toxicity events.

Method:

Patients treated with axi-cel at a single Australian centre between 01/08/2021–31/12/2025 were included. Univariable and multivariable logistic regression was used for the occurrence of toxicity events, while Cox proportional hazards was performed for time to events

Results:

222 patients were included. The median age was 65 (range 16–85) years; 46% were ECOG 1+; 24% received 2L axi-cel; histological subtypes included DLBCL (58%), transformed lymphoma (23%), high grade lymphoma (12%) and other (7%). Median time to onset of first fever $\geq 38.0^{\circ}\text{C}$ ($G \geq 1$ CRS) was 29h (range 5–317h). On univariable analysis, only male sex (HR 1.43; 1.07–1.89) and 2L vs 3L+ therapy (hazard ratio (HR) 1.79; 1.30–2.44) were associated with earlier fever. Only ECOG ≥ 1 (odds ratio (OR) 2.09; 1.03–4.06) and disease bulk $\geq 10\text{cm}$ (OR 3.27; 1.38–7.74) pre-infusion were associated with $G \geq 3$ ICANS. Univariable spline analysis demonstrated a strong association between time to first fever and subsequent occurrence of $G \geq 3$ ICANS (Figure 1). Risk of $G \geq 3$ ICANS was 36% with first fever at < 24 hours, 19% at 24–48 hours, 6% at 48–72 hours and 5% at > 72 hours. On multivariable analysis, this relationship was independent of baseline variables (ECOG, bulk, bridging response and LDH).

Conclusion:

Early onset of fever is strongly associated with subsequent severe ICANS in axi-cel-treated patients with r/r LBCL and may warrant more intensive observation and/or earlier intervention.

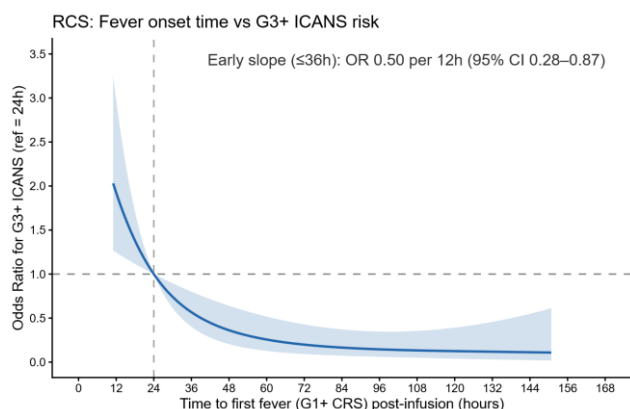


Figure 1: Relationship between time to first fever and OR for severe ICANS (with reference to 24h) in R/R LBCL patients treated with axi-cel.

Superior overall survival from mogamulizumab compared to vorinostat in patients with relapsed/refractory mycosis fungoides or Sézary syndrome: an unanchored matching-adjusted indirect comparison

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Aim: Mycosis fungoides (MF) and Sézary syndrome (SS) are rare, frequently incurable and often debilitating cutaneous T-cell lymphomas, typically necessitating multi-line treatment courses. In the phase 3 MAVORIC trial (NCT01728805), patients with relapsed/refractory MF/SS receiving mogamulizumab had significantly longer progression-free survival compared with those receiving vorinostat. However, >70% patients on vorinostat crossed over to mogamulizumab when permitted by the study protocol, confounding comparison of overall survival (OS). Using real-world data from patients treated with vorinostat, this study aimed to estimate the effectiveness of mogamulizumab relative to vorinostat on OS in patients with MF/SS.

Method: Unanchored matching-adjusted indirect comparisons were performed. Individual patient data from MAVORIC (mogamulizumab arm; N=186; data cut-off 2 March 2019) were reweighted on age group, sex, histology, disease stage at treatment initiation, and Eastern Cooperative Oncology Group performance score to match baseline characteristics of the vorinostat cohort (N=67) from an Australian population-based Cutaneous Lymphoma Database. Hazard ratios (HRs) were estimated using a Cox regression model.

Results: Following reweighting, median OS was not reached for mogamulizumab (effective sample size [ESS]=102, weighted median follow-up 39.6 months, 95% CI 38.1–46.3) and was 31.0 months (95% CI 21.1–41.2) for vorinostat (median follow-up 58.1 months, 95% CI 46.8–non-estimable) (Figure 1). Patients receiving mogamulizumab had significantly longer OS (HR 0.48; 95% CI 0.30–0.76; p=0.002). This significant survival benefit persisted when patients in the mogamulizumab arm who subsequently underwent an allogeneic stem cell transplant were removed from the analysis (ESS=97; HR 0.51; 95% CI 0.32–0.80; p=0.004).

Conclusion:

This study presents the first comprehensive survival comparison of mogamulizumab and vorinostat, leveraging real-world data to overcome treatment cross-over limitations inherent to the earlier phase 3 trial. These findings provide supportive evidence that mogamulizumab may offer an OS advantage over vorinostat, benefitting Australian patients with relapsed/refractory MF/SS.

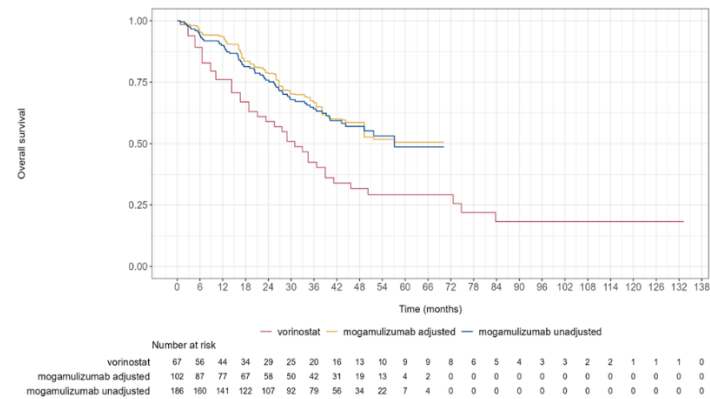


Figure 1. OS in the unadjusted and adjusted MAVORIC mogamulizumab arm and CLD vorinostat cohort

Improved control of patient-reported symptoms and health-related quality of life (HRQL) in patients with mycosis fungoides (MF) and Sézary syndrome (SS) treated with mogamulizumab in the PROSPER study

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Aim:

MF and SS may cause a significant symptom burden and impair HRQL. In the phase 3 MAVORIC trial, mogamulizumab was associated with greater reductions in pruritus and improvements in HRQL than vorinostat. The PROSPER study investigated the impact of mogamulizumab on a wider array of symptoms and HRQL in patients with MF/SS in real-world practice, incorporating cutaneous T-cell lymphoma (CTCL)-specific patient-reported outcome measures.

Method:

Patients starting mogamulizumab completed a CTCL-specific symptom diary (severity of skin itch, pain, redness, and flaking; frequency of sleep problems; difficulty regulating body temperature), an MF/SS-specific measure of HRQL (MF/SS-CTCL QoL), and the Brief Fatigue Inventory (BFI) before treatment and at regular intervals thereafter.

Results:

Seventy-three patients were enrolled: 56% MF, 44% SS; 52% male; 82% white; mean (SD) age 67.2 (12.2) years; mean mogamulizumab treatment cycles 9.3 (4.2); 60, 61, and 58 patients, respectively, completed the Symptom Diary, MF/SS-CTCL QoL, and BFI at baseline. Mean scores for skin itch, flaking, and redness improved from baseline to week 48 (−2.5, −3.1, and −3.1, respectively); all changes exceeded the minimum important difference (MID) from week 4 (Table 1). Skin pain scores improved to −1.7 at week 48; changes exceeded the MID from week 12. The sleep problems score improved by ≥2 points for 4% of patients at week 4 and 30% at week 48. Temperature regulation improved for 23% of

patients at week 4 and 37% at week 48. Improvements in BFI scores were less than the MID at all timepoints but for SS patients were achieved in all scores at week 48. The MF/SS-CTCL QoL score improved from baseline to week 48 (-8.8) and exceeded the MID from week 12.

Conclusion:

Mogamulizumab provides rapid and sustained symptomatic improvements as early as week 4, and in HRQL as early as week 12. The improvements were sustained throughout the 48-week study.

BICICL: A phase IB/II study of BTK and Immune Checkpoint Inhibitor in CNS Lymphoma

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Aim:

The prognosis for relapsed or refractory CNS lymphoma is poor with median survival measured in months. We sought to evaluate the efficacy of the combination of zanubrutinib and tislelizumab in patients with relapsed/refractory (RR) primary or secondary CNS lymphoma (SCNSL) and treatment-naïve patients unfit for chemotherapy (UC).

Method:

Adult patients with histologically confirmed CNS lymphoma, either RR or UC, and without systemic involvement were enrolled. Treatment consisted of 4-9 weeks lead-in with oral zanubrutinib followed by IV tislelizumab. Overall response rate (ORR) defined as the proportion of patients achieving a best response of CR or PR was the primary endpoint. The sample size based on methods by A'Hern and Fleming was 30 with early termination for futility should the observed response rate be <50% at 17 weeks.

Results:

17 patients including 9 with RR PCNSL, 3 with UC PCNSL and 5 with SCNSL were included. Median age was 73 (53-87). The median follow up was 2.6 months with several early progressors. The best ORR was 7/17 (41%) with CR 2 (12%) and PR 5 (29%). At the time of reporting all but 3 (2 PCNSL, 1 SCNSL) had progressed with a median DoR of 6 months. Responses in these 3 were durable and ongoing at 14, 31 and 34 months. Early progression resulted in several patients being unable to receive tislelizumab resulting in a protocol amendment to shorten zanubrutinib lead in. However the study was terminated for futility at the SDMC recommendation based on the low ORR. Patients had high levels of comorbidity and infection was common.

Conclusion:

Clinical studies in CNSL are challenging due to patient age and comorbidity. While ORR was low, a proportion of patients had durable responses. Correlative studies to identify response predictors are ongoing.

Application of machine learning in predicting lymphoma treatment outcomes

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Aim:

To develop and validate predictive models for treatment response to first-line therapy in patients with B-cell lymphomas.

Method:

The study developed and internally validated a nomogram and machine learning (ML) algorithms using universally collected clinical features, biomarkers, and inflammatory nutritional markers from 33 hospitals to assess the predictive value of treatment response. Data from 2763 patients with diffuse large B-cell lymphoma, follicular lymphoma, mantle cell lymphoma and Burkitt lymphoma enrolled in the Lymphoma and Related Diseases Registry (LaRDR) were randomly divided into training (n = 2221, 80%) and validation (n = 553, 20%) cohorts. The performance of six ML algorithms, including K-nearest neighbours, support vector machines, random forests, and extreme gradient boosting, benchmarked against logistic regression, was assessed. Model performance was evaluated using a discrimination metric (area under the curve (AUC)), classification metrics, calibration and decision curve analysis (DCA).

Results:

In the final model, six predictors (stage, ECOG performance status, lactate dehydrogenase, anemia, BCL2 expression, and systemic immune-inflammation index) were included. The performance of all ML algorithms and standard regression was comparable, with validation cohort AUCs ranging from 0.69 to 0.70. The nomogram achieved an AUC of 0.70 (95% CI: 0.65–0.75) compared to the Revised International Prognostic Index (AUC = 0.61, 95% CI: 0.56–0.66) and the National Comprehensive Cancer Network International Prognostic Index (AUC = 0.63, 95% CI: 0.57–0.68). Decision curve analysis demonstrated the superior clinical utility of the nomogram compared with existing prognostic indices.

Conclusion:

While our nomogram, which incorporates routinely collected clinical, inflammatory, and molecular markers, demonstrated improved discrimination and clinical utility compared with existing prognostic indices, further external validation is needed before clinical integration.

CD19-directed third generation CAR T-cells incorporating a Toll-like receptor 2 co-stimulatory domain may confer improved safety via reduced IFN- γ and GM-CSF production

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Aim:

Second-generation anti-CD19 chimeric antigen receptor (CAR) T-cells incorporating CD28 (1928z; axi-cel/brexu-cel) are standard care for refractory/relapsed (r/r) large B-cell and mantle cell lymphomas. However, they are associated with high rates of cytokine release syndrome (CRS) and immune effector cell-associated neurotoxicity syndrome (ICANS). Modifying CAR signalling domains can affect the balance between efficacy and toxicity.

Toll-like receptor 2 (TLR2) is a pattern recognition receptor expressed by activated T-cells, and can serve as a costimulatory signal, enhancing memory formation and modifying cytokine profile. We explored the impact of a TLR2-derived Toll/IL-1 receptor domain (TIR) domain within a 3rd generation CD19-directed CAR T-cell product (1928T2z) on efficacy and safety.

Methods:

We explored the impact of a TLR2 domain on CAR T-cell activity *in vitro*. Clinically, we evaluated 1928T2z CAR T-cells incorporating CD28 and TLR2 costimulatory domains in a phase 1 trial for r/r B-cell lymphomas (ENABLE-1; NCT04049513).

Results:

In vitro, 1928T2z CARs provided comparable cytotoxicity to 1928z, while lower levels of CRS and ICANS-associated cytokines IFN- γ and GM-CSF were observed at both gene and protein levels. Genetic mutation of the TLR2-TIR impeded CAR activity, and TLR2 position relative to CD3 ζ affected cytokine production, indicating that both TLR2 domain activity and position contribute to 1928T2z function. Among heavily pre-treated patients (n=30; median 4 lines of prior therapy; 47% prior stem cell transplantation; dose range $5 \times 10^4 - 1 \times 10^6$ /kg), we observed complete response rate of 53% and favourable safety, with no grade 3+ CRS and a single case of grade 1 ICANS.

Conclusion:

Incorporating a TLR2 co-stimulatory domain into CD28-costimulated anti-CD19 CAR T-cells reduces CRS- and ICANS-associated cytokines in a position-dependent manner, while preserving *in vitro* cytotoxicity. These findings align with phase 1 trial data demonstrating a low incidence of CRS and ICANS. A multicentre phase 2 trial (ENABLE-2; NCT06486051) is enrolling.

A case of IgG-secreting lymphoplasmacytic lymphoma

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Introduction:

Lymphoplasmacytic lymphoma (LPL) is a rare low grade B cell lymphoproliferative disorder. IgM LPL or Waldenström macroglobulinaemia often presents with symptoms of hyperviscosity, however this is reliant on the presence of high molecular weight IgM. Non-IgM subtypes represent 5% of total cases which include IgA LPL, IgG LPL and non-secretory subtypes. Given the rarity of the disease, there is minimal published data available regarding the diagnosis and treatment of non-IgM LPL.

Case Study:

We describe a case of a 70-year-old male with a background of aortic sclerosis, depression and osteoarthritis who was referred for haematological review with fatigue and increased duration and severity of infections. There were no lytic lesions, renal impairment, weight loss or lymphadenopathy. He was found to have mild normocytic anaemia and an IgG kappa paraprotein of 32g/L.

A PET scan showed diffuse sclerotic bone change with mild FDG-avidity in the spleen and bone marrow. Bone marrow biopsy showed a hypercellular marrow with a diffuse interstitial infiltrate which included a spectrum of lymphoid, plasmacytoid and plasma cells. The plasma cells were kappa restricted and CD38 positive, but they showed an unusual immunophenotype for LPL as they were largely CD19 negative and CD56 positive, a phenotype commonly associated with multiple myeloma, whereas LPL plasma cells are typically CD19 positive and CD56 negative. There was also a more typical kappa-restricted lymphocyte population that was CD19 and CD20 positive, and CD5 and CD10 negative. Next-generation-sequencing demonstrated a classical molecular profile for LPL with MYD88 and CXCR4 variants.

In the limited literature on non-IgM LPL, it is associated with a worse overall survival, increased extramedullary disease and shorter time from diagnosis to treatment. Due to the lack of data available, there is no standardised treatment regimen.

Conclusion:

This case adds to the paucity of literature available on the presentation and diagnosis of non-IgM lymphoplasmacytic lymphoma.

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Comparing relative dose intensity and delays of Lymphoma treatment in Māori and non-Māori patients.

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Aim:

Māori have poorer survival outcomes across most cancers, including lymphoma, yet the causes remain unclear. Differences in chemotherapy density could contribute. This study aimed to determine whether a difference exists in lymphoma patients, with respect to relative dose intensity (RDI), dose intensity (DI), or treatment delays between Māori and non-Māori in Hauora a Toi Bay of Plenty.

Method:

A retrospective, single-centre, observational study was conducted across two hospital sites (Tauranga and Whakatāne). The cohort was derived from ePharmacy, identifying all lymphoma patients who received dose-limited chemotherapy between 2020 and 2025. A total of 180 patients were included, 25 Māori and 155 non-Māori. Comparisons of demographic and clinical features between the Māori and non-Māori patients were undertaken using independent t-tests and chi-square or Fisher's exact tests. Logistic regression analysis was used to determine the association between RDI and delay for Māori and non-Māori.

Results:

Māori were significantly younger (mean 56.9 vs 66.8 years, $p=0.003$). There were no significant differences in diagnosis, stage, HCT-CI, or regimen. Logistic regression analyses showed that Non-Māori patients had approximately threefold higher odds, OR = 3.092 (95% C.I. 1.059-9.028, $p = 0.039$), of dose reduction than Māori patients. Toxicity was the primary reason for dose reduction (61%). A delay in treatment was seen in 35% of patients, with no difference between Māori and Non-Māori (OR = 1.331; 95% C.I. 0.694-2.553, $p=0.389$). Almost all delays were shorter than one week.

Conclusion:

Māori patients did not receive lower chemotherapy dose intensity or experience greater treatment delays than non-Māori. These findings suggest that disparities in lymphoma survival are unlikely to be explained solely by differences in chemotherapy delivery and warrant further investigation into other contributing factors.

A single-centre experience of bacterial infections after CAR T-cell therapy for haematological malignancies

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Aim:

CAR T-cell therapy is an effective immunotherapy for haematological malignancies; however, it can result in significant infectious complications. We aimed to evaluate the incidence and outcomes of clinically significant bacterial infections in CAR T-cell recipients at the Alfred Hospital.

Method:

We retrospectively reviewed all adult patients who received CAR T-cell therapy in 2024 and developed positive bacterial cultures during their post-infusion admission. Clinically significant infections were defined as positive bacterial cultures associated with infectious signs or symptoms and requiring systemic antimicrobials. Data included demographic (age, sex), treatment-related (diagnosis, CAR T-cell product, toxicity and immunosuppression rates), microbiological (bacterial species, infectious syndrome) and survival outcomes.

Results:

Fifty-two CAR T-cell infusions were administered in 2024. Median age was 68.5 years (range:32-84). The most common indication was DLBCL (67.3%). Ten patients (19.2%) developed clinically significant positive bacterial cultures, accounting for 12 infectious episodes. Median time from infusion to first positive culture was 8.9 days (range:8-106). Median neutrophil count at the time of first positive culture was $0.17 \times 10^9/L$ (range:0.00-2.41). Bacteraemia was most common (11 cultures), followed by urine (3), faecal (2), and sputum (1). Gram-positive (most commonly staphylococcal species) and gram-negative (most commonly *Escherichia coli*) organisms accounted for seven and four bacteraemia cases, respectively. Sepsis of unclear origin was the most common clinical syndrome (n=6). Four infectious episodes were polymicrobial. Patients with positive cultures had longer admissions than those without (median:28.5 vs 14 days, $p=0.0059$), but similar rates of CRS (90% vs 80.9%, $p=0.67$) and ICANS (40% vs 35.7%, $p=1$). Eighty percent (n=8) of patients with positive cultures received immunosuppressive therapy for CAR T-cell-related toxicities, most commonly dexamethasone and tocilizumab. Three deaths (one infection-related) occurred among patients with positive cultures.

Conclusion:

Clinically significant positive bacterial cultures post-CAR T-cell infusion are common and associated with prolonged hospitalisation, emphasising the importance of early investigations and Infectious Diseases team involvement.

Lymphoma treatment in inborn errors of immunity: The promises and pitfalls in the era of adoptive immunotherapy

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Case Study:

The advent of immunotherapy has transformed lymphoma management, shifting treatment away from conventional chemotherapy. However, these therapies depend on an intact immune system. Although rare, inborn errors of immunity (IEI) comprise a heterogeneous group of disorders characterised by immune dysfunction and are over-represented in lymphoma. We present a case of Autoimmune Lymphoproliferative Syndrome (ALPS) due to FAS mutation complicated by EBV-positive immunodeficiency-associated lymphoproliferative disorder (IA-LPD).

A 34-year-old female presented with bulky mediastinal lymphadenopathy in the context of known ALPS on the basis of family history and FAS mutation. Biopsy confirmed EBV-positive IA-LPD with composite DLBCL/cHL histology. Initial tumour-directed therapies included R-CHOP, GDP, BEAM + AuSCT and brentuximab vedotin which failed to achieve durable remission. The patient was subsequently enrolled on the TREBL-1 trial of novel immunotherapy comprising sequential rituximab/ibrutinib (8 weeks) followed by four infusions of HLA-matched third-party EBV-virus-specific T-cells (EBV-VST). Serial peripheral blood mononuclear cells collected throughout this trial demonstrated poor T-cell viability in culture (6–44%), however polyclonal (PMA/ionomycin) and EBV-specific stimulation showed increasing CD8+ T-cell effector cytokine production during this regimen (Figure 2). Yet, these immunological findings did not translate to a clinical response. However, 7 months after EBV-VST infusion, checkpoint inhibition with pembrolizumab achieved complete response after 4 cycles. This response was consolidated with allogeneic stem cell transplant from a FAS wildtype sibling donor and the patient remains in remission at five years.

Conclusion:

This case highlights the complex interplay between IEI and the emerging armament of immunotherapies in lymphoma. Poor ex-vivo growth kinetics support use of third-party over autologous cell therapies, while restored effector function supports a role for immune adjuvants and third-party cellular therapies. Early identification of IEI at diagnosis should be a consideration in patients with clinical or family history suspicious for IEI and

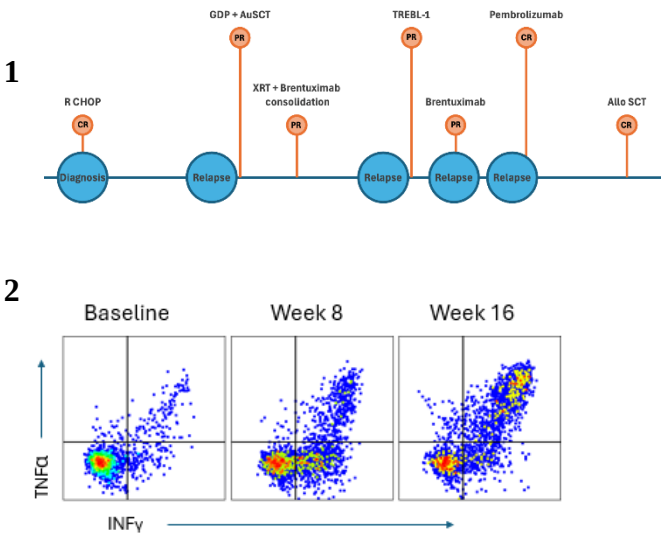


Figure 1: Timeline of diagnosis with therapies, best response in the orange circle.

Figure 2: Flow cytometric analysis of CD8+ T-cell effector cytokine production following polyclonal stimulation (PMA/ionomycin) at A) baseline, B) week 8 following rituximab-ibrutinib and C) week 16 following 4 cycles of EBV-VST therapy, demonstrating progressive restoration of T-cell effector function during treatment

Retrospective audit on the use of soluble CD25 assay (sCD25) as a diagnostic and prognostic tool for haemophagocytic lymphohistiocytosis (HLH) in New Zealand

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Aim:

To evaluate the appropriateness and indication for sCD25 testing at Auckland Hospital LabPlus, identify an optimal cut-off for the Quantikine ELISA assay, and evaluate the prognostic ability of sCD25 in HLH.

Method:

Fifty-eight New Zealand patients had relevant clinical and biochemical parameters collected based on HScore and HLH-2004 criteria. Patients with HLH had prognostic information gathered. Correlation and multivariate regression analysis was performed.

Results:

Nineteen patients had HLH. sCD25 was of utility in conjunction with other HLH-2004 criteria and HScore in diagnosing HLH. However, in isolation, sCD25 did not have diagnostic or prognostic significance. sCD25 correlated with HScore and number of HLH-2004 criteria met prior to considering invasive or specialised investigations.

Conclusion:

The current local restrictive approach to sCD25 testing for diagnosis of HLH continues to be appropriate. Development of formal indications for testing, based on fulfilment of other HLH-2004 criteria, and HScore, may improve consistency and resource utilisation. A local sCD25 cut-off for optimising HLH diagnosis or prognosis was not identified.

High-dose methotrexate for post-transplant lymphoproliferative disorder with central nervous system involvement in patients with kidney failure: a case series

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Background:

High-dose methotrexate (HDMTX) is standard of care for patients with post-transplant lymphoproliferative disorder (PTLD) and central nervous system (CNS) involvement; however, clinical guidelines recommend avoiding HDMTX in kidney failure due to toxicity.

Methods:

We report two cases of HDMTX used for PTLD with CNS involvement following kidney transplant in patients with kidney failure.

Results:

Case 1: A 55-year-old male on chronic haemodialysis (HD) following failed kidney transplant presented with unilateral weakness, a parietal mass on MRI brain and FDG-PET avid lesions in his liver and kidney allograft. A liver biopsy confirmed EBER-positive DLBCL. He was treated with immunosuppression reduction, rituximab and four cycles of 1g/m² HDMTX with daily high volume haemodiafiltration (HDF) until methotrexate cleared. He experienced transient mucositis that did not recur in future cycles. He cleared methotrexate appropriately in all cycles, and achieved a CMR on FDG-PET and PR on MRI brain.

Case 2: A 47-year-old male kidney transplant recipient with CKD IV presented with unilateral weakness and visual disturbance, with a parieto-occipital mass on MRI brain and no extracranial involvement on FDG-PET. A brain biopsy demonstrated EBER-positive DLBCL. He was treated with immunosuppression reduction, rituximab and two cycles of 1g/m² HDMTX. HDF was employed when methotrexate levels were elevated above threshold, however, methotrexate was cleared by 96 hours in both cycles. The patient experienced no toxicity or renal impairment, though had small-volume PD on repeat MRI and is awaiting further treatment.

Conclusion:

We have demonstrated that HDMTX can be effectively and safely delivered to patients with kidney failure through rigorous fluid status monitoring, regular MTX levels and use of high volume HDF if required. HDMTX is the mainstay of front-line treatment for CNS lymphoma and its use should be strongly considered in patients with kidney failure despite minimal historic data, particularly given advances in haemodialysis techniques.

Immunohistochemical practice in the diagnosis of DLBCL, LaRDR study

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Aim:

Diffuse large B-cell lymphoma (DLBCL) is a heterogeneous group of aggressive lymphomas with an array of biological subtypes classified by immunohistochemistry (IHC). Despite published guidelines, approaches to IHC vary by jurisdiction. This study aimed to evaluate IHC testing practices in Australian DLBCL patients using national registry data and benchmark against 5th edition WHO-Haem 2022, National comprehensive care management (NCCN), European haematology association (EHA), Spanish society of medical oncology and Oncology group for treatment and study of lymphomas (SEOM-GOTEL) and Australasian lymphoma Alliance (ALA) criteria.

Method:

This national Lymphoma and Related Diseases (LaRDR) study analysed prospectively recruited adult DLBCL cases between 2016-2025. Source histopathology reports and clinical data entered into the registry were reviewed for IHC results. These were compared against a reference panel developed from above listed guidelines and expert consensus.

Results:

647 eligible patients were included. 15% met recommended panel, 46% met EHA panel, 39% SEOM-GOTEL, and 2% ALA criteria.

CD20 expression was reported in 96%, and cell-of-origin (COO) markers in 86-92% with COO assignment reported in 88% (Table 1). Markers required for excluding differential diagnoses frequently missing; 52% reported the follicular markers CD21/CD23 and markers for mantle cell lymphoma (MCL) were unreported in 20%. Prognostic markers e.g., EBER-ISH were reported in 55% of cases. There were no significant differences in the percentage of complete IHC panel between cases with surgical/excisional biopsies and those with core biopsies, suggesting a lack of tissue was not a that influenced panel completeness.

Conclusion:

Suboptimal uptake of comprehensive IHC panels for DLBCL diagnosis exists in Australia, impacting diagnostic accuracy and treatment selection. Standardised reporting and expert

Table 1: Rates of reporting and positivity in registry patients.

Total evaluable (n=647)				
	Not reported (%)	Reported (%)		
		Total	Positive	Negative
Standard IHC panel				
CD20	26 (4)	621 (96)	615	6
CD3	172 (26)	475 (74)	5	470
CD5	169 (26)	478 (74)	42	436
CD10	50 (8)	597 (92)	289	308
CD23	395 (61)	252 (39)	54	198
CD21	478 (74)	169 (26)	41	128
MUM1	92 (14)	555 (86)	364	191
BCL2	73 (11)	574 (89)	477	97
BCL6	68 (12)	579 (89)	515	64
MYC	117 (18)	530 (82)	350	179
EBER-ISH	289 (45)	358 (55)	26	332
Markers for specific conditions				
CD30	373 (58)	274 (42)	69	205
PAX5	482 (74)	165 (26)	162	3
CD79a	611 (94)	36 (6)	33	3
CD22	600 (93)	47 (7)	44	3
ALK	575 (89)	72 (11)	2	70
Cyclin D1	364 (56)	283 (44)	8	275
SOX11	614 (95)	33 (5)	1	32
Oct-02	631(98)	16 (2)	15	1
BOB1	635 (98)	12 (2)	11	1
FOXp1	645 (>99)	2 (<1)	1	1
GCET1	645 (>99)	2 (<1)	1	1
LMO2	643 (>99)	3 (<1)	3	0
CD38	601 (93)	46 (7)	31	15
CD138	605 (94)	42 (6)	12	30
Cyclin D2	647 (100)	0 (0)	0	0

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review in the context of multidisciplinary team meetings are needed to improve diagnostic fidelity.

Clinical features and outcomes of Methotrexate associated DLBCL-Australian Study

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Aim:

Methotrexate-associated diffuse large B-cell lymphoma (MTX-DLBCL) arises in the setting of chronic immunosuppression for autoimmune disease. Evidence guiding prognosis and treatment, particularly in Western populations, remains limited. We evaluated clinical characteristics, treatment patterns, and survival predictors in a multicentre cohort of patients with MTX-associated DLBCL.

Method:

We performed a retrospective analysis of patients diagnosed with MTX-associated DLBCL across six tertiary centres in Australia. Baseline clinicopathologic features were collected. Overall survival (OS) and progression-free survival (PFS) were estimated using Kaplan–Meier methods, and predictors of outcome were assessed using univariable Cox proportional hazards models.

Results:

Forty-one patients were included. Median age at diagnosis was 68 years (range 29–87), and 73% were female. Rheumatoid arthritis was the commonest underlying autoimmune disease (61%), followed by CNS involvement in 10%. EBV-ISH positivity was detected in 21%. Most patients (83%) received R-CHOP or R-CHOP-like chemoimmunotherapy, with methotrexate withdrawal in 66%; 20% had involved-site radiotherapy. Median follow-up was 44 months. Median OS was not reached, with estimated 5-year OS of 76.7% (95% CI 64.6–90.3) and PFS of 76.5% (95% CI 61.1–92.2).

NCCN-IPI risk category significantly discriminated OS ($p=0.025$), with no deaths in low/intermediate-low risk patients versus median OS of 53 months in intermediate-high/high risk groups. ECOG performance status was also associated with OS (HR 6.56, 95% CI 1.21–34.9; $p=0.027$). Neither EBV status nor treatment with rituximab alone versus chemotherapy significantly impacted outcomes.

Conclusion:

MTX-associated DLBCL in this multicentre cohort demonstrated favourable overall outcomes despite frequent high-risk features. Conventional risk stratification using NCCN-IPI remained prognostic. Further studies are needed to define the role of treatment de-escalation in selected patients.

Advanced stage classical hodgkin lymphoma with antecedent multisystem langerhans cell histiocytosis: a case report and review of the literature

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Aim:

To describe an adult case of stage IV classical Hodgkin lymphoma (HL) arising shortly after a diagnosis of multisystem Langerhans cell histiocytosis (LCH), and to summarise the adult literature on LCH–HL associations.

Method:

We describe the clinical course, pathologic and molecular features of an adult initially diagnosed with LCH who subsequently developed HL, and review adult cases and registry data on LCH-associated lymphoma.

Results:

A 45-year-old man presented with constitutional symptoms and widespread FDG-avid lymphadenopathy with splenic uptake on PET. Supraclavicular lymph node biopsy demonstrated partial nodal effacement with CD1a-positive, CD68-negative histiocytic cells; ALK and CD30 staining were negative, with no Reed-Sternberg cells. Next-generation sequencing (NGS) identified no pathogenic variants including BRAF or C-KIT. He commenced methotrexate and cytarabine but had persistent B symptoms, splenomegaly, and a mixed metabolic response with new nodal sites after 2 cycles. Repeat cervical node biopsy showed large atypical CD30-positive, MUM1-positive cells with a high Ki-67 index, diagnostic of classical HL; RNA fusion analysis and targeted NGS were unrevealing. He commenced escalated BEACOPDac, achieving complete metabolic response on interim and end-of-treatment PET.

A large international dataset describes 154 adult patients with LCH-associated malignancies, of whom 32 had HL. A dedicated lymphoma–LCH series identified five patients with concurrent classical HL; two achieved complete remission with first-line ABVD/AVD, while three were relapsed/refractory requiring salvage therapy. Escalated BEACOPDac has not previously been reported as frontline HL therapy in the LCH setting, making this, to our knowledge, the first such case.

Conclusion:

This case illustrates a rare sequence of multisystem LCH rapidly followed by stage IV classical HL in an adult, both lacking identifiable driver mutations on targeted sequencing yet achieving a durable complete metabolic response to escalated BEACOPDac. New or persistent B symptoms or discordant PET findings after LCH-directed therapy should prompt timely re-biopsy to exclude occult lymphoma, and intensive HL-directed chemotherapy should be considered in fit patients with advanced-stage disease.

Pirtobrutinib in treatment-naïve (TN) patients with chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL): pooled results from BRUIN CLL-313 and BRUIN CLL-314

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Aim:

Pirtobrutinib, a highly selective, non-covalent BTKi, is approved globally for patients with CLL/SLL pre-treated with a covalent BTKi. BRUIN CLL-313 and BRUIN CLL-314 are randomized phase 3 studies evaluating pirtobrutinib in patients with CLL/SLL, including in the TN setting [versus bendamustine+rituximab (BendaR; CLL-313) and versus ibrutinib (CLL-314)].

Method:

Pooled data from TN CLL patients randomized to receive pirtobrutinib from CLL-313 and CLL-314 were used to assess efficacy and safety. PFS and OS estimates were calculated by the Kaplan-Meier method.

Results:

A total of 253 TN patients, median age of 66 yrs, were assigned to receive pirtobrutinib (CLL-313:n=141; CLL-314:n=112); 252 received treatment. Efficacy was consistent between the two studies. Overall, ORR was 93.3%. Median PFS was not reached; the 24-month PFS rate was 93.2% (95%CI:89.1-95.8). Median OS was also not reached; the 24-month OS rate was 97.5% (95%CI:94.6-98.9). Median duration of therapy was 29.1 months. Treatment discontinuation due to TEAEs occurred in 4.8% of pts with 1.6% treatment related. Any-grade infection occurred in 59.9% of pts; neutropenia in 18.3% and grade ≥3 bleeding in 2.4%. Any-grade hypertension occurred in 10.7% of pts and atrial fibrillation/flutter was reported in 2.8%.

Conclusion:

In 253 TN patients with CLL, pirtobrutinib showed a high ORR and favorable 24-month PFS and OS rates. The safety profile was consistent with prior studies using pirtobrutinib in more heavily treated patients, with low rates of atrial fibrillation/flutter, hypertension and TEAE-

related discontinuations. These findings reinforce the potential of pirtobrutinib as a meaningful and clinically relevant treatment option for patients with TN disease.

Prognostic significance of lactate dehydrogenase among the patients with diffuse large B-cell lymphoma: a meta-analysis

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Aim:

The International Prognostic Index (IPI) has proven to be a valuable tool for prognosticating aggressive non-Hodgkin lymphoma. However, its use in accurately identifying high-risk patients and guiding treatment is poor. Further, the prognostic significance of isolated lactate dehydrogenase (LDH) for patients with diffuse large cell B-cell lymphoma (DLBCL) remains under investigated. Thus, the objective of this research was to assess the prognostic significance of LDH on the overall survival (OS) and progression free survival (PFS) of patients with DLBCL by meta-analyses.

Method:

The hazard ratios (HRs) of multivariate or univariate analysis for OS and PFS between the normal LDH and the elevated LDH group were obtained by searching pertinent literature in the PubMed, EMbase, Science Direct, and OVID databases from inception to August 2024. The pooled HR were then calculated using a fixed or random effect using RevMan 5.4 software. The Q test was used to examine heterogeneity. For statistical significance, a p-value of less than 0.05 was used.

Results:

Eight qualifying publications totaling 1599 DLBCL cases were included in the total. The analyses revealed non-significant heterogeneity among set of studies. The pooled results of the univariate analysis showed that elevated LDH was a significant indicator for poor overall survival (OS) (HR = 1.83, 95% CI = 1.58–2.13, $p < 0.00001$, $I^2 = 46\%$). The pooled effect analysis for multivariate OS produced a statistically significant result as well (HR = 1.89, 95% CI = 1.46–2.44, $p < 0.00001$, $I^2 = 0\%$). Further, elevated LDH was significant indicator of poor PFS (pooled univariate PFS, HR = 2.54, 95% CI = 1.69–3.81, $p < 0.00001$, $I^2 = 0\%$).

Conclusion:

LDH strongly correlated with worse OS and PFS in DLBCL patients. LDH might be suggested as a low-cost prognostic biomarker in DLBCL.

NF-E2 variant in an adult patient with isolated thrombocytopenia

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Case Study:

NF-E2 (Nuclear Factor, Erythroid 2) is a heterodimeric transcription factor, important in all steps of megakaryocytic maturation and formation of proplatelets. Structurally, this protein is 373 amino acids long; containing a N-Terminal transactivation domain, Cap'n'Collar domain, Basic region and Leucine Zipper (bZIP) region.

NF-E2 knock-out mice have demonstrated arrest of late megakaryocytic maturation and consequent severe thrombocytopenia. Previous case reports describe the homozygous *NF-E2* mutation as the cause for severe thrombocytopenia in humans. In humans, *NF-E2* has been implicated in a number of myeloid malignancies; including myeloproliferative neoplasms (MPN), myelodysplastic neoplasms (MDS) and myeloid sarcoma (MyS). Mice models suggest that *NF-E2* mutations alone are sufficient to induce an MPN phenotype; whilst in both mice and human models *NF-E2* are associated with a increased risk of transformation to AML.

Here we describe a case of a 56-year-old male with historically intermittent, mild thrombocytopenia (platelet count 80-100x10⁹/L) during periods of intercurrent illness. He was diagnosed with Prurigo Nodularis initially treated with topical steroids followed by methotrexate. This resulted in a precipitous fall in his platelet count (nadir 58x10⁹/L) which did not improve on cessation of methotrexate nor commencement of oral corticosteroids. There was no splenomegaly present. A bone marrow biopsy, demonstrated a normocellular marrow with adequate trilineage haematopoiesis, noting a proportion of small, monolobate megakaryocytes. His cytogenetics were normal. Next Generation Sequencing (NGS) revealed a *NF-E2*p.(Pro82_Tyr83delinsHis) mutation with a variant allele frequency of 3% as the sole abnormality. This mutation lies within the N-terminal transactivation domain and we postulate that it has resulted in impaired production of proplatelets, resulting in thrombocytopenia in our case.

Conclusion:

More research is required to understand the true effect of these mutations on underlying disease biology, as the evidence suggests that some mutations may induce a proliferative phenotype, whilst others induce thrombocytopenia.

Haematoinflammatory diseases: Multidisciplinary team management of VEXAS and beyond.

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Haematoinflammatory disease is an emerging concept which recognises the interplay between haematological diseases and immune dysregulation, encompassing newly recognised conditions such as VEXAS and established haematology–rheumatology overlap conditions. These diseases cross specialty boundaries, leading to diagnostic delay and fragmented care. Multidisciplinary team (MDT) management is recommended in VEXAS guidelines and can improve outcomes in complex multisystem diseases. Thus, a dedicated haematoinflammatory MDT was established at Prince of Wales Hospital.

Aim:

To describe presentations of haematoinflammatory disease, focusing on VEXAS syndrome, and evaluate the impact of our MDT on the diagnosis, investigation, and management of patients with suspected haematoinflammatory disease.

Method:

A 12-month retrospective audit was performed. Cases were categorised into six subgroups using clinical, laboratory, imaging, bone marrow, and genetic data. MDT impact was assessed by diagnostic clarification, investigation and management changes.

Results:

46 cases were reviewed: VEXAS syndrome (n=10), clonal haematopoiesis of immunological significance (n=5), autoinflammatory diseases with haematological features (n=10), primary haematological disorders with inflammation (n=12), haemophagocytic lymphohistiocytosis (n=2) and connective tissue diseases with haematological features (n=7). MDT discussion resulted in a new or amended diagnosis in 13%, cross-specialty investigations in 15%, and management changes in 61%.

Investigation recommendations included bone marrow biopsy and targeted next generation sequencing. Management changes included adjustment of immunomodulatory therapy and initiation of marrow-directed treatments.

The VEXAS cohort included *UBA1* variants M41L (n=4), M41V (n=1), M41T (n=5). Three had additional clonal haematopoiesis variants. Treatments included tocilizumab, JAK inhibitors, and azacitidine.

Conclusion:

We describe the first haematoinflammatory MDT in Australia and the largest Australian VEXAS cohort to date. A dedicated MDT-assisted diagnosis led to management change in 61%, supporting multidisciplinary care. The VEXAS cohort demonstrated a wide range of clinical features. Azacitidine is emerging as a credible therapeutic option for VEXAS.

Clinical characterization and prognostic impact of systemic autoimmune and inflammatory diseases (SAID) in MDS/MPN Overlap Syndromes.

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Background: Systemic autoimmune and inflammatory diseases (SAID) are increasingly recognized as significant comorbidities in myelodysplastic syndromes and myeloproliferative neoplasms (MDS/MPN). Despite their clinical prevalence, the specific impact of SAID on clinical phenotype and overall survival (OS) remains a subject of debate. This study characterizes the prevalence and prognostic significance of SAID within a tertiary care center, at Liverpool Hospital.

Methods: We retrospectively analyzed 71 patients diagnosed with MDS/MPN overlap syndromes. Patients were stratified by the presence of a documented SAID. Clinical parameters, including full blood count and inflammatory markers, were compared between SAID (n=17) and non-SAID (n=54) subgroups. OS was estimated using the Kaplan-Meier method and evaluated via the log-rank test.

Results: The prevalence of SAID in the cohort was 23.9% (n=17). Baseline hematologic profiles were similar between groups; no significant differences were observed in median WBC ($11.7 \times 10^9/L$), hemoglobin (11.4 g/dL), or absolute monocyte counts ($1.9 \times 10^9/L$) ($p > 0.05$). While not statistically significant, the SAID subgroup trended toward a lower median platelet count (143 vs $148 \times 10^9/L$, $p=0.13$). Furthermore, the rate of AML transformation was comparable between the two groups (17.6% vs 13.0%, $p=0.694$) (Table 1). Kaplan-Meier survival analysis demonstrated that the presence of SAID did not significantly affect OS compared to the non-SAID group (Log-rank = 0.135) (Figure 1).

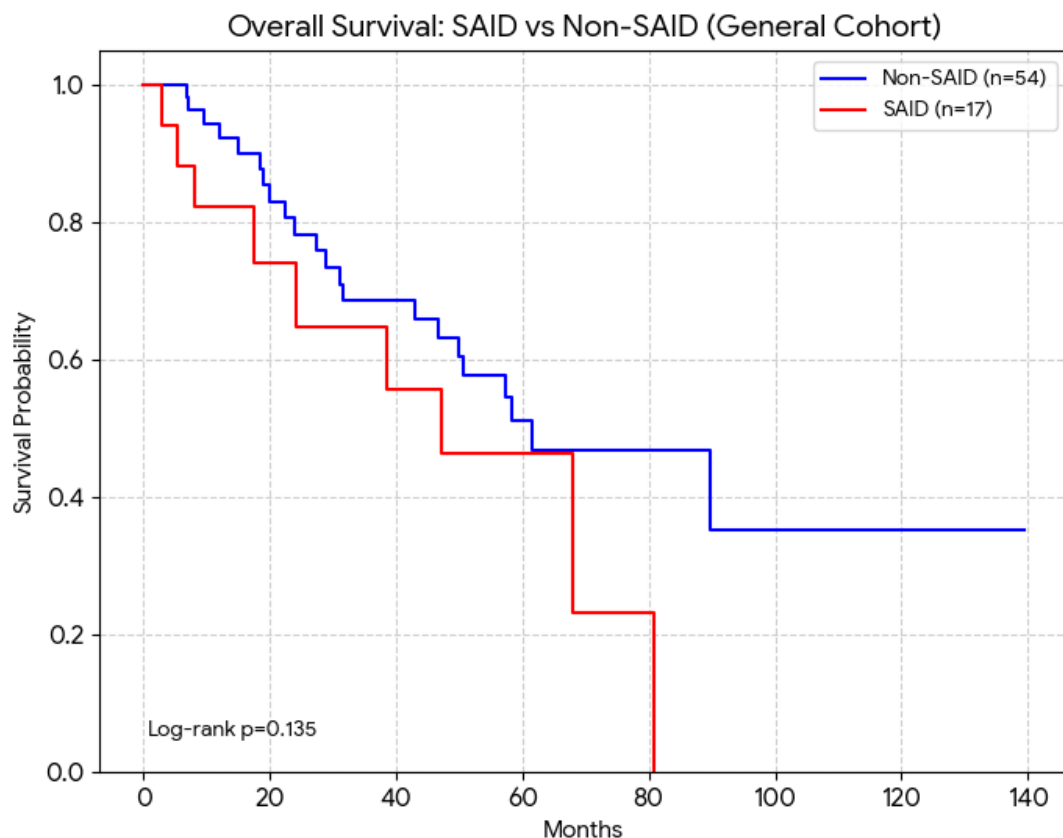
Conclusion: In this cohort, SAID was a frequent clinical feature but did not act as an independent predictor of early mortality or leukemic transformation. These findings suggest that while SAIDs require targeted management for symptomatic relief and quality of life, they do not adversely alter the natural history of the underlying MDS/MPN clone in this population.

Table 1: Clinical and Hematological Characteristics of the Full Cohort (N=71)

Characteristic	All MDS/MPN (n=71)	No Autoimmune (n=54)	Yes Autoimmune (n=17)	P-value
Age, years	75.0 [69.5-80.0]	76.0 [70.0-79.8]	75.0 [69.0-81.0]	0.861
Sex, Female (%)	28 (39.4%)	21 (38.9%)	7 (41.2%)	1
WBC, $\times 10^9/L$	11.7 [7.2-17.8]	11.8 [7.1-18.1]	10.6 [7.5-14.5]	0.681
Hemoglobin, g/dL	11.4 [10.3-12.9]	11.4 [10.3-12.8]	11.4 [10.7-12.9]	0.861
Platelets, $\times 10^9/L$	148.0 [75.0-322.5]	148.0 [95.0-347.0]	143.0 [52.0-198.0]	0.13
Monocytes, $\times 10^9/L$	1.9 [1.4-3.0]	2.2 [1.5-3.3]	1.6 [1.2-2.8]	0.227
ALC, $\times 10^9/L$	2.0 [1.4-3.1]	2.0 [1.4-3.2]	2.0 [1.5-2.6]	1
Peripheral Blasts (%)	0.0 [0.0-1.0]	0.0 [0.0-0.9]	0.0 [0.0-1.9]	0.45
BM Blasts (%)	3.0 [1.0-5.0]	3.0 [1.0-7.0]	4.0 [1.0-4.0]	0.607
LDH, U/L	238.0 [183.5-300.0]	236.5 [186.8-292.8]	238.0 [178.5-357.2]	0.881
CRP, mg/L	4.8 [2.1-13.1]	3.4 [1.9-10.4]	17.4 [7.0-29.2]	0.016
Median Follow-up (mo)	31.6 [13.3-58.3]	40.1 [15.6-60.0]	22.7 [9.9-49.9]	0.13
Overall Survival (mo)	31.6 [13.3-58.3]	40.1 [15.6-60.0]	22.7 [9.9-49.9]	0.13

AML Transformation (%)	10 (14.1%)	7 (13.0%)	3 (17.6%)	0.694
Death (%)	31 (43.7%)	22 (40.7%)	9 (52.9%)	0.546

Figure 1: Overall survival (OS) of MDS/MPN patients stratified by SAID status. Kaplan-Meier estimates of OS in the general cohort (n=71) comparing patients with systemic autoimmune and inflammatory diseases (SAID, red line) vs. those without (Non-SAID, blue line). No significant survival disadvantage was observed (Log-rank $p = 0.135$).



SETBP1 mutations confer adverse prognosis in MDS/MPN Syndromes

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Aim:

To evaluate clinical impact of SETBP1 mutations in MDS/MPN syndromes.

Method:

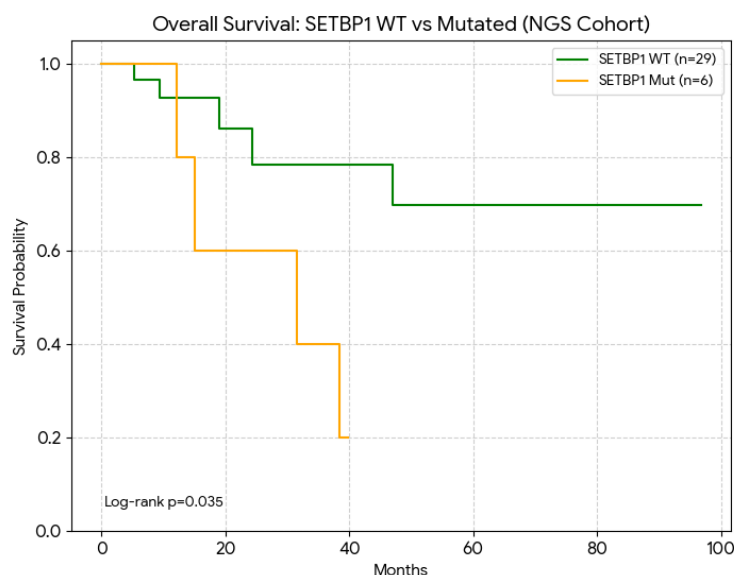
Patients with MDS/MPN diagnosed 2016-2025 were identified in our institutional Leukaemia database. NGS was performed in 35/71 patients (49%). Clinical characteristic and outcomes were sourced from the medical record. Statistical comparisons between SETBP1-mutated and wild-type patients were conducted.

Results:

In the overall cohort median follow-up was 17.4 months, rates of AML transformation and overall mortality were 11.4% and 25.7%, respectively. SETBP1 mutations were identified in 17.1% (n=6). Patients harbouring SETBP1 mutations were younger (age 64.5 vs. 73.0 years; $p=0.023$). SETBP1 mutations were associated with higher percentage of blood blasts (median 2.0% vs. 0.0%; $p=0.014$), higher monocyte count (median 2.8 vs. $1.6 \times 10^9/L$). SETBP1 mutation was associated with five-fold higher rate of AML transformation compared to wild-type (33.3% vs. 6.9%). Survival analysis restricted to the molecularly profiled cohort (n=35) demonstrated significantly inferior OS compared in those mutated SETBP1. (Log-rank $p = 0.035$; Figure).

Conclusion:

SETBP1 mutations were associated with inferior survival in this cohort of MDS/MPN patients



Utility of Iron Staining in Bone Marrow Aspirates in the Era of Next-Generation Sequencing: A Retrospective Single-Centre Study

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Aim:

Bone marrow iron staining is traditionally used to assess iron stores and identify ring sideroblasts (RS), a key feature of sideroblastic anaemia and historically important in the classification of myelodysplastic and myelodysplastic/myeloproliferative overlap neoplasms. Given the de-emphasis on morphology with the adoption of the WHO 2022 classification and increasing availability of next-generation sequencing (NGS), the diagnostic relevance of routine iron staining warrants re-evaluation.

Methods

We retrospectively analysed 101 consecutive adult diagnostic bone marrow examinations (51 myeloid, 50 lymphoid) performed at a regional Australian hospital between January 2023 and June 2024. Perls' Prussian blue staining was routinely performed. Ferritin was available in 76% of cases, and molecular testing in 35% of cases. Two independent reviewers graded bone marrow iron using the Gale score and enumerated RS. Diagnostic impact was categorised as either no impact, supportive but non-essential, or potential diagnostic miss. Interobserver agreement, correlation with serum ferritin, and diagnostic performance for iron deficiency were evaluated.

Results

Iron staining had no diagnostic impact in 94% of cases and was supportive but non-essential in 6%; omission would not have altered the final diagnosis in any case. RS $\geq 15\%$ were identified in seven myeloid cases, including MDS, AML, and therapy-related myeloid neoplasms. SF3B1 mutations were present in three RS-positive cases; RS presence did not independently determine diagnosis. Interobserver agreement for iron grading was good (weighted $\kappa = 0.77$, 95% CI 0.64-0.89). Correlation between marrow iron grade and serum ferritin was weak ($r \approx 0.38$). Low marrow iron grade (≤ 1) showed variable sensitivity (33% to 67%) but high specificity ($>90\%$) for iron deficiency.

Conclusion

Routine bone marrow iron staining rarely influences diagnostic classification in contemporary practice. RS morphology is supportive but not determinative, and marrow iron grading correlates poorly with systemic iron status. These data support a targeted rather than routine approach to marrow iron staining, particularly where NGS is available.

Exceptional long-term remission in therapy-related myeloid neoplasm with azacitidine-based therapy: a case report

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Background:

Therapy-related myeloid neoplasms (t-MN) are associated with a poor prognosis. Reflecting disease heterogeneity, median overall survival ranges from 9-21 months, depending on cytogenetic risk, patient fitness and whether they proceed to allogeneic stem cell transplantation. For transplant ineligible patients, treatment with hypomethylating agents (HMAs) is not considered curative and current guidelines recommend indefinite continuation until disease progression or intolerance. Long-term complete remissions without allogeneic transplantation are exceedingly rare and not well captured in existing literature.

Case:

A 52-year-old female was referred to a tertiary haematology service in Sydney in 2008 with persistent cytopenias following cytotoxic therapy for breast cancer (fluorouracil, epirubicin, cyclophosphamide). Bone marrow assessment demonstrated multilineage dysplasia and 14% blasts, with an aberrant immunophenotype on flow cytometry and random chromosomal losses on karyotype, representing a t-MN by current WHO 2022 classification. Deemed unfit for allogeneic transplantation, the patient was enrolled on a clinical trial of azacitidine and thalidomide. Per protocol thalidomide was discontinued from cycle 13 and she continued on azacitidine monotherapy thereafter. From 2021, dosing frequency was progressively reduced at patient preference, with azacitidine most recently administered six-monthly. A bone marrow biopsy in 2025 demonstrated complete morphological remission with normal karyotype and no mutations detected on myeloid NGS panel. The patient is currently opting for treatment cessation.

Conclusion:

We present a sustained 17-year remission and potential functional cure with azacitidine-based therapy in t-MN without allogeneic transplantation – a duration not previously described in the published literature. Such outcomes are exceedingly rare, reflected by the scarcity of comparable cases. Whether the addition of thalidomide contributed to this exceptional response is unknown. This report asks whether HMA cessation is safe in long-term responders, a scenario not addressed by current guidelines, and raises the possibility that a small subset of patients with MDS/AML may achieve durable remission without allogeneic transplantation. This case adds to the emerging concept of HMA “super-responders” – ultimately challenging the purely palliative framing of azacitidine in myeloid neoplasia.

CEBPA mutations in non-AML myeloid neoplasms

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Aim:

AML with *CEBPA* mutation is a distinct entity associated with favourable risk, characterised by in-frame insertion/deletion mutations within the bZIP domain (bZIP^{InDel}), which may occur alone or as part of biallelic mutations. However, the characteristics of *CEBPA* mutations in non-AML myeloid neoplasms remain unclear. We aimed to define the molecular and clinicopathological features of *CEBPA*-mutated non-AML myeloid neoplasms, namely MDS, MDS/MPN, and MPN.

Methods:

We retrospectively analysed patients with myeloid neoplasms who underwent molecular profiling (AllHaem DNA assay) at the Peter MacCallum Cancer Centre, Melbourne, Australia. Patients harbouring at least one *CEBPA* mutation were identified. Clinical, morphological, cytogenetic, and molecular data were reviewed, including *CEBPA* mutation characteristics and co-mutation profiles.

Results:

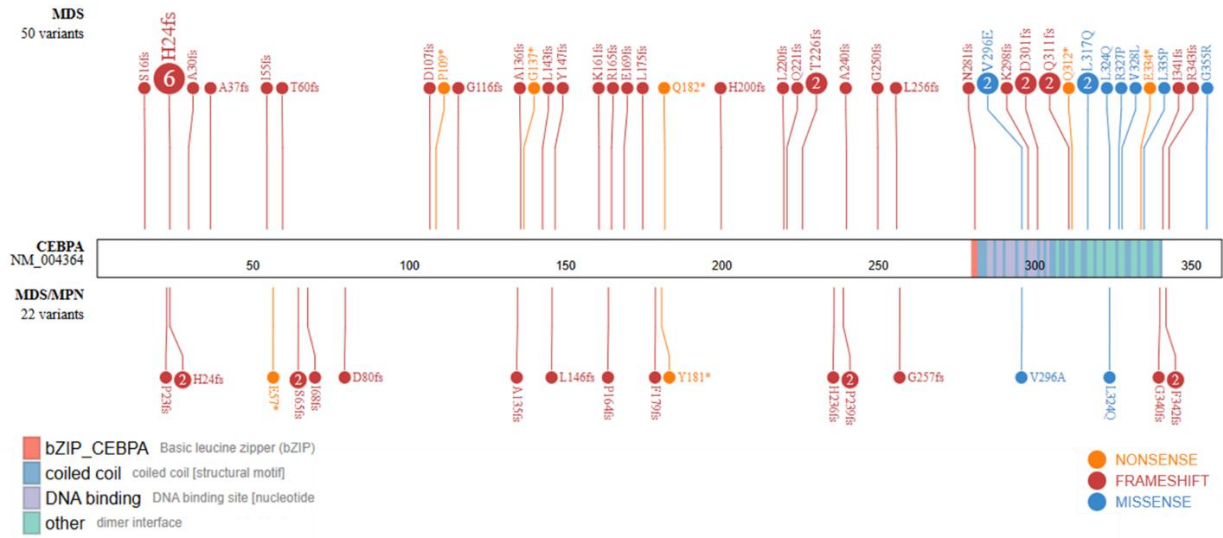
A total of 321 *CEBPA* mutations were identified in 211/6243 (3.4%) patients with myeloid neoplasms: 159/2136 (7.4%) AML, 38/2479 (1.5%) MDS, 13/1127 (1.2%) MDS/MPN, and 4/1456 (0.3%) MPN ($p < 0.001$ by Chi-square test). Out of 79 *CEBPA* mutations in 52 patients with non-AML myeloid neoplasms, 19/50 in MDS, 5/22 in MDS/MPN and 2/7 in MPN were bZIP domain mutations, either truncating (54%) or missense (46%). No bZIP^{InDel} mutations were identified (Figure 1). In contrast, 69% of *CEBPA* mutations in *de novo* AML were bZIP^{InDel}.

In non-AML myeloid neoplasms, *CEBPA* mutations were associated with increased blasts in MDS (76%), MDS/MPN (69%), and MPN (100%, all 4 in blast phase). The most frequently co-mutated genes in non-AML myeloid neoplasms were *ASXL1*, *TET2*, *RUNX1*, *STAG2* and *SRSF2*, in contrast to AML harbouring bZIP^{InDel} mutations, where *WT1*, *GATA2* and *NRAS* predominated.

Conclusion:

CEBPA mutations are uncommon in non-AML myeloid neoplasms but are enriched in patients with high-risk disease and are associated with a co-mutation profile distinct from AML with *CEBPA* mutation. Canonical bZIP^{InDel} mutations were absent in MDS, MDS/MPN and secondary AML, indicating a high specificity for *de novo* AML.

Figure 1: Distribution and type of *CEBPA* mutations in MDS and MDS/MPN.



MDSLink: Update on diagnoses, treatments and clinical outcomes from a Myelodysplastic Syndromes Registry

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Aim:

Update and expand MDSLink registry results with longitudinal follow-up data, including diagnostic, treatment, transfusion and survival data.

Method:

MDSLink is a multicentre, observational, non-interventional cohort study over 270 MDS patients at 4 HREC-approved sites. This analysis presents data from Cabrini and Austin Hospital only (with follow up data available).

Results:

Analysis of 190 patients. Median age 76.7 years; 64% female. Diagnoses: MDS 80.9% (EB 35.5%, MLD 34.9%, SLD 7.9%, RS 11.2%, isolated del(5q) 2.6%, unclassifiable 0.7%), therapy-related myeloid neoplasm 4.3%, MDS/MPN 14.9% (including CMML), other 7.2%. IPSS-R calculated n=161; very low 17.4%, low 36.6%, intermediate 19.1% [*lower risk* 74%], high 13% and very high 13% [*higher risk* 26%].

At baseline, 30% RBC-transfusion-dependent (24.0% of lower risk, 53.3% higher risk) median 4 units in preceding 8 weeks. Platelets administered to 12% (5.8% lower risk, 30.0% higher risk). Growth factors were used in small numbers: EPO 3.4%, GCSF 2.3%. Disease-modifying treatment planned/used in 30.5% including azacitidine 14.4%, chemotherapy 3.4%, venetoclax 2.3%, clinical trial 6.3%.

At median follow up 11.5 months, higher numbers (47.2%) RBC-transfusion-dependent (median 6 units; 41.3% lower, 62.1% higher risk), platelets required 25.0% (median 8 units; lower 17.3%, higher risk 44.8%), EPO 10.2%, GSF 12.0%. Higher numbers were receiving active treatment; azacitidine 27.2%, chemotherapy 10.7%, venetoclax 10.7%.

At any time during follow up, small numbers received immunosuppressive treatment (2.6%), lenalidomide (2%), but substantial numbers (16.1%) participated in clinical trials.

Median overall survival was 59.1months (m); IPSS-R very high 13.9m, high 24.6m, intermediate 59.1m, low/very low not reached.

Conclusion:

MDSlink provides an important resource for describing a cohort of MDS patients not previously captured in Australia. Follow-up data provides a foundation for optimising patient management and informing future clinical decision-making, including resource allocation. Further analysis, including additional patients and subgroups, will be presented.

Childhood MDS driven by somatic co-acquisition of tetrasomy 21 and GATA1 mutation with underlying constitutional t(21;22).

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Case Study:

Acquired somatic mutations in exon 2 of GATA1 are leukemogenic in the context of trisomy 21 and are seen in virtually all cases of Myeloid Leukaemia Associated with Down Syndrome (ML-DS) (WHO 2022), including cases of trisomy 21 mosaicism¹. Co-acquisition of somatic chromosome 21 gain and GATA1 mutation has also been reported in the context of paediatric non-Down syndrome Acute Megakaryoblastic Leukaemia², but not in myelodysplastic syndrome (MDS).

We describe a case of childhood MDS presenting as an incidental finding of macrocytic anemia and thrombocytopenia on routine full blood examination, in a male infant without mosaic or non-mosaic constitutional Down Syndrome. Bone marrow was hypercellular with increased myeloblasts (10-15%), dysmegakaryopoiesis (aberrant CD34 expression and micromegakaryocytes), with mild to moderate dysplasia in the erythroid and granulocytic lineages and secondary myelofibrosis. Flow cytometry detected 5% aberrant erythroid precursors and 0.4% myeloblasts.

G-banded karyotype showed an abnormal male karyotype of 46 chromosomes with an apparently balanced translocation between chromosome 21 and 22 at q?11.2 and p?11.1, respectively. This was subsequently confirmed as constitutional in origin. SNP microarray demonstrated an abnormal male karyotype with gain at 21q (representing tetrasomy 21q) in 20% of cells.

Myeloid panel next generation sequencing on DNA from the diagnostic bone marrow detected a GATA1 frameshift variant in exon 2 (NM_002049.4:c.34_46dup; p.(Pro16LeufsTer28)) at a variant allele frequency (VAF) of 12.2%.

Conclusion:

Co-acquisition of somatic chromosome 21 copy number gain and GATA1 mutation has not previously been described in MDS. We postulate that instability of the constitutional t(21;22) in this case led to tetrasomy 21 and subsequent acquisition of the GATA1 exon 2 mutation, with development of MDS due to a similar mechanism of disease to that of ML-DS.

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Updated phase 2 results of elritercept in patients with transfusion-dependent (TD) lower-risk myelodysplastic neoplasms (LR-MDS)

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Aim:

We report updated safety and efficacy data from a phase 2 trial of elritercept in patients with LR-MDS (NCT04419649).

Method:

The phase 2 study (NCT04419649) enrolled TD patients with IPSS-R Very Low/Low/Intermediate-risk MDS or chronic myelomonocytic leukemia. Dose escalation (n=31) evaluated dosing Q4W; ≤24 cycles; expansion (n=71) evaluated 3.75 mg/kg Q4W (optional up-titration to 5.0 mg/kg). Safety was assessed in all treated patients. Endpoints included RBC TI (≥8 and ≥24 weeks) and hematologic improvement-erythroid (HI-E: Hgb increase ≥1.5 g/dL in low transfusion burden [LTB] or transfusion reduction ≥4 units/8 weeks in high transfusion burden [HTB]) per modified IWG 2006 criteria. TI analyses used mITT24 (≥3.75 mg/kg; baseline ≥2 units; ≥24 weeks on study or discontinued before Week 24).

Results:

As of April 3, 2025, 96 patients were enrolled; median exposure was 13.8 months. Drug-related treatment-emergent adverse events occurred in 44 (45.8%) patients (grade ≥3: 5 [5.2%]); most common were nausea (7.3%) and diarrhea (6.3%). By Week 24, TI ≥8 weeks occurred in 38.5% of evaluable patients (HTB: 29.3%; RS+: 44.2%; non-RS: 28.0%; erythropoietin <500 units/L: HTB 37.2%, RS+ 48.9%, non-RS 43.8%). By Week 48, TI ≥24 weeks occurred in 26.9% (HTB 15.5%); median time to TI was 0.4 weeks (95% CI: 0.3–5.3). Sustained TI ≥24 weeks occurred in 67.3% of patients with TI ≥8 weeks. Median TI duration was 110.9 weeks (95% CI: 24.3–not estimable). By Week 24, HI-E occurred in 49.0% (HTB 48.3%; erythropoietin <500 units/L 51.9%; RS+ 53.1%; non-RS 38.7%); median time to HI-E was 3.1 weeks (95% CI: 1.1–8.1), with median duration 43.9 weeks (95% CI: 24.6–59.1).

Conclusion:

Elritercept was well tolerated and led to rapid, durable responses in patients with LR-MDS, including non-RS and HTB patients.

Hematologic improvement and fatigue reduction with elritercept in participants with lower-risk (LR) myelodysplastic neoplasms (MDS) with non-transfusion dependent anemia: results from an ongoing phase 2 trial

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Aim:

To evaluate hematologic responses and fatigue outcomes with elritercept in non-transfusion-dependent (NTD) participants with LR-MDS and anemia.

Method:

The phase 2 study (NCT04419649) enrolled 15 NTD participants (0 RBC units/8 weeks) who received elritercept at the recommended phase 2 dose (3.75–5 mg/kg, Q4W). Assessments included IWG 2006 hematologic improvement-erythroid (HI-E; mean Hgb increase ≥ 1.5 g/dL over ≥ 8 weeks), hematologic and iron parameters, and quality of life (Functional Assessment of Cancer Therapy-Anemia [FACT-An]; FACIT-Fatigue).

Results:

As of August 30, 2024, 11 of the 15 patients were ring sideroblast (RS) positive and 4 non-RS. Median treatment duration was 84 weeks (13-166). Elritercept was generally well tolerated, consistent with the overall study population. Baseline median Hgb was 9.2 g/dL (8.1-10.5). Thirteen (86.7%) participants achieved HI-E; 11 (73.3%) maintained mean Hgb ≥ 11 g/dL over ≥ 8 weeks. Hgb increases were sustained. Increased Hgb was the most common reason for dose delay (n=8) or reduction (n=5); responses were maintained or regained after modification. Platelet and neutrophil counts were normal at baseline (median 225 and 2.7×10^9 /L) and remained stable or increased within normal limits through 48 weeks. Median baseline ferritin and hepcidin were 417 ng/mL and 9.8 μ g/L, with sustained decreases during treatment. Clinically meaningful improvements in FACIT-Fatigue were observed, particularly in participants with worse baseline fatigue. Among 67% with baseline scores < 40 , improvements exceeded the minimal clinically important difference of 3 by Week 4 and were maintained at Week 24.

Conclusion:

Elritercept was well tolerated and produced robust, durable Hgb responses in NTD LR-MDS, with preserved blood counts, improved iron parameters, and meaningful fatigue reduction, supporting clinical benefit in this population.

Evaluating the prognostic significance of bone marrow fibrosis in patients with Myelodysplastic Syndrome

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Aim:

Over the past years, The Revised International Prognostic Scoring System (IPSS-R) Several studies have shown that bone marrow histology may provide additional diagnostic and prognostic information in patients with myelodysplastic syndrome (MDS). Specifically, bone marrow fibrosis (BMF) has been reported to be associated with poor prognosis in patients with MDS. IPSS-R does not include BMF in its scoring system. The prognostic role of BMF in MDS has not been confirmed in a meta-analysis yet. Thus, the objective of this research was to assess the prognostic significance of BMF on the overall survival (OS) and mortality of patients with MDS by meta-analyses.

Method:

The hazard ratios (HRs) of multivariate analysis for OS between the bone marrow fibrosis grade 0 or I and the bone marrow fibrosis grade II or III were obtained by searching pertinent literature in the PubMed, EMBASE, Science Direct, and OVID databases from inception to December 2024. The pooled HR were then calculated using a fixed or random effect model as per heterogeneity using RevMan 5.4 software. The Q test was used to examine heterogeneity. For statistical significance, a p-value of less than 0.05 was used.

Results:

Seven qualifying publications totaling 2849 MDS cases were included in the total. The analyses revealed non-significant heterogeneity among set of studies. The pooled results showed that marrow fibrosis of grade II or III was a significant indicator for poor overall survival (OS) (HR = 1.70, 95% CI = 1.44–2.01, $p < 0.00001$, $I^2 = 45\%$). Further, higher grades of marrow fibrosis were associated with higher hazards of mortality in MDS patients.

Conclusion:

Bone marrow fibrosis strongly correlated with worse OS in MDS patients. Bone marrow fibrosis can potentially be incorporated in IPSS-R system.

Autoimmune myelofibrosis: case study and literature review

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Case study:

A 54 year old highschool teacher presented with symptomatic anaemia with reticulocytopenia, with a haemoglobin of 64g/L. Her history was significant for subclinical hyperthyroidism for which she had been commenced on carbimazole 6 months prior. Bone marrow biopsy demonstrated panmyelosis with increased reticulin fibrosis, suspicious for myelofibrosis. Her myeloid NGS was negative for clonal mutations. An autoimmune screen demonstrated autoantibodies consistent with lupus, however she had no manifestations of lupus. She was commenced on prednisone 1mg/kg and her carbimazole was ceased due to concerns about drug-induced SLE. Her anaemia resolved after 3 weeks with normalisation of her haemoglobin and reticulocyte count.

Conclusion:

This is the first case report of autoimmune myelofibrosis associated with drug-induced autoantibodies. Autoimmune myelofibrosis is a very rare disorder that should be suspected when patients present with cytopenias and bone marrow features of myelofibrosis however lack clonal markers of a myeloproliferative disorder. It responds to immunosuppression, typically steroids, however a variety of immunosuppressants have been used with varying degrees of efficacy.

A Tale of Two Clones: BCR-ABL1 fusion-positive CML arising in JAK2 V617F mutated MPN with germline DDX41

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Background:

While germline variants in DDX41 are associated with myelodysplastic syndrome (MDS) and acute myeloid leukemia (AML), its presence in patients with myeloproliferative neoplasms (MPN) are rare and occasionally reported^{1,2}.

The coexistence or sequential emergence of distinct myeloproliferative drivers within a single patient, while uncommon but not novel³, highlights the complexity of clonal haematopoiesis.

Against this background of limited reported associations and rare clonal evolution patterns, we describe a patient with germline DDX41 predisposition who developed a JAK2-mutated MPN followed by BCR-ABL1–positive chronic myeloid leukemia (CML), illustrating sequential acquisition of distinct oncogenic drivers within a single disease course.

Case report:

A 73-year-old woman presented in 2021 with elevated haemoglobin and platelet counts. Molecular testing identified a JAK2 V617F variant (VAF 25–50%), with no evidence of BCR-ABL1 fusion transcripts.

In 2024, repeat next-generation sequencing confirmed persistence of the JAK2 variant and detected an additional DDX41p.(Gly173Arg) variant (VAF 51%). Analysis of a hair sample established this as a likely pathogenic germline mutation. Karyotyping was unsuccessful.

In late 2025, a bone marrow examination revealed a *t*(9;22) translocation, and molecular testing confirmed *BCR::ABL1* fusion with a transcript level of 78% (IS). The JAK2 variant persisted at a reduced VAF of 8%. The diagnosis was subsequently revised to CML.

Discussion:

A key question is whether this reflects progression of an underlying MPN or the emergence of a distinct CML clone. The fall in JAK2 V617F variant allele frequency at the time of *BCR::ABL1* detection, together with prior absence of *BCR::ABL1* transcripts, supports the interpretation of two separate clones, with Philadelphia chromosome–positive disease arising independently rather than through MPN evolution, highlighting the importance of longitudinal molecular monitoring. Although JAK2 and BCR-ABL1 coexistence has been reported⁴, the added germline DDX41 variant make this case unique, suggesting germline predisposition may permit multiple independent malignant clones over time.

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Myeloproliferative neoplasm-associated splanchnic vein thrombosis (MPN-SVT): a case report and focused review

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Case Study:

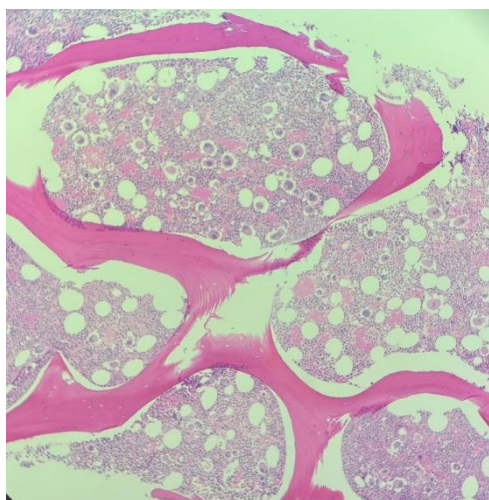
A 41-year-old male with type 2 diabetes presented with two weeks of severe abdominal pain following elective ankle arthroscopy. CT demonstrated extensive porto-mesenteric venous thrombosis and splenomegaly without chronic liver disease (**figure 1**), and no acute intestinal ischaemia. *JAK2 V617F* was detected (variant allele frequency 28%). He was treated with enoxaparin 1mg/kg 12 hourly. Given the extensive thrombosis and severe presentation, tertiary hepatology review was sought; however, systemic thrombolysis and endovascular intervention were not pursued.

Bone marrow biopsy demonstrated age-adjusted hypercellularity, megakaryocytic hyperplasia and atypia with loose clusters, and grade 1 reticulin fibrosis (**figure 2**). A diagnosis of MPN-U was made in the absence of classical peripheral blood features of another MPN.

Thrombophilia screening additionally identified a concomitant prothrombin G20210A mutation. Gastroscopy demonstrated portal hypertensive gastropathy requiring surveillance. Anticoagulation was transitioned to indefinite apixaban, and cytoreduction commenced with pegylated interferon. The patient continues to experience chronic pain at 3 months.

Conclusion:

MPN-associated mutations are identified in up to 30–50% of SVT cases, frequently in the absence of classical haematological abnormalities. This case illustrates diagnostic and therapeutic challenges in MPN-SVT and highlights two under-recognised management considerations. First, the role of cytoreduction in MPN-SVT without overt haematological features has been uncertain. The recent GASTRO-MPN observational study of 757 patients demonstrated that cytoreduction independently reduces recurrent thrombosis (HR 0.67, $p=0.01$), though randomised data are lacking. Second, early multidisciplinary consideration of endovascular intervention is warranted in patients with extensive thrombosis or persistent symptoms, though access to expertise remains limited and high-quality evidence is lacking. Consideration should be given to establishing an Australian registry of MPN-SVT patients to better characterise this unique cohort and address the paucity of randomised evidence.



2A

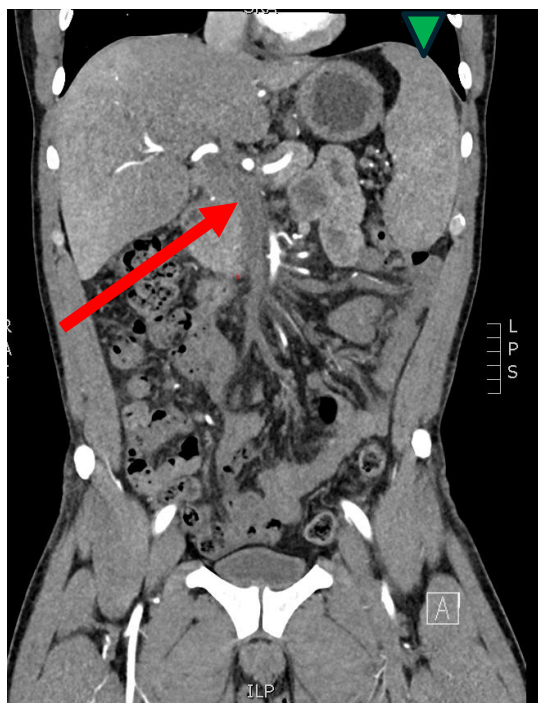
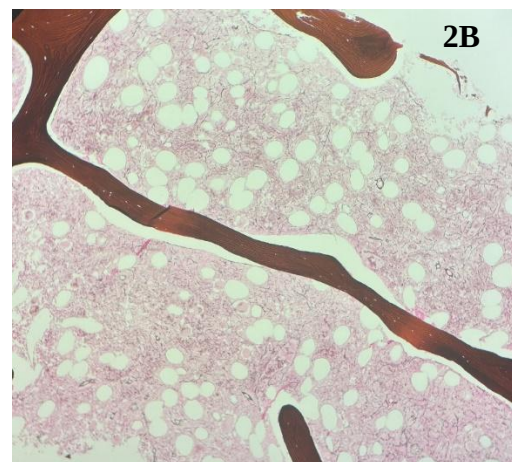


Figure 2. Coronal CT abdomen/pelvis with contrast - demonstrating thrombotic occlusion of the portal vein and superior mesenteric vein (red arrow) and mild splenomegaly (green arrowhead)

Figure 2. Bone marrow trephine biopsy (100× magnification). (A) Hypercellular marrow with megakaryocytic hyperplasia, pleomorphism, and atypia. (B) MF-1 reticulin fibrosis (loose network of thin fibres with intersections).



A preliminary clinical audit of momelotinib therapy in myelofibrosis

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Aim: Myelofibrosis (MF) is a myeloproliferative neoplasm characterized by splenomegaly, progressive anemia, and constitutional symptoms that significantly impair quality of life. Momelotinib is a first-in-class inhibitor of JAK1, JAK2, and ACVR1. This audit evaluates the real-world application of momelotinib following its 2024 PBS approval for patients with myelofibrosis.

Method: A retrospective review was conducted at Gold Coast University Hospital, Queensland, involving seven patients with primary or secondary MF. Most participants had previously failed ruxolitinib therapy. The study tracked hemoglobin (Hb) levels at baseline and at 12, 24, and 36 weeks, alongside transfusion status and treatment-emergent adverse events.

Results: The cohort represented an advanced disease population; four of the seven patients died during the treatment period due to disease progression or comorbidities. One patient discontinued therapy within weeks due to adverse events, specifically headache and dizziness. Overall, participants did not demonstrate significant Hb improvement at the 12- or 24-week intervals and transfusion requirements only improved in 3 patients. While two survivors showed Hb increases (moving from the 80s to >100 g/L) by week 36, these results were confounded by the concurrent use of erythropoiesis-stimulating agents in one patient.

Conclusion: Although modest Hb improvements were observed in surviving patients, the small sample size and advanced disease stage of the participants preclude definitive conclusions. Further investigation with a more substantial cohort is required to determine if the positive hematologic outcomes seen in international Phase 3 trials—such as SIMPLIFY and MOMENTUM—can be replicated within this local clinical setting.

No conflict of interest to disclose.

Evaluating the diagnostic accuracy of basal tryptase level in systemic mastocytosis

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Aim:

In the absence of an associated haematological neoplasm (HN), basal tryptase level (BTL) of >20 ng/mL is a minor diagnostic criterion for systemic mastocytosis (SM). However, BTLs can be elevated in non-SM conditions. We aimed to establish the diagnostic accuracy of BTLs >20 ng/mL for SM.

Method:

We conducted a retrospective study of patients who underwent bone marrow biopsy (BMB) at Eastern Health, Victoria between January 2015 and April 2026 with BTLs performed within 3 months of BMB.

Results:

Eighty-one patients were included. Eleven patients had SM, all without associated HNs. Amongst non-SM patients, 23/70 had active non-SM HN (Table 1). The median (IQR) BTL was 56.9 ng/mL (50.5-132.5) for SM patients and 6.9 ng/mL (4.0-12.1) for non-SM patients. Within the non-SM cohort, the median (IQR) BTL was 6.5 ng/mL (4.5-11.5) for patients with active HN and 6.8 ng/mL (4.0-12.6) for those without. Excluding patients with active non-SM HNs, BTLs of ≥20 ng/mL had 90.9% sensitivity and 88.6% specificity for SM. A BTL cut-off of ≥14.6 ng/mL had the highest sensitivity (100% sensitivity, 83.7% specificity) whilst a cut-off of ≥34.9 ng/mL had the highest specificity (81.8% sensitivity, 100% specificity). Positive predictive value (PPV) of BTLs between 20-39 ng/mL was 14.3%, whilst BTL ≥40 ng/mL had PPV of ≥80%.

Conclusion:

BTL of >20 ng/mL was highly sensitive and specific for SM at our institution. However, BTL cut-off of ≥40 ng/mL had greater PPV and specificity.

Table 1: Diagnoses in 70 patients without systemic mastocytosis (SM)

Diagnosis	Patients (n)
Non-SM haematological neoplasm	
a. Active	23
b. In remission	4
Cutaneous mastocytosis	1
Reactive cytoses	9*
Systemic autoimmune disease	1
Idiopathic/immune cytopenias	2
Hypereosinophilic syndrome	8*
Monoclonal gammopathy of undetermined significance (MGUS)	3
Urticaria/anaphylaxis	8
Bone marrow granulomata	1
No pathological process found	11

*One patient each with hypereosinophilic syndrome and reactive eosinophilia had concurrent MGUS

Adult presentation of CBL syndrome with longstanding massive splenomegaly and bicytopenia

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Aim:

Description of a rare adult presentation of CBL syndrome, highlighting its diagnostic challenges in the context of longstanding splenomegaly and cytopenias.

Case report:

A 32-year-old man presented to a tertiary centre with abdominal discomfort, early satiety, weight loss, night sweats, and cyclical fevers over 4 months, on a background of longstanding massive splenomegaly since adolescence. Laboratory evaluation demonstrated bicytopenia (platelets $68 \times 10^9/L$, haemoglobin 115 g/L) and polyclonal hypergammaglobulinaemia.

PET-CT demonstrated marked splenomegaly (craniocaudal span 26.9 cm) with increased FDG avidity and diffuse mild uptake in the axial and proximal appendicular skeleton. *JAK2* and *BCR::ABL* testing were negative. Bone marrow examination showed a normocellular marrow with normal trilineage haematopoiesis and reactive features, with adequate megakaryopoiesis. NGS identified a *CBL* p.(Lys382Glu) variant with a variant allele frequency of 45%. Splenic biopsy demonstrated expanded red pulp with extramedullary haematopoiesis. These findings supported a diagnosis of CBL syndrome. CBL syndrome is a RASopathy with a highly heterogeneous phenotype. This is often recognised in childhood during evaluation for dysmorphic features or presentation with juvenile myelomonocytic leukaemia.

This case highlights an uncommon adult presentation of CBL syndrome, a disorder more frequently recognised in paediatric populations. Recognition of this entity is important in patients with longstanding splenomegaly, cytopenias, and non-diagnostic marrow findings. Incorporation of molecular testing is critical for diagnosis and requires confirmation with germline testing.

Active Multiple Myeloma with bony-disease despite negative FDG-PET/CT and MRI.

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Given the high sensitivity of both Magnetic Resonance Imaging (MRI) or Fluorodeoxyglucose Positron Emission Tomography-Computed Tomography (FDG-PET/CT), manifestations of multiple myeloma with dual negativity to both modalities pose a significant diagnostic challenge. FDG-PET negative, but active myelomatous lesions are thought to have altered glucose metabolism; and whilst alternative radiolabelled tracers are under investigation in the research setting, these are not yet available in clinical practice. Whilst MRI is considered the gold standard for imaging of the axial skeleton, it has known limitations relating to anatomical distribution, small size of lytic lesions or early stage disease.

The limitations of the imaging modalities in detecting active myeloma highlights the biological heterogeneity of this disease. Here we present a case of a male with active myeloma, proven on bone-biopsy that was non-FDG-avid on PET, and had a low-signal on MRI STIR not suggestive of a myelomatous lesion.

A 77 year old male presented with bone pain and weight loss. He had raised kappa free light chains (110 mg/mL, Lambda 19mg/mL, K/L Ratio 6.0); a faint banding of uncertain significance was found on serum protein electrophoresis, a raised beta-2-microglobulin 4.9mg/L, mild renal dysfunction with serum creatine 108 umol/L and eGFR 57mL/min. Pan-CT scan revealed multiple linear lucencies with cortical breaches involving the spine, pelvis, sternum and proximal femur suggestive of myeloma, which were non-FDG-Avid on PET/CT and had a low signal intensity on MRI STIR. Bone marrow aspirate and trephine biopsy revealed <5% CD138 positive plasma cells, however a kappa-restricted B-cell population was noted. The sternal lesion was biopsied and proven to be a plasmacytoma. He subsequently developed pain corresponding with a lesion in T8; and repeat CT suggested a fracture or instability. He proceeded to a targeted bone biopsy which was diagnostic of a second plasmacytoma with an aberrant immunophenotype (CD19 negative/CD56 heterogenous).

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Seasonality of infection-related hospitalisations in Australian patients with multiple myeloma: a longitudinal analysis of hospital data

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Aim:

Patients with multiple myeloma (MM) experience a substantial infection risk. Immunoglobulin replacement therapy (IgRT) is prescribed for infection prevention in some settings. Australian IgRT access criteria suggest trialling cessation in September/October, but evidence to support this practice in MM is lacking. We examined the association between seasonality and infection-related hospitalisations.

Method:

This population-based analysis used linked longitudinal hospital data from Victoria, Australia. Patients diagnosed with MM, admitted to hospital between 2008 and 2022, were included and followed until death. Patients were excluded once commenced on IgRT. Cox proportional hazards models were used to examine the association between calendar month and infection-related hospitalisation relative to the September-October period, adjusting for age, sex, Charlson Comorbidity Index, selected comorbidities, and history of anticancer treatment.

Results:

We included 10,529 MM patients with a median follow-up of 4 years, of whom 65% had at least one infection-related hospitalisation. Unadjusted infection-related hospitalisations were similar across the year.

Adjusted monthly infection risk, relative to September was lower in November (Hazard ratio [HR], 0.89; 95% confidence interval [CI]: 0.83-0.96), December (HR, 0.91; 95% CI: 0.85-0.98), January (HR, 0.85; 95% CI: 0.79-0.92) and March (HR, 0.92; 95% CI: 0.86-0.99).

When compared to October, only January (HR, 0.90; 95% CI: 0.83-0.97) had a lower risk of infection-related hospitalisations.

Infection related hospitalisation was independently associated with anticancer treatment in the last month (HR, 2.08; 95% CI: 2.00-2.17), 2-6 months (HR, 1.55; 95% CI: 1.48-1.63), 7-12 months (HR, 1.07; 95% CI: 1.02-1.12), chronic kidney disease (HR, 2.28; 95% CI: 2.20-2.37), chronic lung disease (HR, 1.79; 95% CI: 1.72-1.87) and diabetes (HR, 1.34; 95% CI: 1.29-1.39).

Conclusion:

Seasonal differences in infection-related hospitalisations do exist, but are relatively limited. When considering the timing of cessation of IgRT for MM patients, recency of anticancer treatment and presence of comorbidities appear more important.

Plasma cell-free DNA RAS/RAF mutation profiling by droplet digital PCR for risk assessment in plasma cell dyscrasia

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Aim:

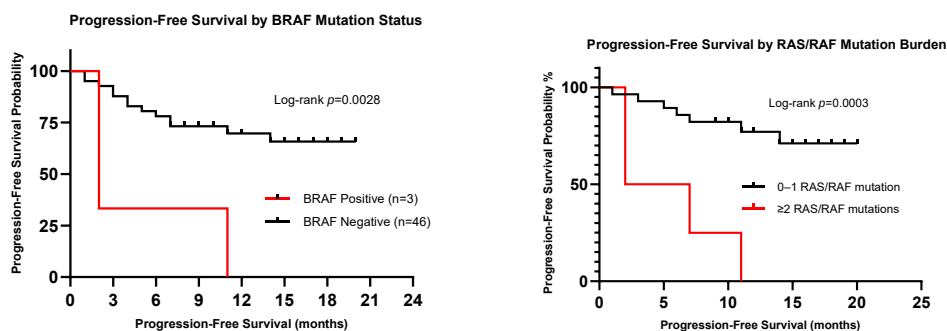
Plasma cell dyscrasias are a spectrum of clonal plasma cell disorders, ranging from precursor states to multiple myeloma (MM). MM is spatially and genetically heterogeneous. Bone marrow biopsy remains the standard for molecular assessment, but it is invasive and limited by single-site sampling. We established a plasma cell-free DNA (cfDNA) droplet digital PCR (ddPCR) assay for KRAS, NRAS, and BRAF mutations and evaluated associations with disease category, cytogenetic risk, R2-ISS stage, and progression-free survival (PFS).

Method:

Peripheral blood samples were collected from 96 patients with plasma cell dyscrasias. Plasma cfDNA was extracted and quantified using a Qubit fluorometer. Mutation detection and quantification were performed using ddPCR with assays targeting NRAS Q61, KRAS G12/G13, and BRAF V600E mutations. Clinical data, cytogenetics, R2-ISS stage, and PFS were collected. PFS was analysed using Kaplan-Meier curves and compared by the log-rank test.

Results:

The cohort included 32 patients with monoclonal gammopathy of unknown significance (MGUS), 15 with smouldering MM, 17 with newly diagnosed MM, and 32 with relapsed/refractory MM. Median age at diagnosis was 68 years (range, 37-91). cfDNA levels were higher in active MM compared with precursor disease. RAS/RAF mutations were detected across R2-ISS stages, with the highest prevalence in Stage III disease. KRAS and NRAS Q61 mutation patients showed trends toward shorter PFS does not reach statistical significance. BRAF mutation was associated with significantly shorter PFS, although the BRAF-positive subgroup was small. Patients with ≥ 2 RAS/RAF pathway mutations had significantly shorter PFS compared to patients with 0–1 RAS/RAF mutation.



Conclusion:

Plasma cfDNA ddPCR analysis enables quantitative RAS/RAF mutation detection in MM. BRAF positivity and accumulation of RAS/RAF pathway mutations may identify patients at higher risk of progression and support liquid biopsy-based risk assessment and longitudinal monitoring.

Encore: Belantamab mafodotin (belamaf), bortezomib, and dexamethasone (BVd) vs daratumumab, bortezomib, and dexamethasone (DVd) in relapsed/refractory multiple myeloma (RRMM): updated 4-year results of the phase 3 DREAMM-7 trial

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Aim:

In DREAMM-7 (NCT04246047), BVd showed superior progression-free survival (PFS) and overall survival (OS) vs DVd. This analysis evaluates the long-term treatment benefits of BVd vs DVd.

Method:

DREAMM-7 is a phase 3, open-label, randomized trial evaluating the efficacy and safety of BVd vs DVd in patients with RRMM and ≥ 1 prior line of therapy. Patients underwent 8 cycles of BVd or DVd (randomized 1:1) followed by belamaf or daratumumab monotherapy, respectively, in cycles ≥ 9 . Primary endpoint: investigator-assessed PFS. Secondary endpoints: OS, response rates, and safety. Data cutoff: Jan 9, 2026.

Results:

At >4 years of follow-up (median [m] 52.9 months), OS and PFS benefits with BVd (n=243) vs DVd (n=251) were maintained. In the intention-to-treat population, mOS with BVd was not reached (NR; 95% CI 63.0 months-NR) vs 58.3 months (95% CI 41.4 months-NR) with DVd (HR 0.62; 95% CI 0.46-0.82). PFS and OS benefit was observed across response categories. With BVd, 38% of patients achieved $\geq$ complete response (CR) vs 21% with DVd. At 4 years, OS rates in the BVd arm were 98% in patients with stringent CR (sCR) and 82% in those with CR. mPFS was NR in patients with sCR or CR treated with BVd and was 56.2 and 45.0 months, respectively, in similar responding patients treated with DVd. No new safety concerns or fatal adverse events (AEs) emerged and AE incidence remained consistent with previous analyses. Health-related quality of life remained stable over time, underscoring the long-term tolerability of belamaf monotherapy.

Conclusion:

At >4 years follow-up for BVd, OS outcomes remained superior to DVd, with many patients achieving deep remission and PFS benefit. The safety profile remained consistent with the

known profile of belamaf. These results further support BVd as a potential new standard-of-care in RRMM.

Comparison of survival outcomes in newly diagnosed multiple myeloma with t(4;14) translocation in isolation and in combination with 1q gain and/or 1p deletion

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Aim:

Until recently, chromosomal translocation t(4;14) has been considered a high-risk feature in association with multiple myeloma (MM). In 2025, the International Myeloma Society/International Myeloma Working Group (IMS-IMWG) reclassified t(4;14) as conferring high-risk only when occurring in combination with 1q gain or 1p deletion. This study is investigating survival outcomes in patients with t(4;14) alone and those with t(4;14) accompanied by gain(1q) and/or del(1p) regarding our cohort of WA patients.

Method:

A retrospective analysis of patients from Western Australia (WA) with a new diagnosis of MM between 2016 and 2025 was performed. Patients were separated in two groups: those with isolated t(4;14) (group 1, n = 24) and those who had t(4;14) accompanied by gain(1q) and/or del(1p) (group 2, n = 42). Statistical analysis is being performed using Kaplan-Meier analysis and the Mantel-Cox log-rank test to compare OS between groups, and also to determine the impact of haematopoietic stem cell transplant, age and hyperdiploidy on OS within groups. The Mann-Whitney U test will be used to determine the significance of remaining data. Significance throughout the study is indicated by *P*-value <0.05.

Results:

Data analysis remains underway, however preliminary results indicate no statistically significant difference in median OS between groups 1 and 2 (65.43 and 59.63 months, respectively; *P* = 0.533), with a trend favouring survival of those with t(4;14) in isolation.

Conclusion:

Early results have not confirmed that isolated t(4;14) is not a poor prognostic factor for MM in the WA community, given similar survival outcomes to those observed with the high-risk combination of t(4;14) with gain(1q) and/or del(1p). Survival outcomes may be influenced by haematopoietic stem cell transplant rates between groups, patient age, co-occurrence of hyperdiploidy, and the study being limited by numbers in each group. Further data and discussion will be presented at the meeting.

Rapid biochemical response to venetoclax-based therapy in heavily pre-treated t(11;14) multiple myeloma with TP53 deletion.

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Aim:

To describe the efficacy and tolerability of venetoclax-based therapy in a patient with heavily pre-treated relapsed/refractory t(11;14) multiple myeloma with TP53 deletion following progression after multiple prior therapies, including BCMA-directed treatment.

Method:

We report a case of lambda light chain multiple myeloma diagnosed in 2019 with extensive lytic bone disease, 60% bone marrow plasma cell infiltration, and cytogenetic abnormalities including t(11;14) and TP53 deletion. The patient received six prior lines of therapy including autologous stem cell transplantation, anti-CD38 therapy, salvage chemotherapy, and the BCMA-targeted bispecific antibody etentamig in combination with iberdomide on a clinical trial. Given refractory disease and limited trial options, venetoclax, selinexor and dexamethasone were commenced in April 2026 following biochemical progression with worsening renal impairment and skeletal disease. Venetoclax was initiated with inpatient dose ramp-up and tumour lysis syndrome (TLS) prophylaxis including rasburicase. Posaconazole was co-administered to enhance venetoclax exposure.

Results:

Prior to treatment, free lambda light chains were 5379 mg/L with associated renal impairment (creatinine 216 µmol/L). Repeat testing three weeks later demonstrated a rapid biochemical response with a 93% reduction in involved free lambda light chains to 371.7 mg/L, consistent with at least a partial response by IMWG criteria. Paraprotein reduced from 3 g/L to 2 g/L with improvement in renal function (creatinine 183 µmol/L). No TLS or significant toxicity was observed.

Conclusion:

This case highlights the potential efficacy and tolerability of venetoclax-based therapy in heavily pre-treated t(11;14) multiple myeloma despite adverse biological features including TP53 deletion and prior exposure to modern immunotherapies. The rapid response observed supports the growing role of biomarker-directed therapy in relapsed myeloma and reinforces the importance of molecular profiling to guide therapeutic selection. Venetoclax-based therapy may also provide a bridging strategy to future GPRC5D-directed or cellular therapies in selected patients. Bone pain resolved within seven days of commencing treatment.

Evaluating tandem and second autologous stem cell transplant for myeloma at Gold Coast University Hospital

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Aim:

At GCUH, patients aged 67 or less with myeloma have sufficient stem cells collected for 2 ASCT. The study has 3 aims:

1. To evaluate the current practice regarding tandem (defined as planned 2 ASCT within 6 months) and the clinical benefit of such an approach with respect to treatment response and progression free survival (PFS).
2. To evaluate the role of a second ASCT (defined as ASCT done for relapsed myeloma) as a treatment strategy with respect to treatment response and PFS.
3. To rationalise the number of stem cell collections in patients with myeloma.

Method:

This is a single-site retrospective analysis of pre-existing data from GCUH of patients with myeloma who have undergone tandem or second ASCT between 1 July 2015 and Dec 2025. To be considered for tandem transplant, patients must have either progressed on front-line bortezomib-based chemotherapy, or had high risk cytogenetics (4:14, 14:16 or del17p / TP53 mutation), and must be aged <65 with good response to first transplant with minimal toxicity.

Second ASCT was considered for patients who had a PFS of at least 2 years from their first ASCT.

Results:

From July 2015 to Dec 2025, 213 patients received an ASCT for the management of myeloma. Of these, 7 patients underwent a tandem transplant, with a median age of 53 years (range 49-65).

Only 2 patients received a second transplant at 3 and 6 years respectively post first transplant. Both patients were <50 years of age at time of second transplant.

Further analysis will be presented regarding depth of response, progression-free survival, toxicity profiles and assessment of patient and disease characteristics.

Conclusion:

The frequency of tandem or second ASCT is low, comprising <5% of ASCT. This study may help inform the current practice of stem cell collection. Further data will be presented at the meeting.

Dexamethasone masks lenalidomide cutaneous toxicity during induction: A real-world cohort analysis of new-onset rash upon transition to Lenalidomide maintenance monotherapy in multiple myeloma

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Background:

Lenalidomide (len) combined with dexamethasone (dex) is the backbone of induction therapy combinations for newly diagnosed multiple myeloma (NDMM) prior to autologous stem cell transplantation (ASCT), after which len continues as maintenance monotherapy. We observed an apparent clinical paradox in which patients tolerating lenalidomide during dexamethasone-containing induction subsequently developed rash upon transition to maintenance monotherapy. We hypothesise that dex mitigates len-related cutaneous hypersensitivity during induction, which is unmasked on transition to monotherapy.

Methods: Single-centre retrospective cohort study, at Fiona Stanley Hospital (2020–2025). Eligible patients had NDMM and underwent ASCT, and initiated len maintenance following a prior len-containing combination regimen with minimum 3-month follow-up. The primary endpoint was new-onset rash within 90 days of maintenance commencement deemed clinically attributable to lenalidomide after chart review.

Results:

Of 108 patients screened, 57 met eligibility (53%), all were off-dex at maintenance initiation. Median time from last induction cycle to maintenance was 137 days (IQR 112–176). New-onset rash developed in 12/57 patients (21.1%) at a median onset of 32 days (IQR 8–39). All 12 had tolerated len without rash throughout prior dex-containing induction. Rash was predominantly grade 2, truncal (75%), and involved >30% body surface area in 42% of evaluable cases. Management was conservative: 75% continued len unchanged, 25% required temporary dose-hold, no patient was permanently discontinued. All rashes resolved (median 30 days). The occurrence of the rash had no impact on progression-free survival ($p=0.193$).

Conclusion:

New-onset len-related rash develops in 1 in 5 patients upon transition to maintenance post ASCT despite prior tolerance during dex-containing induction. The temporal pattern supports the hypothesis that dexamethasone exposure during induction may suppress or attenuate len-associated cutaneous toxicity, unmasked upon cessation. Rash is clinically manageable and does not compromise treatment fidelity or survival outcomes. A prospective trial is warranted to directly test whether gradual corticosteroid withdrawal prevents this clinically important adverse event.

A cross-sectional analysis of serum neurofilament light chain and nerve conduction studies in newly diagnosed paraproteinemia.

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Aim:

This study investigated whether serum neurofilament light chain (sNfL) correlates with electrophysiological markers of peripheral nerve damage in newly diagnosed paraproteinemia, assessing its potential as a biomarker for early neuropathy.

Method:

A cross sectional study done in Hospital Canselor Tuanku Muhriz, Malaysia from February 2021 until March 2022. Newly diagnosed paraproteinemia patients aged ≥ 18 year old were recruited prior to initiating chemotherapy or radiotherapy using purposive sampling. Those who have established other forms of peripheral neuropathy (diabetic neuropathy, CIDP), history of malignancy or autoimmune disease on treatment with immunomodulatory agent or history of exposure to toxins/alcohol were excluded. Demographic data were obtained and patients were assessed for peripheral neuropathy symptoms and underwent nerve conduction study.

Results:

18 patients were recruited (N=18). Mean age was 61.6 years (SD $\pm$ 8.8) with male (12, 66.7%) and Malay (12, 66.7%). Hypertension was the most prevalent comorbidity (12, 66.7%). Plasma cell neoplasms was the most common diagnosis (12, 66.7%) with dominant immunoglobulins was IgG (11, 61.1%). 13 participants (72.2%) exhibited peripheral neuropathy (PN) symptoms, predominantly Grade 2 severity (12, 66.7%) and nerve conduction studies confirmed an axonal pattern of damage in (7, 38.9%). This study compared the demographic, clinical, and laboratory parameters between patients with symptomatic PN (n=13) and asymptomatic PN (n=5). Across all the evaluated parameters, there were no statistically significant differences between the two groups (p > 0.05). However, despite the lack of statistical significance, the symptomatic PN group exhibited higher mean values for most of the clinical parameters including sNfL.

Conclusion:

Although the small sample size failed to show statistical significance value in study populations, the pronounced elevation of sNfL in symptomatic patients strongly supports its clinical utility as a potential biomarker of active peripheral nerve injury.

Ciltacabtagene autoleucel in lenalidomide-refractory multiple myeloma responding to bridging therapy: CARTITUDE-4 cytogenetic subgroup analysis

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Aim:

CARTITUDE-4 (NCT04181827) demonstrated significant overall survival (OS) and progression-free survival (PFS) benefits of ciltacabtagene autoleucel (cilta-cel) in lenalidomide-refractory multiple myeloma (MM) after 1–3 prior lines. Emerging data underscores the importance of successful bridging therapy (BT); deeper responses (partial response or better, $\geq$ PR) during BT were associated with better survival and safety outcomes with cilta-cel. We report efficacy and safety for patients receiving cilta-cel with high- or standard-risk cytogenetics who responded to BT.

Method:

CARTITUDE-4 as-treated set comprised patients who received a single cilta-cel infusion after apheresis, $\geq$ 1 BT cycle, and lymphodepletion. High-risk cytogenetics were defined as positivity for del(17)p, t(14;16), t(4;14) or gain/amp(1q); standard-risk patients were negative for these mutations. Responses to BT were per International Myeloma Working Group criteria. Efficacy and safety were analyzed by cytogenetic subgroup in as-treated patients with $\geq$ PR to BT.

Results:

Of 176 patients treated with cilta-cel (median follow-up, 33.6 months), 64 high-risk and 40 standard-risk patients achieved $\geq$ PR to BT. In high-risk patients, median PFS and OS were not reached; 30-month PFS 65.1% (95% CI, 51.4–75.8); OS 87.2% (95% CI, 76.1–93.4). In standard-risk patients, median PFS and OS were not reached; 30-month PFS 85.0% (95% CI, 69.6–93.0); OS 92.5% (95% CI, 78.5–97.5). Safety (high-risk vs standard-risk): cytokine release syndrome 73.4% vs 70.0%; serious non-haematological AEs 64.1% vs 57.5%; grade 3/4 infections 43.8% vs 30.0%; ICANS 7.8% vs 0. Non-relapse mortality (NRM) occurred in 9 patients (high-risk 7; standard-risk 2); there were 4 infection-related deaths in high-risk patients. No immune effector cell (IEC)-parkinsonism reported.

Conclusion:

Cilta-cel yielded substantial survival and response benefits in high- and standard-risk cytogenetic subgroups achieving $\geq$ PR to BT, with >85% alive at 30 months. Infections were a

principal cause of NRM. These data underscore cilta-cel's benefit when MM is well controlled at infusion.

iMMagine-3: Phase 3, randomized study to compare the efficacy and safety of anitocabtagene autoleucel with standard of care in patients with relapsed/refractory multiple myeloma (RRMM)

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Aim:

Anitocabtagene autoleucel (anito-cel) is an autologous D-Domain–based anti-BCMA CAR T-cell therapy evaluated in RRMM after 3 prior therapies. The phase 1 study showed an overall response rate (ORR) of 100% and 79% complete response/stringent (CR/sCR). At 38.1 months median follow-up, median PFS was 30.2 months. There were no Grade ≥ 3 CRS; Grade 3 ICANS 3%. At 12.6 months median follow-up in the phase 2 iMMagine-1 study, ORR was 97% with a CR/sCR of 68%; Grade ≥ 3 CRS incidence was 1% and no Grade ≥ 3 ICANS. No non-ICANS toxicities or immune effector cell–associated enterocolitis was observed in either study. The Phase 3 randomised iMMagine-3 study (NCT06413498), will assess the efficacy and safety of anito-cel compared with standard of care (SOC) in patients with RRMM with 1-3 prior therapies.

Method:

iMMagine-3 will enrol approximately 450 patients randomized to anito-cel or SOC. Investigators will select the SOC regimen: pomalidomide, bortezomib, and dexamethasone; daratumumab, pomalidomide, and dexamethasone; carfilzomib, daratumumab, and dexamethasone; or carfilzomib and dexamethasone. Patients will receive SOC until unacceptable toxicity, progression, death, or withdrawal. Patients in the anito-cel arm will undergo leukapheresis, bridging therapy, lymphodepleting chemotherapy, and infusion of anito-cel (115×10^6 CAR+ T cells). Inclusion criteria are ECOG 0-1, progressive disease ≤ 12 months of last regimen, and measurable disease at screening. Exclusion criteria include prior BCMA-targeted therapy, T-cell engager therapy, genetically modified T-cell therapy, autologous stem cell transplantation (SCT) < 12 weeks before randomization, allogeneic SCT, and CNS or meningeal involvement. Dual primary endpoints are PFS and MRD-negative CR/sCR rate at 9 months. It is hypothesized that anito-cel will improve PFS or MRD-negative CR/sCR rate at 9 months compared with SOC. Secondary endpoints include CR/sCR, MRD negativity, overall survival, and safety.

Results:

iMMagine-3 will have approximately 130 study sites globally.

Conclusion:

iMMagine-3 is currently enrolling patients.

Functional high-risk (FHR) relapsed/refractory multiple myeloma (RRMM) outcomes with belantamab mafodotin (belamaf): DREAMM-7 and DREAMM-8 subgroup analysis (encore)

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Aim:

This is a subgroup analysis of patients with FHR RRMM (progression ≤ 18 months after transplant or first line of therapy [LOT]) with ≥ 1 prior LOT in the DREAMM-7/8 (D7/8) trials.

Methods:

Patients were randomized (1:1) to belamaf + bortezomib + dexamethasone (BVd) vs daratumumab + Vd (DVd) in D7 (NCT04246047) and belamaf + pomalidomide + dexamethasone (BPd) vs bortezomib + Pd (PVd) in D8 (NCT04484623). Primary endpoint: progression-free survival (PFS). Secondary endpoints: overall survival (OS) and minimal residual disease-negativity (MRD-). Descriptive statistics: response and MRD- (10^{-5}) rates. Cox model: PFS and OS hazard ratios (HRs). The Kaplan-Meier method: median survival times.

Results:

In D7, median (m) follow-up (FU): 28.2 months. Patients with one prior LOT were treated with BVd vs DVd (n=125 each), mPFS: 36.6 vs 19.1 months (HR=0.52; 95% CI, 0.36-0.76); ORR: 83% vs 82%; ≥complete response (CR): 39% vs 24%; ≥CR MRD-: 28% vs 14%; mOS: not reached (NR). In patients with FHR MM, mFU: 39.4 months. BVd vs DVd (n=43 each), mPFS: 28.4 vs 13.4 months (HR=0.65; 95% CI, 0.37-1.14); ORR: 86% vs 74%; ≥CR: 33% vs 21%; ≥CR MRD-: 21% vs 9%; treatment-related grade 3/4 adverse events (AEs): 91% vs 60%.

In D8, mFU was 21.8 months (BPd=82 vs PVd=77), mPFS: NR vs 18.5 months (HR=0.50; 95% CI, 0.30-0.85); ORR: 79% vs 88%; ≥CR: 46% vs 23%; ≥CR MRD: 33% vs 5%; mOS: NR. In patients with FHR MM (BPd=28 vs PVd=31), mPFS: NR vs 14.8 months (HR=0.66; 95% CI, 0.28-1.54); ORR: 82% vs 87%; ≥CR: 50% vs 23%; ≥CR MRD- 36% vs 7%; treatment-related grade 3/4 AEs: 78% vs 71%.

Conclusions:

Patients with FHR RRMM treated with BVd and BPd had extended PFS and deeper responses than DVd and PVd

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New IMS/IMWG risk criteria by next-generation sequencing: Analysis of daratumumab benefit in both high- and standard-risk patients in the PERSEUS study

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Aim:

The IMS/IMWG recently introduced Consensus Genomic Staging (CGS) high-risk criteria for NDMM, including genetic alterations not identifiable by fluorescence in situ hybridisation (FISH) but by next-generation sequencing (NGS) eg; TP53 mutations.

PERSEUS/EMN017 (NCT03710603) evaluated daratumumab added to VRd induction/consolidation and to R maintenance (DVRd arm) vs VRd+R (VRd arm) in transplant-eligible patients. Prior analyses showed DVRd improved progression-free survival (PFS) across traditional cytogenetic risk groups.

Methods:

Of 709 NDMM patients randomised 1:1 to DVRd or VRd, unique molecular assay (UMA)-NGS target panel analysed DNA extracted from 434 patient DNA samples from CD138+ bone marrow cells (664 patients had BM collected). The new IMS/IMWG high-risk CGS status was defined post-hoc by presence of del17p/TP53 mutations; IgH translocations with additional amp1q or del1p; amp1q and del1p; biallelic del1p; or elevated β2-microglobulin with normal renal function. FISH high-risk was defined per-protocol. Minimal residual disease (MRD) negativity was assessed by NGS in patients achieving ≥CR.

Results:

Of 434 evaluable patients, 152 (35%) were CGS high-risk. Common genetic lesions included del17p/TP53 (14%), IgH translocation with amp1q/del1p (12%), and del1p with amp1q (9%); 2% had biallelic focal del1p. CGS criteria reclassified 17% of patients from standard-to high-

risk and 4% from high- to standard-risk. DVRd was associated with significantly higher MRD-neg at 10^{-6} vs VRd in both CGS standard-risk (67% vs 39%; $p=0.0001$) and high-risk groups (56% vs 26%; $p=0.0003$). Sustained MRD-neg (10^{-6}) at ≥ 12 months was higher with DVRd in standard-risk (57% vs 24%; $p<0.0001$) and high-risk patients (41% vs 19%; $p<0.0001$). DVRd improved PFS in standard-risk (HR 0.38; 95% CI; 0.20–0.73; $p=0.001$) and high-risk patients (HR 0.54; 0.31–0.95; $p=0.039$), adjusting for ISS, lactate dehydrogenase and age (>65 years).

Conclusion:

DVRd improved MRD-neg and PFS across CGS risk groups. These findings further support DVRd induction/consolidation and DR maintenance as SOC for transplant-eligible NDMM, regardless of cytogenetic risk.

Anchored transport for pre-market health technology assessment: predicting real-world outcomes from trial evidence in multiple myeloma

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Aim:

Health technology assessment (HTA) agencies face the efficacy–effectiveness gap: benefits observed in trials frequently fail to translate to routine practice. Existing methods for adjusting trial findings to real-world populations require patient-level data that is unavailable before a treatment is licensed. We develop and validate Anchored Transport, which combines aggregate trial data with real-world data on existing treatments to predict real-world effectiveness pre-market.

Method:

We applied Anchored Transport to daratumumab–bortezomib–dexamethasone (DVd) versus bortezomib–dexamethasone (Vd) at second line in relapsed/refractory multiple myeloma in Australia. Aggregate best clinical response (BCR) data came from the CASTOR trial (DVd n=238; Vd n=231); patient-level data came from the Myeloma and Related Diseases Registry (MRDR), including pre-funding Vd (n=70), pre-funding non-Vd (n=2,665), and a held-out post-funding DVd cohort (n=541). Using Vd as the common comparator, we tested whether trial and registry populations were comparable after accounting for treatment selection, then predicted DVd outcomes under actual Australian practice. Predictions were propagated through the EpiMAP Myeloma simulation model to estimate cost-effectiveness against pre-funding standard of care.

Results:

Vd represented only 1.5% of Australian second-line treatment (40/2,735), indicating the trial comparator did not reflect routine practice. After accounting for treatment selection, residual population differences between trial and registry were not statistically significant ($p=0.833$), supporting transportability. Anchored Transport reduced BCR prediction error by 43% versus the trial-based approach. The incremental cost per quality-adjusted life year (QALY) for DVd versus Vd moved from A\$460K (trial-based) to A\$719K (Anchored Transport), towards the observed real-world value of A\$2.1M.

Conclusion:

Anchored Transport offers a feasible pre-market approach to predicting real-world treatment effectiveness using the data available at HTA submission. The mismatch between trial comparator and actual clinical practice, combined with the improvement in prediction accuracy, has direct implications: decisions framed against an unrepresentative comparator may substantially misestimate both clinical and economic value.

Enhancing service provision through strategic collaboration - challenges of delivering subcutaneous Bortezomib based chemotherapy regimens for Multiple Myeloma in a regional setting

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Aim:

Regional myeloma treatment is complex requiring frequent hospital visits with long travel distances and limited access to care. Gippsland Regional Integrated Cancer Service (GRICS) established partnerships to develop a self-administration chemotherapy pathway improving access, supporting safe home-based treatment delivery, promote patient autonomy, and optimise chemotherapy unit (CDU) capacity.

Method:

GRICS coordinated a multidisciplinary working group of haematologists, haematology clinical nurse coordinators, CDU staff, and oncology pharmacy to support implementation in Gippsland. This collaboration created a robust protocol, patient education guidelines, establishing discipline specific roles and responsibilities. Tailored resources were integrated into existing pre-treatment education processes to support patient recruitment.

Results:

The pilot has screened 31 patients and recruited 4 patients (13%) to date. Sixteen patients (52%) were ineligible due to alternative regimens (e.g DVd), 5 (16%) excluded for clinical trial enrolment and 5 (16%) deemed too frail to self-inject.

Implementation leveraged existing patient support structures to ensure seamless integration while maintaining high standards of care. A structured mixed methods evaluation will assess feasibility, safety, effectiveness, and patient and clinician experiences, including clinical time savings, increased CDU capacity and social return on investment. To date, no administration errors or increase in adverse events have been reported, reinforcing patient safety as central to this model.

Implementation leveraged existing patient support structures to ensure seamless integration while maintaining high standards of care.

Conclusion:

This project establishes the framework for an alternative model of treatment delivery to improve access to care. Evaluation findings will inform sustainability and scalability of this self-administration model with potential, pending pilot outcomes, to expand across subregional CDUs and other subcutaneous treatments (e.g. Daratumumab), supporting care closer to home. By optimising resources and equitable access, this approach promotes patient-centered care and quality of life for patients living in geographically dispersed regional communities.

The role of whole-body STIR MRI in assessing first biochemical relapse in multiple myeloma and informing the initiation of second-line therapy

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Aim:

To evaluate how STIR MRI may guide second-line therapy initiation in otherwise asymptomatic first biochemical relapse of myeloma.

Method:

We conducted a single-centre retrospective audit of multiple myeloma patients diagnosed from April 2012 - August 2025 at first relapse from $\geq$ PR to first-line therapy. The preferred restaging imaging modality was whole-body STIR MRI with diffusion weighted imaging and dedicated spinal sequences.

Results:

340 patients achieved $\geq$ PR to first-line therapy (CR 43%, VGPR 27%, PR 30%). Median age at diagnosis was 66 (31-89), ISS stage was I (18%), II (60%), III (22%), and 29% had high-risk cytogenetics. 43% received autologous stem cell transplantation. 162 patients have relapsed (median time: 22 months). At IMWG defined progressive disease, 54% had clear treatment indications: CRAB features excluding MRI findings (19%), high-risk FISH at diagnosis (17%), rapid biochemical progression (10%), or renal failure at diagnosis (8%). 75 patients (46%) experienced slow biochemical progression without urgent salvage indications, of which 46 had restaging MRIs at biochemical progression: 25 demonstrated progressive focal bone lesions, 16 showed stable/treated lesions, 5 had no lesions. Thus, 21 patients had asymptomatic biochemical progression without MRI-detected bone progression. 20 received second-line therapy (median 111 days): 5 commenced immediately, 15 were initially observed until 5 developed progressive bone disease within 6-16 months, 1 developed renal failure after 38 days, 9 remained asymptomatic until retreatment (median 133 days), and 1 remains untreated without MRI progression at 3 years.

Conclusion:

Whole-body MRI identified progressive focal bone lesions in 54% of patients with slow biochemical first relapse without other treatment indications. Of those without MRI-detected progression, 40% subsequently developed progressive lesions predominantly within 1 year, suggesting most patients require therapy at biochemical progression, particularly if access to MRI is limited. A small cohort may be safely observed with short-interval surveillance MRI while planning second-line therapy.

Cevostamab plus pomalidomide (Pom) and dexamethasone (dex) in relapsed/refractory multiple myeloma (RRMM): Phase I dose-expansion results from the CAMMA 1 study

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Aim:

Cevostamab, (FcRH5xCD3 BsAb) has shown encouraging activity and manageable safety as monotherapy in RRMM. Combining cevostamab with anti-myeloma agents that augment T-cell activity could enhance efficacy. We present initial data from the Arm B1E randomised dose expansion study of cevostamab plus Pom-Dex.

Method:

Eligible patients had RRMM and had received ≥ 1 prior line including an IMiD and PI. Pts were randomized (1:1) to 70mg (low-dose [LD]) or 105mg (high-dose [HD]) cevostamab, Q2W in 28-day cycles (C1-6) and Q4W in C7+, after 0.3/3.3mg double step-up dosing. From C1+, Pom (2mg) was given on D1–21 and dex (20mg) on D1, 8, 15 and 22. Treatment was continued until disease progression or unacceptable toxicity.

Results:

At cut-off, 32 pts (n=16 LD; n=16 HD) were treated. High-risk cytogenetics (t(4;14), t(14;16) or del(17p)), (8.3% and 25.0%); and extramedullary disease (18.8% and 25.0%) in the LD and HD cohorts, respectively; median number of prior lines was 2 and 3; ≥ 1 prior BCMA-targeted therapy (1 and 3 patients); triple-class refractory (25.0% and 31.3%), and 68.8% in both cohorts were refractory to their last line.

Median follow-up was 8.9 and 7.5 months, respectively. ORR were 93.8% and 62.5% and $\geq$ VGPR were 81.3% and 62.5%. At cut-off, 13/15 (86.7%) and 9/10 (90.0%) responders were still in response, with responses deepening over time.

Grade 3–4 adverse events occurred in 68.8% and 87.5% of LD and HD pts, respectively. Common Gr 3–4 AEs included neutropenia (56.3%; 62.5%) and anemia (31.3%; 12.5%). CRS occurred in 13 pts (81.3%) in each cohort (LD: Gr 1, 56.3%; Gr 2, 18.8%; Gr 3, 6.3%; HD: Gr 1, 56.3%; Gr 2: 25.0%). Fatal AEs excluding PD occurred in 2 pts both were considered unrelated to treatment

Conclusion:

Cevostamab plus Pom and dex induces deep responses and has manageable safety in RRMM.

Secondary bone marrow disorders after multiple myeloma therapy: clinicopathological features and outcomes post allogeneic bone marrow transplant

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Aim:

Secondary bone marrow disorders (sBMDs) such as myelodysplastic syndrome (MDS) or acute leukaemia are a rare but serious complication following multiple myeloma (MM) therapy, particularly post-lenalidomide exposure (1-3). Allogeneic bone marrow transplant (alloBMT) represents the only potentially curative treatment option, but outcome data are limited (4), a gap which we aimed to address using our institutional BMT database.

Method:

We identified 9 patients who underwent alloBMT at Royal Melbourne Hospital from Sep-2020 to Apr-2026 for sBMD post-lenalidomide exposure for MM to analyse diagnoses, cytogenetic/molecular features, treatments, outcomes, and complications. Kaplan-Meier methods were used to estimate time-to-progression (TTP), overall survival (OS), GVHD-free relapse-free survival (GRFS), and non-relapse mortality (NRM).

Results:

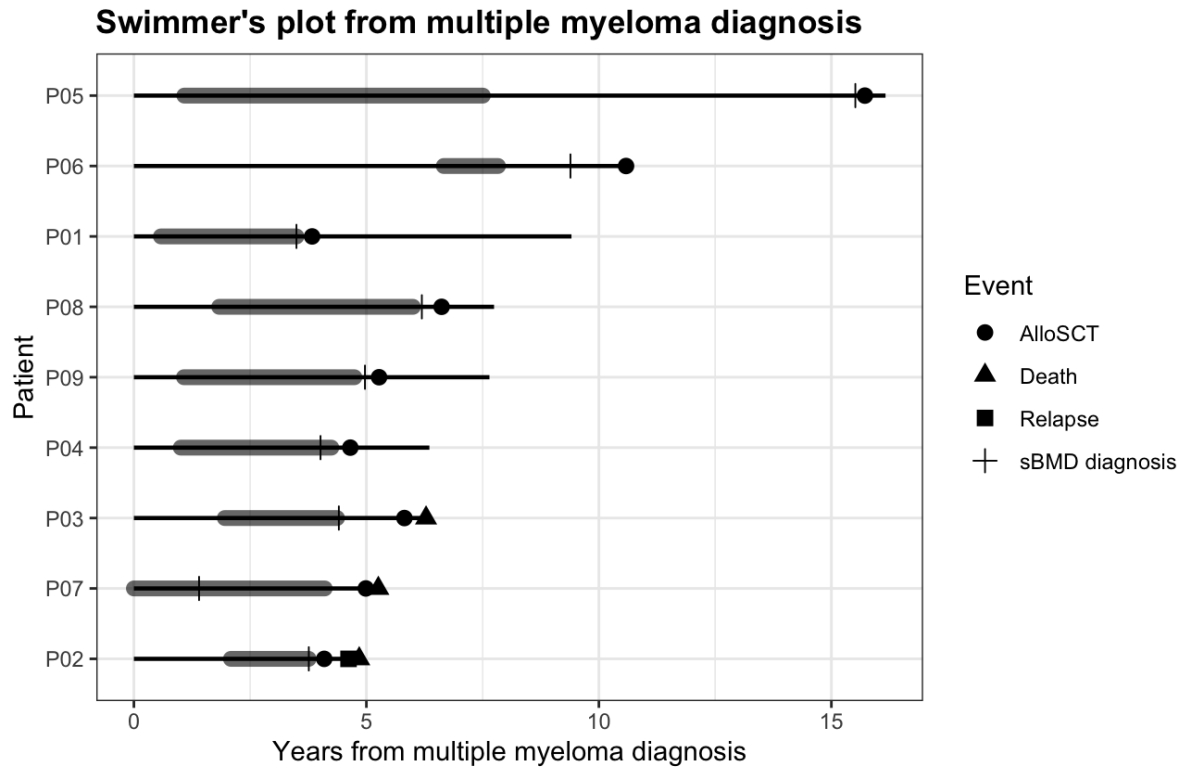
Median age at sBMD diagnosis was 64.4 (range 56.1–71.1) years; 8 were male. sBMD diagnoses were acute myeloid leukaemia (n=4), MDS (n=3), B-acute lymphoblastic leukaemia (n=1), and acute leukaemia of ambiguous lineage (n=1). Median interval from MM to sBMD diagnosis was 4.4 (range 1.4–15.5) years. Median lenalidomide exposure duration was 38.9 (range 14.0–77.0) months. High-risk genetic features were common (complex karyotype, n=3; 7q abnormalities, n=2; *TP53* alterations, n=3; *RUNX* alterations, n=4). At alloBMT, 6 were in CR/CRi. All patients received reduced-intensity peripheral blood alloBMT with the following donor sources: matched related (n=2), matched unrelated (n=3), haploidentical (n=3), mismatched unrelated (n=1). Median HCT-CI was 3 (range 0–10). Among survivors, median post-alloBMT follow-up was 17.0 (1.1–66.9) months. Estimated 12-month TTP, OS, GRFS, and NRM were 80.0%, 58.3%, 31.3% and 27.1%, respectively. Acute and chronic GVHD occurred in 2 and 1 patient, respectively. One patient relapsed post-alloBMT and 3 died (progressive disease, n=1; acute GVHD, n=1; CMV pneumonitis, n=1). No post-alloBMT MM progression was observed.

Conclusion:

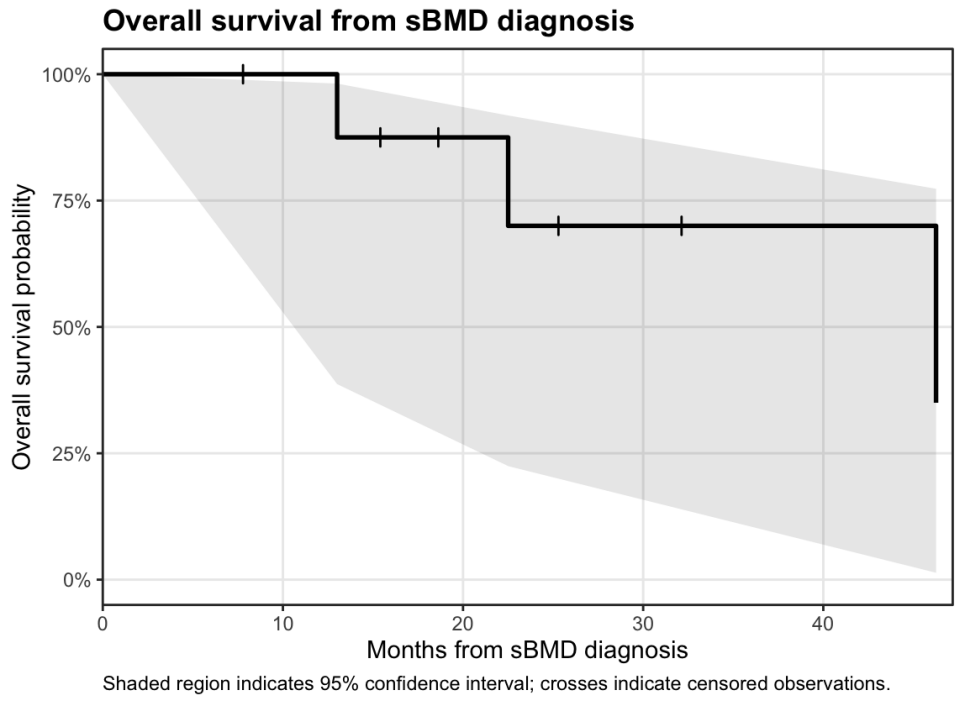
Lenalidomide-associated sBMDs after MM are enriched for high-risk genetic features. AlloBMT can provide durable disease control in selected patients, but early post-transplant morbidity and NRM remain substantial.

Figure 1. (A) Swimmer's plot from MM diagnosis. (B) OS from sBMD diagnosis. (B) TTP, OS and NRM from alloBMT.

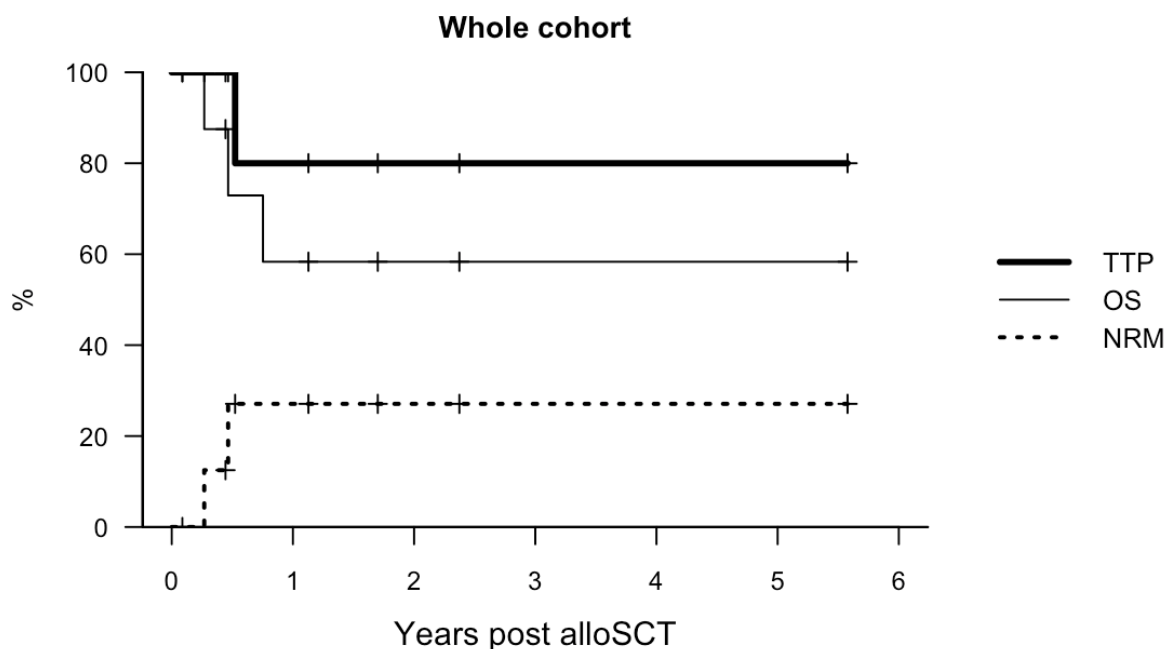
(A)



(B)



(C)



TTP	9	4	2	1	1	1	0
OS	9	4	2	1	1	1	0
NRM	9	4	2	1	1	1	0

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Association of Lenalidomide-based induction and maintenance with post-transplant survival in multiple myeloma: A real-world single-centre cohort

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Background: Lenalidomide-containing induction regimens improve response depth and progression-free survival (PFS) in transplant-eligible multiple myeloma (MM) within clinical trials. However, real-world comparative data against non-lenalidomide based regimens remain limited, particularly when most patients receive post-autologous stem cell transplantation (ASCT) lenalidomide maintenance. We evaluated whether lenalidomide-based induction confers additional survival benefit beyond lenalidomide maintenance in a real-world ASCT cohort.

Methods:

This retrospective single-centre study included consecutive transplant-eligible MM patients undergoing ASCT at Fiona Stanley Hospital (2020–2025). Induction was classified as lenalidomide-based (VRd/Dara-VRd/Rd) or non-lenalidomide-based (predominantly VCD). The primary analysis evaluated PFS using multivariable Cox regression adjusting for maintenance exposure, ISS stage III, and high-risk cytogenetics.

Results:

Among 101 evaluable patients, 80 (79%) received lenalidomide-based induction and 21 (21%) non-lenalidomide induction. PFS did not significantly differ between induction groups (median 57.7 vs 43.9 months; HR 0.84, 95% CI 0.43–1.66; $p=0.595$). Two-year PFS rates were 78.7% versus 75.9%, and 3-year rates 71.2% versus 54.5%, respectively. OS numerically favoured lenalidomide-based induction (3-year OS 91.4% vs 75.7%; HR 0.35, 95% CI 0.12–1.03; $p=0.046$), but interpretation was limited by maintenance imbalance (95% vs 71% received post-ASCT lenalidomide maintenance). Among 91 patients receiving lenalidomide maintenance, median PFS was 57.7 months, with 2- and 3-year PFS rates of 80.5% and 68.4%. In multivariable analysis adjusting for maintenance, ISS III, and cytogenetic risk, lenalidomide maintenance was associated with improved PFS (HR 0.34, 95% CI 0.13–0.91; $p=0.031$), whereas lenalidomide-based induction was not independently associated with PFS (adjusted HR 0.79, 95% CI 0.36–1.74; $p=0.556$). ISS stage III remained the strongest predictor of inferior PFS (HR 3.98, $p=0.002$).

Conclusion:

In this real-world ASCT cohort, post-ASCT lenalidomide maintenance was independently associated with improved PFS. These findings suggest maintenance therapy may have greater association with survival outcomes than induction regimen selection, although interpretation is limited by retrospective design, immortal-time bias, and small comparator groups.

Implementing group based exercise therapy for multiple myeloma: insights from real world practice

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Aim:

Individuals with multiple myeloma (MM) experience a high burden of disease and treatment related side-effects affecting physical function and quality-of-life [1, 2]. Evidence supporting the effectiveness of exercise in improving MM clinical outcomes is accumulating [3, 4]. However, this cohort faces several barriers to engaging in structured exercise, and evidence regarding feasible integration of exercise into routine practice is lacking [5]. This project aims to provide a service-level overview of the implementation of an ongoing MM group exercise program within an established exercise oncology service.

Method:

Patients with MM/associated conditions receiving treatment at a metropolitan comprehensive cancer centre in Sydney were eligible. Participants were referred by the haematologist or MM nurse and screened for exercise contraindications prior to baseline assessment. The exercise program comprised 1x60-minute supervised group exercise session per week for 12 weeks, including aerobic, resistance, and balance exercises informed by exercise oncology guidelines. Exercise programs were individualised according to participant goals, needs, health status, and exercise experience. Feasibility was evaluated by assessing uptake (referral and retention rates), attendance, and acceptability.

Results:

Over six months, 22 of 25 referred patients were eligible to participate. Sixteen (73%) participants were enrolled: seven completed the program attending 82% of sessions, and nine are currently taking part. Reasons for decline included not interested (n=1) and uncontactable (n=2). Three patients withdrew due to medical appointments (n=1), cancer/treatment-related side effects (n=1), and preference for self-managed exercise (n=1).

Conclusion:

This implementation report provides real-world insight into the delivery of group exercise for MM. Preliminary study data demonstrate that a group exercise program for individuals with MM is feasible, based on rates of uptake, adherence, and completion. Evaluation of program acceptability via participant survey is forthcoming, and further investigation into the effectiveness of group exercise for improving patient-reported outcomes and objective measures of physical function is planned.

References:

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Immunoglobulin Use and Infection Rates in Multiple Myeloma Patients on Bispecific and Trispecific T-cell engagers: A Real-World Audit

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Aim:

To evaluate local adherence to NBA criteria for access to IVIG/SCIg in multiple myeloma (MM) patients receiving T cell engager therapy (TCE); to assess the impact of IVIG/SCIg replacement on infection rates; and to estimate the associated health system costs.

Method:

A single-centre retrospective audit of 52 patients receiving TCE therapy at St Vincent's Hospital Melbourne (SVHM) was conducted over a 4.2-year period. Data captured included baseline serum immunoglobulin (Ig) profiles, IVIG/SCIg treatment strategies, and graded infection events. To account for variable treatment duration, infection incidence was calculated per 100 patient-months.

Results:

Substantial discordance was observed between real-world prescribing practices and NBA eligibility criteria. In total, 38.5% of the cohort received upfront prophylactic IVIG, which largely represented the continuation of prophylaxis established during prior lines of therapy rather than de novo initiation. Among episodes of reactive IVIG initiated post-TCE commencement, paraprotein interference artificially elevated total IgG nadir measurements in several cases. However, despite this interference, the subgroup demonstrated profound underlying hypogammaglobulinaemia (median uncorrected IgG nadir 3.4 g/L), thereby confirming broad institutional adherence to the primary NBA eligibility threshold for hypogammaglobulinaemia (< 4.0 g/L). IVIG initiation was associated with clinically meaningful reductions in infection burden: Grade 2 infection rates declined by 50% following commencement (24.6 to 12.3 episodes per 100 patient-months), and Grade ≥3 infection rates decreased by 36% (7.1 to 4.5 episodes per 100 patient-months). The median estimated IVIG product cost was AUD \$19,693 per treated patient.

Conclusion:

Local prescribing patterns demonstrate substantial reliance on prophylactic IVIG, which was associated with meaningful reductions in TCE-associated infections. These findings highlight the importance of reviewing NBA eligibility criteria to better align with international consensus on immunoglobulin replacement in this setting. Clinical monitoring protocols should prioritise the measurement of uninvolved immunoglobulins to accurately assess immunoparesis and circumvent paraprotein interference, particularly in IgG-secreting MM.

Lenalidomide-induced haemorrhagic colitis and delayed pneumonitis: a two-case series

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Aim:

To describe two rare but serious toxicities associated with lenalidomide in patients with myeloma, highlighting diagnostic and management considerations.

Method:

We report a retrospective case series of two patients with myeloma treated with lenalidomide at an Australian regional tertiary centre in 2026. Clinical, radiological, endoscopic, microbiological and histopathological findings were reviewed. Causality was assessed based on temporal association with lenalidomide exposure, exclusion of alternate aetiologies and response to drug cessation.

Results:

A 56-year-old woman receiving frontline lenalidomide, bortezomib, and dexamethasone (RVd) developed acute haemorrhagic diarrhoea after six weeks of therapy. Imaging and colonoscopy revealed diffuse colitis, and biopsies demonstrated inflammatory changes without evidence of CMV colitis. Faecal microscopy, culture and viral PCR studies were negative. CT angiogram showed diffuse hyperaemia of the large bowel consistent with inflammatory colitis rather than focal hypoperfusion or infarction seen with thrombotic ischaemic colitis. Symptoms resolved following lenalidomide cessation.

A 69-year-old woman developed progressive hypoxic respiratory failure five months after commencing lenalidomide maintenance following autologous stem cell transplantation. This was preceded by five months of frontline induction and consolidation RVd. Imaging demonstrated widespread bilateral diffuse alveolar opacities. Bronchoalveolar lavage microscopy, culture, *Pneumocystis jirovecii* PCR and galactomannan antigen were negative. There was no improvement despite broad spectrum antimicrobials. Lenalidomide was discontinued, and high dose methylprednisolone therapy was initiated, resulting in a rapid clinical response.

Both cases demonstrated symptom resolution following drug discontinuation, with no recurrence or alternative cause identified.

Conclusion:

Lenalidomide-induced non-ischaemic haemorrhagic colitis is exceedingly rare, with only two previous case reports. Lenalidomide pneumonitis is well described, and has a median onset of 3-5 months. This case is notable, however, for the significant delay in pulmonary toxicity. Together, these cases emphasise the importance of maintaining a high index of suspicion for atypical toxicities in patients receiving immunomodulatory therapy.

Value of the treatment-free period following ciltacabtagene autoleucel infusion in patients with relapsed/refractory multiple myeloma: preliminary findings from a qualitative interview study

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Aim:

Current treatment options for patients with relapsed/refractory multiple myeloma (RRMM) following ≥ 1 prior line of therapy can include a single ciltacabtagene autoleucel infusion (cilta-cel) without maintenance therapy, contributing to a potentially beneficial “treatment-free” period. We present preliminary findings from ongoing qualitative interviews exploring patient perspectives and experiences of the treatment-free period with cilta-cel for RRMM.

Method:

US-based adult patients with RRMM who received cilta-cel ≥ 6 months before study enrolment and currently treatment free, participated in semi-structured, qualitative audio/transcribed interviews. Thematic analysis identified key themes associated with patients’ interpretation of “treatment free” and their treatment-free experiences.

Results:

Fifteen patients aged 53–78 years were interviewed (9 female/6 male; median time since cilta-cel: 13 months 4 days). Patient interpretations of being “treatment free” included freedom from side effects, absence of symptoms, increased freedom of time, and return to ‘normal’ life. The treatment-free period was mostly a positive experience with substantial health-related quality of life (HRQOL) benefits. Patients reported engaging more in normal, everyday activities with notable improvements in psychological/emotional well-being; 8 patients reported no longer viewing themselves as a ‘patient’ with reduction in medical appointments/absence of continuous treatments. Patients highlighted meaningful and increased involvement in family life because they were treatment free. Challenges associated with the treatment-free period were fear of potential relapse (n=8) or additional treatment. Important experiences reported during the treatment-free period included: improved well-being/HRQOL/increased energy (n=10), increased free time (n=8), feeling cancer/disease free (n=7), freedom from medication/treatment (n=7). For most patients (n=9), being treatment free improved psychological wellbeing.

Conclusion:

These initial interviews provide valuable insights on patient-perceived value of a treatment-free period following cilta-cel for RRMM. Notably, improvements in patients’ overall HRQOL and freedom from disease and continuous treatment changed patients’ perceptions of themselves and their lives. These findings emphasise the positive impact of living without continuous treatment.

Retrospective review of the optimal care pathways at a tertiary referral centre

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Background:

The Optimal Care Pathways (OCPs) are a framework for the delivery of consistent, safe, high-quality, and evidence-based care for people with cancer developed by the Federal Ministry of Health in 2022-23 with key stakeholders including the Leukaemia Foundation. Covering every step from prevention and early detection through to recovery, living with a chronic disease, or end-of-life-care, they aim to improve patient outcomes irrespective of where they live or receive cancer treatment.

Aim:

To assess the OCPs in real-world setting in a single tertiary centre across three disease states: chronic lymphocytic leukaemia (CLL), myelodysplastic syndrome (MDS) and multiple myeloma (MM)

Method:

We conducted a retrospective audit of adherence to the OCPs within our regional tertiary centre using the Optimal Care Pathways Adherence Assessment (OCPAA) tool. Following initial acceptable inter-user concordance assessment of >80-90% across each disease OCPAA, all newly diagnosed cases from September 2023 to September 2024 were included.

Result:

We had 33 cases of CLL, 18 of MM and 41 of MDS. In MM, 2 cases (11.1%) had >4 weeks for their initial review and 12 cases (66.7%) did not have documentation of their ECOG or frailty status. In MDS 5 cases (12.2%) had a delay in review beyond 4 weeks despite being listed as urgent, 7 cases (17%) did not have documentation of ECOG or frailty status, and only 5 cases (12.2%) had documentation of potential clinical trial option. In CLL, 4 cases (12.1%) required initiation of treatment following initial referral, all of whom had no documentation of clinical trial discussion. Across all disease types, there was no MDT discussion (0 of 92).

Conclusion:

This audit highlights some of the challenges in OCP adherence within a large regional tertiary hospital. We await additional data from other regional centres to complete the real-world

experience of OCP adherence and hope that this contributes towards areas of future resource allocation.

A case of idiosyncratic bone marrow failure following lenalidomide therapy

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Case Study:

A 62 year old man was referred to clinical haematology with an IgG paraprotein of 81g/L. He had mild anaemia (103g/L) with normal renal function and calcium. A bone marrow biopsy demonstrated a plasma cell burden of greater than 80% with suppressed trilineage haematopoiesis. FISH demonstrated t(4;14) and gain of 1q21, in keeping with high risk multiple myeloma as per IMS-ISWG 2025 criteria.

Per patient preference, he commenced lenalidomide and dexamethasone therapy. On day 22 he presented to hospital with fevers and pancytopenia (haemoglobin 86g/L, platelets 34 E+/9L and neutrophils 0.05 E+/9L). He was commenced on antibiotics and G-CSF. Blood counts failed to improve after 10 days. Bone marrow examination at this timepoint yielded a dry tap. The trephine biopsies demonstrated marked hypocellularity with marked stromal oedema, sinusoidal dilatation and fibrosis. Plasma cell burden had significantly reduced with a few aggregates remaining.

Two months after the initial presentation, Neutrophils spontaneously began to recover. His paraprotein had fallen to 7g/L. A repeat bone marrow biopsy performed one month later showed reduced stromal oedema, fibrosis and vascular changes with improving cellularity. However, megakaryopoiesis remained markedly reduced. Karyotype was normal and the DNA NGS panel showed no variants. An inherited bone marrow failure panel performed on a germline sample showed no variants of significance.

The patient's neutrophil count has since continued to improve. However, 5 months following the initial presentation he remains platelet and red cell transfusion dependent.

Conclusion:

While, reversible and dose dependent myelosuppression is seen with lenalidomide therapy, we believe this case reflects a severe idiosyncratic stromal injury resulting in protracted bone marrow failure. This has not been previously described.

Updated efficacy and safety results of subcutaneous daratumumab plus lenalidomide versus lenalidomide alone as maintenance therapy in newly diagnosed multiple myeloma after transplant: AURIGA study

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Aim:

Lenalidomide (R) maintenance is the current standard of care following autologous stem cell transplant (ASCT) for patients with MM. Primary analysis of the phase 3 AURIGA trial (NCT03901963) where subcutaneous daratumumab was added to R maintenance (D-R) in anti-CD38-naïve pts who were minimal residual disease (MRD) positive post-ASCT improved MRD-negative conversion by 12 months and progression-free survival (PFS) compared to R maintenance alone.¹ Herein, updated AURIGA efficacy and safety results are reported at 24 months from maintenance initiation.

Method:

Eligible patients (table 1) were stratified by cytogenetic risk status and randomised 1:1 to 28-day cycles of either D-R or R maintenance arms (figure 1). Primary endpoint was MRD-neg (10⁻⁵) conversion by 12 months from maintenance initiation.

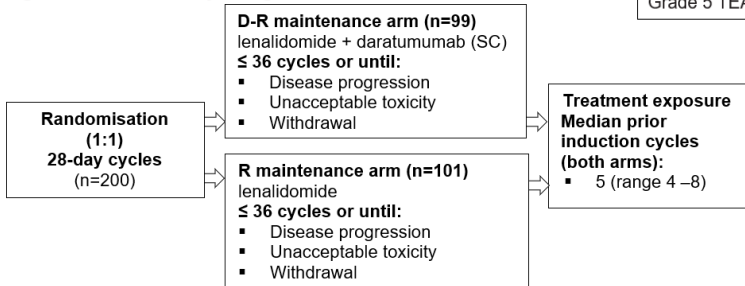
Table 1. AURIGA study inclusion criteria

Key inclusion criteria:	
▪ Newly Dx MM	▪ MRD positive at 10 ⁻⁵ by NGS post-ASCT
▪ Age 18–79 years	▪ Anti-CD38 naïve
▪ ≥ very good partial response (VGPR)	▪ Received ≥ 4 induction cycles
	▪ Enrolled ≤ 6 months of ASCT

Table 2. AURIGA sub-analysis: Safety summary

Treatment emergent adverse events (TEAEs)	D-R patients (n=99)	R patients (n=101)
Grade 3/4 TEAEs	75.0%	73.5%
Most common		
- neutropenia	49.0%	45.9%
- infections	19.8%	14.3%
Serious TEAEs	31.3%	25.5%
TEAEs leading to discontinuation	12.5%	9.2%
Grade 5 TEAEs (all infections)	2 patients	1 patient

Figure 1. AURIGA study design



Results:

Randomised patients received a median of 36.0 (D-R) and 25.5 (R) maintenance cycles respectively. 88.5% and 78.6% completed 12 cycles while 78.1% and 53.1% completed 24

cycles. At a median follow-up of 40.3 months, D-R maintenance continued to demonstrate higher MRD-neg conversion rates vs R at 10^{-5} (60.6% vs 28.7%; OR: 3.92; 95% CI: 2.16–7.14, $p<0.0001$) and MRD-neg (10^{-5}) conversion rates with complete response or better were 55.6% for D-R and 23.8% for R (OR: 4.11; 95% CI: 2.23–7.59; $p<0.0001$). D-R maintenance led to tripling of the ≥ 12 -month sustained rate (29.3% vs 7.9%; OR: 4.88; 95% CI: 2.09–11.38; $p=0.0001$) vs R alone. A 45% reduction in the risk of disease progression or death was seen with D-R versus R (HR: 0.55; 95% CI: 0.33–0.91; $p=0.0183$), with estimated 36-month PFS rates of 76.8% for D-R and 61.4% for R. Safety is summarised in table 2.

Conclusion:

Updated efficacy and safety data from AURIGA continue to demonstrate the value of adding daratumumab SC to R maintenance, as evidenced by continued higher MRD-neg conversion rates and a PFS benefit, with no new safety signals observed.

Reference: 1. Badros A, Foster L, Anderson LD Jr, et al. Oral Presentation. The 21st International Myeloma Society (IMS) Annual Meeting; September 25-28, 2024; Rio de Janeiro, Brazil.

Age and frailty analyses of transplant-ineligible (TIE) patients with newly diagnosed multiple myeloma (NDMM) in the phase 3 MAIA and CEPHEUS trials of daratumumab + lenalidomide-dexamethasone (Rd) and bortezomib-Rd (VRd)

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Aim:

MAIA and CEPHEUS trials demonstrated that daratumumab (D) with standard of care (SOC) VRd or Rd significantly improved clinical outcomes versus SOC in TIE NDMM. Here we describe efficacy and safety in TIE patients from both trials by age and baseline frailty using the latest data cuts.

Method:

The MAIA trial randomised eligible patients 1:1; D+Rd (DRd; n=368) vs Rd (n=369).

CEPHEUS randomised 1:1; D+VRd (DVRd; n=144)

Table 1. MAIA and CEPHEUS study design

MAIA Randomisation 1:1 DRd (n=368) vs Rd (n=369)	CEPHEUS Randomisation 1:1 DVRd (n=144) vs VRd (n=145)
Assessed by age (years/y) <70 y, 70–<75 y, ≥75 y	
<ul style="list-style-type: none"> Progression-free survival (PFS) Complete response or better (≥CR) Overall MRD negativity at 10⁻⁵ with ≥CR Sustained MRD neg with ≥CR (confirmed MRD neg ≥12 ± 1 months apart without MRD positivity in between) Safety 	
Assessed by IFM simplified frailty score	
Baseline frailty:	
<ul style="list-style-type: none"> 0–1= non-frail ≥2 = frail 	

Table 2. MAIA and CEPHEUS age and frailty analysis results

Age/ Frailty status	PFS hazard ratio (95% CI)		≥CR rate, %		MRD neg with ≥CR (10 ⁻⁵) rate, %		Sustained MRD neg with ≥CR (10 ⁻⁵) rate, %	
	MAIA	CEPHEUS	MAIA	CEPHEUS	MAIA	CEPHEUS	MAIA	CEPHEUS
<70 y	0.35 (0.21–0.56)	0.60 (0.31–1.18)	56.4 vs. 31.2	85.7 vs. 68.6	35.9 vs. 11.7	74.3 vs. 42.9	25.6 vs. 3.9	62.9 vs. 28.6
70–<75 y	0.64 (0.45–0.89)	0.60 (0.37–0.99)	56.2 vs. 31.3	77.9 vs. 69.2	36.2 vs. 12.2	55.9 vs. 47.7	20.8 vs. 5.3	45.6 vs. 38.5
≥75 y	0.59 (0.44–0.79)	0.46 (0.22–0.94)	44.4 vs. 28.6	80.5 vs. 44.4	26.9 vs. 9.9	58.5 vs. 26.7	13.8 vs. 3.1	43.9 vs. 15.6
Frail	0.64 (0.48–0.85)	0.62 (0.32–1.18)	44.8 vs. 33.1	72.9 vs. 54.3	25.6 vs. 13.0	56.3 vs. 34.3	15.7 vs. 4.1	39.6 vs. 17.1
Non-frail	0.48 (0.36–0.64)	0.51 (0.34–0.78)	56.6 vs. 27.5	84.4 vs. 63.6	37.8 vs. 9.5	63.5 vs. 41.8	21.4 vs. 4.0	54.2 vs. 32.7

vs VRd (n=145). Study endpoints assessments are shown in table 1.

Results:

Median follow-up was 64.5 months in MAIA and 76.0 months in CEPHEUS. In MAIA, 155 (21%) patients were <70 years (y), 261 (35%) 70–<75 y, and 321 (44%) ≥75 y; 341 (46%) pts were frail, 88.0% of whom were ≥70 y. In CEPHEUS TIE pts, 70 (24%) pts were <70 y, 133 (46%) 70–<75 y, and 86 (30%) ≥75 y; 83 (29%) pts were frail, 86% of whom were ≥70 y.

In both studies DRd or DVRd improved PFS, MRD neg rates, sustained MRD neg rates, and ≥CR rates vs Rd or VRd arms across age and frailty subgroups (table 2).

Safety was consistent with established individual drug profiles, and adverse event rates were generally comparable across treatment arms and subgroups within both trials.

Conclusion:

Daratumumab-based regimens improved efficacy outcomes across subgroups in MAIA and CEPHEUS trials, reinforcing daratumumab-based regimens as SOC in TIE NDMM regardless of age or frailty. These data offer clinically relevant insights to help guide treatment selection for TIE patients.

Encore: Analysis of subsequent T-cell–redirecting therapies (TCRTs) after treatment with belantamab mafodotin (belamaf) in DREAMM-7 and DREAMM-8

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Aim:

In translational studies of patients treated with belamaf, soluble B-cell maturation antigen (BCMA) levels returned to near baseline at time of progression without evidence of T-cell exhaustion, supporting sequencing TCRTs after belamaf. This analysis evaluates efficacy of TCRTs such as BCMA-directed specific antibodies and chimeric antigen receptor T-cell therapies after belamaf in DREAMM-7 (NCT04246047) and DREAMM-8 (NCT04484623).

Method:

This post-hoc analysis included patients in DREAMM-7 and DREAMM-8 who received belamaf + ≥1 subsequent TCRTs at data cutoff (Jan 9, 2026; n=21). Time from end of belamaf to start of subsequent TCRTs, time of TCRTs initiation to progression, death or subsequent therapy, and investigator-reported best response were assessed. Results were summarised using descriptive statistics. Time-to-event endpoints were estimated using the Kaplan-Meier method with Brookmeyer-Crowley 95% CIs. Funding: GSK.

Results:

Nine DREAMM-7 and 12 DREAMM-8 patients received belamaf and subsequent TCRTs after stopping belamaf. Pooled median time from end of belamaf to start of first subsequent TCRT was 84.1 weeks (range 14.4-168.1). Pooled median time from start of subsequent TCRTs to progression or death on TCRT treatment, or until initiation of subsequent therapy was 11.7 months (95% CI 3.8-not reached). Among patients with available data at cutoff (DREAMM-7=8; DREAMM-8=5), response to subsequent TCRTs was seen in 8/8 patients and 4/5 patients in DREAMM-7 and DREAMM-8 respectively. ≥Very good partial response was achieved in 7/8 and 2/5 patients respectively. ≥Complete response was observed in 4/8 and 2/5 patients respectively. A <6-month interval between end of belamaf and start of

subsequent TCRTs was seen in 4 patients (DREAMM-7=1; DREAMM-8=3). Of 2 patients with data (D8), both had a response. At data cutoff, 10/21 patients remained on TCRTs.

Conclusion:

Consistent with translational data, patients achieved deep responses with TCRTs after belamaf, supporting sequencing TCRTs after belamaf.

Mezigdomide, carfilzomib, and dexamethasone (MeziKd) vs carfilzomib and dexamethasone (Kd) in relapsed/refractory multiple myeloma (RRMM): results from the phase 3 SUCCESSOR-2 trial

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Aim:

Increasing numbers of patients (pts) entering second-line treatment (tx) are anti-CD38 monoclonal antibody (mAb)- and lenalidomide (LEN)-exposed, limiting tx options. Mezigdomide (Mezi), a potent oral CELMoD, induces maximal, rapid Ikaros/Aiolos degradation leading to enhanced MM cell death and immune stimulation vs IMiDs[®]. We report initial results from SUCCESSOR-2 (NCT05552976), the first randomised phase 3 study of Mezi in RRMM, evaluating MeziKd vs Kd.

Method:

SUCCESSOR-2 is a phase 3, two-stage, inferentially seamless trial in adults with ≥1 prior line of therapy, including anti-CD38 mAb and LEN. In stage 1, patients were randomised to MeziKd (Mezi 0.3, 0.6, or 1.0 mg) or Kd to select the optimal Mezi dose; stage 2 compared MeziKd versus Kd. Treatment was administered in 28-day cycles. The primary endpoint was progression-free survival (PFS); secondary endpoints included overall survival, overall response rate (ORR), and safety.

Results:

The selected stage 2 Mezi dose was 1.0 mg. 479 patients were analysed (288 MeziKd; 191 Kd). Median age was 68 years, with 25.1% aged ≥75 years, and median prior lines of therapy was 2. Most patients were heavily pretreated: 92.1% were triple-class exposed, 85.8% anti-CD38-refractory, and 75.8% LEN-refractory. Median follow-up was 10.6 months. MeziKd significantly improved PFS versus Kd (median 18.0 vs 8.3 months; HR 0.48; P<0.0001), with consistent benefit across key subgroups. ORR was higher with MeziKd (80.2% vs 53.4%), including complete response or better (26.7% vs 8.9%). Grade 3–4 adverse events were more

frequent with MeziKd, mainly neutropenia and infections; grade 5 infections were infrequent in both arms.

Conclusion:

MeziKd provided a clinically meaningful improvement in PFS from early relapse in a predominantly triple-class-exposed, anti-CD38- and LEN-refractory population, supporting Mezi as a potential new standard-of-care option in RRMM.

Pushing the boundaries of flow MRD in myeloma – validation of a single-tube spectral flow cytometry assay with improved lower limit of detection of $<1 \times 10^{-6}$ in peripheral blood

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Title:

Pushing the boundaries of flow MRD in myeloma – validation of a single-tube spectral flow cytometry assay with improved lower limit of detection of $<1 \times 10^{-6}$ in peripheral blood.

Aim:

The EuroFlow™ (EF) method for Minimal Residual Disease (MRD) detection is the international standard of Next Generation Flow (NGF) and achieves a lower limit of detection (LOD) of 1×10^{-6} . Improving NGF sensitivity may allow less invasive peripheral blood (PB) monitoring to substitute bone marrow MRD testing. Our aim was to develop a novel flow MRD assay using spectral flow cytometry with an improved limit of detection compared to EF in PB.

Method:

We recruited 46 participants: 15 controls and 31 with myeloma, smouldering myeloma, or MGUS. The novel assay uses a single-tube method with 17 antibodies and the ID7000 spectral flow cytometer. A maximum of 9 ml peripheral blood was used. Participants with plasma cell dyscrasias (n=31) were tested in parallel with EF. To determine assay linearity, bone marrow CD138⁺ plasma cells were isolated and spiked into blood of a non-myeloma control. Inter-operator and stability studies were performed. Data was analysed with Infinicyt 2.0 (gating strategy in Figure 1), and statistics were performed on prism 11.0.1.

Results:

All participants with positive results on EF also tested positive with the novel assay. Use of spectral flow cytometry with inclusion of viability staining and exclusion of neutrophils and NK cells resulted in a limit of blank <5 cells and a LOD of 10/20 million cells or 5×10^{-7} .

Conclusion:

This novel single-tube assay demonstrates an improved LOD of 10 cells thus, achieving lower LOD of $<10^{-6}$ when $>10^6$ viable cells are analysed.

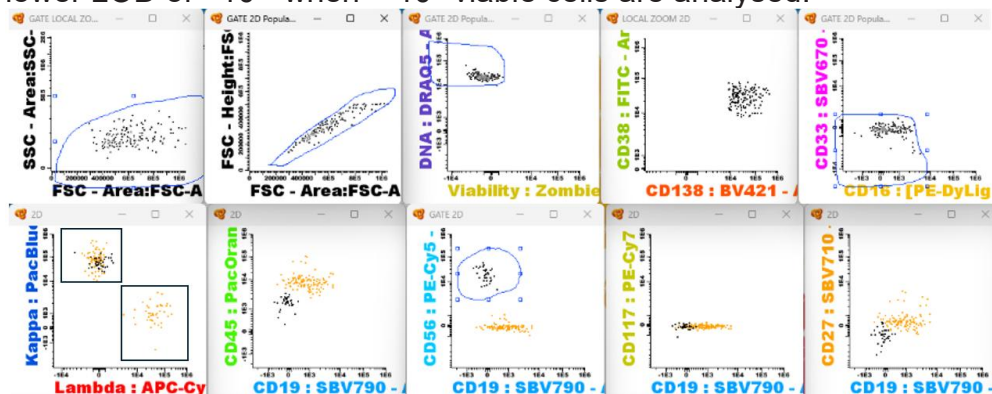


Figure 1:

Single viable cells are defined using SSC/FSC, doublet exclusion and viability. Plasma cell as displayed: Cells expressing CD138/CD38 are followed by excluding CD33 and CD16

expression and back-gating on single viable plots is used to refine the population. Kappa and lambda are then selected. In this example (RPASpec39) an abnormal plasma cell population is identified which is CD45⁻, CD19^{dim}, CD56⁺, CD27^{dim} and kappa restricted.

Single-centre experience establishing a 14-colour flow cytometric panel for measurable residual disease assessment in multiple myeloma using the Sysmex XF-1600 and VenturiOne software

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Aim:

To establish and validate a 14-colour flow cytometry panel for measurable residual disease (MRD) assessment in multiple myeloma using the Sysmex XF-1600 platform and VenturiOne software.

Method:

A single-centre method development and validation study was performed. A 14-colour plasma cell MRD panel was designed and optimised on the Sysmex XF-1600 flow cytometer using VenturiOne software for analysis. The panel incorporated surface and cytoplasmic markers, including cytoplasmic CD38 (cCD38), to improve plasma cell identification in patients receiving anti-CD38 monoclonal antibody therapy, where surface CD38 expression may be reduced or masked. Instrument setup, fluorochrome optimisation, antibody titration, compensation, gating strategy, and assay reproducibility were assessed during validation.

Results:

The 14-colour MRD panel was successfully established and demonstrated stable analytical performance on the Sysmex XF-1600 platform with reliable data analysis using VenturiOne software. Incorporation of cCD38 enabled consistent plasma cell detection despite potential interference from anti-CD38 monoclonal antibody therapy and allowed clear separation of normal and aberrant plasma cell populations. To our knowledge, this represents the first reported multiple myeloma MRD assay established in Australia on a Sysmex platform incorporating cCD38 within a 14-colour panel.

Conclusion:

This study demonstrates the feasibility of implementing high-parameter flow cytometric MRD assessment for multiple myeloma on the Sysmex XF-1600 platform, with analysis using VenturiOne software. Incorporation of cCD38 may improve plasma cell identification following anti-CD38 monoclonal antibody therapy and supports broader adoption of sensitive MRD testing using flow cytometry.

AL Amyloidosis with Progressive Liver Failure: A Transplant Dilemma

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Background:

Solid organ transplantation in AL amyloidosis is rarely performed due to frequent multi-organ involvement. Although the liver is the third most commonly affected organ, isolated or predominant hepatic involvement requiring liver transplantation remains uncommon. Underlying multiple myeloma as the driver of amyloidosis has also historically limited transplant eligibility because of concerns regarding post-transplant outcomes and disease progression. We report a case of myeloma-associated kappa light chain AL amyloidosis presenting with hepatic failure requiring liver transplantation.

Case Report:

A 61-year-old male, with no past medical history, presented with ascites and hepatomegaly of unclear cause. After extensive investigation, a liver biopsy was performed showing diffuse sinusoidal amyloid deposition. Stage I AL amyloidosis secondary to myeloma was diagnosed with raised kappa free light chains (443mg/L), 30% bone marrow plasma cells and associated factor X deficiency. There were no renal or cardiac involvement based on urinalysis, troponin, NT-proBNP and TTE and no evidence of lytic lesions.

Four months post, despite complete response with Daratumumab-Bortezomib-Cyclophosphamide-Dexamethasone therapy, bilirubin worsened from 27 to 440 $\mu\text{mol/L}$ with refractory ascites, hepatorenal syndrome, coagulopathy and MELD-Na peaking at 44. Repeat liver imaging excluded alternative causes and repeat liver biopsy confirmed cholestasis and hepatic atrophy caused by extensive amyloidosis.

Referral for liver transplant was sought and inpatient work up was expedited to meet stringent eligibility criteria. Cardiac MRI excluded cardiac involvement but scant amount of amyloid deposit was seen in the duodenum and non-specific microalbuminuria has developed since diagnosis. After further multi-disciplinary discussion with gastroenterology, nephrology, State Amyloid Clinical Lead and Liver Transplant unit, eligibility was eventually confirmed based on absence of significant other organ dysfunction. Six weeks later, he underwent liver transplantation. At 5-month post-transplant, he remains in complete remission and has not restarted anti-myeloma therapy.

Conclusion:

Predominant hepatic involvement in myeloma-associated AL amyloidosis with progressive liver failure is uncommon. In carefully selected patients with limited extrahepatic disease, liver transplantation may represent a potential life-saving option, particularly in the modern era of improved myeloma survival with advanced anti-plasma cell therapies.

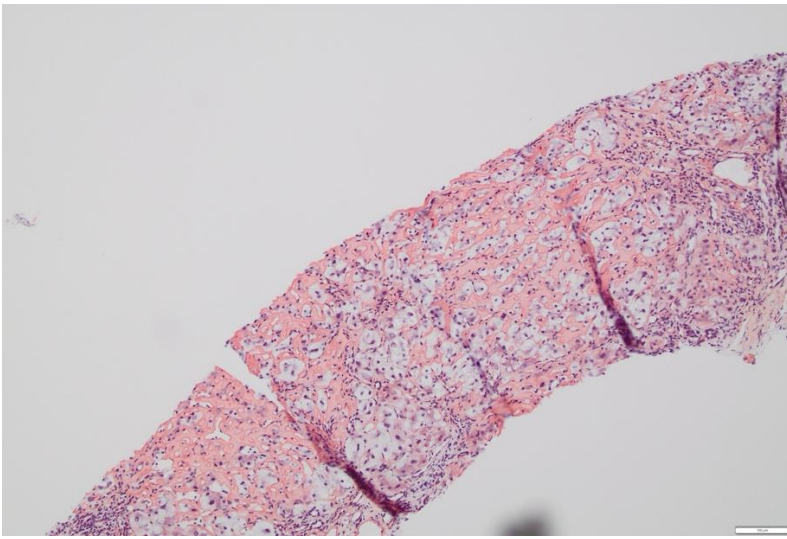


Figure 1 Congo red staining highlights amyloid deposition between hepatocytes.

Elranatamab therapy in relapsed refractory multiple myeloma patients with chronic kidney disease: a case series

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Aim:

Elranatamab monotherapy has demonstrated efficacy in treating relapsed refractory multiple myeloma (MM). However, clinical trials for this therapy excluded patients with stage 4 and 5 chronic kidney disease (CKD). Therefore, safety and efficacy data about Elranatamab therapy in this cohort are limited. This case series contributes to the limited literature about the topic, by describing Elranatamab use in three cases with refractory MM and stage 4 and 5 CKD. We aim to report the safety profile and efficacy of this therapy in this context.

Method:

Three cases were recruited from Sir Charles Gairdner Hospital, a tertiary centre in Perth, Western Australia. Data were extracted from the medical record about the aetiology and degree of renal failure, previous lines of MM therapy used, adverse events related to Elranatamab use and response to therapy (including serum and urine light chains).

Results:

The three cases, including one on haemodialysis, had at least three lines of MM therapy prior to receiving Elranatamab. Only one case experienced grade 1 cytokine release syndrome, successfully managed with Tocilizumab and Dexamethasone. No cases experienced immune effector cell-associated neurotoxicity syndrome. One case decided to cease therapy after one cycle due to non-specific symptoms including fatigue and anorexia. All three cases demonstrated serological response to Elranatamab therapy even after one cycle.

Conclusion:

This case series contributes to the existing but limited literature suggesting Elranatamab monotherapy is safe and effective in patients with relapsed refractory MM with stage 4 or 5 CKD.

MALDI-TOF mass spectrometry with its enhanced specificity reduced therapeutic antibody interference in Multiple Myeloma monitoring

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Aim:

Therapeutic monoclonal antibodies (mAbs), including anti-CD38 agents daratumumab and isatuximab, interfere with serum immunofixation electrophoresis (sIFE) due to shared isotype and electrophoretic co-migration with endogenous monoclonal proteins (M-proteins). Accurate detection of M-proteins is essential for monitoring monoclonal gammopathies and determining treatment response, including complete response (CR). sIFE interference therefore may lead to false-positive results, misclassification of response and possibly affecting patient management. In contrast, MALDI-TOF mass spectrometry (MS) distinguishes immunoglobulins by mass-to-charge (m/z) ratios, with potential limited overlap of ± 4 m/z. Therapeutic antibodies have defined m/z signatures (daratumumab 11,691; isatuximab 11,745).

The aim was to assess the frequency of clinically relevant spectral overlap between endogenous IgG κ / κ M-proteins and anti-CD38 mAbs, and compare interference rates between MS and sIFE.

Method:

A total of 1101 serum samples were retrospectively analysed by MALDI-TOF MS (EXENTTM, The Binding Site) and sIFE (SAS Vitrési, Helena BioSciences). Among these, 505 patients with IgG κ or κ light-chain M-proteins were identified; with 125 were actively receiving anti-CD38 therapy and evaluated for clinically relevant interference. Interference rates between MS and sIFE were compared using Fisher's exact test.

Results:

Theoretical m/z proximity (± 4 Da) was observed in 6.34% (32/505) for daratumumab and 3.76% (19/505) for isatuximab. Among treated patients, clinically relevant MS interference occurred in 2/125 cases (1.9%) versus 43/125 (34%) by sIFE. sIFE showed significantly higher interference (OR 31.5; $p < 0.0001$), corresponding to a 95% relative reduction with MS.

Conclusion:

MALDI-TOF MS significantly reduces therapeutic antibody interference compared with sIFE, improving specificity of M-protein detection. Its adoption may reduce diagnostic uncertainty and improve response assessment, particularly CR determination, in routine practice and in clinical trials.

Carfilzomib-associated posterior reversible encephalopathy syndrome - case series and review of the literature

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Background/Aim:

Posterior reversible encephalopathy syndrome (PRES) is a rare neurological condition generally arising as a consequence of hypertension or drug reactions and can lead to seizures and death. PRES associated with carfilzomib administration has only been described in single case reports. We describe the clinical presentation, investigation, and management of three cases of PRES associated with carfilzomib in patients with multiple myeloma.

Method:

Retrospective case review of three patients with multiple myeloma who developed PRES while receiving carfilzomib-based regimens. Clinical features, diagnostic investigations, management strategies, and outcomes were reviewed retrospectively from medical records across three centres.

Results:

Three patients (73F, 63M, 67M) presented with confusion in two cases and headache in one case. In two cases, hypertension was noted at time of presentation. In one case, concomitant microangiopathic haemolytic anaemia was present. MRI brain confirmed radiological features of PRES in all cases. Management included withholding carfilzomib and managing blood pressure where indicated. In all three cases, there was complete clinical and radiological resolution. In two cases, carfilzomib was successfully reintroduced at a reduced or stepwise-escalated dose without recurrence of PRES. Our experience mirrors four previous single case reports in whom PRES resolved after carfilzomib cessation and supportive management.

Conclusion:

Carfilzomib-associated PRES is a rare complication with heterogeneous presentation. A raised index of suspicion in patients presenting with headache, confusion and/or high blood pressure is important, and early neuroimaging is essential for accurate diagnosis. With appropriate management, outcomes can be favourable, and cautious reintroduction of carfilzomib may be feasible in selected patients. The pathogenesis remains unclear, and further studies could evaluate whether this phenomenon may be associated with carfilzomib-associated endothelial dysfunction/activation.

Not your average marrow – A case of avatrombopag-related reversible myelofibrosis in paediatric immune thrombocytopenia (ITP).

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Introduction:

Thrombopoietin receptor agonists (TPO-RAs) have an established role as second line therapies in the treatment of persistent or chronic paediatric immune thrombocytopenia (ITP). However, there is limited data concerning the long-term effects of second generation TPO-RAs (specifically avatrombopag) in the paediatric population.

Case Presentation:

We report a 4-year-old boy with chronic ITP who developed mild myelofibrosis after therapy with avatrombopag.

SF was diagnosed with acute ITP in July 2023 (age 26 months, initial platelet count 11). Due to frequent injuries, his remote location & chronicity of disease, he was treated with multiple therapies (including eltrombopag & romiplostim) with variable, non-durable responses over the ensuing 18 months. Bone marrow aspirate & trephine (BMAT) prior to treatment with TPO-RAs was normocellular with increased megakaryocytes with left shift consistent with peripheral destruction.

He was commenced on avatrombopag in February 2025 (age 45 months) as a sole agent & escalated to the maximum recommended dose after 4 weeks. An apparent early response (maximum platelet count 65) was not consistently sustained. After 8 months of therapy, his blood film revealed prominent teardrop poikilocytes with an occasional blast (1-2%). Subsequent BMAT showed increased megakaryopoiesis with some left shifted maturation, clustering & abnormal paratrabecular forms. In addition, there was increased fibrosis compared to previous marrows (WHO MF1 with patches of MF2). There was normal erythropoiesis and granulopoiesis & no evidence of a malignant infiltrate.

Based on the above investigations, avatrombopag was ceased & a trial of mycophenolate was commenced. A follow up BMAT 4 months later revealed a return to previous marrow findings with complete resolution of the myelofibrosis.

Conclusion:

This case report of reversible myelofibrosis secondary to avatrombopag in a paediatric ITP patient highlights the importance of ongoing surveillance for adverse long-term effects of second generation TPO-RAs in this population.

Thrombolytic therapy in thrombotic thrombocytopenic purpura presenting with acute ischaemic stroke: a case report and systematic review.

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Background:

Thrombotic Thrombocytopenic Purpura (TTP) can present with acute ischaemic stroke. However, profound thrombocytopenia and the risk of catastrophic haemorrhage limit the use of thrombolytic therapy in these patients.

Aim:

To describe a case of thrombolysis in a patient with TTP presenting with acute ischaemic stroke, and to systematically review published cases evaluating the use and safety of thrombolysis in this setting.

Method:

A case report and a PRISMA-compliant systematic review were conducted. Databases searched included PubMed, Ovid MEDLINE, Embase, and Scopus for studies published within the past 15 years. Primary outcomes were functional neurological recovery and haemorrhagic complications.

Results:

A 20-year-old female presented with expressive aphasia and right-sided hemiplegia consistent with left middle cerebral artery-territory stroke. She received intravenous alteplase within 3 hours of symptom onset following standard acute stroke assessment. A subsequent full blood count revealed severe thrombocytopenia (platelet count $6 \times 10^9/L$) with schistocytes on film, without coagulopathy, and undetectable ADAMTS13 activity, consistent with TTP. She underwent urgent plasma exchange, corticosteroids and rituximab. There were no major haemorrhagic complications, and she achieved complete neurological recovery.

A systematic review with pre-specified search terms identified 117 records, of which 5 studies met the inclusion/exclusion criteria. In all cases, patients presented with acute stroke symptoms before recognition of thrombocytopenia and received tissue plasminogen activator (tPA). Neurological improvement occurred in all patients, with 3 demonstrating minor residual deficits. Haemorrhagic complications were uncommon, with 1 patient experiencing haemorrhagic transformation post-thrombolysis. All patients underwent plasma exchange, 1 also received long-term rituximab, and 1 methylprednisone.

Conclusion:

Thrombolytic therapy may be tolerated in selected patients with unrecognised TTP presenting as acute ischaemic stroke, with favourable neurological outcomes reported in most cases. However, evidence remains sparse, and the risk of haemorrhagic complications requires careful consideration. Early recognition of TTP following thrombolysis remains critical to facilitate urgent plasma exchange and avoid complications.

Comparison of manual left shift index with automated immature granulocyte count in identifying neonatal sepsis

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Aim:

Early identification of neonatal sepsis is challenging due to its non-specific presentation and reliance on blood cultures. The immature-to-total neutrophil ratio (I/T ratio) is commonly used. Automated immature granulocyte (IG) parameters have been validated, but limited data exist for the Sysmex XN-9000. This study compares the left shift index (LSI), analogous to the I/T ratio, with IG measurements for neonatal sepsis detection.

Method:

We retrospectively reviewed neonates admitted to Starship Hospital NICU from November 2024 to February 2025. Full blood counts within 48 hours of blood or CSF cultures were included. Exclusions: repeat samples within 7 days, cord blood and transient abnormal myelopoiesis. Absolute IG counts were quantified on Sysmex XN-9000. Manual differentials were performed on smears. Cases were classified as likely or unlikely sepsis, including both early (<72h) and late (≥72h) onset. Receiver operator characteristic (ROC) curves and box plots were used for analysis.

Results:

Among 264 suspected episodes in 232 neonates, 98 were classified as likely sepsis (9 culture positive). 167 (63.7%) cases were early-onset. Most cases were 28 to 36 weeks corrected gestational age, only a minority were extreme preterm. Only 3.4% cases had preceding surgery. LSI >0.2 had a sensitivity of 60%, specificity of 72%, PPV of 56% and NPV of 76%. IG >0.06 E+9/L had higher sensitivity (76%) but lower specificity (17%), PPV of 35% and NPV of 56%. 17 cases were excluded due to analyser issues; 14 were likely sepsis.

Conclusion:

LSI remains a valuable but imperfect tool in the early evaluation of neonatal sepsis, in the absence of robust alternatives. Automated IG parameters on Sysmex XN-9000 are inferior to manual methods. Larger prospective studies are needed to confirm these findings.

Diagnostic pitfalls: catching HLH before it's too late

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Aim:

Hemophagocytic Lymphohistiocytosis (HLH) is a rare, life-threatening hyperinflammatory condition due to deregulated immune system activation. The incidence of HLH diagnosis is increasing. It is classified into Primary (genetic/familial) and Secondary (acquired). This abstract compares the presentation of HLH triggered by infection, malignancy, and autoimmunity; and the utility of a standardised approach to investigation and treatment.

Method:

Three patients were selected from 2025 to first quarter of 2026 who presented the clinical triad of persistent and antibiotic-resistant fever, falling blood counts, elevated ferritin (the 3 Fs). HLH-2016 and HLH-2024 criteria were used as basis for the tests required. The patients' initial and most abnormal (peak) results were compared for the calculation of H-Score. Identification and classification of triggers were based on multi-disciplinary diagnostic findings.

Results:

The initial H-Score of Patient A and B were 70-80% HLH probability, while Patient C had borderline 40-54% probability. All three patients' peak H-Score were >99% probability. Patient A had Epstein-Barr Virus infection and showed markedly reduced SLAM-associated protein expression (Primary HLH). Patient B was diagnosed with Diffuse Large B-cell Lymphoma which had transformed from Nodular Lymphocyte-Predominant Hodgkin Lymphoma. Patient C returned a weak positive result in Melanoma Differentiation-Associated gene 5 autoantibody, a biomarker of dermatomyositis. Patient B and C were classified as Secondary HLH.

Conclusion:

Increasing HLH awareness and early recognition of 3Fs may lead to fewer missed cases and reduced mortality. This presentation illustrates that the progress of infection-driven HLH is quick, but response to treatment is also prompt. Lymphoma-driven HLH may be explosive, demonstrating severe hyperinflammatory results which may mask the underlying malignancy. Autoimmune-driven HLH may appear as sepsis-like illness and progress to multi-organ effusions and can be refractory to first-line treatment. Getting It Right First Time (GIRFT) is the recommended standard to diagnosis and management of HLH.

A retrospective single-centre scoping study of CHIP/CCUS

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Aim: Clonal haematopoiesis of indeterminate potential (CHIP) and Clonal cytopenia of undetermined significance (CCUS) are increasingly identified on next-generation sequencing (NGS) utilised in daily clinical practice. This study addresses the limited data on the Australian landscape of CHIP/CCUS in haematology clinic cohorts, including the prevalence, risk profiles and non-haematologic complications.

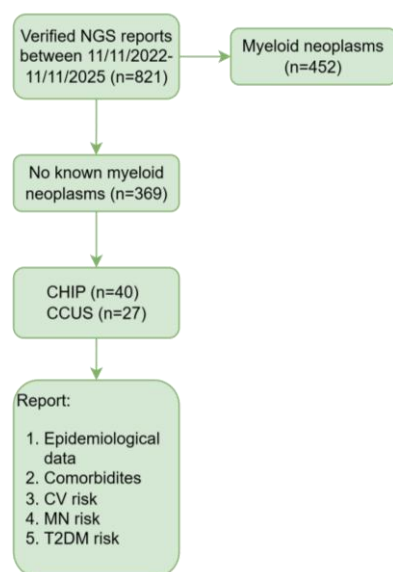
Method: Clinical and laboratory data were extracted between 11/11/2022 and 11/11/2025 to determine the frequency and characteristics of CHIP/CCUS among people who underwent targeted somatic haematological NGS locally (n=821). This was predominantly the combined myeloid and lymphoid panel, including bone marrow and peripheral blood samples.

Results: NGS was performed for myeloid neoplasms (MN) in 55% (n=452). In the remainder (n=369, 45%), there were 40 CHIP and 27 CCUS (total 67; 8.2% of the entire cohort). The median age was 71.9 years, 56.7% males. CHIP/CCUS was identified during investigation for cytopenia, cytoses, or a secondary finding in non-MN (22.4%) and immune/inflammatory conditions (6%). 24% received cytotoxic therapy.

Most common variants were *DNMT3A* (30.5%), *TET2* (24.8%), and *ASXL1* (7.6%). The average VAF was 10% (median 5%, and 36% had a VAF $\geq$ 10%). Three patients were pathogenic germline variant carriers, including *CHEK2*.

MN risk stratification by CHRS was predominantly low (53.7%) and intermediate (41.8%). Three (4.5%) had high risk, all CCUS. However, CCRS stratification yielded 8 high-risk CCUS. 42.2% had cardiovascular (CV) diseases, 40.6% had chronic kidney disease, 22.4% had Type 2 diabetes mellitus, and 10.9% had cerebrovascular disease. 43% had high CV risk (AusCVD), and 73% had high T2DM risk (AUSDRISK).

Conclusion: CHIP/CCUS was identified in 8.2% of this small cohort at risk over 3 years, either during investigation for cytopenia or as a secondary finding. MN risk scores were predominantly low to intermediate. A considerable proportion had CH-associated complications, high AusCVD and AUSDRISK scores.



Retrospective study of clinical features and treatment patterns in patients with Hereditary Haemorrhagic Telangiectasia (HHT).

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Introduction:

HHT is the second most common bleeding disorder in the world, characterised by the development of mucocutaneous telangiectasia and visceral arteriovenous malformations. The condition is autosomal dominant with pathological variants involving the ENG and ACVRL1 gene. Diagnosis is delayed and management is largely supportive. Currently, there is a lack of Australasian data capturing the clinical characteristics of HHT patients.

Aim:

To identify the patient characteristics and management gaps of patients diagnosed with HHT in Australasia.

Method:

We examined HHT patient medical records from two Australian tertiary referral hospitals. Descriptive statistics are reported.

Results:

A total of 28 patients were clinically diagnosed with HHT (Curacao criteria). 53% had a known genetic mutation associated with HHT. Median age of the cohort was 59.5 years and 71% of patients were women. 46% of patients have received bevacizumab in the last 12 months. The average Epistaxis Severity Score (ESS) score for a patient on bevacizumab was 4.25 compared with an average ESS of 3.73 for those not currently on bevacizumab.

50% of patients had an iron infusion in the last 12 months, with a higher proportion of these on systemic therapy (69%). Screening for pulmonary and cerebral manifestations of HHT deviated from current international recommendations as only 43% were fully adherent.

Conclusion:

This data analysis is the first of its kind in Australasia, describing the clinical features and current management of patients diagnosed with HHT. Delay to diagnosis represents an opportunity for improved clinician awareness and better access to genetic analysis.

Our ongoing collaborations with other sites across Australia and New Zealand are critical to collate more information and inform the development of national guidelines to aid diagnosis, management, and improve the standard of care for HHT patients.

Assessment challenges in a malarial parasite density count EQA program

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Aim:

Parasite density counts of asexual plasmodial developmental forms are used in malaria treatment decisions, to distinguish between uncomplicated and severe infections, and to monitor parasite clearance during treatment. These counts are performed on the thick or thin film. The RCPAQAP Malarial Parasite Program issues 2 cases per year for density counts. Assessment of the returned data has proved challenging due to a large variation in the returned data and the implications for clinical interpretation

Method:

Digital blood film (thick and thin) images of *P. falciparum*-positive samples were provided to 250 enrolled participants to perform and report a density count, along with the method used. Participants count parasites on a digital scan in both parasites/uL and/or % density. Results collected over 4 years (8 samples) were evaluated using descriptive statistics (median, mean, SD, and CV%) and z-score assessment (mean $\pm$ 2SD) to determine whether 80% of results in this period met an acceptable clinical standard that would enable assessment using z-score criteria.

Results and Discussion:

89-93% of the 250 participating laboratories returned results within $\pm$ 2SD of the mean across all 8 samples. This indicates that z-score assessment would be a valid indicator of acceptable performance.

Conclusion:

The World Health Organisation requires that a diagnosis or microscopy be supported by quality assurance programs. While there is an existing program for malarial parasite density count, this has previously been issued for educational purposes and has had no assessment applied. This study's results indicate that a z-score assessment is appropriate for this program and would provide participants with a suitable means to gauge the suitability of their methods and calculations.

Red Cell Distribution Width (RDW) in Haematological and Nonhematological Disorders: An Under-Recognised Prognostic Marker

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Background:

Red cell distribution width (RDW) is a routinely reported parameter of the complete blood count and has traditionally been used to assist in the classification of anaemia. Growing evidence indicates that RDW also serves as a useful biomarker across a broad range of nonhematological conditions, where it has been linked to increased disease severity, morbidity, and mortality. As a result, RDW has emerged as a readily available and cost-effective marker with potential prognostic significance beyond haematological disorders.

Aim:

To assess the role of RDW in haematological and nonhematological disorders and its usefulness as a readily obtainable prognostic marker in clinical settings.

Method:

A narrative review of the literature was undertaken focusing on the physiological basis of RDW variation and its reported associations across haematological and systemic diseases. Emphasis was placed on conditions commonly encountered in routine pathology and acute care settings. RDW is measured by automated FBE analysers (e.g. Sysmex which is in operation across Eastern Health Labs). These analysers calculate RDW by measuring red cell volumes to generate an RBC histogram, from which RDW-CV and RDW-SD are automatically derived.

Results:

Elevated RDW is commonly observed across various chronic and inflammatory conditions, including various anaemias, cardiovascular, liver, and kidney diseases. Increased RDW reflects underlying processes such as nutritional deficiency, bone marrow suppression, impaired erythropoiesis, and chronic inflammation. Furthermore, it correlates with disease presence and severity.

Conclusion:

RDW is a simple, inexpensive, and widely available biomarker that provides valuable diagnostic and prognostic information across a spectrum of illnesses when interpreted in appropriate clinical context. Furthermore, RDW is a valuable adjunct laboratory marker that provides important insight into underlying disease processes beyond anaemia and should not be overlooked in routine FBE interpretation.

Current status of the aplastic anaemia and other bone marrow failure syndromes registry (AAR)

Mrs Vanessa Fox¹, Dr Lucy Fox^{1,2}, Dr Laura Sellick¹, Mr Neil Waters¹, Mr Cameron Wellard¹, Dr Nathanael Lucas^{1,3,4}, Dr Elizabeth Prime¹, Professor Zoe McQuilten^{1,5,6}, Prof Frank Firkin⁷, Prof Erica Wood^{1,6}

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Background:

Bone marrow failure syndromes (BMFS) are a heterogeneous group of acquired (e.g. immune aplastic anaemia [iAA]) and inherited disorders (which encompasses hereditary predisposition to haematological malignancies [HPHM]). Diagnosis is challenging but new scientific knowledge and genetic testing availability have enabled better & faster diagnosis, more targeted therapy, and counselling for patients & families. Long-term data are necessary to understand local disease prevalence, natural history, and effectiveness of new therapies.

Method & Results

The AAR is overseen by a multidisciplinary steering committee with patient/family representation, and receives funding from Maddie Riewoldt's Vision, a community organisation. Cases of both acquired and inherited BMFS and HPHM from paediatric and adult patients are contributed from 37 participating Australian hospitals, and 6 sites in New Zealand are in progress. Data collected include patient demographics, diagnosis, family history, clinical presentation and prescribed therapies and outcomes.

Of 637 participants, 49.7% are female and 23.7% children <18 years. Of confirmed diagnoses, 57.5% are iAA, 38.3% inherited BMF disorders and 4.2% clinically unclassifiable.

Inherited disorders include Diamond-Blackfan Anaemia (12.3% cases), Fanconi Anaemia (8.6%), Shwachman-Diamond Syndrome (9.4%), telomeropathies (7.8%) and severe congenital neutropenia (8.2%). The most common HPHM mutations are DDX41 (13.5% cases), GATA2 (5.3%) and RUNX1 (4.9%).

Collaborations

The AAR has supported the MRFF-funded IBMDx study and DIAAMOND trial of avatrombopag, and is currently supporting these collaborative activities:

1. Australian Marrow Failure Biobank – biological samples linked with AAR's comprehensive clinical dataset
2. International initiatives:
 - Telomere Biology Disorders: CCCTAA Consortium, National Cancer Institute
 - Severe Chronic Neutropenia International Registry, Boston Children's Hospital
 - Retrospective study of germline ANKRD26, University of Wisconsin
3. Capacity building: 2 current PhD students

Conclusion

The AAR provides valuable real-world data, including long-term follow-up, and both complements and supports clinical trials & biobanks. New sites & suggestions for analyses of registry data are welcome (contact: aar@monash.edu)

Appropriateness of inpatient intravenous iron infusion at Gold Coast University Hospital: a retrospective audit following identification of adverse infusion-related events

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Aim:

Intravenous iron is indicated for iron deficiency anaemia, anaemia of chronic kidney disease and heart failure with reduced ejection fraction where oral iron is ineffective or contraindicated. Inappropriate use may expose patients to avoidable risks. Among 1,086 inpatient iron infusions administered at our institution between January 2025 and June 2025, 14 adverse infusion-related events were identified, including one case of extravasation requiring ICU admission for septic shock with ongoing dialysis dependence. Of these, 8 were retrospectively judged inappropriate administration. This audit aimed to assess the appropriateness of inpatient intravenous iron and identify common clinical scenarios associated with inappropriate use.

Method:

A retrospective chart review of 200 randomly selected patients who received intravenous iron between January 2025 and June 2025 was performed. Clinical and laboratory data including full blood count, iron studies, renal function and documented indication were extracted. Cases were adjudicated as appropriate or inappropriate using indication-based criteria for iron deficiency anaemia (with age-adjusted thresholds for patients aged over 75 years¹), anaemia of chronic kidney disease and heart failure with reduced ejection fraction.

Results:

Over the six-month audit period, 200 of 1,068 inpatient intravenous iron infusions were reviewed. Of these, 99 infusions (49.5%) were adjudicated appropriate and 101 (50.5%) inappropriate.

Among inappropriate infusions, 61 (60.4%) were administered to patients without anaemia, and in no case was a prior trial of oral iron supplementation documented. Other common issues included iron repletion at time of infusion and administration when intravenous iron is otherwise not recommended, including acute infection and first trimester of pregnancy.

Conclusion:

In this audit, 101 of 200 inpatient intravenous iron infusions did not meet the predefined criteria for prescription, while 99 were assessed as appropriate. Inappropriate infusions commonly involved patients without anaemia, no documented trial of oral iron therapy, or clinical contexts in which intravenous iron is contraindicated. These findings highlight an opportunity to refine local prescribing guidance and better align inpatient intravenous iron use with appropriate clinical indications.

Reference:

1. Fougère B, Morley JE, Decavèle M, et al. Prevalence of iron deficiency in patients admitted to a geriatric unit: a multicenter cross-sectional study. *BMC Geriatrics* 2024;24(1):112.

Thrombophilia testing in a tertiary hospital - who, what, when and why?

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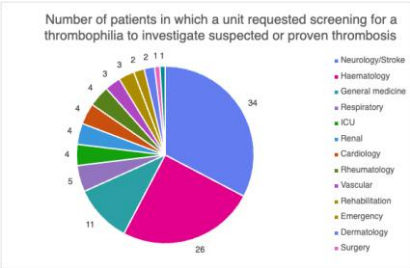
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Aim: Individuals with hereditary and acquired thrombophilia may be predisposed to thrombo-embolic events, more commonly of the venous system (VTE). The utility of testing is somewhat controversial as these conditions are rare, and with few exceptions, identifying them frequently does not change the patient’s management (choice or duration of anticoagulant). We reviewed ordering practices in a single tertiary adult hospital to determine which patients are being investigated for a thrombophilia, how frequently the tests return a positive result, and whether the results affected clinical management.

Method: We performed a retrospective audit of patients who received testing for antiphospholipid syndrome (APLS), protein C or S deficiency, antithrombin deficiency, factor V Leiden and/or thrombin 20210A gene mutation, between 1/1/2024 - 31/3/2024 inclusive at The Royal Melbourne Hospital.

Results: 167 patients were included, with 95 having a history of suspected or proven thrombus (45 venous, 50 arterial); this “thrombosis” sub-group was further analysed. Testing was most frequently ordered by the Neurology unit (34 patients), with Clinical Haematology involved with 26 patients (Figure 1). Three had a family history of VTE. Of the 526 tests performed, 7% showed a positive result (Figure 2). The most common test ordered was lupus anticoagulant though 29% had inconclusive results due to presence of anticoagulant or insufficient sample. 24 patients had at least one test repeated, including unnecessary repeat of previously normal genetic testing. 28 patients had at least one initial positive result; but a new diagnosis of thrombophilia affected management in only one patient.

Figure 1: Requesting units of thrombophilia screens



NB some patients had >1 unit involved in decision-making and are therefore represented twice.

Figure 2: Testing in the “thrombosis” sub-group

Test	Number of tests ordered	Number of positive results
Lupus anticoagulant	84	2 (24 inconclusive)
Anticardiolipin antibody	77	7
Anti-beta-2-glycoprotein 1 antibody	77	3
Protein C	65	3
Protein S	57	4
Antithrombin III	54	9
Factor V Leiden	65	7 – all heterozygote
Prothrombin 20210A gene mutation	47	1 - heterozygote
PNH flow cytometry	12	1
MPN next generation sequencing panel	6	1
Homocysteine	3	0

Conclusion: At our institution during this period, thrombophilia tests were more frequently ordered for arterial than venous thromboembolism. Diagnosis of a new thrombophilia was rare and only led to change in management in a single patient. Our study suggests a more targeted approach to testing should be considered, including appropriate timing and potential management implications.

Effectiveness and safety of avatrombopag for treatment of immune thrombocytopenia in older patients and those with comorbidities or prior TPO-RA exposure: interim results from the phase 4 ADOPT study

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Aim:

To describe interim results from ADOPT among patients aged ≥ 65 years, and those with comorbidities, or prior TPO-RA exposure.

Method:

ADOPT is an ongoing phase 4 observational study across 60 centres in 9 European countries. Adults with established ITP receiving avatrombopag were included; secondary ITP was excluded. Retrospective data was collected for up to 12 months prior initiation, and prospective data for up to 12 months post enrolment. Primary endpoint is cumulative weeks with platelet count (PC) $\geq 30 \times 10^9/L$ during treatment. Secondary endpoints are weeks with PC $\geq 50 \times 10^9/L$, SAEs and AEs of special interest (TEE or clinically significant bleeding). Analyses were descriptive by subgroup: ≥ 65 yrs, comorbidities (TEE risk factors) and prior TPO-RA exposure.

Results:

As of 12 Nov 2024, 200 patients enrolled; 51 (25.5%) completed the study. Subgroups included ≥ 65 yrs (n=73), comorbidities (n=89) and prior TPO-RA exposure (n=128, eltrombopag n=58, romiplostim n=45, eltrombopag+romiplostim n=25). 55.5% were female. Mean age ranged from 50.3 years (ELT+ROM group) to 75.2 years (≥ 65 yrs). Median cumulative dosing duration was 52.3 weeks for all groups. Concomitant ITP therapy was 39% (≥ 65 yrs/comorbidities) and 26.7%-56.0% (prior TPO-RA). Rescue therapy used $\leq 20\%$ of patients.

Median weeks with PC $\geq 30 \times 10^9/L$ ranged from 46.3 (ELT+ROM) to 52.1 (ELT). Median weeks with PC $\geq 50 \times 10^9/L$ ranged from 42.9 (ELT+ROM) to 50.2 (ELT). All patients with ≥ 8 weeks of follow-up maintained PC $\geq 50 \times 10^9/L$ for ≥ 8 consecutive weeks.

16.0% (ELT+ROM) to 23.3% (≥ 65 yrs) 10.3% to 16.9%. of patients experienced an AE or SAE respectively. AESI ranged from 6.7%-8.0% and included atheroembolism, deep vein thrombosis, pulmonary embolism, and cerebral venous thrombosis. To date, 3 non-avatrombopag-related deaths have been reported.

Conclusion:

Avatrombopag was effective across subgroups (≥ 65 y, comorbidities, prior TPO-RA) with no new safety concerns. These findings provide insights for optimising treatment strategies in diverse real-world populations.

Benefit of pegcetacoplan in patients with paroxysmal nocturnal haemoglobinuria irrespective of baseline transfusion status.

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Aim:

Evaluate the effect of baseline transfusion status on key haematological and clinical responses to pegcetacoplan in C5i-experienced and-naïve PNH pts over long-term follow-up.

Method:

This post-hoc analysis assessed long-term efficacy & safety of pegcetacoplan in 2 subpopulations, patients with <4 or ≥4 red blood cell concentrates (RBCs) in the 12 months prior to study enrolment, as part of an integrated analysis of PRINCE, PEGASUS and the subsequent open-label extension. Time-aligned outcomes, including Hb, LDH, ARC and FACIT-Fatigue were assessed for up to 192 weeks.

Results:

In 12 months prior to enrolment, 64 pts had received <4 RBCs and 68 pts had received ≥4 RBCs. At baseline, mean (SD) age was 46.2 (16.0) years and 47.9 (14.8) in the <4 and ≥4 RBCs group, respectively; 50% (32) and 60.3% (41) of patients were female. Overall, improvements in mean Hb, LDH, ARC and FACIT-Fatigue over time were consistent between transfusion status groups (</≥4 RBCs). By Week 4 after initiation, mean (standard error) Hb levels increased from 9.2 (0.2) g/dL and 9.0 (0.1) g/dL at baseline to 12.3 (0.2) g/dL and 12.1 (0.4) g/dL in the <4 RBCs and ≥4 RBCs group, respectively. Improvements were sustained for up to 192 weeks. Median LDH decreased at Week 4 and remained mostly stable below 1.5xULN. Initial reductions in mean ARC were sustained. Improvements in haematological parameters translated into rapid increases in mean FACIT-Fatigue scores and improvements were largely maintained long-term. Safety profile was comparable between the groups. 35 (55%) and 38 (56%) pts with <4 and ≥4 RBCs, respectively, experienced serious adverse events (AE), deemed PEG-related in 2 and 4 pts. 6 (9%) and 11 (16%) pts discontinued PEG due to an AE.

Conclusion:

Efficacy was achieved and maintained for up to 192 weeks regardless of baseline transfusion status, a conventional marker of PNH severity.

Consistent benefits of pegcetacoplan in PNH patients with and without a history of aplastic anemia in real world: Interim analysis of COMPLETE Phase IV observational study.

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Aim:

Describe real-world effectiveness of pegcetacoplan in patients with PNH and a history of aplastic anaemia (HAA) or no history of aplastic anameia (NoHAA).

Method:

COMPLETE (NCT05776472) is a 36-month observational study enrolling 200 adult patients internationally, including Australia. Primary objective is haemoglobin (Hb) levels from pegcetacoplan start to 6 months. Secondary objectives include changes in LDH, ARC and improvement in Hb (Hb ≥ 12 g/dL or increase ≥ 2 g/dL) every 6 months, transfusion requirements and AEs. Baseline disease characteristics were comparable between cohorts.

Results:

As of 12 January 2025, 70 patients were recruited; 24 had a confirmed HAA and 43 have NoHAA. Median baseline Hb (IQR) was 8.7g/dL (8.3-10.0) for HAA patients and 9.4g/dL (8.8-10.3) for NoHAA. 15 and 32 patients were included in the 6-month analysis, respectively.

At 6 months, median (IQR) Hb increase was 2.0g/dL (0.9-3.0) and 2.6g/dL (0.8-3.5). Median (IQR) Hb was 11.2g/dL (10.3-12.5) and 11.7g/dL (10.5-13.0) respectively. 33.3% of HAA patients and 46.9% of NoHAA patients achieved Hb levels ≥ 12 g/dL. Improvements were maintained at 12 months.

Hb increase was accompanied by corresponding benefits in LDH, ARC and Tx regardless of prior AA history. Median (IQR) LDH improved from 340.0U/L (303.0-369.0) to 192.0U/L (161.0-238.0) and from 291.0 U/L (228.0-365.0) to 227.0 U/L (180.0-265.0) for HAA and NoHAA patients respectively. Median (IQR) ARC decreased from 174×10^9 cells/L (145-205) to 96×10^9 cells/L (62.0- 118.7), and from 217×10^9 cells/L (171- 265) to 105×10^9 cells/L (81.8-136.6) respectively. Transfusion requirements reduced compared to the year prior.

No haemolytic events requiring additional intervention were reported at 12 months in the HAA group, compared to 6 NoHAA patients. 1 SAE (headache) lead to discontinuation.

Conclusion:

Pegcetacoplan improved markers of haemolysis in patients with PNH in real world settings, regardless of history of AA.

Characterising intravenous iron prescribing patterns at Northern Health

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¹Northern Health, Melbourne, Australia

Aim:

To characterise intravenous iron prescribing patterns across hospital departments, infusion settings and iron formulations at a local health service.

Method

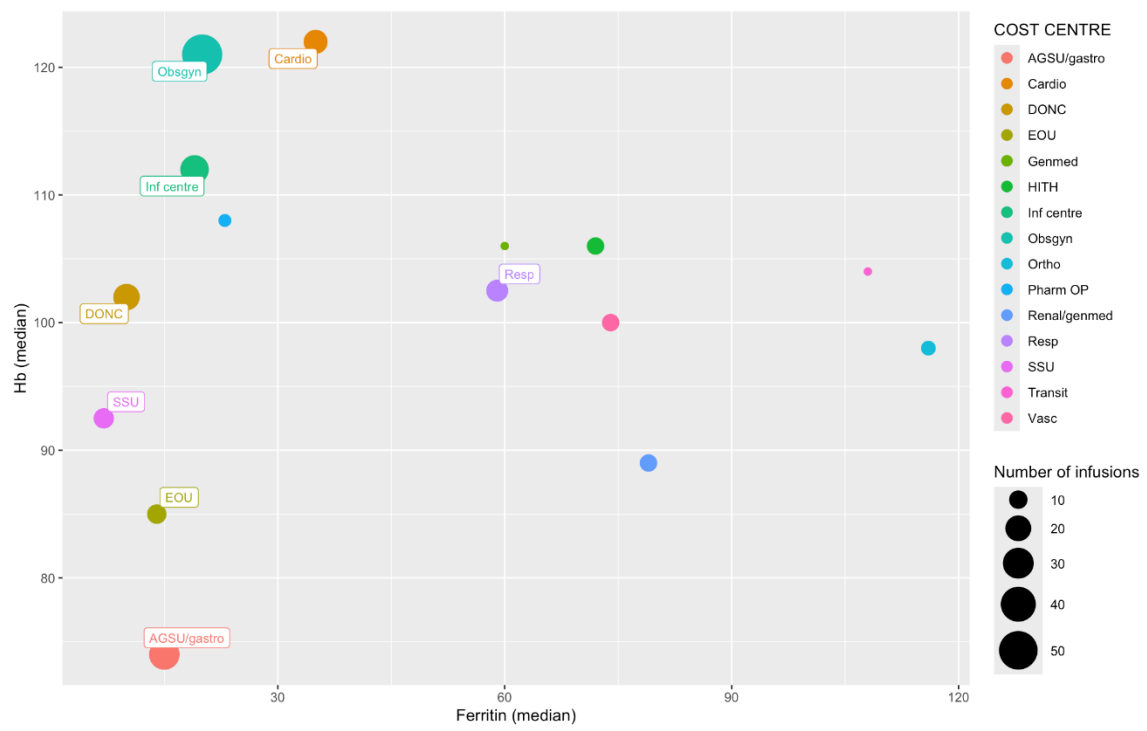
We conducted a retrospective analysis of intravenous iron prescriptions administered at Northern Hospital, Epping, between 1 and 30 November 2025. Pharmacy dispensing records were linked with electronic medical records to extract prescribing location, treating unit, iron formulation, dose, and pre-infusion haemoglobin, mean corpuscular volume, ferritin and transferrin saturation. Prescribing patterns and biochemical parameters were summarised using descriptive statistics.

Results

Over the study period, 246 intravenous iron infusions were administered. Most occurred associated with an inpatient admission (n=187, 76%), with fewer administered as an outpatient (n=56, 22.8%) or through Hospital in the Home (n=3, 1.2%). The most commonly prescribed formulation was ferric carboxymaltose (n=186, 75.6%), followed by ferric derisomaltose (n=43, 17.5%), iron polymaltose (n=14, 5.7%) and iron sucrose (n=3, 1.2%). Pre-infusion ferritin varied substantially across the cohort, with a median ferritin of 21 µg/L and wide range of values (3-872 µg/L, IQR 12-67 µg/L). Median pre-infusion ferritin also varied between departments, ranging from 7 µg/L in the short-stay unit to 116 µg/L in orthopaedics among departments with at least five infusions during the study period. The inpatient department most frequently associated with intravenous iron prescribing was obstetrics/gynaecology, comprising 55 infusions (22.4%).

Conclusion

Intravenous iron prescribing at Northern Hospital varied substantially by department, clinical setting and iron formulation. The majority of infusions were associated with an inpatient admission, indicating that inpatient encounters represent an important opportunity for the identification and treatment of iron deficiency. Variation in pre-infusion ferritin between departments likely reflects differences in patient populations, clinical indications and prescribing thresholds. Our findings support further review of interdepartmental prescribing practices, local guideline implementation and opportunities to improve consistency of intravenous iron use.



Minimising treatment delays and enhancing safety in acute intermittent porphyria: Case-based learnings from a haematology-led, multidisciplinary, streamlined care pathway

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Background

Acute intermittent porphyria (AIP) is a rare autosomal dominant disorder of haem biosynthesis whose attacks mimic surgical, neurological, and psychiatric emergencies. Its rarity contributes to delayed diagnosis, psychiatric misattribution, and uncertainty over admitting teams, compounding treatment delays.

Case

A young woman experienced recurrent abdominal pain and headaches from age 12, alongside significant mental health morbidity. AIP was diagnosed in March 2024 following an ICU admission with abdominal pain, hyponatraemia, and seizures, confirmed by markedly elevated urinary porphobilinogen and ALA. Subsequent presentations were characterised by delays due to admitting-team uncertainty and a complication of upper-limb venous thrombosis following haem arginate administration via a peripheral cannula. To address this, haematology became the default admitting team and led development of a streamlined multidisciplinary pathway with neurology, endocrinology, emergency, clinical pharmacology, and intensive care.

Discussion

AIP is caused by autosomal dominant mutations in the gene encoding hydroxymethylbilane synthase, with overaccumulation of porphyrin precursors (ALA/PBG) results in a “triad” of severe abdominal pain, peripheral neuropathy and central nervous system manifestations which mimic other surgical, neurological and psychiatric emergencies, resulting in diagnostic delays.

Triggers include fasting, infection, hormonal fluctuation, stress and porphyrinogenic drugs. Management involves ALAS1 suppression with timely haem arginate, dextrose loading, verified drug safety reference, acute pain management, monitoring for hyponatraemia, seizures, arrhythmia and disseminated intravascular coagulopathy. Haem arginate is a vesicant requiring central access. Givosiran, a PBS-listed ALAS1-targeting siRNA, reduces attack frequency and biochemical markers and improves quality-of-life.

Transferable pathway principles: (1) early designation of a primary admitting team; (2) multidisciplinary consensus with accessible documentation and pre-approved haem arginate protocol and acute pain team management; (3) formal linkage with tertiary clinical pharmacology expertise; (4) integrated mental health and clinical genetics referral.

Conclusion

Pre-emptive, haematology-led multidisciplinary care pathways transform recurrent emergency presentations into streamlined, protocolised care, reducing complications, improving patient experience, and shortening length of stay.

Anti-Xa marks the spot: a laboratory audit of DOAC drug level testing across two Sydney hospitals

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Aim:

To assess whether requests for DOAC anti-Xa and drug level testing at our tertiary institution aligned with guideline-supported indications. Secondary aims were to review laboratory turnaround times and to determine the extent to which test results influenced clinical management.

Method:

A retrospective laboratory audit was conducted of DOAC anti-Xa and drug level testing performed over a six-month period (April to September 2025 inclusive) across two Sydney hospital sites – a tertiary referral centre where the central laboratory is located and a district hospital requiring specimen transport for analysis. Data was extracted from the electronic medical record. Requests were assessed for appropriateness based on ICSH guidelines. Results were assessed for clinical informativeness and impact on management. Turnaround times were evaluated.

Results:

A total of 170 assay requests were analysed. Overall, 72% were considered appropriate according to guideline-supported indications and timing criteria. Anti-Xa testing was most commonly requested for urgent procedures (48%), clinically significant bleeding (15%) and renal impairment or suspected drug accumulation (10%). Although only 37 tests (22%) resulted in a documented change in management, results were considered clinically informative in 126 cases (74%). Serial testing accounted for 56 requests (33%) and was significantly less likely to be appropriate or clinically informative than initial testing. The median turnaround time was 1.65 hours overall, but differed markedly between sites: 1.42 hours at the tertiary referral centre where the central laboratory is located (n = 140) compared with 5.71 hours at the district hospital requiring specimen transport (n = 30).

Conclusion:

Anti-Xa testing was largely appropriate and clinically informative within this cohort; however, recurrent patterns of inappropriate testing highlight opportunities for improved laboratory utilisation, including optimisation of test requesting practices, pre-analytical factors and turnaround time.

Recurrent normocytic anaemia: A case of maturation arrest

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Blood 2026 Abstract for Poster Presentation

Background/Clinical Case: A 28 year-old male presented in late 2025 with recurrent normocytic anaemia with significant reticulocytopenia, now transfusion dependent, after initial spontaneous resolution in 2016 without acute management.

Initial investigation showed a normocellular marrow with left shifted erythropoiesis and otherwise normal granulopoiesis and megakaryopoiesis without dysplasia. He had a normal karyotype with no somatic variants on his next generation sequencing. He had negative viral serologies including Parvovirus B19, no other drug or toxin cause, and no evidence of malignancy or infection on cross-sectional imaging.

After several months of transfusion dependence, he had a repeat bone marrow which showed a mild reduction in erythropoiesis with more prominent features of dyserythropoiesis, partial maturation arrest at the proerythroblast stage, and low level erythrophagocytosis. He was trialled on ciclosporin, ceased after a three-month trial without response. He was subsequently commenced on sirolimus with improvement in his haemoglobin by week 8 of therapy.

Conclusion: The patient has since been off transfusion support for six months after resolution of his severe anaemia with plan for ongoing weaning of his immunosuppression. This case highlights erythroid failure and the difficult clinical and morphological overlap between pure red cell aplasia and late erythroid precursor maturation arrest. While the patient did have initial spontaneous resolution, he subsequently required therapy with a variable response to immunosuppression including escalation to second-line therapy.

No conflict of interest to disclose.

Ensemble machine learning with optimised feature engineering for amyloid subtype classification from mass spectrometry proteomics: a systematic evaluation

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¹Princess Alexandra Hospital, Brisbane, Australia

Aim: To evaluate machine learning (ML) approaches for automated subtype classification in systemic amyloidosis using laser microdissection and tandem mass spectrometry (LMD MS)-based proteomics, and to identify optimal quantification strategies, feature engineering approaches and model architectures.

Method: LMD MS proteomic data from 106 diagnostic biopsy samples spanning five amyloid subtypes (ATTR, AL- λ , AL- κ , AA, AH) from a single tertiary centre were analysed. Six ML architectures were evaluated: logistic regression, support vector machine, random forest, gradient boosting, multilayer perceptron and a stacking ensemble, alongside a Pearson correlation centroid classifier. Protein identification variables (spectral counts, raw intensity, relative intensity, unique peptides, percent coverage and iBAQ), protein filter strategies and immunoglobulin aggregation approaches were systematically compared. Class imbalance was addressed with SMOTE. Internal validation used a held-out 30% split. Metrics used were accuracy, area under the receiver-operator curve (AUROC) and F1 score.

Results: Tree-based models outperformed linear classifiers and the multilayer perceptron (random forest AUROC 0.999, gradient boosting AUROC 0.994). The stacking ensemble achieved accuracy 94% and AUROC 0.996. Restriction to causally relevant proteins substantially outperformed unfiltered or automated feature selection (mean F1 0.933 vs 0.613). Aggregating immunoglobulin chains into KAPPA, LAMBDA and HEAVY categories restricted to maximum-intensity proteins significantly improved performance over uncombined approaches (mean F1 0.925 vs 0.712).

Conclusion: ML-based classification of amyloid subtypes from LMD MS proteomics achieves excellent performance. Causal protein restriction, immunoglobulin aggregation and multi-variable quantification are critical preprocessing steps. These findings provide a methodological foundation for prospective multi-centre evaluation of ML-assisted amyloid subtyping, with potential to reduce interpretive subjectivity in routine diagnostic practice.

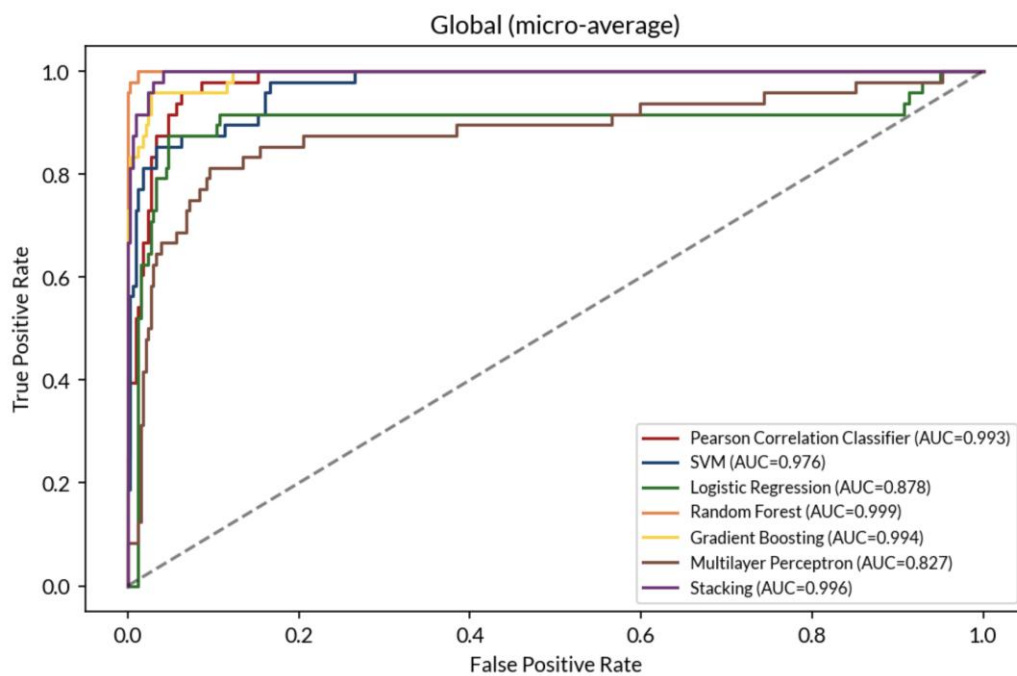


Figure 1: Micro-averaged AUROC curves for each model evaluated on internal validation dataset

Development and validation of a novel multimodal deep neural network model based on CBC digit parameters and scattergrams for rapid hematology malignancy classification: a multicenter cohort study

Prof Hongyan Liao¹, Siyuan Chen¹, Professor Qin Zheng¹

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Aim:

Rapid screening of hematology malignancies (HMs) by complete blood cell count (CBC) is crucial for choosing the next appropriate workup and initiating timely treatment for critical cases such as acute promyelocytic leukemia. However, conventional workflow based on morphology review for HM screening remains time-consuming, labor-intensive, expertise-dependent and subjective. This study aimed to develop an artificial intelligence (AI)-assisted model for rapid and accurate prediction of HMs presented as leukocytosis, thus informing proper further workup and timely treatment.

Methods:

We retrospectively collected a multicenter dataset containing 4,995 CBC records from patients presented with leukocytosis and finally diagnosed of either diseases from six prevalent HMs and acute bacterial and/or acute viral infection for model development and validation. This eight-nomial classification model, on a multimodal basis, integrates the digit parameters and its matching WBC differential scattergram from a single CBC test via a convolutional fusion deep neural network, and was compared with the digit- and scattergram-based unimodal model, as well as the current CBC review rules for performance evaluation.

Results:

The multimodal mDNN-cHM outperformed either unimodal model, as is demonstrated by metrics including precision, recall, F1-score and accuracy (all $p < 0.05$). The model showed striking diagnostic accuracy in both internal and external validations (AUC-ROC all above 0.95, ranging from 0.98-1.00 internally and 0.95-1.00 externally). Further, mDNN-cHM demonstrated a higher prediction rate than the flag prompt by current CBC review rules.

Conclusions:

Our study presents a proof-of-concept AI classifier for HMs in a real-time manner, which potentially maximizes the diagnostic value of the low-cost and widely-accessible CBC within 0.5 h after sample receipt. The framework also underscores the potential of interpretable AI in accelerating early disease diagnosis, mitigating human error and enlightening clinical decision-making via CBC, which complements and enhances standard-of-care diagnostics, particularly for urgent and high-risk diseases including leukemia/lymphoma and acute infection.

Developing the aplastic anaemia and other bone marrow failure registry in Aotearoa New Zealand: Collaboration, data governance, and stakeholder engagement

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Background:

To describe the experience to date of establishing the Aplastic Anaemia and Other Bone Marrow Failure Registry (AAR) in New Zealand (NZ).

Bone marrow failure syndromes (BMFS), including immune aplastic anaemia, inherited BMFS, and hereditary haematologic malignancies (HHM) are rare conditions but collectively contribute significant morbidity and healthcare burden.

The AAR was established in 2013 in Australia, and now has 37 participating hospitals, and 685 patients enrolled. In comparison, little NZ data exists on the epidemiology, management or outcomes of BMFS.

Method and Results

Establishing AAR in NZ required review of NZ-specific considerations working with stakeholders during the 18 months of establishing the AAR.

Three key priorities were:

Stakeholder engagement and collaboration: To ensure culturally informed and patient-centred development of the NZ arm of the AAR protocol, we developed partnerships with and received advice from the University of Otago Māori Health Advancement team, Pasifika experts, Rare Disorders NZ, and Blood Cancer NZ. We also established NZ representation on the AAR steering committee.

Data sovereignty: AAR data are stored in Australia, including genetic data. Working with stakeholders we developed a NZ data management plan incorporating culturally safe data storage methodologies.

Consent: Registry studies have previously adopted an NHMRC-approved opt-out consent model. However following NZ National Ethics Advisory Committee 2021 guidelines, an opt-in consent model is now preferred in NZ, when practical. We developed an e-consent model in REDCap, with ability to re-consent paediatric patients on the AAR at age 16.

Conclusion:

The AAR is now established in New Zealand, with ethics approval and 6 sites preparing/open to recruit patients. We share these experiences to highlight the work undertaken, and hope this may be helpful for others establishing registries in New Zealand.

Diagnosing telomere biology disorders using nanopore sequencing: Proof of concept results and next steps

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Background

Telomere lengths (TL) are the most crucial differentiator between acquired and inherited causes of bone marrow failure. Currently Flow-FISH (FF) is the gold standard method for measuring TL, with this method only available in one laboratory in Australasia; other methods of TL measurement such as qPCR are used in research settings. Nanopore-based DNA sequencing represents a novel way to measure TL – however, it has never been used to diagnose telomere biology disorders (TBD). Our aim was to determine whether a nanopore sequencing assay could identify the short telomeres characteristic of TBDs in a patient with known TBD.

Methods

We completed a proof-of-concept study evaluating the Oxford Nanopore Technology TL Telo-seq protocol. Samples from a 38-year old European patient with a known TBD served as our positive control (measured on FF), and five unaffected 50-year old European patients from the Canterbury Health, Ageing and Life Course (CHALICE) study as normal controls. All controls had TL previously measured using qPCR.

Results

The TBD positive control had the shortest telomeres across three independent sequencing runs (3681 kb, 3802 kb, and 3656 kb). The assay correctly identified the shorter and longer length telomeres in normal control patients as seen by qPCR (*figure 1*). Strong correlation between the nanopore sequencing method and qPCR assay was observed, ($r=0.77$).

Conclusion

This proof-of-concept study demonstrates nanopore sequencing is an effective method for TL measurements. It accurately identified the patient with short telomere lengths. Next steps include partnering with the Australian Bone Marrow Failure Biobank – to further understand sensitivity and specificity diagnosing TBDs and establishing normal reference ranges for patients of different gender, age, and ethnicities.

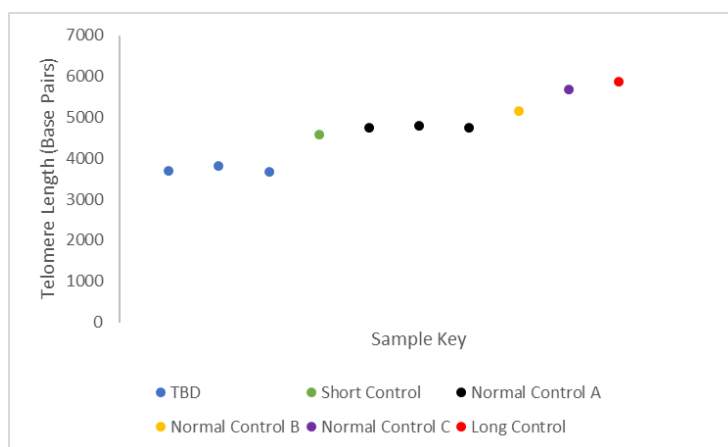


Figure 3: Telomere lengths measured using nanopore sequencing for TBD patient and 5 controls

Somatic 6p loss of heterozygosity and HLA inactivation in aplastic anaemia: A scoping review

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Background

6p copy number loss of heterozygosity (6pLOH) and human leukocyte antigen-inactivating mutations (HLA-IA) can predict a diagnosis of immune aplastic anaemia (iAA). 6pLOH provides a mechanism of clonal escape for haematopoietic stem cells (HSC) in iAA by reducing expression of HLA alleles. Our objective was to assess the available evidence on epidemiology, methods of detection, prognostic significance, and treatment implications of 6pLOH/HLA-IA in the setting of iAA.

Methods

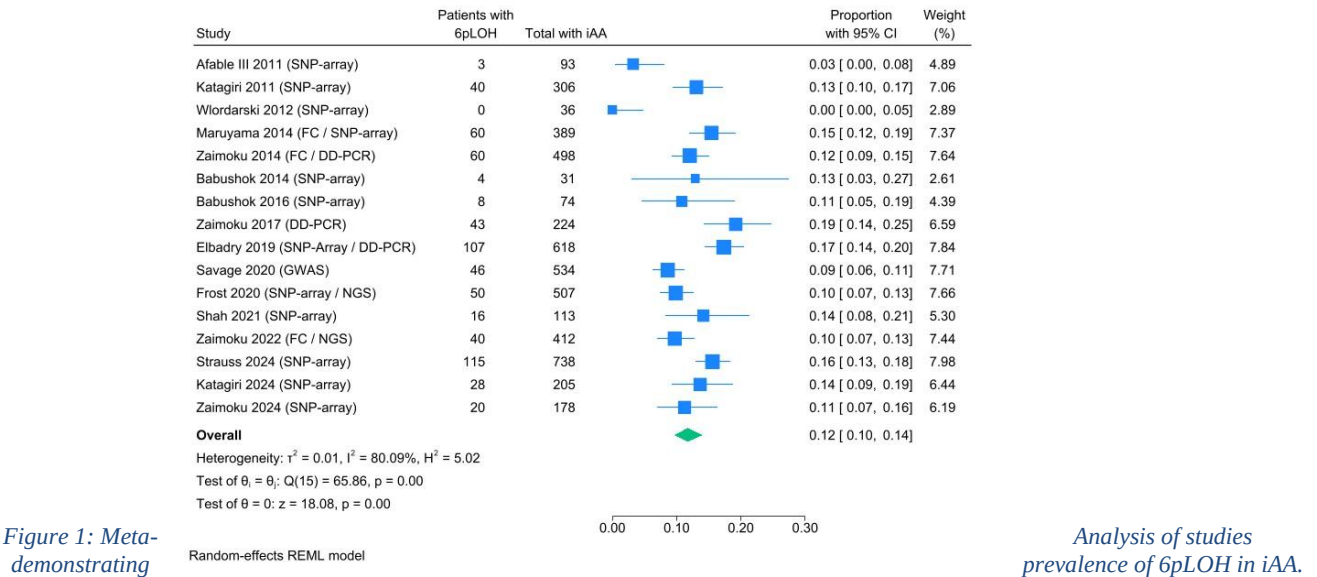
We performed a scoping systematic review and meta-analysis of 6pLOH/HLA IA in iAA using the PRISMA-ScR framework to assess epidemiology, methods of detection, prognostic significance, and impact on treatment. We searched PubMed, Scopus, Embase, and MEDLINE between January 2010 to April 2025. The protocol was registered at PROSPERO (CRD420251013483).

Results

59 studies met inclusion criteria; 71% of publications were from two centres. SNP-array, flow cytometry, digital droplet PCR, and next generation sequencing were all used as methods to diagnose 6pLOH/HLAIA. Pooled prevalence of 6pLOH was 12% (95% CI 10-12%) as shown in Figure 1. HLA-IA was identified in 13% (95% CI 5-23%). Subgroup meta-analysis demonstrated that hepatitis-associated severe aplastic anaemia had a higher prevalence of 6pLOH (29% 95% CI 14-47%). Limited data exist on prognosis of 6pLOH/HLA-IA.

Conclusions

There is a need for high-quality research and prospective trials to establish the importance of 6p LOH/HLA-IA, particularly focussing on the implications for prognosis and management as well as its role in diagnostic work-up of bone marrow failure syndromes



All that PLASMICs isn't TTP – Tumour associated microangiopathy as a TTP mimic

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Case Study:

Thrombotic thrombocytopenic purpura (TTP) requires emergent treatment prior to obtaining ADAMTS-13 laboratory testing results. A 74-year-old woman presented to a tertiary hospital after collapsing at home and was found to have a classical pentad of fevers, neurological symptoms, renal impairment, thrombocytopenia and microangiopathic anaemia. Creatinine was 113umol/L, haemoglobin 67g/L, platelets 76x10⁹/L and WCC of 7.5x10⁹/L. Bedside scoring demonstrated a PLASMIC score of 6 and French-TMA score of 2 consistent with suspected TTP along with an elevated LDH at 1821U/L. PLEX was initiated awaiting the result of an AcuStar® ADAMTS-13 chemiluminescent immunoassay, which returned the following day at 6%. After one cycle of PLEX, her platelets increased to 110x10⁹/L followed by a gradual decline improved by further PLEX cycles, with LDH near normalising to 361U/L after three cycles.

Several incongruent features were noted at presentation including relatively few (~1/HPF) schistocytes and a low-normal haptoglobin of 0.7, as well as an outpatient blood test from two months prior demonstrating anaemia. A CT-CAP performed shortly after admission demonstrated an enlarged axillary lymph node. Core needle biopsy was consistent with adenocarcinoma of likely breast origin, and a subsequent bone marrow demonstrated extensive infiltration consistent with metastatic breast cancer. Despite initial response to PLEX she rapidly deteriorated and after discussion with her family transitioned to palliative care. ADAMTS-13 inhibitors were not detected on her initial samples via Bethesda assay, and a Technozym® ELISA activity assay performed on the diagnostic ADAMTS-13 sample returned at 39%, confirming her pathology was a tumour-associated microangiopathy rather than TTP.

Conclusion:

This case highlights both the importance of differing instrument assessment of ADAMTS-13 in complex cases of TTP, as well as the importance of obtaining definitive diagnostic investigations despite promising platelet and LDH kinetics on PLEX.

A perfect storm: HLH and complement-mediated TMA in MDA5 dermatomyositis requiring coordinated immunomodulation

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Introduction:

Melanoma differentiation-associated gene 5 (MDA5) dermatomyositis is an uncommon trigger of secondary haemophagocytic lymphohistiocytosis (HLH) and may overlap with complement-mediated thrombotic microangiopathy (TMA). Mortality is high, and evidence-based sequencing and dosing of immunomodulatory therapy remains limited, particularly with concurrent severe infection.

Case:

A 33-year-old female presented with fever, rash, cytopenias and ferritin of 14,600µg/L, progressing to shock and neurological deterioration requiring ICU admission and intubation. HLH (H-score>250) secondary to MDA5 dermatomyositis was diagnosed. Intravenous methylprednisolone (1g daily ×3) followed by 1mg/kg/day, anakinra IV 100mg BD (escalated to 300mg BD) and tacrolimus were commenced within 48 hours. Persistent hyperinflammation with rising ferritin and sCD25 by week 1 prompted addition of ruxolitinib 10mg BD, plasmapheresis and IVIG. Her course was complicated by complement-mediated TMA (sC5b-9 >1000ng/mL, red cell fragmentation, thrombocytopenia and renal failure) by week 2, requiring eculizumab which was escalated to 900mg IV twice weekly until sC5b-9 <100ng/mL, followed by maintenance dosing. Ongoing disease activity led to escalation of emapalumab to 10mg/kg every 3 days. Cyclophosphamide was administered at a renally adjusted dose of 12.5mg/kg fortnightly. Renal replacement therapy was required. Ferritin and sC5b-9 trends guided therapy throughout critical illness. Despite disseminated infections, immunomodulation continued under multidisciplinary oversight. Ferritin improved to 7,267µg/L over 11 weeks, allowing stabilisation and repatriation to ongoing care.

Discussion:

Management of MDA5-associated HLH with concurrent TMA requires early combined immunomodulation and rapid, biomarker-directed escalation. Upfront corticosteroids with IL-1 blockade ± calcineurin inhibition provide initial control, with early JAK inhibition in refractory disease. Recognition of TMA and escalation to intensified complement inhibition guided by sC5b-9 are critical. Serial ferritin, sCD25 and sC5b-9 measurements support therapeutic decision-making.

Conclusion:

Overlapping HLH and TMA demand parallel, biomarker-driven immunomodulation. Multidisciplinary coordination is essential to enable safe delivery of high-intensity therapy and access to high-cost agents in critically unwell patients.

Word count: 298 (excluding title)

Cytomegalovirus-induced hemophagocytic lymphohistiocytosis in an immunocompromised patient: a case study

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Introduction:

Hemophagocytic lymphohistiocytosis (HLH) is a rare, life-threatening syndrome marked by uncontrolled immune activation and hyperinflammation. Primary HLH is genetic, whereas secondary HLH is due to infection, malignancy, or autoimmune disease, particularly in immunocompromised patients. Viral infections are a common precipitant, with cytomegalovirus (CMV) frequently implicated. However, the degree of viral load observed in this case has been rarely reported.

Case presentation:

A 38-year-old female initially presented with abdominal pain and diarrhea of unclear etiology, which self-resolved within a week. She was immunosuppressed with mycophenolate mofetil following multiple corneal grafts for corneal ulcerations on the background of ectodermal dysplasia cleft syndrome. She re-presented within 3 days with high fevers, anorexia, and mild abdominal pain. Investigations revealed significant liver dysfunction (GGT 630, ALT 450, ALP 1080, AST 610U/L), elevated INR (1.94) and CRP (150mg/L). As part of the infective screen, her quantitative CMV PCR demonstrated a high viral load of 58,000,000IU/mL. CT abdomen, initially performed for diarrhea, showed progressive transverse colitis. She subsequently developed worsening hypoxia, with CXR showing progressive bilateral infiltrates consistent with CMV pneumonitis, requiring intensive care and high-flow oxygen. HLH was suspected due to persistent fevers despite negative septic workup, falling blood counts, and markedly elevated ferritin (99,800ug/L). Triglycerides were also elevated (9.3mmol/L). Bone marrow biopsy confirmed the diagnosis of HLH. She was commenced on HLH treatment with anakinra, high-dose methylprednisolone, intravenous immunoglobulins, transfusion support and targeted CMV therapy with intravenous ganciclovir. Mycophenolate was temporarily withheld. She gradually improved with laboratory parameters, including viral load, liver function tests, inflammatory markers, and blood counts, near normalising prior to discharge.

Conclusion:

This case highlights the importance of early recognition to reduce morbidity and mortality, and the role haematologists play in the diagnosis of HLH, especially in immunocompromised patients presenting with the three Fs (fever, falling blood counts and raised ferritin).

Beyond microcytosis: red cell clues to cultural sources of lead exposure in children

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Background:

Lead, or *plumbum* (Pb), toxicity although rare is a significant public health concern. Lead exposure has declined due to public health measures, however accidental exposures have serious health impacts. The NHMRC recommends an individual's blood level should be <5µg/dL (0.24µmol/L).¹ Lead is not generally absorbed well via skin, and hence the greatest risk is with inhaled or swallowed particles. The health impacts of lead exposure depend on age, along with the amount and duration of lead exposure. For pregnant women, lead can cross the placenta and affect the developing fetus.

Lead exposure effects haem synthesis. The morphological features of lead toxicity include microcytosis with basophilic stippling. Anaemia is observed where lead levels exceed >50 µg/dL (2.42 µmol/L).² Where there is concomitant iron deficiency or thalassaemia trait, features of lead toxicity may overlap or be underappreciated. Careful morphological review is essential, with the degree of basophilic stippling (striking, coarse) being a differentiating feature. Confirmatory testing, including iron levels, haemoglobin electrophoresis and blood lead levels, is required to distinguish these potentially co-existing conditions.

Table 1. Examples of potential sources of lead exposure in infants and children

Lead-based paint	Toys	Cosmetics & cultural powders (Kohl, Surma, Kumkum, Sindoor) ³⁻⁵	Leaded petrol (now banned)
Contaminated water or roadside soil	Jewellery	Complementary medicines	Mining & smelting (Mount Isa, Port Pirie, Broken Hill) regions
Fish sinkers	Shot & ammunition		

Case Report:

A 4 month old girl was referred for microcytosis and persistent unconjugated hyperbilirubinaemia. Ferritin, LFTs, G6PD and E5M were normal. Haemoglobin electrophoresis confirmed beta thalassaemia trait (HbA 93.4%, HbF 1.4%, HbA2 5.2%), and genotyping identified no alpha-globin gene deletional mutations, or alpha-2 globin mutations. Review of the morphological film features noted coarse, basophilic stippling, and subsequent lead levels were noted to be high (see table 2). Whilst identifying the source of lead, the levels initially increased. The source of lead toxicity was identified as the Bindi / Sindoor being applied by the family, which the girl had inadvertently ingested. Both parents lead levels were normal.

Table 2. Haematological indices, lead levels

Age of patient	Hb, MCV, Ferritin	Lead level µg/dL (µmol/L)
2 months	Hb 100, MCV 73.7	N/A
18 months	Hb 100, MCV 53	0.33
19 months	Hb 104, MCV 53, Ferritin 44	4.6 (0.22)
25 months	Hb 96, MCV 53, Ferritin 78	12.9 (0.62)
26 months	Hb 99, MCV 54	10.8 (0.52)
29 months	Hb 95, MCV 52, Ferritin 53	4.4 (0.21)
40 months	Hb 97, MCV 53	2.9 (0.14)

Figure 1. Differentiated morphology for concomitant thalassemia & lead toxicity
Poster will include dedicated images of the film for reviewers' interest.

Summary/Conclusions:

Lead toxicity is an important differential for microcytosis, with the peripheral smear remaining one of the most important diagnostic modalities. Traditional cosmetics and powders should be considered as potential sources of lead, and all family members should be tested where an exposure is identified.

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Coexistence of primary myelofibrosis and paroxysmal nocturnal haemoglobinuria: a case report

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Introduction

Paroxysmal nocturnal haemoglobinuria (PNH) arises through a somatic mutation of the phosphatidylinositol glycan A (*PIG-A*) gene in stem cells, leading to deficiency of complement regulatory proteins CD55 and CD59. This results in complement-mediated haemolysis and increased thrombotic risk (1). Whilst PNH is notoriously associated with myelodysplastic syndromes, it rarely coexists with myeloproliferative neoplasms (MPNs), such as primary myelofibrosis (PMF)(2). Here, we report a case of concurrent PMF and PNH harbouring a *JAK2* mutation.

Case

A 66-year-old male presented with one week of coryzal symptoms and two days of cola-coloured urine, nine days after a PRBC transfusion. He had a recent diagnosis of *JAK2*-positive pre-fibrotic MF (40.8% VAF) and had commenced ruxolitinib. He also had known anti-E alloimmunisation from previous transfusions for a CABG in 2021. Thus, his working diagnosis was a delayed haemolytic transfusion reaction. Investigations were indicative of intravascular haemolysis: elevated reticulocytes (3%), bilirubin (81 µmol/L), LDH (2534 U/L; baseline 1000 U/L), decreased haptoglobin (0.02g/L) and a weakly positive Coombs test. Rhinovirus was also detected. However, no new alloantibodies were identified, prompting further investigations, which revealed a large PNH clone (87%) and haemosiderinuria. He was commenced on ravulizumab alongside ruxolitinib due to high thrombotic risk from concurrent MF and PNH. Interestingly, retrospective review revealed a prominent haemolytic episode during his CABG, exceeding expected cardiopulmonary bypass-related haemolysis. Thus, these events suggest a previously undetected PNH cell population, unmasked by complement amplifying conditions (CACs).

Discussion/Conclusion

This case demonstrates a rare association between MF and PNH presenting with significant haemolysis. Given such a large PNH clone, it may represent expansion of a *JAK2*-mutated clone within PNH cells, supporting the notion that acquisition of MPN driver mutations confers an intrinsic growth advantage to PNH cells (3). *PIGA* gene sequencing has been sent, and updated results will be presented. In conclusion, testing for PNH should be prompted in patients with MPNs with signs of haemolysis.

References

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Diagnostic and therapeutic challenges of CNS EBV-driven polymorphic PTLD after haploidentical allogeneic HSCT for XLP1-associated EBV-HLH

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Aim:

To describe the diagnostic and therapeutic challenges of CNS EBV-PTLD occurring after haploidentical allogeneic HSCT for XLP1-associated EBV-driven HLH.

Method:

We present a case report of a 17-year-old male diagnosed with XLP1 following severe EBV-driven HLH with probable CNS involvement. Initial manifestations included fulminant hepatic dysfunction, coagulopathy, respiratory failure, cytopenias, hyperferritinaemia, marrow haemophagocytosis, and detectable EBV within bone marrow and CSF.

Management prior to transplant included dexamethasone, rituximab, ruxolitinib, etoposide, anakinra, emapalumab, IVIg, serial intrathecal methotrexate, rituximab, and hydrocortisone. He subsequently underwent haploidentical peripheral alloHSCT using alemtuzumab, fludarabine, and treosulfan conditioning with post-transplant cyclophosphamide, tacrolimus, and mycophenolate mofetil for GvHD prophylaxis.

Results:

On day +73 post-transplant, the patient developed progressively worsening headaches and visual blurring. MRI brain demonstrated multiple supra- and infratentorial ring-enhancing lesions associated with raised intracranial pressure. Differential diagnoses included opportunistic infection, recurrent CNS-HLH, and PTLD.

CSF analysis showed elevated protein and persistent low-level EBV positivity without alternative infective pathogens. Due to lesion location and procedural risk, biopsy was initially deferred and empirical treatment for intracranial opportunistic infection commenced with voriconazole, ceftazidime, and high-dose trimethoprim-sulfamethoxazole. Concurrently, he received EBV-specific cytotoxic T-lymphocyte therapy.

Despite clinical improvement, repeat MRI after three weeks demonstrated interval progression in lesion burden, prompting diagnostic reconsideration. Subsequent stereotactic biopsy confirmed polymorphic EBV-driven PTLD involving the CNS. Antimicrobial therapies were ceased, and follow-up imaging demonstrated marked reduction in lesion size, enhancement, and surrounding oedema, with complete resolution of neurological symptoms.

Conclusion:

This case highlights the diagnostic complexity of ring-enhancing CNS lesions following alloHSCT in patients with XLP1-associated immune dysregulation. It demonstrates the importance of tissue diagnosis when feasible, limitations of low-level EBV viral load interpretation, and the potential role of EBV-specific cytotoxic T-lymphocyte therapy in CNS PTLD.

Moderate to severe thrombocytopenia in pregnancy does not negatively impact on maternal and neonatal outcomes: A single centre, retrospective study

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Aim:

Thrombocytopenia is a common haematological complication in pregnancy. Data on moderate to severe cases (platelets $\leq 100 \times 10^9/L$) are limited. This study aims to investigate aetiology and peripartum management in this subgroup.

Method:

We performed a single-centre retrospective study conducted at Northern Health in Victoria, Australia. Pregnancies with platelets $\leq 100 \times 10^9/L$ between January 2019 to December 2024 were included. Relevant clinical and investigations data are collected via electronic medical record. Outcome measures were: (1) causes of thrombocytopenia, (2) peri-partum management, including mode of delivery, use of neuraxial anaesthesia, and thrombocytopenia-targeted therapies, (3) postpartum haemorrhage (PPH) and blood products usage, (4) neonatal platelet count and bleeding in immune thrombocytopenia (ITP) pregnancies.

Results:

117 pregnancies were included in total. The most common aetiology was gestational thrombocytopenia (n=83, 70.9%) followed by ITP (n=25, 21.4%), and hypertensive disorders (n=8, 6.9%). Mean nadir platelet count was $77.1 \pm 18.1 \times 10^9/L$. 61 (53.0%) pregnancies received neuraxial anaesthesia at delivery, with lowest peri-partum platelet count of $69 \times 10^9/L$, without bleeding complications at anaesthetic site. PPH occurred in 40 pregnancies (34.8%), and five (4.3%) required red blood cell transfusions, with no associations between thrombocytopenia severity and PPH risk. In the ITP cohort, 16 (65%) pregnancies received steroids, intravenous immunoglobulin and/or platelet transfusions, with eight (32%) achieving platelet count $>70 \times 10^9/L$ peripartum. Four (16%) out of 22 neonates born to ITP pregnancies had thrombocytopenia (nadir platelet count of $44 \times 10^9/L$) in the first seven days without haemorrhagic complications.

Conclusion:

Moderate thrombocytopenia in pregnancy does not confer increased risk of maternal PPH and neonatal haemorrhage. Neuraxial anaesthesia can be safely administered without complications. Early treatment of ITP could improve peripartum platelet count with low risk of adverse effects, and enables safe use of neuraxial anaesthesia. Larger prospective study would be helpful to enable meaningful statistical analysis.

Less is more for patients with Haemophilia B

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Aim:

Haemophilia B is a rare bleeding disorder affecting approximately 1 in 25,000-30,000 males in Australia. It occurs due to a deficiency of Factor IX.

Patients requiring prophylaxis treatment to prevent bleeding have several treatment options. Current treatments available include standard half-life (rFIX) and extended half-life (rFIX-Fc) factor IX, both given intravenously. A new extended half-life (rFIX-FP) became available on the Australian market from July 1st, 2025, and patients were given the opportunity to switch treatments.

The aim was to demonstrate switching to the newer rFIX-FP decreased factor consumption, increased factor levels and extended median dosing intervals.

Method:

A retrospective review of five patient records who swapped from rFIX or existing rFIX-Fc to the new option rFIX-FP from August 2025 to present.

Patient records were reviewed to compare:

- Amount of factor product used before and after switching.
- Factor IX trough levels before and after switching.
- Treatment intervals before and after switching.

Results:

The review demonstrated:

1. Reduced units/kg/year in four out of the five patients and a similar units/kg/year for the fifth patient.
2. An increase in trough factor IX levels for all patients
3. An extension in intervals of treatment for two out of the five patients.
4. Nil observed breakthrough bleeds

Conclusion:

Changing from either a rFIX or existing rFIX-Fc to the newer rFIX-FP on the market, resulted in a better quality of life, reduced treatment burden and increased median dosing intervals resulting in improved factor IX levels in this paediatric population.

All patients with Haemophilia B receiving prophylaxis will be offered all treatment options, including the newer rFIX-FP now available.

Granulomatous bone marrow involvement in Crohn disease

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Aim:

Description of a case of granulomatous bone marrow involvement in Crohn disease presenting with radiological and clinical features concerning for haematological malignancy, to highlight the associated diagnostic challenges.

Case report:

A 31-year-old man with a background of Crohn disease with chronic active ileitis and primary sclerosing cholangitis was referred to Haematology for evaluation of intra-abdominal moderately FDG-avid lymphadenopathy, splenomegaly, and diffuse marrow uptake on PET-CT. Imaging was performed during an episode of presumed cholangitis.

Laboratory evaluation demonstrated a mild longstanding anaemia (haemoglobin 110 g/L) without additional cytopenias. Liver function tests showed a predominantly cholestatic pattern, with intermittent mild hypercalcaemia. Peripheral blood flow cytometry did not show evidence of a monoclonal B- or aberrant T-cell population.

Bone marrow aspirate and trephine biopsy revealed a hypercellular and disorganised marrow with multiple granulomas and mixed interstitial and paratrabecular lymphoid aggregates. A single multinucleated giant cell was identified, characterised by central and peripheral nuclei that contained a single prominent nucleoli. A background reactive infiltrate, including eosinophils and plasma cells, was present.

Given the atypical findings, differential diagnoses included infectious granulomatous processes (including tuberculosis; Ziehl–Neelsen stain was negative), sarcoidosis, Langerhans cell histiocytosis, and foreign body-type granulomatous inflammation. In the context of known Crohn disease and the absence of infection or haematological neoplasia, the findings were considered most consistent with granulomatous marrow involvement as a rare extraintestinal manifestation of Crohn disease.

This case highlights the importance of integrating clinical, radiological, and pathological findings and a multidisciplinary approach in difficult cases.

Australian clinical practice guideline for the diagnosis and treatment of idiopathic multicentric Castleman disease (iMCD)

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Aim: Idiopathic multicentric Castleman disease (iMCD) is a rare and heterogeneous lymphoproliferative disorder associated with significant diagnostic and therapeutic challenges. The Australian iMCD Interest Working Group aimed to develop a multidisciplinary Australian clinical practice guideline to improve diagnosis and management of iMCD in Australia.

Method: A multidisciplinary working group comprising seventeen Australian experts in haematology, rheumatology, immunology, and pathology developed the guideline through expert meetings, literature review, and consensus discussions. The guideline incorporated international diagnostic criteria, World Health Organization classification updates, clinical trial data, retrospective studies, registry data, and existing international treatment recommendations. Evidence grading followed National Health and Medical Research Council (NHMRC) guidelines.

Results: The guideline highlights the heterogeneous presentation of iMCD and emphasises multidisciplinary evaluation (including close collaboration between haematologists, pathologists, immunologists and rheumatologists) and excisional lymph node biopsy for diagnosis. International consensus diagnostic criteria and structured investigation pathways are recommended to improve diagnostic accuracy and differentiation from infectious, autoimmune, inflammatory, and malignant mimics. Targeting interleukin-6 (IL-6) activity with siltuximab is recommended as first-line therapy for both severe and non-severe disease, supported by level II evidence. The guideline also discusses considerations unique to Polynesian populations and management challenges associated with relapsed or refractory disease. Please refer to Table 1 for Summary and key recommendations.

Table 2. Summary and key recommendations

Recommendations	Level	Grade
1. The diagnosis and management of iMCD is challenging. Therefore, a multidisciplinary approach leveraging relevant expertise is recommended.		
2. The clinical presentation is heterogeneous, ranging from mild constitutional symptoms to severe multi-organ dysfunction.		

3.	It is important to be aware that the incidence of iMCD is higher amongst Polynesians. The phenotype may be milder with excellent response to IL-6-directed therapy.		
4.	The 2017 international consensus criteria are recommended to establish the diagnosis.	IV	C
5.	Histopathological assessment of the lymph node is an essential part of the diagnosis.	IV	C
6.	A core needle biopsy may provide information on the lymph node architecture, but is generally suboptimal compared to an open excisional biopsy.		
7.	Fine needle aspiration can only provide cytological analysis and should not be used in the diagnosis.		
8.	A bone marrow biopsy is warranted to assess for differential diagnoses and may demonstrate histological changes that support the diagnosis.	IV	D
9.	In addition to histopathology, a panel of other investigations is required, including cross-sectional imaging, blood and urine tests.	IV	C
10.	Assessment of disease severity according to the CDCN guidelines is recommended to tailor therapy.	IV	C
11.	Targeting IL-6 activity forms the cornerstone of modern therapy for iMCD, with siltuximab recommended as first-line therapy.	II	B
12.	The recommended regimen for siltuximab is 11 mg/kg every 3 weeks.	II	B
13.	Patients who achieve at least a PR should remain on siltuximab maintenance therapy indefinitely until disease progression.	IV	C
14.	Patients with severe disease should receive first-line siltuximab in combination with high-dose steroids.	IV	D
15.	Rituximab-based regimens are recommended for second-line therapy.	IV	C
16.	Third-line agents include cyclosporin (especially for TAFRO), sirolimus, anakinra, and thalidomide.	IV	D
17.	Chemotherapy is recommended as a treatment option in severe, refractory iMCD or TAFRO	IV	D
18.	We recommend using the CDCN-defined response criteria to guide, rather than dictate, treatment selection and duration.		

CDCN, Castleman Disease Collaborative Network; iMCD, idiopathic multicentric Castleman disease; IL, interleukin; PR, partial response; TAFRO, thrombocytopenia, anasarca, fever, reticulon fibrosis, renal dysfunction, organomegaly. The levels of evidence and grades of recommendation follow the NHMRC guidelines.¹¹ Statements without grading were considered justified standard clinical practice by the experts.

Conclusion: This guideline provides a practical framework for the diagnosis and management of iMCD in Australia and may reduce diagnostic delay, standardise treatment approaches, and improve patient outcomes.

Sensitivity of ClotPro to apixaban in patient samples compared with routine anti-Xa assay in a single centre

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Aim: Apixaban is the most commonly used oral anticoagulant in Australia, with an estimated 16,000 cases of major bleeding annually. Routine coagulation assays (PT, aPTT) do not reliably detect apixaban, leading to empirical use of reversal agents such as 4-factor prothrombin complex concentrate. The aim of this study was to evaluate the sensitivity of the ClotPro viscoelastic assay to detect apixaban compared with anti-Xa assays, assess reversal with Beriplex® AU spiking, and examine feasibility of implementation.

Method: This was a prospective single centre study conducted at Royal Prince Alfred Hospital, Sydney Australia between January 2025 and March 2026. Blood collected into sodium citrate tubes underwent RVV_{test} and EX_{test} analysis on the ClotPro device, measuring clotting time (CT), A5 and A10. Parallel Apixaban anti-Xa levels were measured using a standard laboratory assay. Two samples were spiked with Beriplex® AU (1 U/mL). A total of 25 patients receiving apixaban for venous thrombosis were included. Linear regression and correlation analyses were performed using GraphPad Prism 10.

Results: RVV_{test} CT and A5 significantly correlated with plasma apixaban levels, whereas EX_{test} CT, A5 and A10 did not (**Fig 1**). Compared with healthy controls, the RVV_{test} CT has a higher sensitivity and specificity than A5 and A10 to differentiate patients who have received Apixaban. Addition of Beriplex® AU did not decrease the ClotPro RVV_{test} or EX_{test} CT. Use of the ClotPro device was able to provide values on CT within 5 minutes, with a total test run time of 40 minutes. Technical considerations include the manual pipetting and cost of reagents which may limit routine implementation.

Conclusion: The apixaban effect on ClotPro clotting time is not neutralized by Beriplex in vitro. ClotPro provides a quick and sensitive point of care test to exclude residual Apixaban in the blood in Emergency settings.

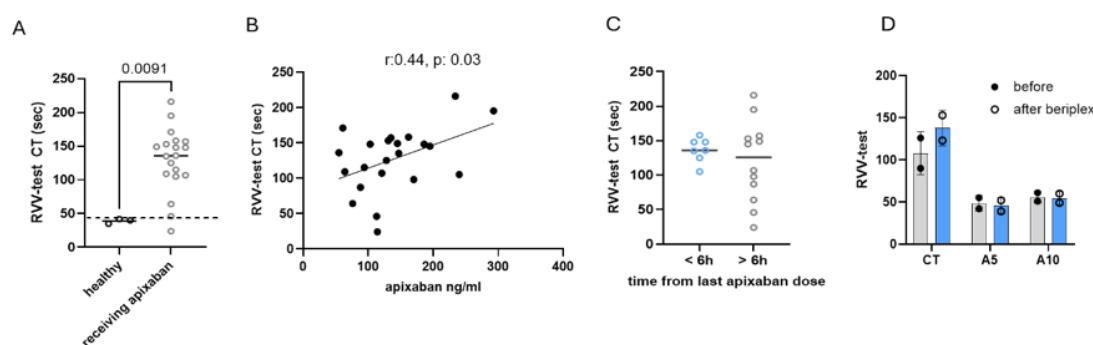


Figure 1.
ClotPro
RVV-test
clotting
time (CT) A.

in individuals and patients receiving apixaban, Mann Whitney test **B.** correlation with apixaban levels, simple linear regression, **C.** range depending on time from last apixaban dose, **D.** Effect of Beriplex on RVV tests.

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Influenza A-associated Thrombotic Microangiopathy: A Case Report

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Thrombotic microangiopathy (TMA) encompasses a heterogeneous group of disorders characterised by microangiopathic haemolytic anaemia, thrombocytopenia and microvascular thrombosis.¹ Influenza A-associated TMA is exceedingly rare, with fewer than 30 reported cases in the literature.² Here, we describe a case of influenza A-induced TMA, which was successfully treated with complement inhibition. Genetic complement studies remain pending at this time, however, the presentation was deemed consistent with complement-mediated haemolytic uraemic syndrome (CM-HUS). This was supported by low-normal ADAMTS13 activity excluding thrombotic thrombocytopenic purpura (TTP), absence of diarrhoeal illness suggestive of shiga toxin-producing *Escherichia coli* (STEC)-HUS, and unremarkable malignancy screening. Following complement inhibition, the patient achieved complete renal recovery and remains in remission five months later.

Case:

A previously well 21-year-old Caucasian female presented with a 3-day viral prodrome. Initial investigations demonstrated severe anuric acute kidney injury (creatinine 633 $\mu\text{mol/L}$), thrombocytopenia ($20 \times 10^9/\text{L}$), haemoglobin 119 g/L, white cell count ($8.7 \times 10^9/\text{L}$) and MCV 88 fL. Peripheral blood film demonstrated marked schistocytosis. Haemolytic studies revealed normal reticulocyte count, haptoglobin and indirect bilirubin, with negative direct antiglobulin testing. Respiratory PCR confirmed influenza A. Coagulation studies were unremarkable and stool shiga toxin testing was omitted given absence of diarrhoea. ADAMTS13 activity was 5.7% (via chemiluminescence immunoassay, AcuStar), inconsistent with severe acquired TTP. Vasculitic screening and serum complement levels were normal. Renal biopsy on day 21 demonstrated resolving thrombotic microangiopathy.

Empirical treatment for presumed TTP included prednisone 1 mg/kg daily and two sessions of therapeutic plasma exchange, discontinued following ADAMTS13 results on day 2. The patient subsequently received eculizumab induction therapy before transition to maintenance ravulizumab, and intermittent haemodialysis was required for two weeks.

Summary:

This case contributes to the growing body of evidence that recognises influenza A as a trigger for TMA. It highlights atypical features, including absence of classical haemolytic markers, necessitating a high index of clinical suspicion in such presentations. It also demonstrates that early presumptive treatment for TTP whilst awaiting definitive ADAMTS13 testing is safe and did not adversely affect clinical outcomes.

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Early recognition of microangiopathic hemolytic anemia through peripheral blood smear in a pediatric case of suspected hemolytic uremic syndrome

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Background:

Microangiopathic hemolytic anemia (MAHA) is one of hematologic emergencies in the pediatric population. Hemolytic anemia with characteristic morphologic findings including schistocytes (fragmented red blood cells) and thrombocytopenia are suggestive of thrombotic microangiopathy (TMA), often manifesting as Hemolytic Uremic Syndrome (HUS) in children. Early detection is essential to support prompt management.

Case Presentation:

A 9-year-old male presented with a history of fever, fatigue, and macrohematuria. Initial laboratory evaluation demonstrated acute hemolytic anemia with consumptive thrombocytopenia. Laboratory follow-up showed progressive decline of hemoglobin levels and platelet count with elevated unconjugated bilirubin, consistent with ongoing hemolysis. Peripheral blood smear (PBS) examination revealed significant schistocytosis (quantified at 2-4%) with associated anisocytosis, polychromasia, and giant platelets, strongly suggesting microangiopathic hemolytic anemia.

Further evaluation showed elevated urea and creatinine levels, supporting the clinical suspicion of renal involvement secondary to HUS. Based on hematologic and renal findings, the patient was managed with supportive treatment and therapy for underlying conditions. Further testing at the national referral hospital revealed a negative ANA-IF, which supports diagnosis of MAHA rather than autoimmune etiology.

Discussion:

This case demonstrates the critical role of PBS review in the early recognition of MAHA. The identification of prominent schistocytosis and giant platelets prompted further evaluation for thrombotic microangiopathy. In low-resource settings, peripheral blood morphologic assessment remains a robust, cost-effective, and rapid diagnostic tool for early detection of MAHA.

Conclusion

This case highlights the significant role of PBS examination in the early recognition of MAHA as a hematologic emergency. Prompt identification of schistocytosis in PBS and thrombocytopenia, together with laboratory evidence of renal dysfunction, is essential for early diagnosis and timely initiation of appropriate patient management.

Vaccination is not enough: breakthrough meningococcaemia in a ravulizumab-treated aHUS patient

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Aim:

Complement inhibitor therapy with ravulizumab confers significant susceptibility to encapsulated bacterial infections, particularly *Neisseria meningitidis*. Vaccination is a mandated risk-mitigation strategy and antimicrobial prophylaxis is recommended, yet breakthrough infections remain a recognised but rare complication. We report a case of breakthrough meningococcaemia in a fully vaccinated patient receiving cefalexin prophylaxis and ravulizumab for atypical haemolytic uraemic syndrome (aHUS).

Method:

A 19-year-old female with aHUS (harbouring a pathogenic C3 variant and homozygous deletion of *CFHR1/CFHR3*) was diagnosed in 2020 and initially managed with eculizumab before transitioning to ravulizumab in March 2024. She had received full meningococcal vaccination (MenACWY and MenB at diagnosis, with a booster in October 2024) and was maintained on cefalexin prophylaxis following a documented penicillin hypersensitivity reaction. In July 2025, she presented with a one-day history of fever (39.4°C), severe headache, myalgia, arthralgia, and rigors, without meningism or rash. Empirical intravenous ceftriaxone and trimethoprim–sulfamethoxazole were commenced per meningitis protocol. Blood cultures, cerebrospinal fluid (CSF) analysis, meningococcal PCR, and whole genome sequencing (WGS) were performed.

Results:

Neisseria meningitidis was confirmed on blood culture and PCR. CSF analysis was unremarkable. Serogroup-specific PCR for B, C, W135, and Y was negative; WGS to determine the causative serogroup is pending. Trimethoprim–sulfamethoxazole was ceased and ceftriaxone continued, with significant clinical and biochemical improvement. Formal penicillin allergy assessment subsequently resulted in delabelling of the documented allergy.

Conclusion:

This case demonstrates that meningococcal breakthrough infection can occur in complement-inhibited patients despite full vaccination and antibiotic prophylaxis. Clinicians should maintain a low threshold for empirical treatment and prompt infectious disease consultation in this population. Ravulizumab was safely continued, with transition to erythromycin prophylaxis.

The effects of midazolam-based versus propofol-based sedation for bone marrow examination on patient and clinician experience

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Aim:

To compare patient and clinician experience of bone marrow aspiration and trephine biopsy (BMAT) performed under midazolam-based sedation versus propofol-based sedation.

Method:

This ongoing single-centre, prospective observational study included adults undergoing BMAT under either midazolam-based sedation (intravenous midazolam + intravenous fentanyl + local lignocaine; target n=50) or propofol-based sedation (intravenous propofol + intravenous fentanyl + local lignocaine; target n=50) across two sites of a major Australian hospital. Following BMATs, patients completed questionnaires assessing pain and anxiety, while clinicians assessed medication effectiveness and procedural experience. Adverse events and bone marrow sample quality metrics were also recorded. The primary endpoint was patient-reported worst pain intensity during BMAT on a Numerical Rating Scale (NRS). Categorical variables were compared using chi-square test. NRS outcomes, Global Medication Performance (GMP), and sedation assessments were analysed using the Mann-Whitney test. Agreement between patient and clinician GMP assessments was analysed using weighted kappa.

Results:

Between March-May 2026, 47 patients (midazolam-based sedation group n=31; propofol-based sedation group n=16) were enrolled and included in analysis. The hypothesis that patient-reported worst pain intensity during BMAT would be lower under propofol-based sedation than midazolam-based sedation was supported (median 0 [p25-p75=0-1] vs 2 [p25-p75=1-4], $p<0.001$). The propofol-based group experienced deeper sedation ($p<0.001$) and higher patient-reported GMP scores ($p=0.012$) compared to the midazolam-based group. Overall, patients rated medication effectiveness higher than clinicians (median GMP Excellent vs Good, $p<0.001$). Clinicians reported similar procedural experience between the midazolam-based and propofol-based sedation groups (median 8 in both groups, $p=0.434$). Biopsy sample quality metrics and adverse events have not yet been analysed. The study is on-going.

Conclusion:

Preliminary results suggest that propofol-based sedation is associated with clinically and statistically significant reductions in patient-reported pain during BMAT compared with midazolam-based sedation, although interpretation is limited by the small sample size.

Zopiclone-associated haemolytic anaemia: an underrecognised association

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Introduction:

Zopiclone; a non-benzodiazepine hypnotic widely prescribed for short-term management of insomnia, is generally regarded as having a favourable safety profile. Although its neuropsychiatric and gastrointestinal adverse effects are well recognised, haematological complications remain rare and likely underappreciated. Several literatures described the association between zopiclone use and haemolytic anaemia; however, awareness among clinicians remains limited. This case report aims to further highlight this adverse effect, contributing to the growing body of literature and reinforcing the need for heightened clinical suspicion in patients presenting with unexplained haemolysis.

Clinical case:

A 47-year-old female with a history of previous gastric sleeve surgery and anxiety presented with worsening lethargy 2 weeks after hospital admission for vitamin B12 deficiency. Despite treatment, lethargy and macrocytic anaemia persisted (Hb 59 g/L). Further investigations revealed a DAT negative haemolysis (LDH peak 537 U/L (120-250), reticulocytosis, haptoglobin undetectable), with morphological features (bite cells, irregularly contracted cells) suggestive of oxidative haemolysis. G6PD enzyme activity was normal. Additional history divulged the consumption of excess zopiclone up to 6 times (45 mg) of the recommended daily dose (7.5 mg) due to sleep deprivation. Her haemoglobin improved with blood transfusion and cessation of zopiclone.

However, she was once again sent to the Emergency Department with severe anaemia (Hb 66 g/L) and features of oxidative haemolysis, further history revealed the resumption of zopiclone precipitating this episode. Again she improved with drug cessation and small volume transfusion support.

Conclusion:

Zopiclone is not commonly associated with oxidative haemolysis, and previous literatures have primarily described haemolysis in the context of significant zopiclone overdose. This case underscores that even doses mildly exceeding recommended therapeutic levels may precipitate clinically significant haemolytic anaemia. The patient's initial delayed diagnosis and re-prescription of zopiclone emphasizes the need for greater awareness of this drug association.

Determinants and trends of bone mineral density in transfusion-dependent thalassaemia: a retrospective single-centre cohort analysis

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Aim:

Bone disease is a major complication of transfusion-dependent thalassaemia (TDT), but longitudinal site-specific bone density trajectories and their clinical and biochemical determinants remain incompletely characterised. We aimed to define these trajectories and identify key correlates of skeletal deterioration.

Methods:

Retrospective single-centre cohort study of 74 patients with TDT. 71 had analysable DXA data, contributing 424 scans (median 5 per patient; IQR 3.0–8.5). Linear mixed models assessed change in lumbar spine, femoral neck, and total-hip BMD and Z-scores over time.

Results:

The cohort was predominantly beta thalassaemia (93.2%). Median follow-up was 15.1 years (IQR 7.3–21.4); median scans per patient were 5 (IQR 3.0–8.5). Comorbidity burden was substantial: splenectomy 56.8%, hypogonadism 29.7%, diabetes 21.6%, hypothyroidism 20.3%, hypoparathyroidism 10.8%, and fragility fracture 16.2%. At latest DXA, mean age was 39.0 ± 11.4 years; mean lumbar, femoral-neck, and total-hip BMD were 0.976, 0.845, and 0.824 g/cm², respectively. At latest DXA, Z-score ≤ -2 was present in 36.6% at lumbar spine, 31.0% at total hip, and 12.7% at femoral neck. In mixed models, femoral-neck BMD declined significantly (-0.0053 g/cm²/year, $p < 0.001$) while lumbar spine BMD was stable. Lumbar Z-score improved modestly ($+0.016$ /year, $p < 0.001$), whereas femoral-neck and total-hip Z-scores declined (both approximately -0.020 /year, $p < 0.001$). Hypogonadism was the most consistent adverse clinical determinant, independently associated with lower femoral-neck BMD, total-hip BMD, and total-hip Z-score. ALP was the most reproducible biochemical correlate, with higher values associated with lower femoral-neck BMD and lower Z-scores at all three sites. Higher PTH was associated cross-sectionally with lower BMD at all sites. Ferritin showed no independent association with BMD.

Conclusions:

In TDT, longitudinal skeletal deterioration is most evident at the hip, particularly the femoral neck. Hypogonadism, elevated ALP, and PTH dysregulation may be more informative correlates of adverse bone health than ferritin, supporting targeted endocrine surveillance and hip-focused DXA monitoring.

Developing a nurse- led supportive care model for haematological cancers

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Aim:

To develop a nurse-led supportive care model for haematological cancers that focuses on equity of care, to be implemented by the McGrath Cancer Care Nurse workforce.

Method:

The McGrath Model of Care for haematological cancers was developed using a co-design methodology that centred the voices of people with a lived experience and clinicians and is underpinned by evidenced-based practices.

Initially, a haematological cancer expert advisory group was established with a diverse range of clinicians from across Australia. Secondly, in-person and online workshops were held with multidisciplinary clinicians and those with a lived experience of cancer. The workshops' purpose was to identify, define and understand the distinct aspects of supportive cancer nursing care in the haematological setting. Workshop data was analysed using a content analysis process to identify key themes. In the final stage, cancer nursing experts provided feedback on the feasibility of implementing the model of care

Results:

The advisory group provided expert input at three focus groups at different stages of the development of the model of care. Five workshops were held in Sydney, Melbourne and online for clinicians (n=42) and people with a lived experience (n=26). Key considerations for the model of care were the complexity of the disease impact and treatment regimens, rapid diagnosis and acute nature of severe and complex complications and ongoing monitoring and assessment, immunosuppression, as well as long-term nature of care and ongoing support. Other outcomes and the final model of care will be presented at the congress.

Conclusion:

The purpose of developing a McGrath Model of Care for haematological cancers is to meet the complex and diverse needs of people diagnosed with blood cancers. It supports a nation-wide focus on equitable care as well as evidenced based nurse-led supportive care interventions. The model of care provides an opportunity for McGrath Cancer Care Nurses to provide best practice supportive care for individuals with haematological cancers.

Real-world subcutaneous immunoglobulin utilisation and administration patterns in secondary immunodeficiency: Data and insights from a national patient support program

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Aim:

Secondary immunodeficiency (SID) is an acquired impairment of immune function in previously immunocompetent individuals, commonly associated with haematological malignancies or immunosuppressive therapies. Subcutaneous immunoglobulin (SCIg) acts as replacement therapy to restore effective antibody function. Understanding how patients utilise SCIg in routine practice, including dosing patterns, administration and persistence, may help to inform and facilitate patient care. This review interrogated the CSL CARES patient support program (PSP) database to describe real-world patterns of SCIg use and associated self-administration competency and persistence in patients with SID.

Method:

This retrospective review analysed de-identified data from consented patients with SID enrolled in the CSL CARES PSP who received at least one in-home nurse-led education session (June 2018 to December 2025). Descriptive analyses summarised demographics, dosing and administration attributes, competency and treatment persistence.

Results:

A total of 791 patients (51.6% females; aged 07-91 years) were included. SCIg was predominantly administered weekly (94.1%;744/791), with an average weekly administration volume of 42.7 mL and dose of 7.74 gr. Most (79.1%, 626/791) used pump-assisted infusion, typically in ≥ 2 injection sites. Two-thirds of patients (68.5%;542/791) had previously received intravenous Ig and 20.6% (163/791) were Ig-naïve; half (54.6%;432/791) had received in-hospital SCIg education. After a mean of 2.14 nurse education visits, 98.5% (779/791) of patients achieved self-administration competency. Among 185 patients with 12-month follow-up after achieving competency, 11 discontinued SCIg because treatment was no longer required. Of the remaining patients, persistence with SCIg was 84.5% (147/174), and 97.3% (143/147) of those retained competency.

Conclusion:

In this real-world cohort of patients with SID, SCIg utilisation was characterised by consistent weekly dosing, frequent use of pump-assisted, multi-site administration, and sustained persistence and competence over time after nurse-led education. These findings highlight usage patterns that may help to inform the adoption of SCIg as a practical, home-based therapy for patients with SID.

Implementation of a multidisciplinary model

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Background: Chimeric antigen receptor (CAR) T-cell therapy was introduced at Epworth HealthCare in 2024 through commercially sponsored clinical trials. Private hospitals face unique challenges with CAR T-cell delivery, including limited access to government funded CAR T-cell products, funding gaps for essential support services such as apheresis and cryopreservation, and the need to build specialised workforce capability in areas not traditionally embedded in private hospital models. These challenges required the development of a coordinated multidisciplinary service model to support safe implementation and ongoing delivery.

Methods: A review of the required stakeholders was conducted (Figure 1).

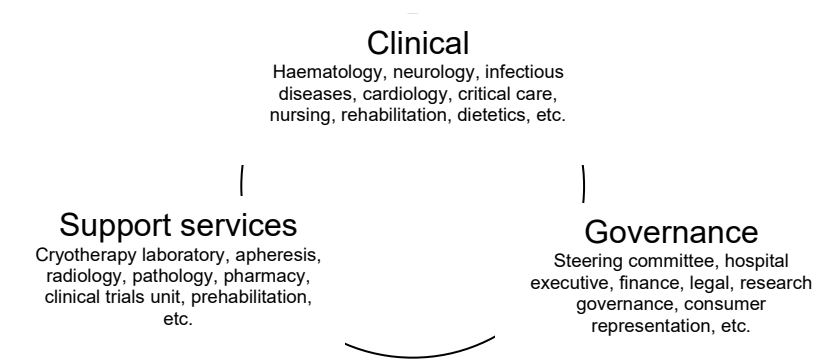


Figure 1. An overview of the stakeholders involved

Results: Introducing CAR T-cell therapies in a private hospital setting presented unique challenges. There was a need to specifically develop the workforce (e.g. registrars, nursing competency, apheresis), requiring governance oversight and funding support. Investment into support services required innovative funding models, including philanthropy and proceeds from commercial clinical trials. Due to the lack of government and private health insurer funding of CAR T-cell products, clear directives with stakeholders were required to ensure appropriate invoicing of services.

Methods for ensuring coordinated care across teams were introduced. Due to the complexity and time-critical nature of scheduling CAR T-cell therapy, additional communication pathways were necessary at key timepoints in the patient’s treatment schedule. These timepoints included at first identification and scheduling, on confirmation of the planned infusion date, and on discharge from acute care following infusion. Existing hospital communication channels were utilised and adapted where applicable.

Conclusion/future directions:

Clear communication pathways and early stakeholder engagement is critical in providing appropriate care of patients receiving CAR T-cell therapies in a private hospital. The methods established here will be used at Epworth to expand the CAR T-cell service to include additional indications and products.

You want to transfuse what cells? Granulocyte transfusions in neutropenic suspected sepsis: a 10 year review (PMH/PCH)

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Background:

Granulocyte transfusions have been used (rarely) for decades in patients with severe neutropenia: proven or highly suspected fungal or bacterial infections unresponsive to appropriate anti-microbial therapy, receiving maximal doses of granulocyte stimulating factor, on active treatment in remission and where neutrophil recovery is expected in the near future (weeks). There are no randomised studies and few clinical reports in the literature.

Granulocyte infusions can be provided from a single donor (usually family member) or as pooled granulocytes (available through Life Blood). Their implementation is often: urgent, difficult to arrange, associated with complications, expensive and perhaps not successful.

At PCH we have a SOP for pooled and directed donor granulocyte infusions.

Aim:

The aim of this study is to review our experience over a period of 10 years: looking at the patient diagnosis, the type of infusion, complications and their outcomes.

A review of the current paediatric granulocyte infusion literature with diagnosis, indications, infusion type, complications and outcomes.

Method:

Retrospective review of paediatric patients receiving granulocyte transfusions for severe neutropenic proven and suspected sepsis from Jan 2015- Dec 2025 at Perth Children's Hospital and Princess Margaret Hospital.

Review of the literature.

Results:

3 patients had Directed granulocyte infusion

- SAA survived
- Metabolic disorder –survived
- ALL- died

3 patients had Pooled Granulocytes

- SAA-survived
- 2 patients with leukaemia-died

Conclusion: This small single institution and literature study will review the complexity of granulocyte infusion use and possible outcomes regarding malignant and non malignant diagnosis. The plan will be to extend this small study to a national paediatric review.

Filgrastim induced cutaneous haemangioma

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Introduction:

Filgrastim (GCSF) injections are widely used to improve neutrophil counts to reduce the risk of neutropenic bacterial infections from therapy, non-malignant severe chronic neutropenia and for peripheral blood stem cell mobilisation. Adverse events are usually mild and manageable, with benefits exceeding their occurrence. Skin and subcutaneous disorders are listed on the Nivestim® data sheet and are limited to alopecia, rash and cutaneous vasculitis, rate common ($\geq 1/100$ to $< 1/10$).

Case History:

A 19-year-old female with moderate to severe neutropenia present since age 12 years was seen in haematology clinic. History is relevant for recurrent mouth ulcers, a reported increase in non-severe infections compared to peers with six courses of antibiotics over the preceding 12 months and subsequent increased infectious precautions including social isolation. No significant bacterial infections had occurred. She is under investigation with Gastroenterology services for an unclassified dysmotility syndrome.

Investigations revealed normal neutrophil count age 11, current neutrophil count of $0.1 \times 10^9/L$, no cyclical pattern, normal blood film morphology and viral serology, non-significant ANA, and unremarkable bone marrow biopsy with karyotype 46,XX. A presumed diagnosis of severe chronic idiopathic neutropenia was made. Following informed consent and patient and family preference to attempt to improve general wellbeing by increasing the neutrophil count, GCSF 300mcg intermittently was commenced.

Within three months of initiating treatment, palpable erythematous nodules began appearing over face and torso. Excision biopsy confirmed lobular capillary haemangioma. Spontaneous regression commenced with cessation of GCSF.



Figure A&B: right forehead and neck.

Conclusion:

Haemangioma have not previously been reported with filgrastim use. This case reminds us to ensure therapies are initiated within accepted guidelines, benefit-risk frameworks and to counsel patients about the known and potential for unknown off target impacts. Reporting of post-marketing side effects strengthens the information we can provide patients.

Patient preferences for infection prevention in haematological malignancies: a discrete choice experiment

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Background: Patients with haematological malignancies (HM) are susceptible to life-threatening infections due to immunosuppression. Immunoglobulin replacement therapy (IgRT) and oral antibiotics (Ab) are often used for prophylaxis, but comparative- and cost-effectiveness evidence is limited. IgRT is expensive and made from scarce donated plasma, while Ab carry risks of antimicrobial resistance. With limited evidence, governments, clinicians and patients must navigate difficult prophylaxis decisions.

Objectives: To quantify patient preferences for infection prophylaxis (IgRT vs Ab) and estimate trade-offs between efficacy, treatment burden, and out-of-pocket costs using a discrete choice experiment (DCE).

Methods: Adults with HM completed one of two online DCE surveys on prophylaxis initiation (IgRT naïve) or continuation (current IgRT users). Participants completed 9 (of 72) choice tasks from a D-efficient design, selecting between labelled IgRT vs Ab profiles defined by 8 attributes: dosing frequency, route/setting, time burden, side-effects, out-of-pocket costs, and 12-month mild/serious infection risks. Data were analysed using a multinomial logit model.

Results: Across both surveys (n=121; 45% using IgRT; median age: 67 years; 60% female), there was no significant preference for IgRT vs Ab, though patients showed clear preferences for treatment characteristics. They preferred less burdensome, non-hospital-based delivery: home-based SC IgRT over hospital-based IV infusions, and less frequent dosing.

In both surveys, patients were willing to trade a ~3% increase in annual serious infection risk for home-based SC (vs hospital-based IV) IgRT, and ~7% and ~9% increase in annual serious infection risk to avoid frequent flu-like and gastrointestinal side effects, respectively. Preference heterogeneity was evident; those with serious infection history, urban residence, or >5 years since diagnosis were more infection risk averse.

Conclusion: Patients value the impact prophylaxis has on their lives, trading infection risk for convenience and less side effects. This combined with preference heterogeneity, supports a shift toward personalised prophylaxis to optimise allocation of scarce, high-cost IgRT and Ab therapies.

Evaluating the quality of cardiovascular risk assessment in adult patients with Hodgkin lymphoma who received Anthracycline therapy: single centre retrospective audit.

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Aim:

The aim is to assess the completeness of the baseline cardiovascular risk assessment prior to treatment with Anthracyclines in patients with newly diagnosed Hodgkin's lymphoma according to the ESC-cardio- oncology guidelines (2022).

Method:

This audit was conducted in a tertiary care referral centre. Cases were identified using the referral database to lymphoma multi-disciplinary team meetings between August 2023 to April 2026. Case-matching with pharmacy database was used to identify the patients who received Anthracycline-containing regimens. Cases referred to MDT but treated at an alternative chemotherapy site were excluded (figure 1).

Audit records utilised digital medical records and clinic letters to assess the completeness of baseline cardiovascular risk assessment. A score system was developed to assess the completeness of the cardiovascular risk assessment based on ESC-2022 guidelines. The cardiovascular risk profile completeness would be assessed with respect to the following:

1. Cardiovascular risk factor identification through history and physical examination
2. Cardiac function assessment by either ECHO or MUGA
3. Performance of complementary tests to identify the cardiovascular risk factors.
4. Counselling on lifestyle factors such as smoking cessation, weight reduction.

Data analysis completed using descriptive statistics. Where appropriate, paired t-test is applied to detect differences in risk-assessment by treatment regimen.

Results:

Consort diagram for study inclusion criteria is shown in Figure 1. 31 patients with newly diagnosed HL were reviewed according to the audit plan. The median age at diagnosis was 38 (range 17–87). The chemotherapy regimens utilised included; ABVD (n= 14), BVAVD(n=3), CHOP (n=5), esc/BEACOPP (n= 4), R-CHOP (n=2), mini-CHOP (n=1) and Nivo- AVD (n=2).

Cardiovascular risk score assignment and treatment-specific screening to be reported. Final analysis pending at the time of submission.

Conclusion:

Cardiovascular risk assessment is ideally done routinely for all new cases of Hodgkin lymphoma. However, age and treatment intensity may lead to potential bias in the degree of cardiovascular screening. This audit hopes to increase awareness of the current guidelines, noting the potential for late/long-term toxicity for HL survivors.

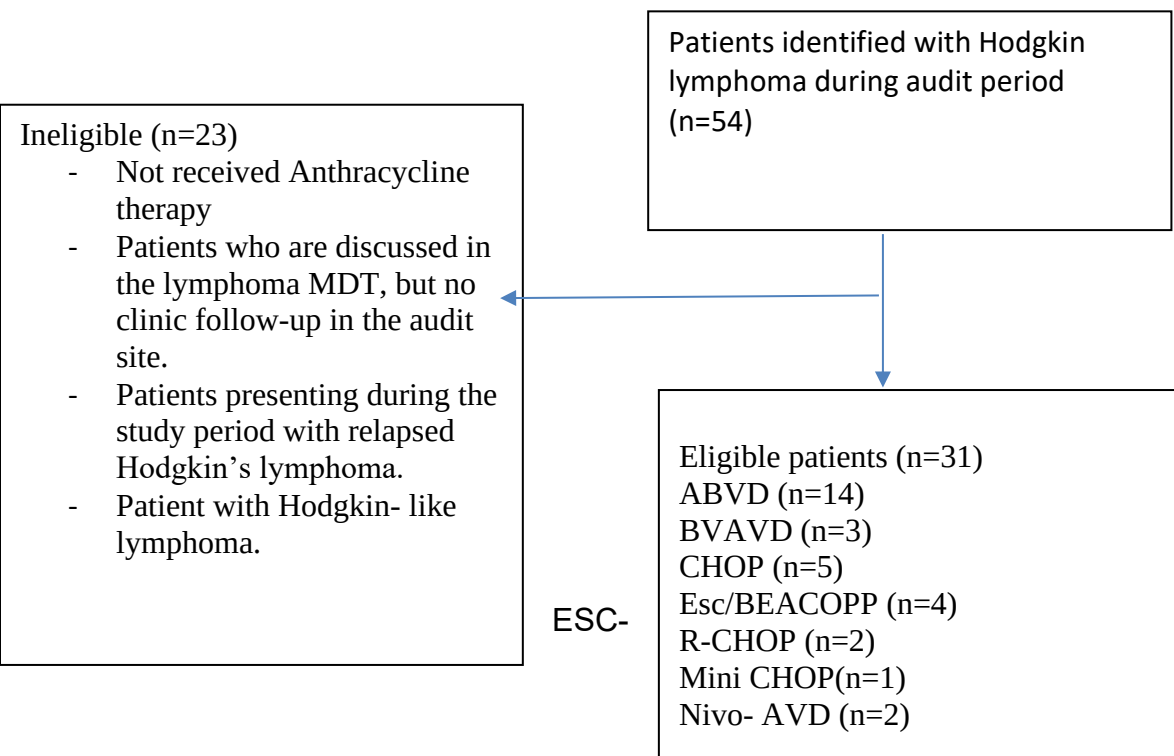


Figure 1

Reference:
Cardio- oncology
guidelines 2022

Closing the invisible gap: A transferable implementation science model for multidisciplinary haematology care coordination - Addressing safety, equity and health system efficiency in a culturally diverse metropolitan district

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Background and Aim:

Haematology patients face disease trajectories comparable to solid organ cancers in complexity, multidisciplinary intensity, and supportive care burden, yet no defined model of care coordination has been implemented, evaluated and shown adaptable across diverse Australian haematology services. Coordination is the multidisciplinary work of all team members connecting care across the patient trajectory – the connective tissue preventing fragmentation, duplication, and unmet need. We aim to design, adapt, implement, and evaluate a haematology care coordination model, generating learning to inform sustainable, transferable practice.

Method:

Whole-of-service diagnostic assessment of a haematology service within a large metropolitan CALD health district applied clinical redesign methodology alongside a comprehensive benchmarking series. A district-level, executive-sponsored implementation science programme bridges the gap between model design and sustained local delivery – addressing context, adoption and pressures that determine endurance. Iterative co-design of care pathways proceeds through a Multidisciplinary Working Party, with mixed-methods longitudinal evaluation under participatory action research principles.

Results:

Diagnostic assessment identified the gap in formalised care coordination as the principal driver of process inefficiencies that compound capacity constraints, fragmented transitions, and unmet supportive care needs – with disproportionate impact in CALD populations. Benchmarking confirmed the absence of an implementable coordination model adaptable to the Australian context. The model under development integrates disease-streamed pathways, a risk stratification instrument targeting resources to higher-need patients under workforce constraint, and supportive care streams spanning malignant and non-malignant haematology. Early implementation is generating learning on operationalising efficiency tools and standardised pathways, closing priority gaps, and supporting adaptive behaviour and cultural change.

Conclusion:

Care coordination is an invisible system gap with measurable consequences for patient safety, experience, and health system benefits. The programme's key transferable contribution is its methodology and design process, informed by real-time application of implementation science to support context-adapted haematology care coordination models in complex, resource-constrained and culturally diverse settings.

Optimising immunoglobulin replacement dosing in secondary hypogammaglobulinaemia following allogeneic stem cell transplantation and CAR-T therapy: an Australian multicentre pharmacokinetic study

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Background:

Secondary hypogammaglobulinaemia (SHG) is a common complication following allogeneic haematopoietic stem cell transplantation (allo-HSCT) and chimeric antigen receptor T-cell (CAR-T) therapy, contributing to infectious morbidity and hospitalisation. In Australia, immunoglobulin is a limited resource, and expenditure on immunoglobulin alone for SHG is approximately \$33.3 million (AUD) per year and rising. Despite widespread use of intravenous immunoglobulin (IVIG) and subcutaneous immunoglobulin (SCIG) replacement, dosing practices remain highly variable with limited evidence guiding precision dosing strategies in these populations.

Aim:

To develop population pharmacokinetic (PopPK) models to optimise IVIG and SCIG dosing in patients with SHG following allo-HSCT and CAR-T therapy.

Method:

This pharmacokinetic study is embedded in a broader multicentre retrospective cohort study investigating immunoglobulin use and infections in cellular therapy recipients across ten tertiary Australian hospitals. Of the 1000 patients' data collected, a cohort of 30 allo-HSCT and 30 CAR-T recipients that received immunoglobulin replacement therapy will be included in the pharmacokinetic study. Collected variables include patient demographics, transplant characteristics, serial serum immunoglobulin concentrations, IVIG and SCIG dosing regimens, and infection rates and severity.

PopPK modelling will be performed using nonlinear mixed-effects modelling to characterise immunoglobulin disposition and interpatient variability. Structural model development will evaluate one- and two-compartment models with assessment of first order elimination kinetics. Covariate analysis will explore the influence of patient-specific factors on pharmacokinetic parameters and immunoglobulin exposure.

Potential Outcomes:

Data collection and analysis is underway to characterise variability in practices and dosing approaches. Individualised precision dosing will reduce the variability in serum immunoglobulin concentrations and achieve higher trough levels to optimise its therapeutic effect. Precision immunoglobulin replacement will help identify which patients, at what level threshold, dose exposure, and immune reconstitution state, may experience fewer severe or recurrent infections.

Patient-reported quality of life outcomes after chimeric antigen receptor T-cell therapy: implications for ICANS risk stratification and management

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Aim: Chimeric antigen receptor T-cell therapy (CAR-T) is rapidly changing the treatment landscape of haematological malignancies and is expected to be similarly successful in neuroimmunological conditions. While CAR-T can achieve durable responses in haematological cancers, the associated toxicities, such as immune effector cell-associated neurotoxicity syndrome (ICANS), are common and potentially life-threatening. Research to date on ICANS and CAR-T therapy more broadly has focused primarily on clinical outcomes, which may not accurately reflect patients' lived experiences. This research aimed to investigate the patient-reported quality of life and its association with ICANS.

Methods: In this longitudinal study, 88 CAR-T recipients (69% male, median age of 67.8 years at infusion) for haematological malignancies completed select Quality of Life in Neurological Disorders (NeuroQoL) scales and a pain intensity scale from the Patient-Reported Outcomes Measurement Information System (PROMIS) at pre-infusion, inpatient review (median = 8 days), and at chronic review (median = 6.5 months). Total raw scores were utilised for statistical analyses. Thirty-one (35%) patients developed ICANS.

Results: In a multivariable logistic regression, poorer pre-infusion self-reported cognitive function was associated with higher odds of ICANS (odds ratio = 2.50, 95% CI 1.07 – 5.85, $p = .034$). Anxiety, depression, fatigue, sleep disturbance, and pain scores were not significant predictors of ICANS group. The ICANS group reported greater symptoms of anxiety, depression, sleep disturbance, fatigue, and cognitive dysfunction across most timepoints. Nevertheless, the symptom burden reported by most CAR-T recipients fell within normative limits.

Conclusion: Patients with greater cognitive complaints prior to CAR-T therapy may be at increased risk of developing ICANS. This finding can improve risk stratification for toxicity management. Finally, while patients who develop ICANS report increased symptom burden, the severity of symptoms is generally mild. This suggests that CAR-T is not associated with significant long-term deterioration in patients' quality of life.

A computerised cognitive test for immune effector cell-associated neurotoxicity syndrome in chimeric antigen receptor T-cell therapy recipients: a pilot study

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Aim: Cognitive dysfunction is a common manifestation of immune effector cell-associated neurotoxicity syndrome (ICANS) following chimeric-antigen receptor (CAR) T-cell therapy. ICANS may be life-threatening and so necessitate rapid recognition and intervention. This study investigated the utility of a computerised test of attention and processing speed (CARTcog) for monitoring ICANS.

Methods: In this prospective pilot study, 89 CAR-T patients (71% male, mean age at infusion = 67.18 years) completed 1,149 CARTcog tests and 5,347 ICE scores during their inpatient stay.

Results: Of the 89 participants, 30 (34%) developed ICANS. Receiver operating characteristic (ROC) analysis demonstrated that five of six CARTcog scores had moderate discriminatory power in identifying patients who develop ICANS in the following 12 hours (Area Under the Curve [AUC] = 0.77 – 0.79). Cutoffs were derived, and Bayesian generalised linear mixed models demonstrated that the reaction times above the cutoff on the choice reaction task were associated with an almost 20-fold increase in the odds of developing ICANS (OR = 19.64 [95% CI 5.14 – 96.20]). Three case studies illustrate the practical utility of CARTcog.

Conclusion: CARTcog may facilitate early detection of ICANS and thereby enhance patient safety and treatment outcomes.

More efficient delivery of high-cost standard-of-care therapies in relapsed multiple myeloma using real-time feedback of patient-reported outcome measures: the MY-PROMPT-2 trial

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Aim:

patients with multiple myeloma (MM) discontinue therapy prematurely, often due to treatment-related symptoms and reduced quality of life (QoL). Shortened duration on treatment may compromise survival. Real-time feedback from patient-reported outcomes (PROs) to clinicians are reported to improve outcomes in patients with solid cancer, due to earlier recognition and proactive management of toxicities. However to date no such trials have been performed in patients with MM.

We aim to determine whether routine real-time PROM reporting improves event-free survival (EFS; time from randomisation to permanent treatment discontinuation, progression, or death) compared with standard-of-care alone in patients with MM.

Method:

MY-PROMPT-2 is a pragmatic, multicentre, open-label, parallel-group Bayesian randomised controlled trial with 1:1 allocation, stratified by regimen. We will perform EFS subgroup analyses by stage, regimen and age.

In the intervention arm, PROMs are distributed to participants electronically via REDCap one week prior to clinic visits, for ≤12 months. PROM summaries are provided to clinicians upon completion to consider in patient care at clinic visits.

PROMs include MyPOS (a MM-specific tool assessing symptoms, mood, and healthcare) and two separate questionnaires targeting adverse effects of Carfilzomib or Daratumumab..

Health-related QoL (EORTC QLQ-C30) and treatment satisfaction (TSQM-9) are collected in both arms as secondary outcomes.

A Bayesian adaptive design is used. EFS evaluation begins after ≥60 events, with pre-specified rules for early stopping for inferiority or declaring superiority (proof-of-concept), enabling efficient signal detection with a smaller sample.

Results:

Recruitment is ongoing across seven sites, with 35 participants enrolled. Qualitative interviews exploring experience with PROM integration have commenced.

Conclusion:

MY-PROMPT-2 is the first multicentre trial in MM to evaluate the impact of real-time feedback from PROM on duration of therapy and clinical outcomes. Its pragmatic design, REDCap platform, and Bayesian framework support efficient evaluation in a rare disease setting and facilitate translation into practice.

Troponin I elevation and cumulative doxorubicin exposure in cancer therapy-related cardiac dysfunction among patients with malignant lymphoma

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Aim:

Cancer therapy-related cardiac dysfunction (CTRCD) is associated with cumulative doxorubicin exposure, but cumulative dose alone may not capture dynamic cardiotoxic risk during lymphoma treatment. We investigated whether cardiac troponin I (TnI) elevation, interpreted with cumulative doxorubicin exposure, was associated with CTRCD frequency in malignant lymphoma.

Method:

This single-centre retrospective study screened 62 patients with malignant lymphoma receiving doxorubicin-containing chemotherapy. Eligible patients had baseline echocardiography, at least two TnI measurements, and follow-up echocardiography during treatment or within 12 months after the last doxorubicin dose. CTRCD was defined as a ≥ 10 percentage-point left ventricular ejection fraction decline to $< 50\%$ and/or $> 15\%$ relative global longitudinal strain (GLS) reduction. TnI elevation was defined as at least one post-baseline value above the institutional upper reference limit before or at CTRCD detection or censoring. Cumulative doxorubicin exposure was calculated up to CTRCD detection or censoring. CTRCD frequency was compared by TnI status and cumulative exposure (< 300 vs ≥ 300 mg/m²) using Fisher's exact test.

Results:

Fifty patients were included. TnI elevation occurred in 31 (62.0%), and CTRCD occurred in 16 (32.0%). CTRCD was numerically more frequent in TnI-positive than TnI-negative patients (13/31 [41.9%] vs 3/19 [15.8%]; $p=0.068$). Most CTRCD events were GLS-only (14/16, 87.5%). Cumulative exposure at CTRCD detection or censoring was < 300 mg/m² in 20 patients and ≥ 300 mg/m² in 30. In the < 300 mg/m² subgroup, CTRCD occurred in 10/14 TnI-positive patients and 0/6 TnI-negative patients (71.4% vs 0%; $p=0.011$). In the ≥ 300 mg/m² subgroup, CTRCD occurred in 3/17 and 3/13, respectively (17.6% vs 23.1%; $p=1.000$).

Conclusion:

TnI-positive patients showed higher CTRCD frequency, with the clearest separation among patients with < 300 mg/m² exposure at CTRCD detection or censoring. Cumulative exposure alone may not fully capture dynamic CTRCD risk. Integrating TnI monitoring with cumulative exposure may guide intensified echocardiographic surveillance before conventional cumulative-dose thresholds.

Home treatment and supportive care for patients with blood cancers: An Australasian survey

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Aim:

Interest in moving care closer to, or into, the home is increasing due to rising inpatient bed demand and recognition of patient-centeredness. Blood cancer patients can receive outpatient treatment and supportive care at home, such as transfusion and chemotherapy, but availability varies. This study aims to describe home-based care offered in Australia and New Zealand, with a focus on home transfusion.

Method:

Cross-sectional survey of healthcare practitioners working in haematology or Hospital-in-the-Home (HITH) services in Australia and NZ. The survey was distributed through haematology, nursing and HITH professional groups between Oct 2025 and April 2026. Data were collected using the Qualtrics online survey platform and analysed descriptively, with a content analysis approach for open-ended responses.

Results:

75 respondents from 43 healthcare services completed the survey, from each state/territory and NZ (15%). The majority were nursing staff (59%) from inner metropolitan (44%) or middle/outer metropolitan (29%), public (96%) and tertiary (93%) healthcare services, with a small proportion of private services. The most common current home-based services were intravenous antibiotics (73%), line care (69%) and subcutaneous chemotherapy (54%). Desired services to offer in the future for blood cancer patients are seen in Figure 1. Commonly experienced or perceived barriers to commencing these services at home included capacity and lack of staffing, funding concerns, and geographical distance. Perceived barriers to commencement of a home-based transfusion service are depicted in Figure 2, with safety and deliverability as primary concerns. Free-text responses included concerns about staffing capacity and education, travel times, infusion times, and blood product transportation.

Conclusion:

Among survey respondents, there was variability in the care provided at home and in the identified barriers to commencing other home care. Part 2 of this study involves semi-structured interviews with services focusing on home transfusion to ascertain their logistics, barriers, safety aspects, and funding models.

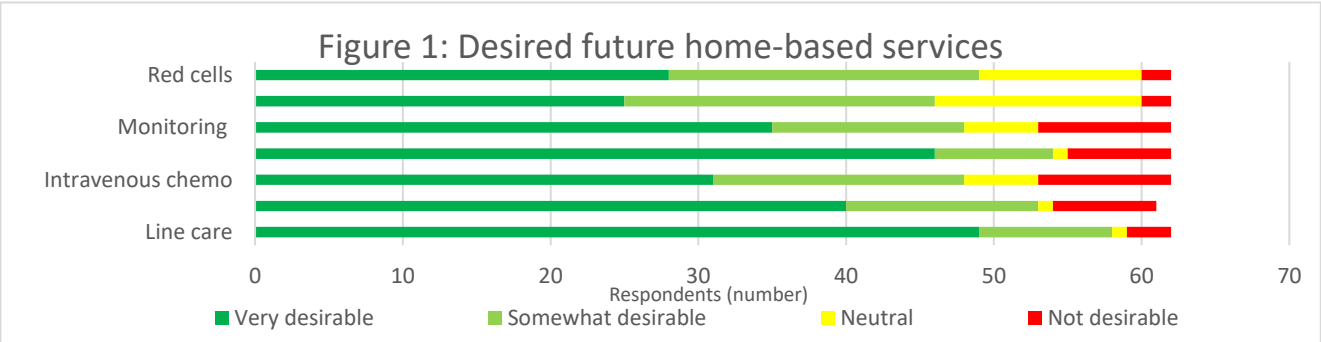
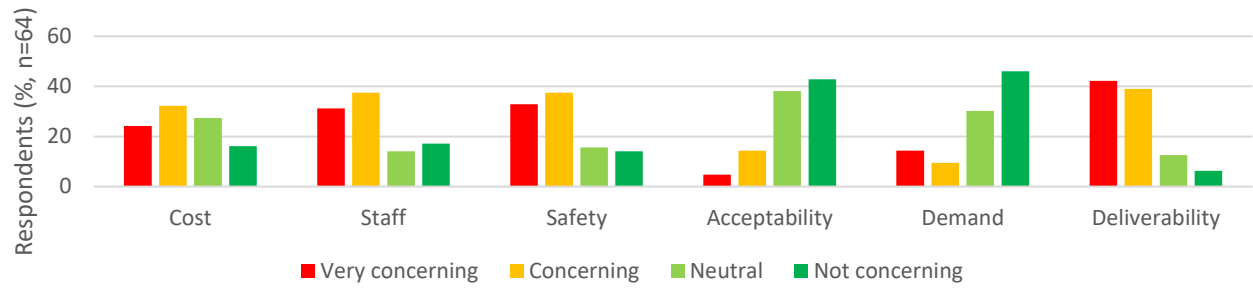


Figure 2: Barriers to home-based transfusion



Promoting clinic-based vaccination of patients with haematological malignancies via a pharmacist screening pilot

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Aim: Vaccination of patients with haematological malignancies (HM) is challenging due to recommendation heterogeneity, concerns about efficacy and safety between different malignancies, treatments and vaccine types, leading to under-vaccination. Clinic time resource is also limited as is the information interface with general practitioners. A local working group developed a guideline and piloted a pharmacist-led vaccination project in haematology clinics. This project aims to audit program implementation.

Method: We prospectively audited vaccination delivery in a Victorian tertiary hospital whereby a pharmacist identified vaccine eligible patients in haematology clinic. The pharmacist provided recommendations for influenza and pneumococcal vaccine prescribing and coordinated nurse administration. Data were collected from May 2025 to March 2026 on demographics, vaccination uptake and safety outcomes.

Results: Twenty-four patients were assessed over 9 clinic sessions: 21 patients (87.5%) in haematology clinic and 3 (12.5%) post referral to immunisation clinic. All patients assessed had vaccination gaps; none declined assessment or vaccination. Demographics are depicted in Table 1. Nine patients (37.5%) were vaccinated prior to cancer treatment, nine (37.5%) mid-treatment and six (25%) post-treatment. In 12 patients planned for first or subsequent cytotoxic chemotherapy cycle, vaccination was delivered a median of 7 days prior to cycle commencement (IQR 3-13.3). Vaccinations delivered were pneumococcal (n=16, 66.7%), influenza (n=15, 62.5%), inactivated shingles (n=3, 12.5%) and COVID-19 (n=3, 12.5%).

Vaccines were tolerated with no immediate reaction or chemotherapy delay. Staging PET post-vaccination for one patient showed uptake deemed as ‘reactive nodes’, not affecting treatment selection. There were no vaccine-preventable infections noted during median follow up of 10.2 months (IQR 9.5-10.3).

Conclusion: Pharmacist-led vaccination identified gaps in coverage with high uptake and acceptability to patients. Vaccination of patients with HM appears well tolerated and accepted despite concurrent chemotherapy. A systems approach for vaccination is necessary for standard-of-care infection prevention.

Table 1: Demographic and treatment data

Demographic data	All patients (n=24)	Treatment types	Patients on treatment (n=18)
Age (median [IQR])	70 (59-77)	Chemoimmunotherapy	7 (38.9)
Male (n [%])	14 (58.3)	BTKi	4 (22.2)
Malignancy (n [%])		ABVD	3 (16.7)
Indolent NHL *	9 (37.5)	Lenalidomide monotherapy	2 (11.1)
DLBCL	5 (20.8)	Rituximab monotherapy	1 (5.6)
HL	5 (20.8)	DVd	1 (5.6)
MM	3 (12.5)		
MCL	1 (4.2)		
ALL (post-treatment)	1 (4.2)		

*MZL n=4, CLL n=2, FL n=2, LPL n=1

CAR T-cell therapy in adults with down syndrome: practical challenges in supportive care and ICANS assessment

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Background:

Published data regarding CAR T-cell therapy in patients with Down syndrome (DS) are extremely limited, particularly in adults. Existing evidence is largely restricted to small paediatric and adolescent registry cohorts with limited toxicity and supportive care data. CAR T-cell therapy causes prolonged immune suppression, including B-cell aplasia, hypogammaglobulinaemia and cytopenias. These effects may be particularly relevant in patients with trisomy 21, who have baseline immune dysregulation and increased infection-related mortality during conventional chemotherapy. Assessment of immune effector cell-associated neurotoxicity syndrome (ICANS) is also challenging in patients with intellectual disability, as neither standard adult ICE scoring nor paediatric tools have been validated in this population.

Case:

We describe an adult patient with Down syndrome undergoing tisagenlecleucel for relapsed/refractory B-lymphoblastic leukaemia. Due to intellectual disability and developmental delay, conventional ICE scoring was not appropriate. A modified assessment strategy was developed using multidisciplinary input including haematology, nursing, neuropsychology/developmental assessment, allied health, and caregiver input to establish an individualised neurological baseline and modified ICE score. Clinical outcome is pending.

Discussion:

This case highlights practical challenges in delivering CAR T-cell therapy to patients with DS. Modified ICANS assessment relies on subjective clinician interpretation and local adaptation, risking under-recognition and over-treatment of neurotoxicity. Additionally, the effects of CAR T-associated immunosuppression in DS remain poorly characterised, including risks of severe infection, prolonged hypogammaglobulinaemia, and delayed immune recovery.

Conclusion:

Given the rarity of CAR T-cell therapy in patients with adult DS, collaborative institutional and multicentre case series are needed to define toxicity, infectious outcomes, and supportive care requirements. Separate collaborative efforts are also required to develop standardised approaches to modified ICE scoring for patients with baseline intellectual disability undergoing CAR T-cell therapy.

Enhancing timely palliative care communication through a multidisciplinary educational intervention designed for and with cancer specialists

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Background:

Timely referral to palliative care, in parallel with standard of care treatment, improves quality of life, symptom control, survival and reduces hospital stays. Despite known benefit, Australian data indicate many patients either do not access specialist palliative care or are referred late in the disease trajectory. Barriers to timely referral include time constraints, clinician discomfort with initiating discussions and persistent misconceptions regarding the role of palliative care.

Aim:

To develop a communication-focused educational intervention to address known barriers.

Method:

A multispecialty clinical working group was convened to explore the issue of timely referral and develop an educational resource to address the issues explored. The working group comprised consumer representatives, specialist physicians in haematology, medical oncology, radiation oncology, palliative care, as well as trainees ensuring a comprehensive and person-centred approach. After a facilitated workshop an agreed course content and design was determined.

Result:

A recognised online Continuing Medical Education (CME) program designed for specialists and trainees in adult haematology, medical oncology, and radiation oncology has been developed. The course emphasises a shift from an “end-of-life” perception of palliative care towards a personalised, needs-based model of “timely” referral integrated alongside active cancer treatment.

This is grounded in contemporary evidence demonstrating benefits of palliative care and incorporating practical communication frameworks, including structured approaches to information delivery, recognition and response to emotional cues, and strategies to address common misconceptions. The course promotes clinician self-reflection and supports skill development required for effective and compassionate communication.

Peer reviewed testing delivered universal support regarding quality and clinical relevance, noting the tailored content as a highlight.

Conclusion:

This open-source CME course aspires to improve clinician skills and lead to earlier integration of palliative care and improved patient and caregiver outcomes. When applied, it will reduce late, referrals in cancer care. This initiative highlights the value of multi-disciplinary collaboration when addressing complex issues.

Helping paediatric patients improve health outcomes through appointment attendance.

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Aim:

Paediatric patients with Thalassemia who receive regular transfusions must be carefully managed due to the risk of iron overload. Iron chelation therapy helps reduce this risk but must also be monitored to check for potential adverse effects.

Our unit has 45 patients receiving regular transfusions. A high percentage of patients were found to not be attending annual screening for audiology and ophthalmology. In addition, medication compliance with iron chelation therapy was low in this patient cohort. Many patients are from non-English speaking backgrounds or refugee families, with varying levels of health literacy.

The aim was to improve compliance by consolidating appointments and improve health literacy by providing information on the importance of medication adherence and appointment attendance in different languages.

Method:

An audit was conducted examining the past 3 years of appointment attendance for all transfusion patients which demonstrated poor attendance. We liaised with the audiology and ophthalmology clinics and proposed a new referral and booking process that allowed patients to be seen when attending the transfusion clinic, to reduce the number of days families needed to attend the hospital.

Results:

Changes brought on by this study has seen a significant increase in attendance to clinic appointments. Moreover, feedback from the families has shown considerable improvement in the patient experience.

Conclusion:

This study has had a positive impact on current and future patients as the improved attendance in screening clinics allows for adverse effects to be found and managed in a timely manner. Furthermore, it has improved holistic patient care by enabling the families to spend less time in hospital.

Patient recruitment challenges in fetal RHD genotyping – the role of the transfusion nurse specialist.

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Aim:

To highlight the contribution of relationship-focused Transfusion Nurse Specialist (TNS) leadership of participant recruitment during a national fetal RHD genotyping validation project at New Zealand Blood Service (NZBS).

Method:

In October 2024, renewed engagement strategies were introduced to improve participation in the fetal RHD validation project, supported by Transfusion Nurse Specialists at NZBS. The Waikato TNS used existing clinical and community relationships to increase awareness and enrolment, beginning with the Whānau Mai team, who provide antenatal and postnatal care. Followed by key stakeholders at Waikato Hospital, including the Antenatal Clinic Charge Nurse Manager, Director of Obstetrics and Gynaecology, and Midwifery Director. Although supportive, they advised that formal hospital ethics approval was required before recruitment could proceed.

Results:

Although overarching approval for patient recruitment had been granted by the Health & Disability Ethics Committee, hospital ethics approval was required before recruitment could proceed at Waikato Hospital. Securing all approvals took four months and included engagement with the hospital's Māori Research Committee, to ensure cultural responsiveness and equity.

Following approval, referral pathways were identified, however, limited capacity among Lead Maternity Carers to undertake the consent process, which could take up to twenty-minutes, resulted in no enrolments during the first two months.

Further engagement with the Whanau Mai coordinator led to an agreement to support recruitment, with the TNS undertaking participant consent discussions. This collaborative approach enabled progress, with the first participant enrolled in April 2025, reaching a total of thirty participants by December 2025.

Conclusion:

This experience highlights the importance of culturally grounded engagement, flexible recruitment pathways and strong interprofessional partnerships in achieving equitable patient participation. TNS leadership played an important role in progressing participation within this fetal RHD genotyping validation project, supporting the alignment with international standards of care for RHD negative pregnant women at NZBS.

Applied muscle tension education and vasovagal reaction reduction in whole blood donors

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Proposed Abstract

Background:

Vasovagal reactions are the most common adverse events in whole blood donation and can adversely affect donor experience and return behaviour. Applied Muscle Tension (AMT) is an evidence-based technique shown to reduce vasovagal reaction risk when correctly performed. A systematic review was completed to establish a best practice standard. A national clinical audit identified inconsistent staff practice in offering AMT education to donors, highlighting an opportunity to standardise and strengthen preventative care.

Aim:

To reduce the rate of vasovagal reactions in whole blood donors by improving staff adherence to best practice in delivering Applied Muscle Tension education.

Methods:

A baseline national clinical audit assessed current practice regarding AMT education. Findings informed a multi-component intervention consisting of updated donor-facing educational resources, revised staff guidance, and targeted staff education. A follow-up audit was completed three- and six-months post interventions, to measure changes in practice. National donor adverse event data were examined to identify trends in vasovagal reaction rates before and after implementation.

Results:

Baseline audit results demonstrated variation and gaps in adherence to the best-practice standard. Post-implementation audit data collection is ongoing. Preliminary analysis of national donor adverse event data suggests a downward trend in vasovagal reactions, coinciding with the implementation of the interventions.

Conclusion:

This quality improvement initiative focused on strengthening adherence to evidence-based AMT education practices across whole blood donation settings. Post-implementation evaluation provides a comprehensive assessment of changes in staff practice and vasovagal reaction rates. Preliminary observations suggest improved consistency in delivery of AMT education and a potential reduction in vasovagal reactions. These findings will inform ongoing strategies to enhance donor safety, experience, and retention.

A patient-centred evaluation of a nurse practitioner model of care in a regional haematology outpatient department

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Aim:

To determine the effectiveness of a nurse practitioner (NP) model in a regional haematology outpatient department.

Method:

A service evaluation was conducted in the Haematology Outpatient Department at a regional hospital. All patients who were reviewed by the nurse practitioner candidate (NPC) over a three-month period were eligible to participate. An anonymous patient survey was employed, consisting of eight Likert-type scale questions and two free-text items for open-ended feedback. The questions were designed to explore four domains: (1) patient satisfaction; (2) perceived safety and confidence in care; (3) accessibility and effectiveness of communication; and (4) barriers and limitations of an NP model of care. Data was analysed for both quantitative and qualitative measures. Free-text responses were reviewed and coded to identify recurring themes.

An initial sample of five patients were surveyed to assess the acceptability of the questionnaire and gain an insight to views of a NP model of care, before expanding to a target sample size of 50 patients.

Results:

Results from target sample size will be finalised in July 2026. Initial sample of five patients indicated the survey was appropriate. All patients were satisfied after their review, agreed that the NP model improved their access and that communication was effective. Four patients agreed that an NP model was safe and felt confident in the care provided.

Conclusion:

This evaluation supports the effectiveness and acceptability of the NP model in a regional haematology outpatient setting. The findings will be used to inform ongoing service improvement and optimisation of the NP role, identify areas for enhancement in patient experience and care delivery, support workforce planning and potential expansion of nurse practitioner-led services. It will contribute to the broader evidence base for advanced practice nursing in haematology.

Influenza vaccine hesitancy in patients with hemoglobinopathies in the Post-COVID era: A retrospective cohort study

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Background

Patients with haemoglobinopathies, including sickle cell disease and thalassaemia, are at increased risk of severe influenza-related complications. Despite recommendations for annual vaccination, hesitancy remains a poorly understood barrier. The COVID-19 pandemic has influenced public perceptions of vaccination, potentially affecting uptake of other vaccines; however, the impact on influenza vaccination in chronically ill and immunocompromised populations in Australia is not well defined.

Objectives

This retrospective study aims to evaluate influenza vaccination uptake and identify patterns of vaccine hesitancy among patients with haemoglobinopathies at a large Australian tertiary hospital in the post-COVID period (2023–2025), with comparison to the COVID period (2020–2022). A secondary objective is to assess demographic and clinical factors associated with non-uptake. Findings will inform the development of a targeted nurse-led vaccination clinic.

Methods

A retrospective cohort study will be conducted using linked administrative data. Patients with confirmed haemoglobinopathies will be identified via the local electronic medical record (EMR). Influenza vaccination status for 2020–2025 will be obtained from the Australian Immunisation Register (AIR), with linkage to Medicare Benefits Schedule (MBS), Pharmaceutical Benefits Scheme (PBS), and EMR data. Descriptive statistics will summarise vaccination uptake, and multivariable logistic regression will identify predictors of hesitancy, including age, sex, geographic remoteness, socioeconomic status, and comorbidity burden.

Significance

Findings will inform the design of a nurse-led vaccination clinic aimed at improving uptake in this high-risk population. This model highlights the role of specialist nurses in promoting vaccine education and access, and contributes to understanding the longer-term impact of the COVID-19 pandemic on vaccine confidence in Australia.

Closing the gap on intimacy and exposure risk guidance: anti-myeloma therapies

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Background and Aim:

Numerous requests were received from myeloma patients and carers around the non-pregnancy related risks for intimate partners and household contacts from exposure to bodily fluids. A search of consumer and product information, Micromedex, other treatment information resources and requests submitted directly to the manufacturing pharmaceutical companies, found that there is a paucity of data available to provide guidance on non-pregnancy related risk of exposure to non-cytotoxic, anti-myeloma therapies. This project aimed to provide expert-endorsed, practical guidance on the risk of exposure to non-cytotoxic anti-myeloma therapies for intimate partners and household contacts of myeloma patients.

Method:

A survey was circulated amongst haematologists with a special interest in myeloma via Microsoft Forms. Respondents assessed whether selected anti-myeloma drug classes posed low or high risk for exposure to bodily fluids during intimacy (e.g. open-mouth kissing, unprotected sexual activity unrelated to pregnancy prevention) and household exposure (e.g. shared facilities and utensils)

Results:

16 participants completed the survey. All respondents indicated that all assessed anti-myeloma therapy classes are considered low risk for both non-pregnancy-related intimacy and household contact exposure. They also endorsed wording to include in treatment infosheets.

Conclusion:

These findings address a current gap in patient information, where existing guidance primarily focuses on fertility, pregnancy, and breastfeeding, with minimal direction on other forms of exposure. This expert consensus addresses a key area of uncertainty within the myeloma community. The findings support the inclusion of clear, practical guidance in treatment information resources, improving patient and caregiver reassurance and quality of life. Future directions include broad dissemination of this guidance, encouraging similar evaluations across other therapeutic areas, and advocating for updates to national resources.

Equity and access in lymphoma care across regional, rural, and remote Australia: a scoping survey by Lymphoma Australia

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Aim:

To explore the experiences of cancer nurses delivering lymphoma care in regional, rural, and remote (RRR) Australia, and to identify strengths, challenges, and inequities influencing patient outcomes.

Method:

A national scoping survey was developed to examine factors impacting lymphoma care delivery in RRR settings. The survey targets nurses involved in delivering lymphoma treatment and providing supportive care to patients with lymphoma. Key areas include access to systemic therapies and clinical trials, supportive care services, survivorship care, and perceived inequities affecting lymphoma patients and carers. Geographic data is collected to enable analysis of regional variation and localised service gaps. Descriptive statistical methods will be used to summarise quantitative data, while thematic analysis will be applied to qualitative responses to identify recurrent themes and priority areas.

Results:

Data collection is ongoing, with the survey to close in June 2026. Preliminary findings are expected to highlight significant barriers to timely diagnosis and treatment, including limited access to specialist services, diagnostic delays, and reduced availability of clinical trials in RRR areas. Additional anticipated findings include workforce shortages, gaps in supportive and survivorship care, and the impact of travel burden on patients and carers. Variability in service availability across regions is also expected to emerge.

Conclusion:

This study will provide insights into the delivery of lymphoma care across RRR Australia by centring the perspectives of cancer nurses. Findings will inform advocacy and targeted resource allocation to address identified inequities. This work aims to support the development of more equitable and accessible lymphoma support across Australia in order to improve outcomes for patients and carers in underserved regions.

This research was supported by BeOne. The company had no role in analysing the data or preparing the abstract.

A pathway for subcutaneous immunoglobulin in a regional New Zealand hospital: a collaborative quality improvement initiative

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Aim:

To demonstrate how a review of intravenous immunoglobulin (IVIG) use as a result of increasing demand in a regional New Zealand hospital led to the planning and development of a patient-centred subcutaneous immunoglobulin (SCIG) pathway to improve patient autonomy and quality of life.

Method:

Immunoglobulin therapies are widely used to treat primary and secondary immune deficiencies. Intravenous Immunoglobulin (IVIG) is the most common route of administration although the subcutaneous immunoglobulin (SCIG) alternative is recognised by the New Zealand Blood Service as safe and effective.

A retrospective review of IVIG use was conducted in 2025 at a regional New Zealand hospital. Patients receiving IVIG were assessed for potential suitability for transition to SCIG. This led to the formation of a working group and a review of available local and national resources with the aim of developing a streamlined, patient-centred pathway for SCIG use.

Results:

This review suggested that approximately 65% of patients receiving IVIG could potentially be transitioned to subcutaneous therapy. However, no clear process existed to support such transitions, and awareness among healthcare providers that SCIG was a viable alternative option was limited. In response, available national and local resources were reviewed with the aim of developing a streamlined, patient-centred pathway for SCIG use. This involved the development of a structured pathway and supporting guidelines to assist staff in providing patients with the tools, education, and resources required for self-management of long-term conditions requiring immunoglobulin therapy.

Conclusion:

Multidisciplinary collaboration, stakeholder and consumer engagement and feedback were central to this quality improvement initiative. Ongoing monitoring, regular review, and feedback from both staff and patients, alongside clear communication, flexibility, and shared ownership, were identified as essential factors to support the successful development and implementation of a safe, effective, and patient-focused model of care.

Paroxysmal nocturnal haemoglobinuria: 2 case reports and why nursing awareness matters in rare, non-malignant haematology.

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Paroxysmal Nocturnal Haemoglobinuria (PNH) is a rare, potentially life-threatening chronic haematological disorder caused by a mutation in the PIG-A gene in haematopoietic stem cells. PNH is characterized by bone marrow failure, with acute episodes of haemolytic anaemia and thrombosis. Clinical manifestations of PNH may resemble autoimmune or systemic inflammatory diseases, making diagnosis challenging despite advances in confirmatory testing.

Aim:

To describe the complexities of PNH by comparing two patient case studies and highlighting the role of a non-malignant clinical nurse consultant (CNC) in the management of symptoms and treatment.

Method:

A retrospective case study of two PNH patients at University Hospital Geelong, comparing their symptomatology, diagnosis and the importance of a non-malignant CNC in overall patient experience.

Results:

Case 1:

A 37-year-old male, presented with fever, coryzal symptoms and haematuria. Noted to have previous admissions to ED, with recurrent episodes of haematuria post viral illness. Laboratory investigation reported features of intravascular haemolysis and elevated LDH. Flow cytometry along with FLAER assay confirmed a diagnosis of PNH, prompting referral to the non-malignant CNC. Treatment discussion and complications with disease were effectively managed with CNC guidance and support.

Case 2:

A 55-year-old male, presents in his early 20's with transient abdominal pain and sudden haematuria, which continues for over a decade with associated anaemia and multiple cardiac complications. Initially managed under urology, later referred to haematology after prolonged symptoms. PNH was suspected and subsequently confirmed through diagnostic testing. After years of misdiagnosis and no CNC role at time of diagnosis, the patient felt unsupported and hesitant to engage with treatment decisions. Since the establishment of the non-malignant CNC role, this patient cohort has benefited from diagnosis and treatment specific education.

Conclusion:

These two cases highlight the critical role of a non-malignant CNC in rare haematological conditions, by facilitating patient education and supporting treatment decision-making to improve patient engagement and outcomes in PNH.

Transfusion nurse specialist and practitioner roles across Aotearoa New Zealand, the United Kingdom and Australia: An exploratory horizon scan

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Aim:

To compare the scope, structure and governance of the Transfusion Nurse Specialist (TNS) role in Aotearoa New Zealand with equivalent Transfusion Practitioner (TP) roles in the United Kingdom (UK) and Australia, identifying similarities, differences and opportunities to inform workforce development and transfusion safety strategy.

Method:

A semi-structured open-ended questionnaire was developed by the New Zealand Blood Service (NZBS) TNS team and distributed to selected key transfusion practitioners and leaders across England, Scotland, Wales, Northern Ireland and Australia in 2025. Responses examined role titles, professional backgrounds, academic requirements, governance arrangements, funding models and core functional responsibilities. Findings were collated and mapped against the New Zealand TNS role using a comparative matrix and thematic analysis. This horizon scan provided a broad macro-level overview of how the NZ TNS role compares to international counterparts.

Results:

Across all countries, TNS/TP roles shared core responsibilities including transfusion education, haemovigilance, incident investigation, audit and quality improvement. Nursing was the predominant professional background, although greater multidisciplinary diversity was reported in the UK. No country reported a formalised national training pathway for entry into the role. Governance models varied considerably, ranging from highly centralised national frameworks in Scotland to more decentralised, trust-based models in England. New Zealand's TNS role aligned strongly with international counterparts in scope and expertise, but differed in its nationally coordinated, partnership-based approach across both blood service and hospital settings.

Conclusion:

This comparative analysis demonstrates strong international alignment in the purpose and value of transfusion nurse specialist and practitioner roles. Variability in governance, education structures and workforce models highlights clear opportunities for shared learning, particularly in developing consistent training frameworks, visibility of impact and sustainable workforce planning to support safe, equitable transfusion practice.

Establishing a dedicated allogeneic bone marrow transplant (allograft) survivorship clinic

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Aim:

Survivorship is an essential element of ongoing cancer care, as emphasised in the Optimal Care Pathways and in pillar three of the Victorian Cancer Plan. Allograft recipients can have several, unique late effects related to their treatment. These late effects are often different to that of the general haematology patient population.

Austin Health currently runs a general haematology survivorship clinic. Allograft patients' complex post-transplant needs are not being sufficiently addressed in the current clinic model.

This project aims to build on our current model of care to implement an allograft survivorship clinic tailored to the unique needs of this population of patients.

Method:

A dedicated allogeneic transplant survivorship clinic will be developed at Austin Health. A fit-for-purpose, allograft-specific survivorship care plan will be developed and implemented to communicate with patients and primary clinicians. A dedicated database will support ongoing monitoring and evaluation. Shared care will be strengthened through engagement with community providers, including general practitioners.

Results:

- A dedicated allograft survivorship clinic has been implemented.
- Patient-specific survivorship needs have been evaluated using locally developed questionnaires.
- An allograft-specific survivorship care plan was developed to address the needs of this population and was positively received by general practitioners.
- A dedicated allograft survivorship database has been established to support ongoing monitoring and evaluation and to track whether patient needs are being met; further analysis will be completed at project end.

Conclusion:

A dedicated allograft survivorship clinic has been successfully implemented at Austin Health, incorporating the use of questionnaires, an updated allograft survivorship care plan and a purpose-built database. These elements have enabled a more comprehensive assessment and management of the unique late effects experienced by this population. Further data analysis will be undertaken at the conclusion of the project to evaluate the service and help guide its future development.

Establishing a Nurse Practitioner Model of Care for Lymphoma and Chimeric Antigen Receptor T-cell (CAR T) within a Cancer Clinical Trials Unit

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Aim:

To describe the implementation and early outcomes of a Nurse Practitioner (NP) led model within a cancer clinical trials unit, providing continuous expert nursing practice, early toxicity identification and management, and long term follow up (LTFU) for patients receiving investigational therapies for lymphoma and CAR T.

Method:

A prospective service evaluation was conducted using the electronic medical record system within the Parkville Cancer Clinical Trials Unit (PCCTU), Peter MacCallum Cancer Centre, following the introduction of a dedicated NP role in August 2025.

The NP model integrates advanced clinical practice into trial delivery through NP led ambulatory clinics, including in person, telehealth, and telephone reviews. Core functions include pre-screening, eligibility, comprehensive clinical assessment, toxicity identification and management, supportive care prescribing, medication reconciliation, and coordination of escalation to the multidisciplinary team.

Data is being collected from August 2025 to September 2026, including number and type of patient encounters, indications for review, and NP led clinical interventions.

Results:

A total of 169 NP led patient reviews have been conducted to date (August 2025–April 2026), with data collection ongoing through to September 2026. These included scheduled on treatment reviews, LTFU and unscheduled assessments of unwell patients, reflecting the NP's role across the continuum of trial care.

Management included treatment related toxicities, lymphoma related symptoms, and LTFU care, with coordination of investigations and escalation to the haematology fellow or principal investigator where clinically indicated.

Further analysis of review types, including unwell presentations and LTFU activity, will be presented.

Conclusion:

As clinical trial complexity increases, advanced nursing models of care are required to support continuity of care. Embedding a NP within a cancer clinical trials unit offers a sustainable, scalable approach that strengthens patient safety and integrates clinical care with trial delivery.

Circulating beyond the city: A single regional experience in establishing a haematology trials program

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Aim: To describe the development of a regional haematology clinical trials program at Coffs Harbour Cancer Institute and to evaluate how strategic partnerships and capacity building enabled delivery of increasingly intensive collaborative and sponsored studies outside a metropolitan setting.

Method: A descriptive review of the program's progression from an oncology-based trials unit to a functioning haematology service. The review drew on operational experience, trial-activation milestones, recruitment outcomes, patient demographics, clinical service availability, and inter-site coordination processes.

Insights were informed by staff feedback, innovation in governance methods, and reflection on the practical challenges and successes encountered during each stage of growth. This evaluative approach allowed identification of the factors that enabled the program to expand capability, strengthen collaboration, and support increasingly complex trial models.

Results:

Access to clinical trials in Australia has largely been metropolitan, leaving regional patients underserved. Coffs Harbour built its program from an existing oncology trials framework, with early haematology work through the LARDR registry, strengthening research culture, staff capability, and governance.

Collaboration with the ALLG advanced the program, with Coffs Harbour joining Port Macquarie and Orange in the POLAR BEAR trial. Although no patients were enrolled, the trial improved workflows, strengthened inter-site links, and confirmed regional trial feasibility. A major step followed with the first independent pharmaceutical study, ELEMENT MDS, recruiting six local patients. This enabled the more complex AbbVie M25 study, delivered through a Coffs Harbour–Port Macquarie; lead–satellite model. M25 was the first industry haematology trial in MNCLHD using new multi-centre processes and a district-wide one-stop shop to expand Multiple Myeloma trial access.

The program now supports a growing portfolio including BRUIN, ELRiSE, Takeda MF, NBCR, and a Daratumumab-at-home protocol.

Conclusion: This experience demonstrates that regional centres can deliver high-quality and complex haematology trials, improving equity and access for patients who would otherwise be excluded from clinical research.

Primary palliative care in acute haematology nursing: A protocol for a qualitative evidence synthesis of content, process and context

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Aim:

Despite growing evidence that early palliative care improves outcomes for people with haematological malignancies, its integration in acute haematology settings remains inconsistent and poorly understood.^{1–5} Haematology nurses are uniquely positioned to deliver primary palliative care (PPC) through sustained therapeutic relationships across the illness trajectory, yet how they enact this role in practice and what enables or constrains it remains largely unexplored.^{1,6–9} This qualitative evidence synthesis (QES) aims to synthesise international qualitative evidence on haematology nurses' experiences of delivering PPC in acute care settings, examining what constitutes this care (content), how it is delivered (process), and what shapes its delivery (context).

Method:

A QES will be conducted in accordance with JBI methodology and reported using PRISMA 2020 guidelines.^{10–12} The research question was structured using the SPIDER framework (Sample: registered nurses in acute haematology/bone marrow transplantation settings; Phenomenon of Interest: PPC delivery; Design: qualitative and mixed methods studies).¹³ A systematic bilingual search (English and Chinese) will be conducted across at least five databases, including CINAHL, MEDLINE, Scopus, Airiti Library, and CNKI. Two independent screeners will apply inclusion and exclusion criteria at title/abstract and full-text stages. Included studies will be critically appraised using the JBI qualitative appraisal checklist. The protocol will be registered on PROSPERO.

Results:

This review is expected to identify key PPC competencies, care delivery processes, and multi-level contextual factors (nurse, team, organisational, and system) that facilitate or constrain nurse-led PPC. Findings will be synthesised into an integrated content-process-context framework.

Conclusion:

This QES will generate an evidence-based framework on haematology nurses' experiences of providing PPC in acute haematology settings. An in-depth understanding of this phenomenon will identify opportunities to support earlier, more equitable and person-centred care for people living with haematological malignancies and their families.

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International perspectives on stem cell donor collection and registry operations: insights from DKMS

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Aim:

To describe professional observations and learning gained through visits to the DKMS Collection Centre and DKMS Life Science Lab in Dresden, Germany, and attendance at the European Society for Blood and Marrow Transplantation (EBMT) 2025 conference in Florence, Italy.

Method:

An observational professional development study tour was undertaken in March–April 2025 at the DKMS Collection Centre and DKMS Life Science Lab in Dresden, Germany, and during attendance at the European Society for Blood and Marrow Transplantation (EBMT) 2025 conference in Florence, Italy. Observations focused on donor workup, mobilisation, collection procedures, donor care practices, laboratory technologies, and registry operations. Comparative reflections were made between DKMS operational processes and local Australian stem cell collection and donor search practices.

Results:

The DKMS Collection Centre demonstrated a highly efficient large-scale donor collection model, completing approximately 10–12 collections daily with dedicated staffing and infrastructure. Compared with local Australian practice, observed differences included donor mobilisation timing, venous access approaches, citrate protocols, donor workup investigations, and post-procedure donor support practices. The DKMS Life Science Lab demonstrated high-throughput next-generation sequencing capabilities processing up to 1.3 million donor samples annually. Attendance at EBMT 2025 further highlighted the importance of international collaboration and evolving practices in stem cell transplantation and donor coordination.

Conclusion:

This study tour improved understanding of the complex international processes underpinning unrelated donor transplantation, including donor recruitment, workup, collection, and high-throughput registry operations. Exposure to alternative donor care and collection practices reinforced the importance of international collaboration and operational efficiency in supporting timely donor identification and stem cell procurement for patients requiring allogeneic transplantation. These insights may help inform future donor coordination practices and contribute to ongoing improvement in Australian transplant and collection services.

The development of a nursing and donor technician strategy

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Aim:

In 2023, a newly appointed Chief Nurse at a national blood service was tasked with developing an organization-wide nursing strategy. Significant system pressures, including increasing demand for plasma products, growth in cancer and chronic disease, expansion of therapeutic services, workforce shortages, and rising organ donation demand, highlighted the need for a cohesive, future-focused nursing and donor technician strategy.

The strategy aimed to provide clarity of purpose, professional direction, and a structured governance framework to support nurses and donor technicians to work to the top of their scope of practice. Key objectives included alignment with legislative and regulatory requirements embedding contemporary professional nursing practice, strengthening clinical governance and continuous quality improvement, and incorporating consumer experience and equity commitments, including obligations under cultural requirements.

Methods:

A co-design approach was adopted, engaging nurses and donor technicians across the blood service through national workshops and structured collaboration. Six priority areas were identified and agreed: Senior nurse leads and co-leads supported implementation, performance measurement, and outcome evaluation, within these groups.

Results:

A bespoke nursing and donor technician strategy was produced, owned by nursing staff and embedded across the organisation. Quantitative and qualitative outcome measures were established across all priority areas, supporting cultural safety, workforce development, quality improvement, and clinical excellence. This strategy was endorsed by the executive team and the Chief Nurse and regulatory body.

Conclusion:

This strategy provides a robust, adaptable framework to strengthen nursing leadership, workforce sustainability, and clinical quality within a complex national blood service, offering transferable insights for other specialized healthcare settings.

Comparison of plasma proteomic signatures in chronic kidney disease versus healthy controls utilising data-independent acquisition mass spectrometry (DIA-MS)

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Aim:

Cardiovascular disease (CVD) is the leading cause of mortality in chronic kidney disease (CKD). We aim to characterise plasma proteomic differences between CKD patients and healthy controls to identify potential biomarkers of CVD.

Method:

We conducted a comparative biomarker discovery study, comparing plasma samples of 60 CKD patients (eGFR<30ml/min/1.73m²) enrolled in a prospective observational cohort with 28 healthy controls at Northern Health, Australia. Baseline demographics and plasma was collected at recruitment. Optimised on-bead enzymatic digest protocols were applied and unbiased proteomic profiling performed using high-resolution data-independent acquisition mass spectrometry (DIA-MS) on a Bruker timsTOF HT platform. Data was processed using Spectronaut, and protein-level abundance estimates using limma. Gene ontology biological process enrichment was assessed via gene set enrichment analysis (GSEA), with normalised enrichment scores calculated.

Results:

The CKD cohort and healthy controls had similar median age (64.5 vs 63.5 years, p=0.45) and sex split (65% vs 57.1% male, p=0.48). The median eGFR of the CKD cohort was 7ml/min/1.73m² with 78.3% (n=47) dialysis dependent.

GSEA was performed on 34 molecular signature database (MSigDB) pathways relevant to CVD to identify functional impacts of the proteomic differences. CKD patients demonstrated significant (FDR<0.1) enrichment in upregulation of Hp abnormal cardiovascular system physiology which is associated with cardiovascular dysfunction. Downregulation of genes associated with coagulation pathways were identified, involving intrinsic and common pathways, fibrinogen and fibrinolysis and with blood microparticles (phospholipid microvesicles) was identified. This likely reflects mechanisms of the coagulopathy seen in CKD patients contributing to their CVD risk.

Conclusion:

We identified a plasma proteomic signature in the CKD cohort reflecting abnormalities of cardiovascular physiology along with altered coagulation pathways including multiple fibrin and fibrinolysis pathways. This data identifies likely mechanisms leading to the high CVD risk in CKD patients and presents future opportunities for development of risk stratifying targeted biomarkers.

Life-threatening haemorrhage from acquired factor V inhibitor: Case report and 10-year literature review

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Background: Acquired Factor V deficiency (AFVD) is a rare but potentially fatal bleeding disorder with poorly identified triggers and management. We report a case of a 75-year-old woman who was diagnosed with AFVD following presentation with critical gastrointestinal and pulmonary haemorrhage and we synthesise contemporary evidence from the past decade.

Method: A literature review of published AFVD cases using **MEDLINE**, **PubMed**, and **Embase** with keywords “*acquired factor V deficiency*” and “*factor V inhibitor*” since 2016. Exclusions for irrelevance, non-English text and/or accessibility were applied.

Results: 60 reports comprising 66 patients were analysed (Age range 13-95, median 74). Bleeding occurred in 71% of cases (Intracranial haemorrhage in 11%, with a haemorrhage-associated mortality of 9%). Thrombotic events were reported in 9%. Various triggers were identified of which antibiotics were most common (Table 1). Factor V inhibitor (FVi) was detected in 71% of patients- median 13 Bethesda Units. 80% required treatment (Table 2). Where immunological assays detected inhibitors and Bethesda assays did not, clearance antibodies over neutralising were suspected. Clinical/biochemical improvement was seen in 65% of patients, spontaneous resolution (without inhibitor eradication therapy) in 23% and a relapse-remitting course in 3%.

Table 1. Suspected AFVD Triggers

Trigger	Frequency
Antibiotics	24%
Idiopathic	21%
Malignancy	6%
Sars-Cov-2	5%
Immune checkpoint inhibitor	3%
Anticoagulant	3%
Amyloidosis (no detectable FVi in all cases)	3%

Table 2. AFVD Treatments (% of total patients)

Haemostatic Interventions	Inhibitor Eradication Therapy
Fresh Frozen Plasma (48%)	Steroids (64%)
Platelets (21%)	Intravenous Immunoglobulin (15%)
Factor concentrates (11%)	Rituximab (12%)
Factor Eight Inhibitor Bypassing Activity (6%)	Plasma Exchange (9%)
Recombinant FVIIa (8%)	Cyclophosphamide (14%)

Conclusion: AFVD is associated with significant bleeding morbidity/mortality with most patients requiring immunosuppressive therapy. Antibiotics represented the most common identifiable trigger as reflected in our patient. Early recognition and tailored immunosuppression are critical in this condition.

Drug-induced thrombocytopenia (DIT): a retrospective audit on a single tertiary referral centre

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Aim: To describe the incidence, review clinical presentations, and outcomes of DIT.

Method: All patients with a diagnosis code of “secondary thrombocytopenia” (D69.5) were examined at a single regional tertiary referral centre using electronic health records for a 12-month period (1/1/2023-30/12/2023). Case records were reviewed and any suggestion of a drug association was evaluated.

Results: There were 98 patients diagnosed with secondary thrombocytopenia, of whom nine were found to be likely DIT (9%) and six cases (6%) were heparin-induced thrombocytopenia (HIT). Out of all 98 patients, 38 patients died (39%). Out of patients that died, 20 patients had cancer (53%).

Nine DIT patients had a median age of 71 years, all-cause mortality 44%, median nadir platelet count $15 \times 10^9/L$ and 89% male. Three patients had WHO grade I, II, III bleeding respectively. Three cases were caused by antibiotics (Piperacillin-Tazobactam, Meropenem, Linezolid), two were caused by antipsychotics (Clozapine and Risperidone) and the rest were caused by other medications (Ibuprofen, Apixaban, Nivolumab and Abciximab respectively).

Six HIT patients had median age of 63.5 years, all-cause mortality 50%, median nadir platelet count $29 \times 10^9/L$ and 67% were male. No bleeding occurred amongst these but 50% had thrombosis.

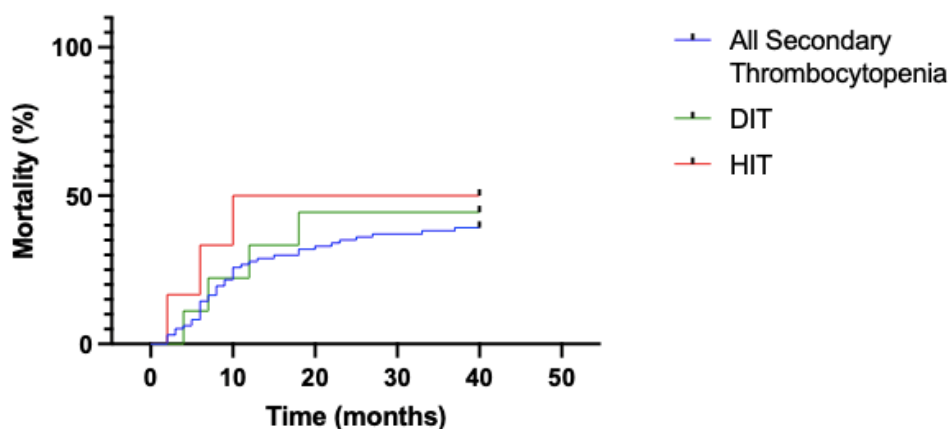


Figure 1. Kaplan-Meier graph for mortality.

Conclusion:

Notably, patients with secondary thrombocytopenia (of any cause) exhibited a strikingly high mortality rate. High all-cause mortality associated with a diagnosis of “secondary thrombocytopenia” merits further observational studies to better understand the determinants of mortality and in the case of drug-induced thrombocytopenia, to better differentiate the culprit agents and develop strategies for their identification.

Evaluation of visco-elastic whole-blood coagulation testing (VET) to detect thrombosis risk in patients with upper gastro-intestinal (GI) cancer

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Aim: This pilot feasibility study was conducted to identify any VET parameters that could predict for thromboembolic events in upper GI cancer patients.

Method: We recruited 14 patients with a new diagnosis of metastatic upper GI cancer. Blood samples were collected at study enrolment. VET assays (NA-test, EX-test, Fib-test and TPA-test) were performed within 4 hours of blood collection using ClotPro™. Non-parametric Mann Whitney tests were performed to compare each parameter in each test.

Results: Among 14 patients, the mean age was 64 years (SD = 11 years), 12 male patients (86%), and 12 month mortality 50%. We identified 4 patients who developed thrombosis after cancer diagnosis. TPA-test showed a trend towards markedly longer lysis time (LT) in the group of patients with thrombosis events (median = 331.5 seconds) compared to without thrombosis (median = 227.0 seconds), but was not significant (p=0.33) in this pilot study. Patients who died within 12 months also trended towards longer LT in TPA-test compared to those who survived (median = 232 vs 215 seconds) (p=0.18).

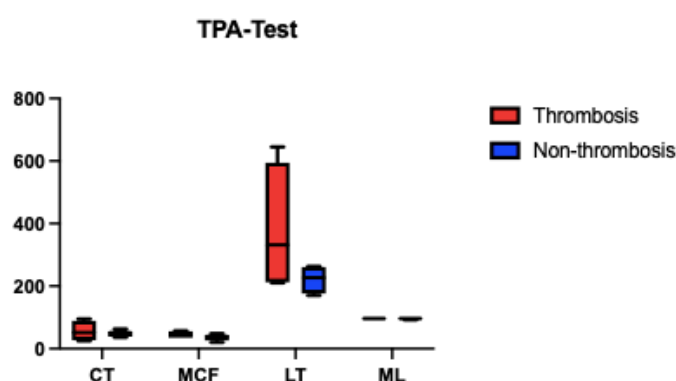


Figure 1. TPA-Test: Clotting Time (CT), Maximum Clot Firmness (MCF), LT and Maximum Lysis (ML).

Conclusion: This pilot study showed that VET was feasible for patients with upper GI cancer and raises the potential utility of assessing LT on the TPA-test to identify patients who may be at higher risk of developing thrombosis. TPA-test uses exogenous tissue plasminogen activator (tPA) to induce clot breakdown, which overrides the natural tPA inhibitors in the blood, plasminogen activator inhibitor-1 (PAI-1)[1]. Longer lysis time in TPA-test indicates potentially impaired fibrinolysis related to higher PAI-1 level, which correlates with poor prognosis in malignancies [2]. Small sample size in this study warrants further investigation and TPA-test may become priority over other tests in VET.

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Development of an Australian and New Zealand point-prevalence audit to assess anticoagulation use and appropriateness

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Background:

Anticoagulants are high-risk medicines frequently used in hospitalised patients. Inappropriate use or omission can lead to substantial harm, with prescribing errors reported in up to 43% of anticoagulants prescribed in Australia (1-5). Variability in prescribing practice and limited access to anticoagulation stewardship (ACS) services hinder optimal anticoagulant management. A key component of ACS programs is qualitative assessment of prescribing appropriateness; however, this is rarely performed due to the lack of available standardised audit tools.

Aim:

This project aims to develop a validated point-prevalence survey for hospitals across Australia and New Zealand (ANZ) to assess anticoagulation use and appropriateness.

Method:

A multidisciplinary steering group comprising haematologists, specialised nurses and ACS pharmacists from ANZ will establish consensus-based criteria and measures for appropriateness, including indication, dosing, duration, and adherence to contemporary guidelines.

The audit tool will support efficient data collection across diverse hospital settings and enable aggregation of results for trend analysis. It will be conducted annually using a core dataset with an optional rotating focus topic (e.g. obesity or ICU venous thromboembolism prophylaxis) to address emerging priorities. The survey will be distributed via the Thrombosis and Haemostasis Society of Australia and New Zealand ACS Network, with all hospitals invited to participate.

Pilot testing and validation will be undertaken at selected sites to ensure usability, reliability, and clinical relevance.

Expected Results:

The initiative will deliver a streamlined audit tool enabling benchmarking of anticoagulation practices across institutions. It will facilitate identification of practice gaps, inform quality improvement initiatives -including the implementation of ACS programs, and enable longitudinal monitoring through annual surveys. Its adaptable design will facilitate ongoing focus on emerging clinical issues.

Conclusion:

This project represents the first large-scale, structured audit developed by a multidisciplinary group to assess inpatient anticoagulant practices. It will support standardisation of care and promote the importance of ACS programs within Australia and New Zealand.

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Subcutaneous cytarabine and pegylated interferon for rapid platelet reduction in myeloproliferative disorders requiring parenteral treatment: report of 2 cases

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Case Study: Myeloproliferative disorders (MPD) can present with concurrent thrombosis and bleeding, creating major therapeutic challenges. Standard therapy includes oral hydroxyurea or pegylated interferon,¹ however, rapid parenteral platelet reduction is occasionally required. Here we describe 2 cases of JAK2 positive MPD admitted to ICU for synchronous thrombosis and bleeding where a fast control of platelet count was required. We based our approach on older studies in chronic myeloid leukemia² and an EviQ protocol for acute myeloid leukemia.³

Patient 1 is a 44 year old woman treated previously with venesection and hydroxyurea. She presented with cerebral venous sinus thrombosis and, despite anticoagulation, developed recurrent ischaemic strokes and aspirin was added. This was complicated by a massive retroperitoneal haematoma. Neurological deterioration necessitated intubation, with platelet counts peaking at $2013 \times 10^9/L$ (**Fig.1**). As oral hydroxyurea could not be administered, she received subcutaneous cytarabine 20 mg/m^2 daily for 7 days with pegylated interferon, resulting in platelet reduction over 10 days.

Patient 2 is a 40 year old man with JAK2 positive MPD who had not received treatment. Following a motor vehicle accident, he sustained catastrophic abdominal injury requiring extensive surgery, prolonged ICU stay and total parenteral nutrition. He developed bilateral arm DVT and received enoxaparin. Despite this, he developed superior mesenteric artery thrombosis and aspirin was added. This was complicated by a large intrabdominal bleed whilst platelets were $1500 \times 10^9/L$. As hydroxyurea could not be administered, he received subcutaneous cytarabine 20 mg/m^2 daily for 7 days with pegylated interferon with improvement in the platelet count. Both patients remain well on pegylated interferon and hydroxyurea 2 years and 6 months after discharge respectively.

Conclusion: Subcutaneous cytarabine can be considered in patients with extreme thrombocytosis where platelet reduction is required to manage bleeding and clotting complications and where oral hydroxyurea is not an option.

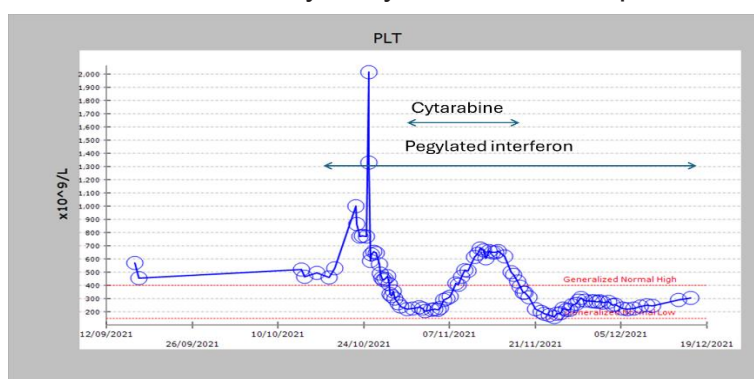


Figure 1. Platelet count in patient 1 over the course of her ICU stay, initially treated with pegylated interferon followed by a course of subcutaneous cytarabine.

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Overcoming interference in fibrinogen measurement in *Clostridium perfringens* induced severe intravascular haemolysis: a case report.

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Case Study: *Clostridium perfringens* is an anaerobic, alpha toxin secreting, gram-positive bacterium causing fatal septicaemia. Alpha toxins damage and lyse erythrocytes. Rapid diagnosis and treatment are critical.

A 74-year-old woman with acute fever and confusion presented. Haemoglobin was 93g/L and rare rod-like inclusions within toxic neutrophils and marked spherocytosis were seen on blood film microscopy. Elevated bilirubin and LDH, with negative DAT, were consistent with intravascular haemolysis. Rapid deterioration occurred with jaundice, metabolic acidosis, renal failure and worsening anaemia. A CT scan showed a gaseous liver abscess. With suspicion of *Clostridium perfringens* septicaemia, clindamycin and tobramycin were added. Blood cultures confirmed gram-positive bacilli under gram-staining microscopy. Bacterial growth was positive after ~5 hours incubation with *Clostridium perfringens* identified. Disseminated intravascular coagulation (DIC) required exclusion, but coagulation testing in the setting of marked haemolysis was challenging. Both clot-based detection and immunological methods on the ACL TOP 500 (Werfen, Bedford, Massachusetts) measure relative light absorbance based off sample turbidity at different wavelengths. Haemolysis obstructs light absorption interfering with the detection of sample turbidity. PT and aPTT were prolonged and the derived fibrinogen could not be calculated. A direct Clauss fibrinogen method was performed. Based on clot curves and milli-absorbance, a clot had formed, confirming the presence of fibrinogen, but haemolysis interference prevented an exact result. Rotational Thromboelastometry (ROTEM) avoids haemolytic interference. The Extrinsic Thromboelastometry (EXTEM) clotting time (CT) was normal. EXTEM A5 was slightly prolonged, but a normal Fibrinogen Thromboelastometry (FIBTEM) A5 demonstrated a normal fibrinogen level. A second sample <3 hours later showed prolonged EXTEM CT (factor deficiency) and FFP was given. EXTEM A5 was mildly prolonged and FIBTEM A5 was not reduced, consistent with normal fibrinogen level but thrombocytopenia. Conclusion: ROTEM enabled rapid guidance to coagulation factor replacement, but despite aggressive interventions the patient passed away from pulmonary haemorrhage.

Surgical outcomes and haemostatic management in people with haemophilia A in New South Wales: a registry-based analysis

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Aim:

To describe the characteristics, peri-operative haemostatic management, and surgical outcomes of people with haemophilia A undergoing surgery in New South Wales (NSW).

Surgical procedures in people with haemophilia A (HA) remain associated with significant bleeding risk and resource utilisation. Despite advances in factor concentrates, including extended half-life factor VIII (FVIII) products and non-factor therapies such as emicizumab, real-world data describing surgical management and outcomes are limited.

Method:

We conducted a retrospective cohort study using data from the Australian Bleeding Disorders Registry (ABDR). People with haemophilia A receiving care at NSW Haemophilia Treatment Centres who underwent surgical procedures during the study period were included. Extracted variables included haemophilia severity, inhibitor status, baseline prophylaxis regimen, and peri-operative haemostatic strategy. Outcomes included reported peri-operative bleeding complications and need for additional haemostatic treatment. Descriptive analyses were performed, with subgroup analyses by disease severity and inhibitor status.

Results:

Between 2015 and 2025 there were 3,261 procedures identified among 1,263 individuals with haemophilia A (37% severe) in NSW. Orthopaedic surgery accounted for 19% of procedures with 63% on hips, knees and ankles. Most procedures required peri-operative FVIII replacement, including among individuals receiving emicizumab prophylaxis. There were 6% of individuals with inhibitors who underwent surgery and they required bypassing agents and their admission was associated with a longer hospital stay. Substantial variability was observed in haemostatic product use across surgery types. Data will be presented on these outcomes.

Conclusion:

Surgery in people with haemophilia A continues to require complex peri-operative management and is associated with ongoing bleeding risk, even in the era of novel therapies. Registry-based data highlight variability in practice and outcomes across surgical contexts. Real-world such as this can inform clinical practice, service planning, and evaluation of high-cost therapies, and provide a foundation for future linked data analyses of surgical outcomes.

Antithrombin use in heparin resistance: A retrospective audit at a tertiary hospital

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Aim:

To evaluate the appropriateness of antithrombin (AT) use in patients with suspected heparin resistance and assess adherence to evidence-based practice, including adequate heparin dosing and activated clotting time (ACT) monitoring.

Method:

A retrospective audit was conducted at a tertiary hospital between 2023 and 2025. A total of 54 AT administrations were identified from electronic medical records. Thirty-four (63%) of these were administered in cardiothoracic patients for the indication of heparin resistance. Data collected included indication for AT use, patient weight, total heparin dose (units/kg), ACT and activated partial thromboplastin time (APTT) values, and complications (bleeding and thrombotic events).

Appropriateness was assessed using a predefined criterion of heparin resistance, defined as failure to achieve ACT ≥ 480 seconds following a heparin dose of 500 units/kg. Descriptive analysis was performed to evaluate adherence to these criteria and identify practice variation.

Result:

In the cardiothoracic cohort (n=34), 7 patients (20.6%) received AT without meeting criteria for heparin resistance. Among these, 4 patients had not received the recommended heparin dose, precluding assessment of true resistance, while 3 patients achieved ACT ≥ 480 seconds yet were still administered AT. ACT monitoring was inconsistent with 4/34 (12%) of patients lacking ACT measurements post-heparin and post AT administration. One patient developed a left middle cerebral artery territory infarction on day 1 following AT administration; however, causality could not be established. No other significant complications were identified.

Conclusion:

Our audit identified inappropriate AT use and inconsistent ACT monitoring, highlighting gaps in adherence to established guidelines. Ensuring adequate heparin dosing prior to AT administration and standardizing ACT monitoring may improve patient safety and reduce unnecessary use of this high-cost therapy. These findings support the need for institutional protocols and re-audit to optimize anticoagulation practices.

Activated platelets are detrimental drivers to stem cell health in autologous harvest products

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Aim:

Autologous stem cell transplantation (ASCT), a crucial therapy for haematological malignancies, relies on harvesting adequate viable haematopoietic stem and progenitor cells (HSPCs). Co-collection of apheresis-activated platelets may compromise graft quality. This study aimed to determine whether activated platelets injure autologous HSPCs and identify the key mediators responsible.

Method:

498 autologous HSPC harvests (2016-2025) were retrospectively analysed for CD34⁺ HSPC viability and platelet burden. In a prospective cohort, platelet-HSPC interactions (CD41a/CD34; n=24) and platelet degranulation (P-selectin; n=7) were assessed using imaging and flow cytometry. Supernatants from peripheral blood, fresh and freeze-thaw harvests were profiled for inflammatory mediators using ELISA. Mass spectrometry (MS) was performed on n=12 representative supernatants and cell-sorted HSPCs with or without bound platelets (n=6).

Result:

Peripheral platelet counts strongly predicted HSPC recovery ($P < 0.0001$) and viability was inversely correlated with platelet count in harvest bags ($r = -0.45$, $P < 0.0001$). Platelet-HSPC aggregates (Figure 1 lower panel) were P-selectin-positive, and aggregates increased in freeze-thawed product (20% vs 49% of HSPCs). Post-thaw supernatants had 2- to 5-fold increases in platelet activation markers and pro-inflammatory tumour necrosis factor (TNF) α and transforming growth factor (TGF) β . MS analysis of harvest product supernatants detected high levels of TGF β , platelet factor (PF)4 and pro-platelet basic protein (PPBP) and many platelet cytoskeletal proteins. Differential pathway analysis revealed signatures of platelet-driven neutrophil activation associated with acute inflammatory and oxidative stress pathways and reduced DNA synthesis in HSPC preparations containing high platelet concentrations.

Conclusion:

Increased platelet burden is associated with greater risk of HSPC injury. Data identified that activated platelets directly engaged HSPCs and released soluble mediators that can generate a pro-inflammatory/apoptotic microenvironment. Activated platelets and signalling pathways are modifiable therapeutic targets that may elevate HSPC viability and preserve graft quality, leading to better patient outcomes.

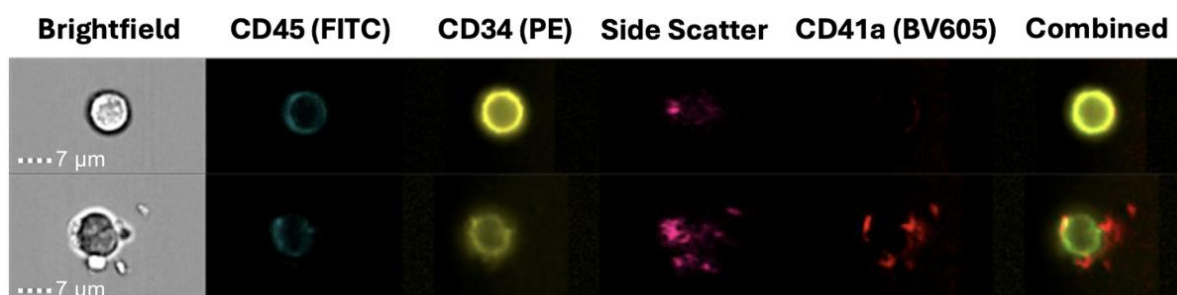


Figure 1. Representative CD34⁺ HSPCs from fresh harvest. CD34⁺ HSPCs defined as dim-CD45⁺/high-CD34⁺ in absence (CD41a⁻; upper panel) or presence (CD41a⁺; lower panel) of bound platelets by imaging cytometry (60x magnification; Amnis ImageStream Mk II). Channels labelled as Brightfield (cell morphology), fluorophore-conjugated antibodies or side scatter for cell granularity. A merged (Combined) image of CD45, CD34 and CD41a channels is shown.

Real-world epidemiology of heparin-induced thrombocytopenia in a regional centre

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Aim:

Heparin-induced thrombocytopenia (HIT) is an uncommon but serious immune-mediated complication of heparin exposure. We aimed to describe HIT epidemiology.

Method:

A retrospective laboratory and clinical audit was performed for HIT antibody screening episodes from 1 January 2023 to 31 December 2024. Screening used the HemosIL AcuStar HIT IgG immunoassay. Positive/equivocal episodes underwent clinical and laboratory review of platelet trends, heparin timing, thrombosis, 4T score, functional testing and final adjudication.

Results:

Across 289,814 admissions, 224 laboratory HIT screening requests were identified: 16 positive, 3 equivocal, 171 negative and 34 cancelled. Review of 19 positive/equivocal screens determined 13 as HIT-positive, 4 clinically equivocal and 2 HIT-negative.

Among 13 HIT-positive cases, median age 67 years, range 21-83, 7 males and 6 females. Median AcuStar HIT IgG was 4.60 U/mL, range 1.17-66.46, platelet nadir $43 \times 10^9/L$ [range 5-87] and 4T score 5 [range 2-7]. Thrombosis after heparin exposure occurred in 6/13 and 6-month mortality was 46.2%. In contrast, the non-HIT cases were predominantly female (5/6), had lower 4T score (3 vs 5) and none had died within 6 months follow-up.

Platelet aggregometry was performed in 14 of 19 positive/equivocal episodes with 8 positive, 3 equivocal and 3 negative results. Five episodes were not tested due to death, low clinical probability, alternative thrombocytopenia causes or clinical context. Two cases were referred to an external laboratory for serotonin release assay (SRA) testing: one low-probability but local functional testing positive case was SRA-negative while one high-probability case (4T score 7) had AcuStar 66.46 U/mL, local functional testing negative, but positive functional confirmation on SRA by send away.

Conclusion:

HIT screening and diagnosis rates were 77.3 and 4.5 per 100,000 admissions, respectively, or an incidence of 1.4 per 100,000 population per year (ABS population data).

Diagnostic pathways and outcomes in suspected heparin-induced thrombocytopenia: a regional Australian experience

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Aims:

To audit HIT investigation, management, and outcomes at a regional Australian tertiary centre, with attention to 4Ts score utilisation, immunoassay performance, and the role of the TORADI-HIT post-test probability calculator.

Methods:

Retrospective single-centre audit of adults tested for HIT at Townsville University Hospital between 1 January 2020 and 23 October 2025. The 4Ts score was reconstructed retrospectively. Clinically adjudicated HIT was defined as a positive AcuStar HIT-IgG titre (≥ 1 U/mL) in an appropriate clinicopathological setting; one patient with a positive LIA who died prior to AcuStar testing was included on clinical adjudication. Statistical analyses used Fisher's exact and Mann–Whitney U tests.

Results:

Of 184 evaluable patients, 26 (14.1%) had a positive screen and 13 (7.1%) had clinically adjudicated HIT, including one probable case of spontaneous HIT. Ninety-six (52%) had a 4Ts score ≤ 3 , yielding a negative predictive value of 99.0% (95% CI 94.3–99.8%) for clinically adjudicated HIT. Functional confirmatory testing was performed in only 4/13 cases. Among clinically adjudicated HIT patients, 62% developed new thrombosis, in-hospital all-cause mortality was 54%, and median length of stay was 33 days (IQR 14–69). The post-test probability, as calculated by TORADI-HIT probability calculator, showed incremental rise across the 4Ts scores. Results are shown in **figure 1**.

Conclusions:

The 4Ts score remains an effective first step in determining the need for HIT testing. Send-away functional testing limits real-time decision-making in regional settings, where quantitative immunoassay titre combined with the 4Ts score, supplemented by tools such as TORADI-HIT, may aid management. Consideration should be given to establishing an Australian HIT registry to examine national trends and outcomes across metropolitan, regional, and rural settings.

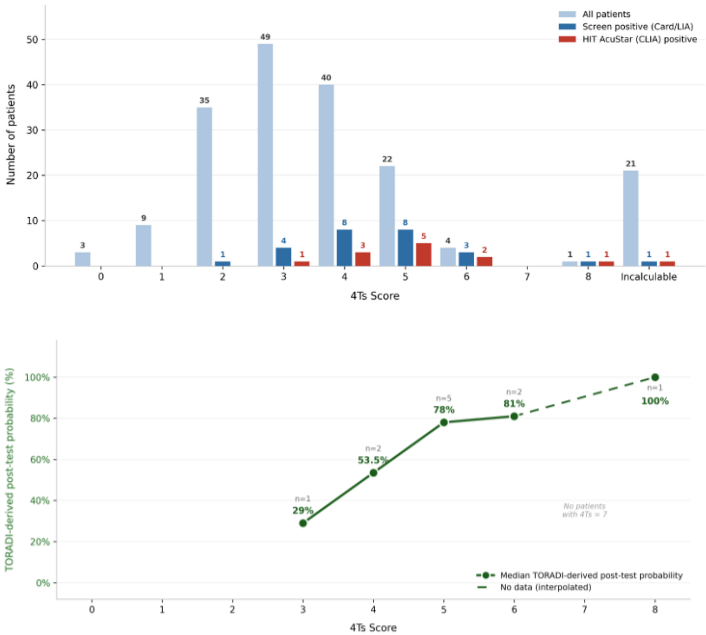


Figure 1.
(4A) 4Ts score distribution with HIT screening outcomes. No patients with a 4Ts score of 7 were identified in this cohort.

(1B) Median TORADI-HIT post-test probability by 4Ts score in patients with clinically adjudicated HIT. Patients with incalculable 4Ts score or lacking HIT AcuStar were excluded from this analysis.

Efanesoctocog alfa prophylaxis for patients with severe hemophilia A: Third interim results from the XTEND-ed long-term extension study

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Aim:

This analysis presents the third interim results from the XTEND-ed (NCT04644575) long-term extension study evaluating safety and efficacy of efanesoctocog alfa prophylaxis in patients with severe hemophilia A.

Methods:

Participants who had completed XTEND-1 (≥ 12 years) and XTEND-Kids (< 12 years) could continue once-weekly efanesoctocog alfa prophylaxis (50 IU/kg) in XTEND-ed (Arm A). The primary endpoint was FVIII inhibitor incidence; secondary endpoints included ABRs, bleed treatment, and safety (treatment-emergent adverse events [TEAEs]). Data cut: 21 Feb 2025.

Results:

A total of 146 adults/adolescents and 71 children rolled over from XTEND-1/XTEND-Kids to XTEND-ed. The median (range) cumulative treatment duration from parent study baseline to the third interim data cut of XTEND-ed was 212.2 (46.3–244.8) weeks (adults/adolescents) and 169.8 (88.2–204.7) weeks (children). No FVIII inhibitors developed. During the entire XTEND-ed efficacy period, mean (95% CI) model-based ABRs for adults/adolescents and children were 0.60 (0.47; 0.76) and 0.64 (0.48; 0.85) for treated bleeds, and 0.20 (0.15; 0.28) and 0.08 (0.04; 0.15) for treated spontaneous bleeds, respectively. The mean (SD) proportion of adults/adolescents with zero bleeds per 6-month interval was 80.7% (4.83) for all bleeds and 91.7% (3.10) for spontaneous bleeds over 36 months in XTEND-ed. The mean (SD) proportion of children with zero bleeds per 6-month interval was 77.1% (5.19) for all bleeds and 97.7 (0.63) for spontaneous bleeds over 24 months. Most bleeds in XTEND-ed were resolved with a single injection (adults/adolescents: 94.0%, children: 91.0%). Participants rated 87.8% (adults/adolescents) and 94.1% (children) of injections as having an excellent/good response. Four patients in total had treatment-related TEAEs (facial paralysis,

reduced FVIII levels, asthma, post infusion pain and headache). No treatment-related discontinuations or serious TEAEs were reported.

Conclusions:

XTEND-ed long term data up to 4 years demonstrates once weekly efanesoctocog alfa is well tolerated and provides highly effective bleed protection for patients with severe haemophilia A.

Joint health outcomes with efanesoctocog alfa prophylaxis for patients with severe hemophilia A: Third interim analysis of the phase 3 XTEND-ed study

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Aim:

Efanesoctocog alfa is a first-in-class, high-sustained factor VIII replacement therapy that overcomes the von Willebrand factor-imposed half-life ceiling. XTEND-1 (NCT04161495) showed once-weekly efanesoctocog alfa was well tolerated in adults/adolescents with severe hemophilia A, providing superior bleed prevention over prior factor VIII prophylaxis. Participants completing XTEND-1 could continue weekly efanesoctocog alfa (50 IU/kg) in XTEND-ed (NCT04644575) arm A. This analysis reports long-term joint health outcomes in adults/adolescents aged ≥ 12 years from XTEND-1 baseline through the XTEND-ed third interim analysis (data cut: 21 February 2025).

Method:

Participants provided informed consent; the study was approved by applicable review boards. Change in HJHS; (range 0–124) from XTEND-1 baseline up to XTEND-ed Month 36 are presented descriptively. Higher HJHS scores denote worse joint health. Individual joints (left/right elbows, knees, ankles) were scored per 8 HJHS domains for total joint score; gait score ranged 0–4. Improved/worsened HJHS was defined by ≥ 4 -point decreases/increases and unchanged (constant) between -3 and +3 points.

Results:

Of 146 participants, 132 had evaluable HJHS at XTEND-1 baseline; median (range) total HJHS was 19 (0–98) (mean [SD]: 20.5 [18.4]). For participants with evaluable data at 12-month intervals, gradual HJHS improvements occurred over 4 years of efanesoctocog alfa prophylaxis, from XTEND-1 baseline to XTEND-ed Month 36. By XTEND-ed Month 36, HJHS total score improved or remained constant in 85.6% of evaluable participants with a mean (SD) change of -3.5 (9.6) (n=90); the largest domain changes were observed for strength -0.6 (2.6) and swelling -0.5 (1.7). Mean (SD) HJHS gait scores stayed constant: XTEND-1 baseline 1.7 (1.6); Month 36, 1.5 (1.6).

Conclusion:

Long-term once-weekly prophylaxis with efanesoctocog alfa for up to 4 years continues to improve and/or maintain joint health in adults and adolescents with severe hemophilia A.

Clot waveform analysis reveals distinct qualitative clot dynamics between AML and ALL despite limited quantitative discrimination

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Aim:

To evaluate whether clot waveform analysis (CWA) provides additional discriminatory information beyond conventional coagulation tests in differentiating acute myeloid leukemia (AML) from acute lymphoblastic leukemia (ALL).

Method:

This prospective study included 216 consecutive patients with newly diagnosed acute leukemia (AML: 113; ALL: 54). Conventional coagulation parameters (activated partial thromboplastin time [APTT], prothrombin time [PT], fibrinogen, D-dimer), complete blood counts, and disseminated intravascular coagulation (DIC) scoring using International Society on Thrombosis and Haemostasis criteria were performed. APTT- and PT-based CWA were obtained on the ACL TOP 500 analyser. Quantitative parameters and qualitative waveform patterns were assessed. Statistical comparisons were performed using the Mann–Whitney U test and chi-square/Fisher's exact test.

Results:

AML patients showed significantly prolonged PT compared with ALL (13.54 ± 2.20 vs 12.96 ± 2.58 s; $p = 0.031$) and higher mean DIC scores (2.35 ± 1.47 vs 1.78 ± 1.34 ; $p = 0.023$), along with lower hemoglobin levels (6.98 ± 1.91 vs 7.77 ± 2.31 g/dL; $p = 0.014$). Other conventional coagulation parameters were comparable between groups. Quantitative CWA parameters derived from APTT and PT did not differ significantly between AML and ALL. However, qualitative analysis demonstrated distinct differences: a normal APTT waveform was more frequent in AML (47.9% vs 26.5%; $p = 0.006$), whereas a shoulder pattern in the second derivative peak was more common in ALL (13.1% vs 4.8%; $p = 0.018$).

Conclusion:

AML is associated with greater coagulation derangement and higher DIC scores compared with ALL. While quantitative CWA parameters do not significantly differentiate between these entities, qualitative waveform patterns reveal distinct clot dynamics. CWA may provide complementary insights into leukemia-associated coagulopathy, although its incremental clinical utility over standard testing appears limited.

Epidemiology and management of relapsed acquired haemophilia A: a single referral centre study

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Aim:

Acquired Haemophilia A (AHA) is a rare autoimmune condition caused by autoantibodies directed against Factor VIII, resulting in a high risk of bleeding. While there are clear guidelines regarding the diagnosis and management of newly diagnosed cases, less is known about the incidence, management and outcomes of those who relapse. We therefore aimed to identify the incidence of relapsed AHA, how they were managed and the outcomes in our centre.

Methods:

Retrospective, single-centre cohort study involving a state-wide Haemophilia Treatment Centre. All cases of AHA registered or previously registered as of April 2026 were identified using medical records and the Australian Bleeding Disorders Registry. Data was collected on demographics, treatment and outcomes.

Results:

We identified 55 patients in our database with AHA in the study period. 14 (25.5%) relapsed. 9 (64%) were male and the median age was 72.5 years. Interim analysis demonstrates the median time to relapse was 8 months; 10 relapsed within the first 12 months of diagnosis and 4 relapsed beyond 24 months. Five (35.7%) had more than one relapse. In most cases, management involved one, or a combination, of rituximab, prednisolone, cyclophosphamide and mycophenolate. One patient with concomitant chronic lymphocytic leukaemia was able to access a BTK inhibitor. One highly refractory patient was given bortezomib and daratumumab without a remission being achieved.

Conclusion:

Relapses of AHA occurs in a significant number of patients suggesting that long term follow up is needed. While most respond to standard immunosuppression, some require novel therapies.

Potentially inappropriate reduced dose apixaban prescribing across tertiary hospitals: a multi-site retrospective analysis

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Aim:

Inappropriate apixaban dosing is linked to poorer outcomes, but its prevalence remains poorly understood.

This study evaluated the prevalence of potentially inappropriate apixaban 2.5mg prescribing across two Australian tertiary hospitals.

Method:

A multi-site retrospective audit was undertaken at two metropolitan tertiary hospitals in Western Australia.

All adult inpatients dispensed apixaban 2.5mg between January 2023 and December 2024 were identified via pharmacy records.

Patient demographics, anticoagulation indication, renal function, body weight, bleeding history, laboratory results, and concomitant medicines were extracted from medical records.

Prescribing appropriateness was evaluated against guideline-based dose-reduction criteria, with quantitative statistical analysis performed.

Results:

Across both hospitals, 555 patients were dispensed apixaban 2.5mg. Patients were predominately older adults, with comparable demographics between sites (mean age 79 years [standard deviation, SD 12.6] at Site 1 and 75 years [SD 13.0] at Site 2, with similar proportions of female patients (49.2% vs 41.6%, $p=0.08$)).

Among 195 patients newly initiated for non-valvular atrial fibrillation (AF), the mean CHA₂DS₂-VA score was 3.8 (SD 1.5) and HAS-BLED score 2.6 (SD 1.2). Site 1 contributed the majority (66.0%) and had higher mean CHA₂DS₂-VA and HAS-BLED scores than Site 2 (4.0 vs 3.4 and 2.7 vs 2.5, respectively; $p<0.05$).

Overall, 77 patients (39.5%) received a potentially inappropriate reduced dose, with similar rates between sites (41.4% vs 35.8%, $p=0.54$).

Potentially inappropriate low-dose prescribing was also observed in the treatment of acute venous thromboembolism (VTE), affecting 19 patients at Site 1 and 28 patients at Site 2.

Rates of potentially inappropriate prescribing were comparable between sites, suggesting consistent prescribing patterns. Contributing factors may include advanced age, bleeding risk, and concerns regarding drug interactions.

Conclusion:

A significant proportion of patients initiated on apixaban 2.5mg received potentially inappropriate doses, particularly in AF and acute VTE.

Similar rates across two tertiary hospitals suggest a widespread issue, highlighting the need to better understand prescribing drivers and support targeted anticoagulation stewardship initiatives.

(299 words excl. title and section headings)

Thrombo Thursday: a pharmacist led point prevalence survey to assess VTE risk assessment documentation in a multi-site hospital network without an electronic medical record

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Aim:

In hospitals without an electronic medical record (EMR), monitoring venous thromboembolism (VTE) prevention performance is labour intensive and often limited to small sample sizes.

This project evaluated a pharmacist-led, EMR-independent point prevalence survey (PPS), branded “Thrombo Thursday”, to assess VTE risk assessment documentation and determine its feasibility for efficient, repeatable monitoring using paper-based records.

Method:

A hospital-group-wide PPS was conducted across one tertiary and two secondary hospitals within a metropolitan health service operating without an EMR.

All adult inpatients listed on the electronic patient journey board at the start of the audit day were eligible.

More than 50 pharmacists participated in simultaneous chart review of medication charts and clinical records.

Documentation was assessed against local VTE prevention policy requirements, including completion within 24 hours of admission and reassessment every seven days or following significant clinical change.

Results:

A total of 1,089 inpatients were identified, with 1,065 patients successfully reviewed (98%). Overall, 244 patients (23%) had a VTE risk assessment documented in accordance with policy. Compliance varied between clinical specialties, with markedly higher rates observed in intensive care (100%) and obstetrics (75%), reflecting the impact of established workflows or electronic subsystems.

Broad pharmacist participation enabled rapid hospital-wide data collection and immediate ward-level feedback.

Conclusion:

Thrombo Thursday proved to be a feasible and efficient method for collecting network-wide data from paper-based medical records, enabling regular monitoring of risk assessment practices across multiple sites.

The approach supported rapid data collection, multidisciplinary engagement, and immediate feedback to clinical areas, facilitating evaluation of VTE prevention initiatives.

The survey will now be undertaken biannually, with future iterations expanding to include anticoagulant prescribing.

The model has been shared through the THANZ Anticoagulation Stewardship Network, with emerging interest in broader adoption, analogous to established point prevalence programs such as the National Antimicrobial Prescribing Survey (NAPS).

Optimising antiphospholipid antibody testing: real-world performance of chemiluminescent immunoassays and revised clinical cut-offs in a hospital setting

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Aim:

While 2023 EULAR/ACR classification criteria recommend ELISA for antiphospholipid antibody detection, many laboratories have transitioned to automated chemiluminescent immunoassays (CLIA) due to faster turnaround times and reduced manual handling. However, manufacturer-defined CLIA cut-offs are derived from healthy populations and may not reflect hospital cohorts, leading to misclassification. Guidelines therefore advise establishing local clinical decision points for non-ELISA assays.

We evaluated the Werfen AcuStar CLIA platform for anticardiolipin (aCL) IgG and anti-β2 glycoprotein I (B2GPI) IgG and determined revised cut-offs based on the 99th centile of hospital patients without antiphospholipid syndrome (APS).

Methods:

A retrospective audit was conducted of aCL and B2GPI tests performed on AcuStar over 12 months (August 2024–July 2025) at Northern Pathology Victoria, Australia. Positive results were adjudicated by two clinicians to confirm APS diagnosis.

Results:

186/881 aCL and 114/845 B2GPI tests had levels ≥20 CU, including 19 patients meeting APS criteria. Using manufacturer cut-offs, aCL demonstrated a sensitivity of 89.5% and specificity of 90.3%, while B2GPI achieved 100% sensitivity and 95.1% specificity (Table 1). However, positive predictive value (PPV) was low at 18.7% for aCL and 33.3% for B2GPI, indicating high false-positive rates.

Using 99th centile thresholds, PPV improved to 66.7% for aCL (≥65 CU) and 68.0% for B2GPI (≥90 CU), with only a modest reduction in sensitivity (84.2% for aCL and 89.5% for B2GPI). Combined antibody positivity using revised cut-offs yielded sensitivity of 94.7%, specificity of 98.4%, and PPV of 60.0%. Importantly, only one APS case would have been missed using revised cut-offs, but remained diagnosable with lupus anticoagulant testing.

Conclusion:

Manufacturer cut-offs for CLIA-based testing may overestimate positivity in hospital populations. Revised thresholds based on the 99th centile substantially improve PPV without compromising sensitivity. We recommend adopting revised cut-offs with an “equivocal” category and confirmatory testing for new positives to enhance diagnostic accuracy.

Table 1: Performance metrics summary comparing recommended Instructions For Use (IFU) cut-offs to revised thresholds.

Cut-off Strategy	Sensitivity	Specificity	PPV
aCL ≥20 CU	89.5%	90.3%	18.7%
B2GPI ≥20 CU	100%	95.1%	33.3%
aCL ≥65 CU	84.2%	99.0%	66.7%
B2GPI ≥90 CU	89.5%	99.0%	68.0%
Combined (revised cut-offs)	94.7%	98.4%	60.0%

Long-term trends in incident venous thromboembolism: an Australian experience

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Aim:

Venous thromboembolism (VTE) remains a major cause of morbidity and healthcare utilisation. Amid increasing patient complexity and the introduction of direct oral anticoagulants (DOACs), contemporary Australian data on temporal trends in VTE remain limited. We examined trends in incident deep vein thrombosis (DVT) and pulmonary embolism (PE) at a large metropolitan health service.

Method:

This retrospective cohort included imaging confirmed, first-episode VTE presentations to the Emergency Department at Northern Health, Melbourne, Australia, between June 2010 and June 2024. Patients were identified using hospital records and Centre for Victorian Data Linkage data. The DOAC era was defined as 2015 onwards.

Results:

There were 2160 first-presentation VTEs (Table 1). Presentations increased 5.2% over this period (95% CI -8.0% to +20.2%, $p=0.46$), accompanied by rising patient complexity (14.5%, 95% CI 11.9% to 17.2%, $p<0.001$). Despite this, inpatient length of stay (LOS) decreased substantially after DOAC introduction (PE median LOS: 6 to 3 days, DVT: 5 to 1 day, PE+DVT: 8 to 4 days; $p<0.001$). PE and PE+DVT LOS reductions remained significant after excluding hospital-in-the-home days. Ninety-seven patients accounted for 105 symptomatic VTE recurrences over the study period (median time-to-first-recurrence 21.8 months). Recurrence did not differ between pre-DOAC and DOAC eras (HR 0.97, 95% CI 0.62–1.51, $p=0.888$). 131 patients experienced bleeding within 90 days (median time-to-bleed 25 days). The DOAC era was associated with significantly less bleeding (HR 0.64, 95% CI 0.44–0.95, $p=0.025$), with increasing age, female sex and active cancer independently associated with bleeding risk.

Conclusion:

In this single-centre cohort, VTE presentations increased modestly over time. DOAC-era management was associated with shorter inpatient LOS despite rising complexity, reduced bleeding and stable 2-year recurrence rates.

Median age (IQR), years		62.5 (47.0–75.0)
Female, n (%)		1121 (51.9)
VTE presentation	DVT alone, n (%)	794 (36.8)
	PE alone, n (%)	811 (37.5)
	PE and DVT, n (%)	555 (25.7)
Non-English-speaking background, n (%)		394 (18.2)
Aboriginal or Torres Strait Islander, n (%)		29 (1.3)
Primary hospital catchment, n (%)		1606 (74.4)

Major complexity*, n (%)	1026 (47.5)
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Table 1. Patient demographics for first VTE presentation. *≥3 organ systems treated during admission. ^Excluding hospitalisations for childbirth.

The Halo Fluorescence Fibrinolysis (HoFF) test identifies the effective tranexamic acid concentration required to suppress fibrinolysis in whole blood

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Aim:

Tranexamic acid (TXA) is widely used to reduce bleeding in major surgery, but it is generally administered at empiric doses of 1–2 g without assessing its actual effect in individual patients. As TXA may cause dose-related adverse effects, including seizures, with reported incidence increasing at blood concentrations above 100 mg/L, and depends on renal clearance, a rapid method to identify the minimum effective dose may enable safer and more personalized treatment. This study aimed to determine whether the Halo Fluorescence Fibrinolysis (HoFF) test can quantify TXA-mediated inhibition of fibrinolysis in whole blood and identify the concentration required for effective suppression.

Methods:

Citrated whole blood from healthy donors was spiked with increasing concentrations of TXA and analysed using the HoFF test. This assay incorporates fluorescence-labelled fibrinogen into halo-shaped clots and enables real-time monitoring of fluorescent fibrin degradation products released during tPA-induced fibrinolysis of these clots. The percentage of fluorophore release at 15 minutes was used to quantify fibrinolytic activity and determine the extent of inhibition at each TXA concentration.

Results:

The HoFF test demonstrated clear dose-dependent inhibition of fibrinolysis by TXA in whole blood. Complete or near-complete suppression of fibrinolysis was generally achieved at TXA concentrations of approximately 10–30 mg/L, substantially lower than the estimated blood concentration associated with commonly used clinical dosing (50–150 mg/L). Marked inter-individual variability was observed, with more than 10-fold differences among donors in the TXA concentration required to fully inhibit fibrinolysis.

Conclusion:

The HoFF test provides a robust and translationally relevant platform for quantifying the antifibrinolytic effect of TXA in whole blood. These findings suggest that the TXA dose required to suppress fibrinolysis varies considerably between individuals and is often lower than current empiric dosing, supporting the potential for personalized TXA therapy and future point-of-care application.

Disconnect between appropriate thromboprophylaxis and formal VTE risk assessment: Findings from a quality improvement program

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Aim:

Venous thromboembolism (VTE) is a leading cause of preventable hospital-associated mortality. While appropriate thromboprophylaxis is paramount, guidelines also recommend structured VTE risk assessment. In practice, substantial discordance between these processes exists. We aimed to evaluate performance across VTE prevention domains, identify barriers to comprehensive care and inform focused interventions to sustainably address system gaps.

Method:

Mixed-methods study at a quaternary centre participating in a statewide quality improvement (QI) collaborative. Longitudinal data were collected for surgical and medical inpatients, including measures of thromboprophylaxis appropriateness, pulmonary embolism (PE) incidence, VTE risk assessment completion and anticoagulant plans documented on discharge. Compliance rates were assessed using monthly random samples from Oct2025-Mar2026. In parallel, a clinician survey was distributed to identify perceived barriers to VTE risk assessments. A gap analysis was conducted, with local interventions developed iteratively using QI principles.

Results:

The overall rate of appropriate VTE prophylaxis was 88.3% (318/360), with 96.7% (174/180) in surgical patients and 80% (144/180) in medical patients.

PE occurred in 0.8 per 1000 medical inpatient episodes. The overall rate of documented VTE risk assessment was 4% (8/200). Survey responses (N=33) identified key barriers to completion as unclear clinical responsibility (36%), time constraints (33%), and electronic workflow limitations (9%).

The rate of anticoagulant plan documentation on discharge was 62.5% (75/120), with 95% (57/60) in surgical patients and 30% (18/60) in medical patients. Following digital health and key stakeholder engagement we have implemented an 'anticoagulant treatment' field in the electronic discharge summary. Other interventions include redesign of prescribing order-sets.

Conclusion:

Despite high performance in appropriate thromboprophylaxis and low rate of PE, significant shortfalls in documentation of formal VTE risk assessment and anticoagulant plans persist, especially in medical patients. These data highlight disconnect between appropriate practice and the need to complete guideline-recommended processes, which are undergoing clinician co-design to address targeted opportunities for system-level changes.

Evaluating the impact of a clinical decision support tool for venous thromboembolism prophylaxis

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Background:

Hospital-acquired venous thromboembolism (HA-VTE) is associated with significant morbidity and mortality. VTE prophylaxis (VTEP) prescribing can minimise the incidence of HA-VTE in hospital inpatients. A clinical decision support (CDS) tool within the Electronic Medical Record (EMR) was implemented by the anticoagulation stewardship (ACS) program to support guideline-compliant VTE risk assessment (RA) and VTEP prescribing.

Aim:

To assess the impact of the CDS tool on VTE risk assessment (RA) completion, VTEP prescribing rates, and appropriateness of prescribed VTEP.

Method:

A retrospective audit of patients admitted for a minimum of 48 hours to a medical, obstetric, surgical or subacute unit before (2/6/2024 to 1/6/2025) and after implementation (2/6/25 to 2/6/26) of the CDS tool across a large tertiary multisite hospital system in metropolitan Melbourne. A minimum of 200 patients pre- and post-implementation were randomly selected. Chart reviews were conducted to ascertain rates of VTE RA completion, VTEP prescribing, HA-VTE. Descriptive statistics (median, IQR, mean, SD, %) for patient characteristics and Chi square analyses for risk assessment and prescribing compliance were conducted.

Results:

A total of 735 patients were included in the preliminary audit; 240 (32.65%) patients in the pre-intervention group and 495 (67.35%) in the post-intervention group.

There was a significant improvement in risk assessment documentation (13.33% vs 64.24%, $p<0.001$), without significant variation in VTEP chemoprophylaxis prescribing (84.6% vs 84.2%, $p=0.88$) or guideline compliance (90.7% vs 92.1%, $p=0.66$). There was a significant increase in mechanical VTEP prescribing of intermittent pneumatic compression devices (IPCs) (5.9% vs 11.1%, $p<0.001$).

Conclusion:

Implementation of the CDS tool was associated with significant improvements in VTE risk assessment completion rates, however the impact on prescribing practices and guideline adherence is less clear. There was variable uptake across specialties, therefore further data are required to assess barriers to use and improve practice.

Figure 1: Preliminary data observations

Total			
	Pre (n=240)	Post (n=495)	p value
VTE risk assessment completed (%)	32 (13.3%)	318 (64.2%)	$p<0.001$
VTEP prescribed (%)	198 (84.6%)	410 (84.2%)	$P = 0.88$

Appropriateness of prescribed VTEP (based on weight and renal function) (%)	167 (92.1%)	328 (90.7%)	P=0.66
VTEP prescribed within 24 h (%)	126 (70.2%)	265 (70.4%)	P=0.94
Mechanical VTE prophylaxis prescribed (IPCs) (%)	14 (5.9%)	56 (11.1%)	P<0.05
HA-VTE during admission (%)	5 (2.1%)	17 (3.5%)	P=0.31

Figure 2: Patient characteristics

Unit	Patients		Medical		Obstetrics		Subacute		Surgical	
Period	PRE	POST	PRE	POST	PRE	POST	PRE	POST	PRE	POST
Patients (n)	240	495	143	298	34	100	10	13	53	84
Sex										
Female (%)	125 (52%)	300 (61%)	65 (45.5%)	160 (53.7%)	34 (100%)	100 (100%)	5 (50%)	5 (38.5%)	21 (39.6%)	35 (41.7%)
Male (%)	115 (48%)	195 (39%)	78 (54.5%)	138 (46.3%)	0 (0%)	0 (0%)	5 (50%)	8 (61.5%)	32 (60.4%)	49 (58.3%)
Age (Median, IQR)	64 (41,79.25)	64 (37,78)	70 (53.5-82)	73 (58-82)	32 (29.25-36)	32 (27.75-37)	75.5 (69.8-82)	70 (64-85)	70 (53-79)	63 (47-74)
Creatinine (Median, IQR)	80 (62,98)	81 (62,107)	79 (61.5-99.5)	82 (63-117.75)	50.5 (47-59.25)	51 (43-57.25)	90 (81-96)	67.5 (54.5-92.25)	81 (69,103)	85 (69.5-98)
Platelets (Median, IQR)	235 (187,301)	228 (178,288.5)	229 (183.5-290)	229 (176-289)	225 (187.5-248)	214 (179.5-253.5)	339 (275-469)	290 (188.25,331.75)	261 (217-320)	252 (197-308.5)

Therapeutic anticoagulation on admission (%)	33 (14%)	78 (16%)	24 (17%)	63 (21%)	0 (0%)	0 (0%)	2 (20%)	4 (30%)	7 (13%)	11 (13%)
HA-VTE during admission (%)	5 (2.1%)	17 (3.5%)	3 (2.1%)	11 (3.7%)	0 (0%)	0 (0%)	1 (10%)	1 (7.7%)	1 (1.9%)	5 (5.9%)

Impact of the 2024 ICSH guidelines on interpretation of coagulation mixing studies in routine practice.

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Aim:

Mixing studies assist in differentiating coagulation factor deficiencies from circulating inhibitors, but interpretation is complicated by intermediate or borderline results. The 2024 International Council for Standardization in Haematology (ICSH) guidelines propose a standardised use of Rosner Index (RI), percentage correction (PC), and subtraction analysis to improve interpretive consistency.

The aim is to evaluate how application of the guidelines would influence interpretation of mixing studies performed at a public pathology service.

Method:

A retrospective review of mixing studies performed from 2021 to 2025 at Northern Pathology Victoria, Australia, was undertaken. Results were reinterpreted according to the 2024 ICSH guidelines (Table 1) and correlated with lupus anticoagulant testing and intrinsic factor assays. Factor deficiency was defined by levels below reference interval.

Results:

A total of 213 mixing studies were performed: 87 (41%) had RI>15% and 126 (59%) had RI≤15%, with no cases <0 by subtraction. Among RI>15%, 45/87 (51.7%) proceeded to lupus anticoagulant testing of which 25/45 (55.6%) were positive, and 8 of 19 (42.1%) which had intrinsic factor testing were deficient, all multifactor, suggesting non-specific interference. Eighty-four of RI>15% had PC<70% (96.6%). For samples with PC<70% (n=159), 29/61 (47.5%) were lupus anticoagulant positive and 13/40 (32.5%) factor deficient.

Among RI≤15% cases, 17/47 (36.2%) were factor deficient and 9/29 (31.0%) were lupus anticoagulant positive. 51 concurred with PC≥70% (40.5%). Across all PC≥70% (n=54), 12/26 (46.1%) had factor deficiencies and 5/13 (38.4%) were lupus anticoagulant positive.

Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) for RI and PC relative to lupus anticoagulant and factor deficiency are summarised in Table 2.

Table 1. Recommended Calculations based on 2024 ICSH guidelines.

Method (units)	Formula
Percentage Correction (%) (PC)	

	$\left(\frac{\text{Patient Baseline Result} - 1:1 \text{ Mix Result}}{\text{Patient Baseline Result} - \text{NPP Result}} \right) \times 100$
Rosner Index (%) (RI)	$\left(\frac{1:1 \text{ Mix Result} - \text{NPP Result}}{\text{Patient Baseline Result}} \right) \times 100$
Subtraction (seconds)	1:1 Mix Result – NPP Result

Abbrev: NPP: normal pool plasma

Ref: Adcock et al. *Int J Lab Hematol.* 2024;46:777-788.

Table 2: Sensitivity, specificity, PPV and NPV of RI and PC for lupus inhibitor and factor deficiency.

	Lupus anticoagulant positive	Factor deficiency
Number of tests performed	74	66
Positive/deficient	34	25
Rosner Index >15%	25/74 (33.8%) Sensitivity = 73.5% Specificity = 58.3% PPV = 83.3% NPV = 43.8%	8/66 (12.1%) *
Rosner Index ≤15%	9/74 (12.2%)	17/66 (25.8%) Sensitivity = 36.2% Specificity = 57.9% PPV = 68.0% NPV = 26.8%
Percentage Correction <70%	29/74 (39.2%) Sensitivity = 72.5% Specificity = 16.7% PPV = 85.3% NPV = 8.3%	13/66 (19.7%) *
Percentage Correction ≥70%	5/74 (6.8%)	12/66 (18.2%) Sensitivity = 46.2% Specificity = 67.5% PPV = 48.0% NPV = 65.9%

*All were multi-factor deficiencies suggestive of unlikely true deficiency.

Conclusion:

Application of the 2024 ICSH guidelines did not resolve diagnostic ambiguity - RI>15% aligned with PC<70% (96.6%), whereas RI≤15% vs PC≥70% showed weaker concordance (40.5%) and subtraction analysis was unemployable. RI>15% and PC<70% showed good sensitivity and high PPV for lupus anticoagulant but poor specificity. Neither RI≤15% nor PC≥70% reliably predicted factor deficiency, although multifactor deficiencies suggest non-specific interference rather than true isolated deficiency.

HIT testing and diagnosis in Australia: a multicentre study of ordering practices and clinical outcomes

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Aim: Heparin-induced thrombocytopenia (HIT) is a rare but severe immune complication of heparin exposure that can cause thrombosis and death. Older estimates suggested an incidence of 2.6% among heparin-exposed patients (Martel, *Blood* 2005) but contemporary Australian data are lacking. This multicentre study aims to define HIT testing patterns, diagnostic yield and clinical outcomes in Australia to inform screening and management.

Method: This retrospective cohort study includes eight hospitals across NSW, VIC, WA, SA, and ACT with additional sites opening in other states. Patients were identified from HIT screening tests requested during 2018-2019 and 2023-2024. A REDCap database was established to incorporate laboratory testing and clinical outcomes extracted from electronic medical records. Site investigators adjudicated the final diagnosis of HIT, typically requiring positive screening and functional assays, whereas non-HIT patients had positive screens with indeterminate or negative functional assays.

Results: Interim analysis of data from 67 patients with a positive HIT screen from 4 hospitals showed that RPA, St George, Austin and Canberra Hospitals recorded an average of 3.9 patients (range 2 - 7) with confirmed HIT per year. Patients with HIT had significantly higher 4T scores (median 5) than non-HIT patients (median 3.5, **Fig 1A**). Screening tests included STAGO ELISA, STic, and Acustar (**Fig 1B**), while functional assays included the serotonin release assay and platelet aggregation. Bivalirudin was the most common anticoagulant used (**Fig 1C**). Radiologically confirmed thrombosis occurred in 56% of HIT patients versus 25.6% in non-HIT patients (**Fig 1D**). Median hospital stay was comparable between groups (**Fig 1E**).

Conclusion: HIT screening practices vary across sites but patients with confirmed HIT had approximately double the rate of thrombosis compared with non-HIT patients. Completion of data collection across all sites will provide the first contemporary national insight into HIT diagnosis and management in Australia.

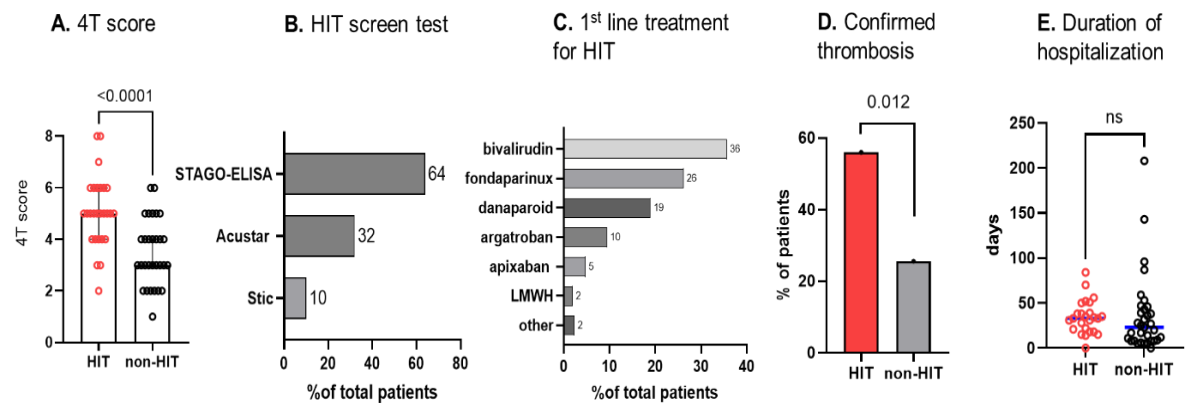


Figure 1. Characteristics of HIT and non-HIT groups across 4 hospitals. A. 4T score in HIT and non-HIT groups, Mann Whitney test. **B.** HIT screening tests used. **C.** First-line anticoagulants used. **D.** Percentage of patients with confirmed thrombosis in HIT and non-HIT groups, Fisher's exact test. **E.** Duration of hospitalization in HIT and non-HIT groups.

Immune acquired factor XIII deficiency: A rare cause of life-threatening bleeding

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Case study:

Acquired factor XIII (FXIII) deficiency is a rare and potentially life-threatening bleeding disorder caused by autoantibodies directed against FXIII, resulting in accelerated clearance or functional inhibition. Diagnosis is challenging as routine coagulation studies are normal, often leading to delayed recognition and significant morbidity. The true incidence is unknown and likely underreported with only case reports and case series published in the literature, with no consensus guidelines on the management of these challenging cases. We describe the clinical course and management of a patient with immune acquired FXIII deficiency at a haemophilia treatment centre.

The patient was a previously well 65-year-old man who presented with a 2-year history of abnormal bleeding including an intracranial haemorrhage, compartment syndrome and severe soft tissue bleeding. Investigations revealed a FXIII activity <0.03 U/mL with a high titre FXIII inhibitor of 79 Bethesda U/mL. Autoimmune and malignancy screen to investigate a possible underlying cause was negative. Management included recombinant FXIII replacement, tranexamic acid, corticosteroids, intravenous immunoglobulin, rituximab, and cyclophosphamide. Cessation of bleeding occurred after 5 weeks of treatment with gradual inhibitor reduction with slow recovery of FXIII levels with ongoing regular FXIII replacement after 14 months (FXIII 0.06 U/mL, inhibitor 1.9 BU/mL).

Conclusion:

This case highlights the importance of considering acquired FXIII deficiency in patients with severe unexplained bleeding and normal routine coagulation studies. Early recognition and prompt initiation of haemostatic and immunosuppressive therapy are critical given the high rates of morbidity and mortality associated with this rare condition.

Real world perioperative outcomes in patients with haemophilia A receiving emicizumab prophylaxis: A multicentre Australian retrospective review

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Background:

Haemophilia A is an X-linked inherited bleeding disorder resulting in reduced levels of FVIII. Emicizumab is a humanised bispecific monoclonal antibody which mimics FVIII by bridging activated FIX and FX. It is used as prophylaxis against bleeding in people with haemophilia A (PWA) with severe bleeding phenotypes and in PWA with inhibitors. The perioperative management of patients receiving emicizumab remains an evolving area of clinical practice, particularly regarding the use of adjunctive haemostatic therapies during procedures.

Aim:

To evaluate perioperative management strategies and surgical outcomes PWA receiving emicizumab prophylaxis across Australian Haemophilia Treatment Centres (HTCs).

Methods:

We performed a multicentre retrospective review of surgical procedures undertaken in PWA receiving emicizumab prophylaxis between January 2021 and June 2026 across HTCs in Australia. Data collected included haemophilia severity, inhibitor status, surgical type and complexity, perioperative haemostatic regimens, bleeding complications, thrombotic events, postoperative outcomes and rates of use of DVT prophylaxis.

Results:

Completion of data collection due June 2026. It is expected that >150 procedures will be described. In the preliminary data, PWA underwent a broad range of minor and major procedures including orthopaedic, dental, abdominal, cardiac, vascular and endoscopic interventions. Perioperative management varied between centres. Procedures overall were performed safely with excellent haemostasis with very low rates of bleeding.

Conclusion:

Surgery in patients with haemophilia A receiving emicizumab prophylaxis can be performed safely with appropriate multidisciplinary planning and tailored perioperative haemostatic support. Findings from this review will contribute important real-world evidence to guide perioperative management strategies in the era of emicizumab therapy.

Not all haemophilia is lifelong: Lessons from Haemophilia B Leyden

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Case study:

Haemophilia B is a congenital, X-linked bleeding disorder caused by reduced factor IX (FIX) activity, with bleeding severity correlating with baseline factor levels. Haemophilia B Leyden is a rare subtype characterised reduced FIX levels in childhood with an increase in the FIX activity with age.

We describe male triplets with a promoter-region mutation in the FIX gene, involving the Leyden-specific region (c.-18A>T). The triplets were diagnosed with mild haemophilia B at 6-12 months of age with baseline FIX levels of 11-12%. Genetic testing had not been performed at diagnosis. All 3 brothers had not had any bleeding complications or required factor replacement since at least 6 years of age. On transition to the adult service at 18 years of age, repeat FIX levels were performed with all 3 brothers demonstrating normal FIX levels between 55 and 69%.

Haemophilia B Leyden occurs due to mutations within the FIX promoter region between nucleotides c.-50 to c.-18, known as the Leyden-specific region¹. Depending on the gene variant, some individuals initially can have FIX levels <1%, whereas others have a milder phenotype². Historically, the rise in FIX was attributed to androgen-mediated upregulation at puberty, however emerging evidence suggests that a more complex mechanism involving binding of other transcription factors which are thought to respond to an increase in growth hormone leading to an increase in FIX production³.

Conclusion:

In this case series we highlight the importance of genetic diagnosis in identifying this unique subtype of haemophilia B as it informs prognosis, guides management, and enables accurate counselling within affected families.

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Cardiovascular procedures in patients with haemophilia: A 10-year retrospective review at an Australian Haemophilia Treatment Centre

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Background:

As life expectancy in patients with haemophilia improves, cardiovascular disease and the need for invasive cardiovascular procedures is increasingly. Management remains challenging due to competing risks of thrombosis and bleeding, with limited evidence guiding peri-procedural haemostatic and antithrombotic management.

Aim:

To review the outcomes of cardiovascular procedures performed in patients with haemophilia at an Australian Haemophilia Treatment Centre over a 10-year period.

Methods:

We performed a retrospective review of patients with haemophilia undergoing cardiovascular interventions between 2016–2026. Procedures included diagnostic angiography, percutaneous intervention, cardiac surgery and electrophysiology procedures. Data collected included bleeding disorder diagnosis and severity, haemostatic management, antithrombotic therapy, and bleeding or thrombotic complications.

Results:

Patients with mild, moderate, and severe haemophilia A and B underwent a total of 25 interventions. All patients received peri-procedural clotting factor replacement regardless of severity of their bleeding disorder. Rates of bleeding due to procedural complications were low with 2 patients experiencing minor access-site bleeding. Significant bleeding events occurred in 2 patients with preexisting pathology. Patients receiving DAPT or low dose anticoagulation while on regular factor or emicizumab prophylaxis tolerated therapy without major complications.

Conclusion:

Perioperative management of patients with bleeding disorders undergoing cardiovascular procedures remains a significant challenge. A multidisciplinary and individualised approach with close monitoring is required to optimise outcomes. Further multicentre studies are necessary to strengthen the evidence in this area.

Can routine coagulation assays provide guidance on drug levels when Xa testing is not available in Western Australia? A retrospective single-center analysis.

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Background:

Oral factor Xa inhibitors (FXa-i) variably prolong routine coagulation assays. This is clinically relevant in Western Australia, where geographic dispersion limits access to drug-specific anti-Xa testing hindering decision making regarding urgent surgery, procedural delay, reversal, or use of prohemostatic blood products.

Aim:

To determine whether routine coagulation assays can identify or exclude clinically relevant rivaroxaban or apixaban concentrations in patients undergoing urgent laboratory assessment.

Method:

A retrospective single-centre study was performed in Western Australia including 50 adults who had rivaroxaban or apixaban levels measured and had routine coagulation studies performed within 1 hour of sampling performed during 2025. Drug concentrations were measured using drug-specific chromogenic anti-Xa assays, and associations with PT, INR, aPTT, and fibrinogen were assessed using scatter plots and simple linear regression.

Results:

Routine coagulation assays showed only modest correlation with measured oral factor Xa inhibitor concentrations. In rivaroxaban-treated patients, PT/INR correlated better with drug level than aPTT or fibrinogen, consistent with prior data.^{2,3} Apixaban had less of a relationship with PT/INR and aPTT. Across both drugs, abnormal PT/INR values were more useful as a qualitative rule-in signal of on-board anticoagulant effect than as a rule-out test. For rivaroxaban, INR cut-offs ≥ 1.6 – 1.8 had high specificity for drug levels ≥ 50 – 75 ng/mL (no patients with INR ≥ 1.8 had rivaroxaban < 50 ng/mL) but sensitivity was limited, with up to half of patients with rivaroxaban ≥ 75 ng/mL having INR below threshold. Normal or near-normal PT/INR and aPTT values did not reliably exclude clinically relevant drug concentrations.

Conclusion:

In this real-world Western Australian cohort, routine coagulation tests showed only modest correlation with rivaroxaban and apixaban levels. In geographically large jurisdictions, our data support using markedly abnormal PT/INR or APTT as a rule-in signal for significant FXa-i effect, whilst “normal” routine assays cannot be used to rule out clinically meaningful rivaroxaban or apixaban concentrations prior to urgent surgery or invasive procedures.

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Laboratory analysis of freeze-dried plasma (FDP) as a viable blood product line for regional and remote Western Australia

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Aim:

Remote and regional areas of Western Australia (WA) face significant obstacles in ensuring access to fresh frozen plasma (FFP) for trauma care, including transport constraints, geographic isolation and limited laboratory access. FDP, a lyophilised pooled plasma product, can be stored up to 2 years at 5-25°C and offers several logistical advantages. This laboratory-based study aimed to assess the coagulation profile of FDP when stored under, and beyond, manufacturer's specifications. As lyophilisation is known to preserve biological activity, it is hypothesized that FDP will maintain a comparable coagulation profile despite exposure to various environmental conditions relevant to remote and regional WA.

Method:

FDP is produced commercially from pooled plasma of group A and AB blood groups and is approved by the US FDA under Emergency Use Authorisation (EUA) only; it is not approved by the Australian TGA. FDP was stored at temperatures above 5°C to simulate real-world conditions in remote and regional WA. Following incubation, FDP was reconstituted according to the manufacturer specifications (reconstitution time <15 minutes), and coagulation factors were measured using standard assays. Additionally, reconstituted FDP was incubated separately for a further 4 hours in different temperatures to simulate delays in administration. Multiple unpaired t-tests were compared with FFP controls.

Results:

The levels of coagulation factors were similar in FDP and FFP immediately after reconstitution ($p>0.05$, Mann-Whitney tests). Following 4-hour incubation at 4°C, FDP showed significantly longer aPTT ($p=0.02$), lower FXIII antigen ($p=<0.01$) and greater vWF:Ag ($p=0.02$).

Conclusion:

FDP and FFP demonstrate comparable levels of all tested coagulation factors immediately post-reconstitution. Refrigeration after reconstitution may impact these results. Further study is required to assess the impact of this in real-world trauma care. FDPs stability, ease of storage and delivery (<15-minute preparation time) makes it an attractive option in management of haemorrhage in remote and regional WA.

Diagnosis and clinical management of Factor XIII deficiency

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Aim:

Factor XIII (FXIII) deficiency is a rare bleeding disorder affecting approximately one in two million people. Diagnosis often correlates with disease severity but remains challenging as routine coagulation studies are normal despite abnormal bleeding.

This study describes the variability in presentation and management of four congenital cases of FXIII deficiency in the Western Sydney Local Health District (WSLHD).

Method:

Hospital electronic medical records and the Australian Bleeding disorders registry were reviewed. Patients with congenital FXIII deficiency seen in WSLHD within the past 10 years were included. Data collected included demographics, FXIII assays, bleeding phenotype, family history, and treatment. Data were de-identified and analysed using Microsoft Excel.

Results:

Four patients (3male, 1female) were included. Age at diagnosis ranged from 0-17years and did not correlate with disease.

Baseline FXIII levels (chromogenic assay) ranged from <1%–14%, with two severe, one moderate, and one mild case. Two patients had a family history of abnormal bleeding, including one confirmed FXIII deficiency. ISTH BAT scores ranged from 6–17. Grade IV bleeding occurred in the patient with moderate deficiency; all others had Grade II bleeding. Common complications included perioperative bleeding (n=4), oral mucosal bleeding (n=3), bruising (n=3), delayed umbilical stump bleeding (n=2), and haemarthrosis (n=2); one patient had intracranial haemorrhage.

All patients received plasma-derived FXIII (Fibrogammin), as monthly prophylaxis (n=2) or on-demand (n=2), with good efficacy except in intracranial haemorrhage requiring additional cryoprecipitate and fresh frozen plasma. Prophylaxis doses were increased perioperatively or after injury, and all used tranexamic acid on demand.

Conclusion:

FXIII deficiency demonstrates highly variable presentation, with imperfect correlation between severity, age at diagnosis, and bleeding phenotype. Management should be individualised, considering disease severity, bleeding pattern, and patient factors, highlighting the importance of clinical judgement across the lifespan.

Outcomes in intermediate-high risk PE patients at a single Australian tertiary institution

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Aim:

Intermediate-high risk pulmonary embolism (PE) is defined as PE with evidence of right ventricular (RV) dysfunction, elevated cardiac troponin levels and clinical parameters of PE severity but without haemodynamic instability (1). Reported in-hospital mortality ranges from 1 – 5% (2), up to 10%. Guidelines recommend reperfusion therapies (systemic thrombolysis or catheter directed therapies) be considered for intermediate-high risk PE although an improvement in mortality or long term complications such as chronic thromboembolic pulmonary hypertension (CTEPH) with reperfusion therapies compared to anticoagulation alone has not been demonstrated (3-6).

We report treatment strategies and complications rates for intermediate-high risk PE at a single Australian tertiary institution.

Method:

We identified all adult patients admitted with an acute intermediate-high risk PE (ESC criteria(1)) in a 5 year period. Exclusion criteria included pre-existing RV dysfunction or conditions known to cause RV dysfunction, and patients with < 6 months follow up. Electronic medical records were reviewed retrospectively to determine treatment, CTEPH rate and mortality.

Results:

Using ICD-10 data, there were 1524 coded PEs of which 520 (34%) met the inclusion criteria. There were 12 (2%) high risk, 77 (15%) intermediate-high risk, 49 (9%) intermediate-low risk and 382 (73%) low risk PEs.

All intermediate-high risk PE patients received anticoagulation. Four patients (5%) received upfront thrombolysis (systemic in 3, catheter directed in 1). One patient (1%) initially treated with anticoagulation alone required rescue thrombolysis due to haemodynamic deterioration.

There were 3 deaths (4%) by 30 days. 2 of 73 patients treated with initial anticoagulation alone died (1 due to sepsis; 1 due to haemodynamic deterioration). 1 of 4 patients treated with upfront thrombolysis died due to complications of haemorrhage and haemodynamic deterioration.

There were no intermediate-high risk PE patients with confirmed CTEPH via right heart catheterization.

Conclusion:

Intermediate-high risk PE patients have low 30-day mortality and CTEPH rates with anticoagulation alone. The role of reperfusion therapies remains uncertain.

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Level up: anti-Xa monitoring practices in patients receiving low-molecular-weight heparin

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Aim:

Low-molecular-weight heparin (LMWH) is dosed according to patient weight and renal function. Its anticoagulant effect may be assessed using peak anti-factor Xa (anti-Xa) levels measured 4-6 hours post-administration. Routine monitoring is not recommended; uncertainty remains whether anti-Xa guided dose adjustments improve clinical outcomes.

As part of our Anticoagulation Stewardship service, we audited LMWH anti-Xa monitoring practices to assess whether levels led to appropriate clinical action.

Method:

We identified all LMWH anti-Xa assays performed at our tertiary referral centre during 2024. Electronic medical records were reviewed to determine anticoagulant intensity, clinical indication for anti-Xa monitoring, and appropriateness of dosing modifications relative to anti-Xa results. Therapeutic peak LMWH anti-Xa target ranges were defined as: 0.5–1.0 IU/mL for twice-daily dosing, 0.8-1.6 IU/mL for once-daily dosing.

Results:

There were 651 LMWH anti-Xa assays performed hospital wide, most frequently in the General Medicine (12%) and Trauma Units (10%). Initial review demonstrated 53% of anti-Xa assays were performed on patients in the Intensive Care Unit (ICU) [344 levels on 142 patients].

Given the above, we further audited anti-Xa testing in ICU patients. Overall, 90% (n=308) of anti-Xa assays were performed in ICU patients receiving therapeutic LMWH and 28% had no apparent indication for anti-Xa monitoring. Thrombosis was the most common primary indication for anticoagulation (85%). Seventeen (5%) assays were performed in patients not receiving LMWH. Of those receiving therapeutic LMWH, one-third of anti-Xa levels were performed at the incorrect time relative to LMWH administration; 11% of these mistimed assays prompted a dose adjustment. Inappropriate dose adjustments occurred in 13% of anti-Xa results. Six (2%) anti-Xa assays were inappropriately performed during transition to alternative anticoagulation.

Conclusion:

Anti-Xa LMWH monitoring is frequently undertaken with unclear benefit. In our ICU, anti-Xa LMWH monitoring was frequently performed without a clear indication, at inappropriate time points, and occasionally led to suboptimal anticoagulant dose adjustments.

Management of cancer-associated disseminated intravascular coagulation (DIC) using IV heparin - a case series.

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Background:

Solid tumour cancer-associated disseminated intravascular coagulation (DIC) can present with marked prothrombotic and fibrinolytic features, delaying oncological treatment due to concerns regarding bleeding during invasive procedures. Given the central role of pathological thrombin generation, we have previously demonstrated the efficacy of direct thrombin inhibitors in cancer-associated DIC. Here, we present a case series showing that continuous intravenous heparin can effectively control both thrombotic and bleeding manifestations, providing a bridge to definitive surgical diagnosis and treatment.

Case 1:

72 year-old female admitted with widespread ecchymoses, malaena and haemoglobin drop of 50g. Fibrinolytic DIC was confirmed with platelets $80 \times 10^9/L$, fibrinogen 0.46g/L, elevated D-dimer 72.70mg/L which progressed through 24 hours of sub-cutaneous heparin. Intravenous heparin infusion (anti-FXa target 0.3-0.7) led to rapid normalisation of fibrinogen, platelet count, paradoxically controlling bleeding. Periprocedural pause (<4 hours) saw a doubling of D-dimer (20mg/L-46mg/L) with control regained after IV heparin resumption. Control of haemostatic parameters enabled biopsy of FDG-avid pelvic sidewall mass at a site of prior radiotherapy.

Case 2:

46 year-old female admitted with multifocal acute ischaemic stroke; renal, splenic and pulmonary infarction and 1-cycle heavy menstrual bleeding. CT revealed a solid/cystic ovarian mass. Within 72 hours, she developed thrombocytopenia $97 \times 10^9/L$, critically low fibrinogen 0.72g/L and d-dimer 23.66mg/L consistent with DIC – presumed cancer-associated. IV heparin was associated with rapid normalisation of DIC parameters, stabilisation of organ infarction and PV bleeding. Transient cessation of heparin for percutaneous biopsy twice, resulted in resurgence of DIC. A decision was therefore made to continue low-dose intravenous heparin perioperatively during surgical resection of the ovarian mass.

Discussion:

Effective management of cancer-associated DIC requires treatment of the underlying malignancy; however, uncontrolled thrombosis and bleeding can delay diagnostic and therapeutic interventions. Therapeutic thrombin inhibition, using either intravenous heparin or direct thrombin inhibitors, can stabilise haemostasis and achieve downstream control of DIC, enabling timely procedures to address the underlying cancer.

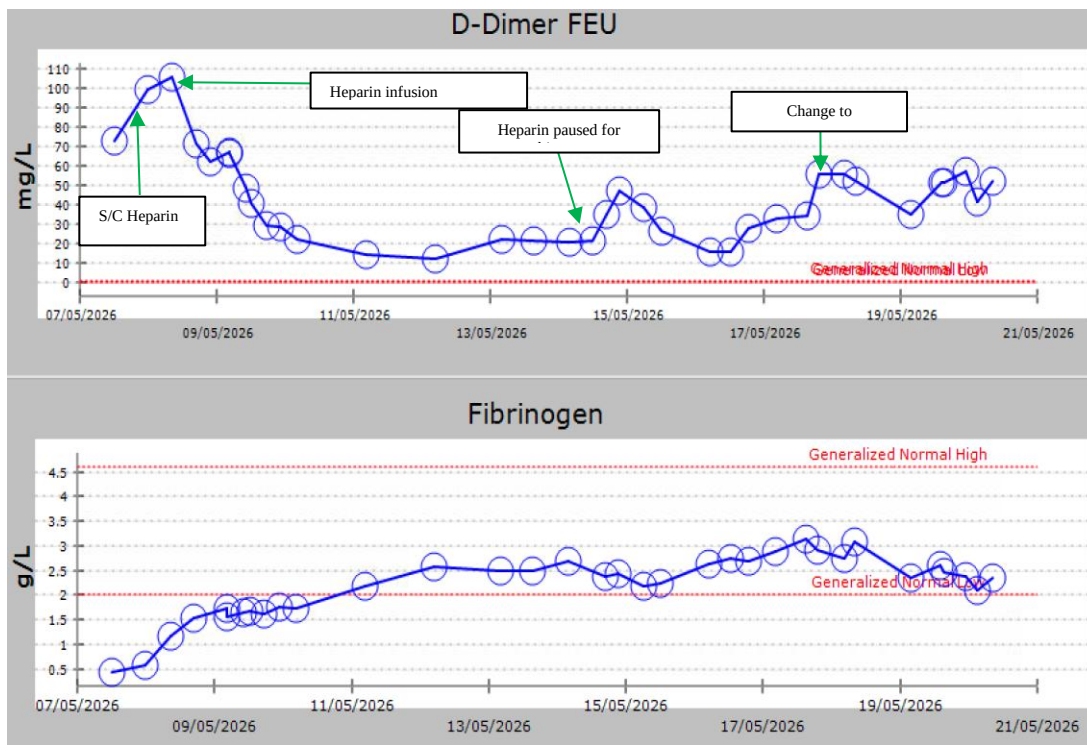


Fig 1. (Case 1): Initial use of subcutaneous heparin inadequate for DIC control, worsening d-dimer over 7/5/26 to 8/5/26 prompting change to intravenous heparin. Resurgence of DIC on 14/5/26 after pause of heparin infusion for biopsy 1. Ultimately DIC no longer controlled by heparin after Biopsy 1, anticoagulation changed to bivalirudin.

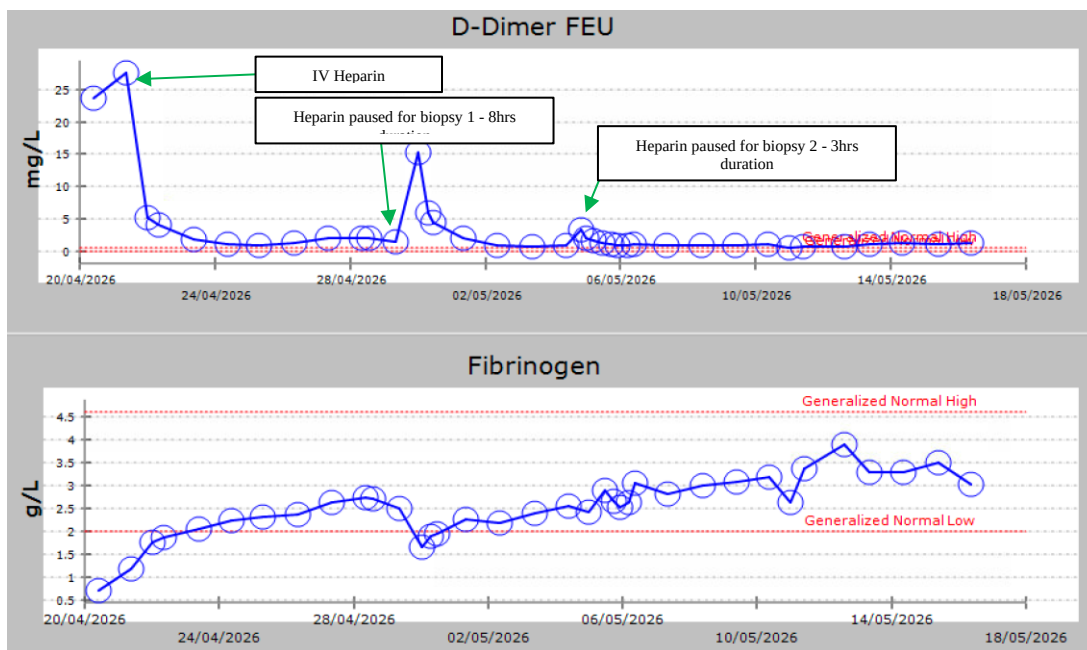


Fig. 2 (Case 2) - control of DIC achieved with IV heparin, with resurgence of DIC noted on 29/4/26 at time of heparin cessation for biopsy (total cessation time 8 hours). Rapid control regained with reinstitution of heparin infusion. Repeat biopsy performed with 3 hour duration of heparin interruption only, with much smaller rise in D-dimer as shown.

Semi quantitative D Dimer performance in an EQA program: A three-year review

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Aim:

The Royal College of Pathologists of Australasia Quality Assurance Programs (RCPAQAP) offers a D-dimer option for semi-quantitative methods. We sought to evaluate the performance and potential limitations of semi-quantitative D-dimer devices enrolled in the program.

Method:

Data from a three-year period (2023-2025) with an average annual participation rate of 19 were evaluated. Eight EQA samples were distributed annually across four dispatches, giving a total of 24 samples to review. Samples were produced in-house from pooled fresh-frozen plasma to represent semi-quantitative D-dimer concentrations of DD <0.2 mg/L, 0.2–0.4 mg/L, 0.4–0.8 mg/L, and 0.8–1.6 mg/L. Duplicate samples were issued twice per year under different sample identifiers to assess interpretative consistency.

Participating laboratories reported qualitative and semi-quantitative results using BioMedica DIMERTEST® Latex, Dialab D-Dimer Latex Agglutination Kit, or Stago D-DI test methods. Assessment was based on qualitative interpretation (detected/not detected), with results classified as concordant, minor discordance and discordant. Performance evaluation for this study included concordance with expected interpretations and comparison of paired results for duplicate sample levels.

Results:

Qualitative interpretation showed a clear concentration-dependent trend. For samples with a target of <0.2 mg/L, substantial variability was observed, with “not detected” responses ranging from 68.8% to 88.9% and “detected” responses from 11.1% to 31.3%. At 0.2–0.4 mg/L, concordance improved, with 93.3–94.4% reporting “detected”. Detection rates remained high for 0.4–0.8 mg/L (93.3–100%) and 0.8–1.6 mg/L (87.5–100%), with only infrequent discordant negative interpretations at these high concentrations.

Conclusion:

Semi-quantitative D-dimer testing demonstrates reliable qualitative performance at moderate to high concentrations; however, variability near the lower detection limit is clinically significant. Misclassification of a positive D-dimer as “not detected” carries the risk of inappropriate exclusion of venous thromboembolism. Greater awareness of assay limitations, harmonisation of interpretation, and continued participation in EQA may support safer patient management.

Venous thromboembolism in newly diagnosed multiple myeloma: incidence and thromboprophylaxis patterns in the contemporary era

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Aim:

Venous thromboembolism (VTE) is a significant complication in newly diagnosed multiple myeloma (NDMM), particularly with immunomodulatory drug (IMiD)-based regimens. Contemporary, real-world data on VTE incidence and effectiveness of guideline-recommended thromboprophylaxis strategies remain limited. We aimed to evaluate VTE event rates, prophylaxis prescribing, and associated risk factors in a modern NDMM cohort.

Methods:

Observational, registry-based cohort study of adults with NDMM at an Australian quaternary centre. Patients enrolled on the Myeloma and Related Diseases Registry between July 2021 and December 2024 were included, with follow-up to April 2026. Data were retrospectively extracted from registry and electronic medical records. The primary outcome was incidence of radiologically confirmed VTE. Secondary outcomes included thromboprophylaxis use and risk factors associated with VTE. Statistical analyses were descriptive.

Results:

Eighty-four patients were included (median follow-up 32 months). Median age was 71.9 years (IQR 65-78.5), 67.9% with a BMI ≥ 25 kg/m² and 26.2% had R-ISS stage III disease. IMiD-based induction therapy was used in 67 (79.8%) patients. VTE occurred in 9.5% of patients, corresponding to 3.5 events per 100 person-years. Most events (87.5%) occurred within 12 months of diagnosis. VTE prophylaxis was prescribed in 81.0% (n=68), most commonly low-dose aspirin (79.4%). Thrombotic events occurred in 11.1% (6/54) of patients receiving aspirin prophylaxis. There were no events observed in the 11 patients receiving direct-acting oral anticoagulants. No statistically significant predictors of VTE were identified, though trends toward higher disease burden were observed.

Conclusion:

In this contemporary NDMM population, VTE risk remains substantial despite widespread prophylaxis, with events clustering early after diagnosis. Breakthrough events on aspirin raise concerns regarding the adequacy of current routine practice. These findings support improved implementation of risk stratification and consideration of different thromboprophylaxis in higher-risk patients. Larger prospective, multicentre studies are required to define optimal prevention strategies in the era of novel myeloma treatment paradigms.

Statewide anticoagulation stewardship to improve medication safety and VTE prevention

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Background:

Anticoagulants are high-risk medicines associated with significant morbidity and mortality. In Tasmania, clinical governance for anticoagulation safety and implementation of the Venous Thromboembolism (VTE) Clinical Care Standard lacked a coordinated statewide structure, contributing to practice variation and recurring safety risks.

Objective:

To establish a multidisciplinary statewide anticoagulation stewardship program to improve anticoagulant safety, optimise VTE prevention, and standardise anticoagulation practices across Tasmania.

Action:

A statewide anticoagulation stewardship committee was established in November 2024 under the governance of the statewide Medication Safety Committee. The committee includes haematology, pharmacy, nursing, medication safety, and governance representatives across Tasmania's major health services.

Initial priorities included standardisation of anticoagulant prescribing practices, optimisation of peri-procedural anticoagulation management, review and harmonisation of statewide guidelines, and implementation of anticoagulation safety monitoring frameworks. Quarterly statewide reporting processes were established, incorporating safety events, hospital-acquired complications, anticoagulant-related readmissions, mortality data, and intravenous heparin prescribing practices.

These data were used to identify system-wide safety risks, guide quality improvement initiatives, and provide feedback to frontline clinicians, treating teams, and governance groups.

Discussion:

The anticoagulation stewardship program has established a coordinated statewide framework for anticoagulation safety and VTE prevention. It has enabled jurisdiction-wide guideline harmonisation, strengthened clinical governance, and facilitated data-driven identification of safety priorities. This model demonstrates the potential value of statewide anticoagulation stewardship programs in improving medication safety and supporting implementation of the VTE Clinical Care Standard.

The importance of multi-method factor VIII activity testing in the evaluation of reverse assay discrepancy associated with the F8 p.Tyr365Cys variant

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Background:

Missense variants in the *F8* gene are a well-recognised cause of discrepancy between Factor VIII assays, typically the one-stage assay (OSA), and other methods of Factor VIII coagulant activity (FVIII:C) measurement, including the chromogenic substrate assay (CSA). Certain *F8* variants, as well as treatment with emicizumab, can result in a discrepancy between assays in which the OSA result exceeds the chromogenic FVIII result. However certain variants, including the *F8* p.Tyr365Cys variant, can result in the less common reverse assay discrepancy, where chromogenic FVIII values are typically twofold or more times higher than OSA FVIII result.

Case Study:

We report a patient referred to the Sullivan Nicolaides Specialised Coagulation laboratory, who was found to have a normal coagulation screen, but reduced FVIII:C by OSA. Review of the patient's clinical history identified that the patient was known to be a carrier of the rare *F8* p.Tyr365Cys variant. Subsequent measurement of FVIII:C by the chromogenic method yielded a result within the normal reference interval, confirming a reverse assay discrepancy.

Conclusion:

This case illustrates the importance of employing multiple FVIII:C measurement methodologies and integrating all available clinical information when evaluating discrepant results in specialised coagulation laboratories, including discrepancies caused by rare *F8* variants. The potential clinical implications of failing to appropriately investigate using multiple methods could include misclassification of haemophilia A severity or carrier status.

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Ravulizumab for refractory antiphospholipid syndrome: experience in two patients

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Introduction

Antiphospholipid syndrome (APS) patients can enter a catastrophic phase characterised by widespread thrombosis and high mortality despite high intensity anti-thrombotic and immunomodulating therapies. Complement is implicated¹, with C5 inhibitor eculizumab showing efficacy in retrospective series²⁻⁴. Ravulizumab is a long-acting C5 inhibitor with reduced dosing frequency (8 vs 2 weekly).

Case 1

73-year-old man with lupus anticoagulant-positive APS previously stable on warfarin and hydroxychloroquine, developed refractory APS (July 2024 - May 2025) with recurrent arterial, venous, and microvascular thromboses. Complications included mesenteric infarction requiring bowel resection, PE/DVT, thrombocytopenia, pulmonary microvascular infiltrates despite escalating low molecular weight heparin (LMWH) with aspirin, plasma exchange (PLEX), mycophenolate, rituximab, and methylprednisolone. Anti-thrombotic intensification was complicated by recurrent major bleeding. He spent 38% of this period hospitalised. Ravulizumab commenced May 2025. Disease activity is now controlled with only minor features (splinter haemorrhages, thrombocytopenia). Immunosuppression and anticoagulation were de-escalated without further major thrombosis, and hospitalisation fell to 3% over the next 9 months.

Case 2:

65-year-old female with 40-year history of triple positive APS characterised by recurrent macrovascular thrombosis and microvascular vasculitis (pulmonary, adrenal, cerebral) with haemorrhage from vessel friability, triggered by infections and responsive to escalated immunosuppression (methylprednisolone, PLEX, rituximab). Early combination anticoagulant and antiplatelet therapy was replaced by BD LMWH to manage breakthrough thromboses and bleeding risk during concurrent ITP flares. Disease control improved from 2019 on maintenance immunomodulation (rituximab, hydroxychloroquine, statin and SCIg), until a further infection-triggered event in 2024: spontaneous intracranial haemorrhage, with imaging suspicious for antecedent cerebral vasculitis. Since C5 inhibition in November 2024 (eculizumab then ravulizumab), no further APS flares have occurred, permitting de-escalation in rituximab and SCIg frequency.

Conclusions

Ravulizumab was successfully used in two cases of refractory APS to facilitate rapid disease control, anti-thrombotic and immunosuppression de-escalation, and reduced inpatient utilisation, thus supporting C5 inhibition in high-risk APS.

Word Count: 300 words

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Resolving haemostasis assay issues related to therapy with emicizumab and efanesoctocog alfa

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Aims:

1. To validate the process of FVIII removal before performing emicizumab assays (1).
2. To apply a corrector to the efanesoctocog alfa (Efa) levels obtained by chromogenic FVIII assay to facilitate Efa measurement in the presence of emicizumab.
3. To adapt the Actin FSL FVIII assay on a Sysmex to Werfen and Stago analysers to allow accurate measurement of Efa using standard plasma calibrator.

Method:

1. Four samples of known emicizumab level were mixed 3:1 with in-house high titre FVIII inhibitor then incubated 30 minutes at 37°C. Subsequent emicizumab assays were corrected for the dilution factor and compared to the predicted emicizumab levels.
2. Forty-five Efa samples (FVIII range 0-175%) were measured by the reference Actin FSL assay (target level) and Siemens chromogenic assay on the Sysmex CS2500. Equations relating chromogenic levels to clotting levels were generated.
3. Ten samples with varied Efa levels were assayed by the Sysmex Actin FSL method. The Actin FSL protocol was transposed to Werfen and Stago analysers(x2), including calibrator, reagents, dilutions and incubation times.

Results:

1. Antibody treatment completely neutralised up to 200% FVIII. Mean emicizumab levels (n=4) for measured versus predicted were 23.7ug/mL and 22.4ug/mL, respectively ($P=0.15$).
2. Samples with chromogenic FVIII levels <10% (n=7) did not require correction. Most remaining samples (n=38) were corrected to within 20% of target by a 3rd order polynomial equation applied to the chromogenic result.
3. Mean (range) of 10 Efa samples assayed on Sysmex, Werfen and Stago(x2) analysers were 82.4% (10.9-175.8), 85.3% (11.3-187.4), 83.6% (13.1-172.6) and 85.7% (15.4-180.4), respectively, with most values within 20% of the Sysmex target.

Conclusion:

Each solution to measuring emicizumab or Efa required a different approach to achieve a satisfactory resolution of the measurement problem. These and similar approaches will be needed as more therapeutic agents are developed and come into use.

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Smarter systems, safer patients: advancing VTE prophylaxis through digital innovation

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Aim:

To evaluate the impact of a live Venous Thromboembolism (VTE) prophylaxis dashboard to improve VTE risk assessment (RA) documentation and appropriateness of prescribed prophylaxis.

Method:

A four-month pilot was conducted from December 2025 to March 2026 in a general medical unit at one site of a multicentre tertiary hospital. Unit pharmacists utilised the live dashboard to screen and prioritise patients without documented prophylaxis and/or incomplete or incorrect RA. The dashboard displayed real-time electronic medical record data, including pathology, medications, weight and RA status, using a red–amber–green classification to identify patients requiring review. Red and amber patients were prioritised due to absent or inappropriate prophylaxis and/or RA.

Data were collected for 30 randomly selected patients per month over a four-month period before and after implementation. Audits assessed RA completion and appropriateness of prophylaxis in accordance with hospital guidelines. Descriptive statistics were used for analysis. Qualitative feedback from pharmacists evaluated usability and workflow impact.

Results:

Following implementation, RA documentation improved from baseline average of 74% to 78%. RA completion peaked at 90% in February and remained high at 87% in March. Appropriate VTE prophylaxis prescribing was high at baseline (91%) and improved to 98%.

Pharmacists reported high acceptance of recommendations by medical teams, with prescribing identified as the priority. The dashboard was described as intuitive and provided concise, clinically relevant information to support decision-making. However, consistent use was challenging due to competing priorities and difficulties integrating into established workflows.

Conclusion:

The live VTE dashboard provided an effective overview of patient's at-risk, and a positive impact was seen with improvements in both RA documentation and prescribing. Sustained improvement will require multidisciplinary engagement, ongoing education and targeted strategies to embed dashboard use into routine clinical workflows.

A rare inhibitor: an unusual case of acquired coagulopathy

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Aim:

A 20-year-old female with Ehlers–Danlos syndrome, chronic gastrointestinal pathology, and May–Thurner syndrome (treated with a short course of unknown antithrombotic therapy) was referred to the haematology clinic. Before 2025, her ISTH bleeding score was 12 with mild mucocutaneous bleeding including epistaxis requiring cauterisation, menorrhagia controlled with oral contraceptives, and intermittent rectal bleeding. From 2025, she developed worsening symptoms including severe epistaxis, prolonged post-operative oozing following laparoscopic ileostomy requiring re-suturing, and delayed healing of minor wounds. The patient denied the use of any antithrombotic medications. Laboratory tests were conducted to investigate the possible underlying bleeding disorder.

Methods:

Initial laboratory evaluation (November 2025) performed by PathWest included coagulation studies, mixing studies, platelet aggregation, von Willebrand testing, and factor assays (VIII, IX, XI, XII). Repeat testing (February 2026) included coagulation profile, mixing studies, factors II and X assays, thrombin clotting time (TCT), reptilase time, anti-factor Xa activity, antiphospholipid antibody screen, and rotational thromboelastometry (ROTEM). Liquid chromatography–quadrupole time-of-flight (LC-QTOF) mass spectrometry was performed by Pathology Queensland.

Results:

Initial tests showed prolonged PT (44.1s), INR (3.5), and APTT (47.1s), correcting on mixing, with normal fibrinogen and unremarkable platelet function and von Willebrand studies. Factors VIII, IX, XI, and XII were normal. Repeat testing confirmed persistent prolongation of PT (48.0s), INR (4.0), and APTT (51.9s), again correcting on mixing. Common pathway factors X and II showed reduced levels with evidence of inhibition. Anti-factor Xa activity was markedly elevated (>2.00 U/mL). TCT and ROTEM were normal, and reptilase time slightly reduced. Lupus anticoagulant and antiphospholipid antibodies were negative. Mass spectrometry confirmed the presence of rivaroxaban.

Conclusion:

Findings were consistent with exogenous rivaroxaban exposure mimicking an acquired coagulopathy. The patient later disclosed surreptitious rivaroxaban ingestion. This case highlights the importance of considering undisclosed direct oral anticoagulant use and the diagnostic value of anti-factor Xa assays and mass spectrometry.

Red Blood Cell Distribution Width Predicts Hemorrhagic Transformation in Ischemic Stroke: A Meta-analysis

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Aim:

Hemorrhagic transformation (HT) is a serious complication that occurs spontaneously or after thrombolysis or mechanical thrombectomy in acute ischemic stroke (AIS). Red blood cell distribution width (RDW) is a cost-effective parameter associated with incidence and prognosis of cerebrovascular diseases. The association of RDW with the risk of HT has been variably analyzed. The purpose of our research was to explore the predictive effect of RDW for HT in patients with AIS.

Method:

PubMed, Web of Science, EMBASE, MEDLINE, Cochrane, and Google Scholar were searched. The primary endpoint was HT. Review Manager software version 5.3 was used to statistically analyze the outcomes. Q test was used to examine heterogeneity. For statistical significance, a p-value of less than 0.05 was used. Forest plots were used to depict the combined Odds ratio.

Results:

A total of four studies including 2305 AIS patients who underwent thrombolysis or mechanical thrombectomy met the inclusion criteria. The pooled odds ratio (OR) value of the high RDW that predicted HT in AIS patients was 2.42 (95% CI, 1.10–5.34; $p = 0.03$, $I^2=93\%$). The association was statistically significant.

Conclusion:

A high RDW can predict HT in patients with AIS. RDW with a cutoff value of 11.74–14.55 was independently associated with HT in AIS patients. RDW can be used as a readily available biomarker for the HT prediction in patients with AIS.

Recurrent venous and arterial thromboses in congenital fibrinogen disorder with an FGG exon 7 variant

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Background

Congenital fibrinogen disorders are clinically heterogeneous. Although hypofibrinogenaemia is typically associated with bleeding, paradoxical thrombosis is increasingly recognised and remains a clinical challenge.

Case presentation

A previously well 20-year-old male with no family history of venous thromboembolism first presented in April 2022 with an unprovoked left lower limb deep venous thrombosis (DVT) extending proximally into the common femoral vein. Thrombophilia and antiphospholipid screens were negative. There was no evidence of May-Thurner syndrome. Fibrinogen level was reduced at 0.5 g/L on functional assay and 0.9 g/L on antigenic assay, with prolonged reptilase time and thrombin clotting time. Variant gamma chain was not detected by mass spectrometry, supporting a predominantly quantitative fibrinogen defect. Genetic testing identified an FGG c.700T>G (p.Trp234Gly) missense variant. He had no personal history of bleeding. D-dimer was never elevated throughout multiple thrombotic presentations.

Management and outcome

He was treated initially with rivaroxaban following first two DVT episodes. A subsequent pulmonary embolism with lung infarction was initially attributed to anticoagulation non-adherence. However, he later developed arterial ischaemia with 'trash foot' appearances despite a sustained period of anticoagulant adherence. Management was escalated to therapeutic low-molecular-weight heparin in combination with aspirin and iloprost. Twice-weekly fibrinogen concentrate was trialled as an adjunct to address potential increase in circulating thrombin with moderate hypofibrinogenaemia given recurrent thrombosis despite rivaroxaban. Gradual clinical improvement of ischaemic symptoms was seen with this multimodal approach. He was later transitioned to dabigatran with continued aspirin, and fibrinogen concentrate was stopped after sustained clinical stability without recurrence.

Conclusion

This case demonstrates the complex, thrombotic paradox of congenital hypofibrinogenaemia and the challenges of management in face of recurrent thrombotic events. We describe our approach to management of arterial ischaemia which occurred despite rivaroxaban therapy.