International Trends for the Blood Sector

January – March 2023

The NBA monitors international developments that may influence the management of blood and blood products in Australia including but not limited to:

- information that may have an impact on global supply, demand and pricing
- potential new product developments and applications
- global regulatory and blood practice trends
- other emerging risks or opportunities.

Highlights

The following paragraphs summarise high-level themes of information that have appeared in the news media, online publications, industry, research updates over the last quarter (January – March 2023) captured across the blood sector.

In **Australia**, Lifeblood have stepped up appeals for **blood donations** including (but not limited to) rare blood types. In addition, Lifeblood is involving a range of ethnic communities (for example the Islamic community) as a way of increasing donor involvement more generally. Demand for blood and plasma continues to rise, and Lifeblood have requested that the Therapeutic Goods Administration (TGA) remove all questions relating to sexual encounters and sexuality from the plasma donor questionnaire to remove barriers to donation.

In the **US**, the FDA is proposing changes from time-based deferrals to assessing donor eligibility using individual risk-based questions to reduce the risk of transfusion-transmitted HIV. At the same time, blood centres and the Association for the Advancement of Blood and Biotherapies (AABB) continue to mitigate misinformation about COVID-19 vaccination and long COVID-19 in relation to blood safety.

In **Belgium**, despite a growing shortage of blood donors, Belgium's Superior Health Council is advising against donations from non-regular donors over 65 years of age.

In the last three months, a series of studies have been released that include retrospective and meta-analyses to assess **immunoglobulin product efficacy**. These variously focus on comparison of subcutaneous immunoglobulin (SCIg) versus intravenous immunoglobulin (IVIg); optimal therapeutic windows for treatment; potential adverse reactions; and an evaluation of immunoglobulin replacement therapy for secondary immunodeficiency.

A University of Technology Sydney (UTS) study used flow cytometry to identify distinct **platelet populations** in thawed cryopreserved platelets, and the PRPCalc2 application has been developed to enable platelet-rich plasma (PRP) preparation with minimal equipment.

A range of articles and papers have been published on **recombinant and monoclonal antibody** treatments for Haemophilia A and B, including studies on Hemlibra, Altuviiio, and the potential of monthly injections of fitusiran (a synthetic small interfering RNA - siRNA).

Crovalimab (Roche), a **novel monoclonal antibody** is in Phase 3 trial for paroxysmal nocturnal haemoglobinuria (PNH). Other developments include recent approvals by the FDA of two lymphoma treatments - Lunsumio and Polivy.

Internationally, the clinical landscape continues to adapt to new treatments for blood-related diseases. Following the approval of **Hemgenix** in the US in November 2022, this **gene therapy** for treatment of haemophilia B has now been approved by the European Medicines Agency and the UK Medicines and Healthcare Products Regulatory Agency (MHRA) has granted conditional marketing authorisation in February 2023. While the EU approved **Roctavian** (a gene therapy treatment for haemophilia A) was approved in August 2022, the FDA has extended the target action date in the US to June 2023. Still on gene technology, a review of a **new gene editing approach** for **sickle cell disease** and transfusion-dependent **thalassemias** indicates a new therapeutic option.

The US FDA has provided Caribou Biosciences with fast-track approval for CB-011 which allows for creation of genome edited **cell therapies**. Positive results have been published in CAR T-cell trials for treatment of lymphoma, myeloma, and leukaemia, while the biotech company ImmuneBridge has raised $12 million in seed financing to develop natural killer (NK) cells (from umbilical cord blood) for cancer treatment.

The first Bruton's tyrosine kinase (BTK) inhibitor, **Jaypirca (pirtobrutinib)** has been approved by the US FDA to treat relapsed or **refractory mantle cell lymphoma** (MCL), while the European Medicines Agency's Committee for Medicinal Products for Human Use (CHMP) has recommended approval of **liso-cell (Breyanzi)** for treatment of **diffuse large B-cell lymphoma (LBCL)**.

Assays for weak ABO variants, blood bank information systems software and algorithms to predict deferrals due to haemoglobin levels were the subjects of various studies to **optimise blood donation** and management, along with optimisation of prediction and use of transfusion and reporting on haemovigilance studies.

COVID-19 continues to impact blood product supply and use, and evidence-gathering for the longer-term impacts and complications of COVID-19 is ongoing. A range of COVID-19 related articles is covered in section 6, including evidence regarding the use of **convalescent plasma therapy (CPT) or hyperimmune immunoglobulin (HI) to treat seriously ill COVID-19 patients**.

In **R&D** news, technological advances such as machine learning and bioinformatics may be driving a new era of precision oncology, and the need for dynamic data feeds for successful machine learning models is critical.

Meanwhile, the Medicines Australia public consultation for the **Health Technology Assessment** Policy and Methods review closed in January 2023.

The **environment** continues to have indirect impacts on the blood sector. A systematic review has linked the potential impact of climate change to blood transfusion safety, as risk of human exposure to novel zoonotic pathogens, and the spread of known pathogens increases.

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1 Blood supply and demand

1.1 Blood supply - Australia

Lifeblood have stepped up appeals for blood donations including rare blood types. In addition, they are reaching out to a range of ethnic communities (for example the Islamic community) as a way of increasing donor involvement more generally. Demand for blood and plasma continues to soar, and Lifeblood have requested that the Therapeutic Goods Administration (TGA) remove all questions relating to sexual encounters and sexuality from the plasma donor questionnaire to remove barriers to donation.

- Jase faced his cancer with an army of donors | Lifeblood
- Camilla Franks designs must-have accessory to help boost blood donations
- Lifeblood urging people to donate blood ahead of World Cancer Day
- Plasma's back: Boost for CSL as collections troubles ease
- RACGP - Potential blood donation changes for MSM
- Australian Islamic community donates to Lifeblood to increase rare blood type supplies
- Urgent appeal to Jews for blood donations to save life of Australian man
- Lifeblood makes urgent appeal for blood donors over Easter as demand reaches a 10-year high
- Giving blood: Gay, bisexual ban on blood plasma donation could be lifted in world-first move (SMH)

1.2 Blood supply - United States

The U.S. FDA is proposing changes to deferral policy from time-based deferrals to assessing donor eligibility using individual risk-based questions to reduce the risk of transfusion-transmitted HIV. At the same time, blood centres and AABB continue to mitigate misinformation about COVID-19 vaccination and long COVID-19 in relation to blood safety.

- FDA Proposes Individual Risk Assessment for Blood Donations, While Continuing to Safeguard U.S. Blood Supply
- Joint Statement: Blood Community Reiterates the Safety of America's Blood Supply for Patients
- DARPA Team Begins Work on Field Deployable Whole Blood Equivalent
- Church unites community against sickle cell disease by hosting blood drives
- Blood donor participation remains low as pandemic fades
- Republicans want to ban people vaccinated for COVID from donating blood

1.3 Blood supply - World news

- 100,000 new donors: Canadian Blood Services' goal for 2023
- Canadian Blood Services and first responders campaign for new donors
- 'One body': Gaza launches blood donations after deadly earthquake
- Thai Red Cross urges foreigners to donate Rh-negative blood to assist western tourists in emergencies
- Belgium advises against blood donations for over-65s

- Students from a high school in San Fernando de Henares promote the blood donation 'marathon' at the Hospital del Henares

2 Product development and applications

2.1 Immunoglobulin

A retrospective study on the efficacy of subcutaneous immunoglobulin as compared to intravenous formulation in patients with chronic lymphocytic leukemia and secondary antibody deficiency

This observational, retrospective, multicenter study from Italy aimed to evaluate the efficacy and safety of subcutaneous immunoglobulin (SCIg) compared to intravenous immunoglobulin (IVIg) in patients with **chronic lymphocytic leukemia (CLL)** and **secondary antibody deficiency (SAD),** according to clinical practice. One hundred and sixteen CLL patients were recruited with a median age of 68 years and of the recruitment cohort, 63% males. Forty-nine patients received IVIg, and 88 received SCIg, including 28 patients who shifted from IVIg to SCIg. The study demonstrated that SCIg is active and well tolerated by patients, and that patients reached higher IgG levels and the rate of infection was lower than IVIg, specifically when IgG levels reach 6 g/L.

Evaluation of immunoglobulin replacement therapy in secondary immunodeficiency at three British Columbia hospitals

A retrospective chart review was conducted across three hospitals in Canada to determine whether immunoglobulin (Ig) usage for patients with **secondary immunodeficiencies (SIDs)** was appropriate noting ongoing shortage concerns of the product. The Australian *Criteria for the Clinical Use of Immunoglobulin* was used as the benchmark. The review found high rates of inappropriate Ig usage in SID patients in both new and chronically treated groups, suggesting that more stringent local guidelines and processes for assessing initial and ongoing Ig replacement are warranted.

The therapeutic window of intravenous immunoglobulin (IVIg) and its correlation with clinical outcomes in Kawasaki Disease: a systematic review and meta-analysis

In response to debate about the optimal therapeutic window to **start intravenous immunoglobulin (IVIg) for Kawasaki disease**, this study (using data from multiple countries) has found IVIg treatment within 7 days of illness seems to be the optimal. IVIg treatment within 7 days is found to be effective for reducing the risk of coronary artery lesions and cardiac sequelae in KD patients. The study found that early IVIg treatment within 4 days could result in IVIg resistance, but that large multi-center, randomised trials are needed to provide more evidence.

Adverse reactions associated with intravenous immunoglobulin in the treatment of neurological disease: A systematic review

Intravenous immunoglobulin (IVIg), which is used to treat multiple neurological conditions, may be associated with serious adverse reactions. This systematic review of literature reporting adverse reactions found rates varied widely (between 25-34%), as did reactions from mild to very serious. There is limited evidence to support the effectiveness of prevention and treatment strategies, which may include modification to dose, reduced infusion rate, and premedication. Further studies regarding methods to prevent and treat IVIg related adverse reactions in neurology patients are required.

2.2 Platelets

Freezing platelets changes the way that they look

Cryopreserved platelets undergo marked changes and previous data has suggested that post-thaw platelets are heterogenous. This study confirms, for the first time, that cryopreserved platelets are procoagulant, rather than apoptotic, which aligns with their procoagulant functional capacity.

Platelets are haemostatic cells, which perform many different roles in the complex process required to prevent and/or stop bleeding. Subpopulations of platelets exist, which perform different functions within the haemostatic process. The study (published in Nature) identified distinct platelet subpopulations within thawed cryopreserved platelets, and a proportion of these were aligned morphologically and phenotypically with traditional procoagulant platelets.

This work is relevant to the Australian Defence Force frozen blood program as well as the CLIP-II clinical trial (funded through the NHMRC), as it gives insight into the impact that cryopreservation has on platelets. Cryopreserved platelets were given to Australian soldiers in Afghanistan, 2006-2010, with apparently good effect. However, supporting evidence is limited to animal and in vitro studies and a single trial in which 24 patients were transfused. While universally encouraging, this is insufficient to justify change in practice. The CLIP II trial is a phase III multi-centre blind randomised controlled clinical non-inferiority trial of cryopreserved platelets vs. conventional liquid-stored platelets for the management of post-surgical bleeding.

Letter to the Editor: Experience with subcutaneous desmopressin in patients with von Willebrand disease (VWD) and qualitative platelet function disorders

This retrospective cohort study found subcutaneous **desmopressin** (a synthetic analog of vasopressin) should be considered as an alternative to the intranasal formulation for home therapy in prevention and treatment of bleeding diathesis in patients with VWD. Additionally, subcutaneous desmopressin testing should be considered for patients unresponsive to intranasal desmopressin.

PRPCalc2: An App for Platelet-Rich Plasma Preparation

PRPCalc2 (an App) has been developed to enable practitioners to set up an easy method for reliable, consistent platelet-rich plasma (PRP) preparation with only a centrifuge and blood drawing supplies. PRP is a widely used, relatively inexpensive treatment for a range of uses including supporting wound healing in trauma and joint injury.

2.3 Recombinant products and monoclonal antibodies

Efanesoctocog Alfa Prophylaxis for Patients with Severe Haemophilia A

Efanesoctocog alpha (Sanofi) is a **novel recombinant factor VIII (FVIII) therapy**. This phase 3 study compared patients with **severe haemophilia A** who received once-weekly prophylaxis for 52 weeks, with patients who received on-demand treatment for 26 weeks followed by one-weekly prophylaxis for 26 weeks. The study showed that once-weekly efanesoctocog alfa provided superior bleeding prevention to pre-study prophylaxis, normal to near-normal FVIII activity, and improvements in physical health, pain, and joint health.

Roche Reports Positive Data for Rare Blood Condition Treatment – **Paroxysmal Nocturnal Haemoglobinuria**

This update outlines a phase 3 study (COMMODORE 2) evaluating the efficacy and safety of crovalimab, a novel anti-C5 recycling monoclonal antibody, in people **with paroxysmal nocturnal hemoglobinuria (PNH)**. The treatment is a subcutaneous injection every 4 weeks for PNH patients who have not been previously treated with complement inhibitors. The study results indicated that the drug achieved its co-primary efficacy endpoint of disease control with less frequent treatment intervals to the current standard.

Eliminating the monitoring period with subcutaneous daratumumab: a single-center experience

Daratumumab is a monoclonal antibody approved for the treatment of **relapsed/refractory multiple myeloma** with a historically high incidence of infusion-related reactions (IRRs). This single-centre, retrospective analysis sought to find the optimal observation time after the administration of **subcutaneous (SC) daratumumab in comparison to the standard intravenous (IV) daratumumab**. The use of SC daratumumab saw lower rates of IRR with the data suggesting that patients can safely receive SC with no observation period and prefer this administration over IV. Reducing post-administration chair observation time to zero can lead to cost savings, an increase in chair availability[1] and decreased time at the cancer center for the patient and burden on healthcare staff.

FDA Authorizes Roche's Lymphoma Treatment

The Food and Drug Administration (FDA) granted accelerated approval to **mosunetuzumab-axgb (Lunsumio,** Genentech, Inc.), a bi-specific antibody. The therapy will be available for adult patients with **relapsed or refractory follicular lymphoma** with limited alternate treatment options across the United States and is expected to cost around $180,000 for a cycle of eight treatments.

Briquilimab may boost success of sickle cell stem cell transplant

This Phase 1/2 trial is assessing whether treatment with **briquilimab** - a monoclonal antibody conditioning therapy (Jasper Therapeutics), in addition to standard therapies - can improve the success of stem cell transplant in people with **sickle cell disease (SCD) and beta thalassaemia**. Early data shows that there has been success in three SCD patients.

BioNTech and OncoC4 team up on novel checkpoint monoclonal antibody candidate

BioNTech and OncoC4 have announced a worldwide license and collaboration agreement to develop and commercialise OncoC4's next generation **anti-CTLA-4 monoclonal antibody candidate ONC-392** as a therapy for various cancer indications. Drug trials are in Phase 1/2 for use alone or in combination with personalised immunotherapies. CTLA-4 inhibits the activity of immune cells, and ONC-392 aims to delete immunosuppressive regulatory T-cells in the tumor microenvironment but spare these cells in healthy tissue. ONC-392 has already received Fast Track designation from the FDA as a monotherapy for immunotherapy-resistant non-small cell lung cancer (NSCLC).

It is expected that a phase 3 trial assessing ONC-392 will begin this year, although it is currently also being evaluated in a phase 2 trial as a combination therapy alongside pembrolizumab to treat platinum-resistant ovarian cancer.

[1] Chair in this instance refers to the chair used by the patient during treatment

2.4 Gene therapy

Pfizer says hemophilia B gene therapy-controlled bleeding in key study

Pfizer has provided early results from Phase 3 **BENEGENE-2** study evaluating *fidanacogene elaparvovec*, an **investigational gene therapy**, for the treatment of adult males with moderately severe to severe **haemophilia B**. The study showed a single dose of Pfizer's therapy lowered participants' annual bleeding rates by an average of 71% over one year, compared to their pre-treatment baseline.

Two-Year Outcomes of Valoctocogene Roxaparvovec Therapy for Hemophilia A

This study is a year two follow-up of patients who received the gene therapy **valoctocogene roxaparvovec (Roctavian)** (BioMarin) to treat their **hemophilia A** as part of an open-label, single-group, multi-centre trial. All patients in the trial were previously on factor VIII prophylaxis and received a single infusion of valoctocogene roxaparvovec. Results showed a durable reduction in mean annualised treated bleeding rate by 84.5%. A discussion of the publication in Healio suggests that the findings may inform therapy choices in Europe, where the therapy has received conditional approval, and possibly in the United States, where a Biologics License Application (BLA) is under review.

Gene editing for sickle cell disease and transfusion dependent thalassemias- A cure within reach

This study reviews results of a **gene editing approach** that can induce foetal haemoglobin production in patients with **sickle cell disease (SCD) and transfusion dependent thalassemias**. Recent improvements in the understanding of the molecular pathways controlling erythropoiesis (formation of red blood cells) and globin switching from foetal haemoglobin to adult haemoglobin offer a new and exciting therapeutic option.

Long-Term Durable FVIII Expression with Improvements in Bleeding Rates Following AAV-Mediated FVIII Gene Transfer for Hemophilia A: Multiyear Follow-up on the Phase I/II Trial of SPK-8011

Spark Therapeutics, a member of the Roche Group, announced updated multi-year results from its Phase 1/2 clinical trial of **investigational *SPK-8011*** for patients with **haemophilia A.** With up to five years of follow-up, the data showed that a single infusion resulted in sustained factor VIII (FVIII) expression and clinically meaningful reductions in annualized bleed rate and annualized FVIII infusion rates. This data was presented at the 64th American Society of Hematology (ASH) annual meeting in December 2022.

CSL's Hemgenix approved in EU and UK

The European Medicines agency (EMA) has approved CSL's candidate **Hemgenix (etranacogene dezaparvovec**), the first gene therapy for the treatment of haemophilia B, three months after the FDA granted market approval in November 2022. The UK Medicines and Healthcare products Regulatory Agency (MHRA) has granted conditional marketing authorisation to **Hemgenix.**

FDA grants RMAT designation to Intellia's NTLA-2002 – the third of such designations. HAE International (HAEi)

The US Food and Drug Administration (FDA) has granted Regenerative Medicine Advanced Therapy (RMAT) designation to Intellia Therapeutics Inc (Intellia) for NTLA-2002. NTLA-2002 is an in-vivo CRISPR-based investigational therapy designed to inactivate the target gene, Kallikrein B1 (KLKB1) to potentially prevent life-threatening swelling attacks in people with HAE. The RMAT designation was

established to expedite the development and review of promising therapeutic candidates (such as gene therapies) to treat, modify, reverse, or cure serious or life-threatening disease. The RMAT is the third special regulatory designation received by Intellia for NTLA-2002. NTLA-2002 was also granted Orphan Drug Designation by the FDA and the Innovation Passport by the UK Medicines and Healthcare products Regulatory Agency.

2.5 Cell therapy

ImmuneBridge raises $12 million to source natural killer therapies from umbilical cord blood

Biotech startup ImmuneBridge has raised $12 million in seed financing to drive development of natural killer (NK) cells that can be used in cell therapies for cancer. These cells require less preparation and can attack tumor cells faster than T-cells and have less propensity to trigger negative effects such as cytokine storms. The seed investment will be used to help ImmuneBridge create a screening dataset that the company can use to identify the best NK cells for cell therapies. The company also plans to demonstrate its platform can manufacture NK cells at scale, and to develop a lead product at the preclinical stage. While its initial focus is on NK cells, the company has the option to develop therapies based on other kinds of immune cells as well.

Growing blood stem cells in the lab to save lives (phys.org)

A team led by researchers at the University of Tsukuba in Japan has established a novel culture system that supports long term *ex vivo* expansion of haematopoietic stem cells (HSCs). Previous methods for HSC expansion have not achieved high enough yield to transplant into patients. This method uses an optimal, fully defined cell culture medium and may help to advance development of HSC related therapies.

3 Blood diseases and treatment

3.1 Haemophilia

Monthly injections of fitusiran reduces bleeds in patients with haemophilia A and B

Fitusiran is a novel siRNA therapy that reduces antithrombin synthesis in the liver, ultimately rebalancing haemostasis. Synthetic small interfering RNAs (siRNA) reduce levels of their target factors by interfering with gene expression. Prophylactic use of fitusiran significantly cut bleeds in patients with **haemophilia A and B.** Two international, Phase 3, randomised controlled trials – funded by Sanofi and published in *The Lancet* and *The Lancet Haematology* journals – have shown that monthly subcutaneous injections were effective at reducing bleeds in patients with or without inhibitors. The authors say that fitusiran is the first prophylactic treatment effective in treating both haemophilia A and B, and in both patients with and without inhibitors. Further studies are needed to assess its safety profile and refine dosing.

Emicizumab (Hemlibra) in people with moderate or mild haemophilia A (HAVEN 6): a multicentre, open-label, single-arm, phase 3 study

This multicenter, open-label study assessed the long-term safety and efficacy of **emicizumab (Hemlibra)** prophylaxis, specifically in people with non-severe **haemophilia A**. Only patients with mild or moderate haemophilia without FVIII inhibitors, who required prophylaxis were included in the study. The results demonstrated a favourable benefit–risk profile of emicizumab in people with non-severe haemophilia A without FVII inhibitors.

Emicizumab prophylaxis in haemophilia A with inhibitors: Three years follow-up from the UK Haemophilia Centre Doctors' Organisation (UKHCDO)

The UK National Haemophilia Database (NHD) collects data from all persons with **haemophilia A** with inhibitors. To determine safety, bleeding outcomes and early effects on joint health, researchers analysed data from people with ≥6 months **emicizumab (Hemlibra**) use compared with previous treatments. The results found that emicizumab was associated with sustained low bleeding rates and was generally well-tolerated in people with haemophilia A and inhibitors.

FDA approves once-weekly hemophilia A therapy

The FDA has approved Sanofi and Sobi's **Altuviiio** (efanesoctocog alfa), a recombinant factor VIII replacement therapy, for the treatment of adults and children with **haemophilia A**. It is the first and only haemophilia A treatment to deliver normal to near-normal factor activity levels with once-a-week dosing, and significantly reduces bleeds compared to prior factor VIII prophylaxis. Regulatory submission in the EU is expected in the second half of 2023.

3.2 Multiple myeloma

Carfilzomib, lenalidomide, and dexamethasone or lenalidomide alone as maintenance therapy after autologous stem-cell transplantation in patients with multiple myeloma (ATLAS): interim analysis of a randomised, open-label, phase 3 trial

This is an interim analysis of ATLAS – a multi-centre, open label, randomised, phase 3 trial being undertaken in 12 academic and clinical centres in the USA and Poland. The study compared treatment options for patients with **newly diagnosed multiple myeloma** following induction therapy and autologous stem-cell transplantation. It was found that a triple-drug maintenance combination of **carfilzomib, lenalidomide and dexamethasone** appeared to improve progression-free survival (PFS) compared with treatment with **lenalidomide** alone. The median PFS was 59.1 months for patients treated with the combination therapy compared with 41.4 months for those treated with just lenalidomide.

Overall Survival With Daratumumab, Lenalidomide, and Dexamethasone in Previously Treated Multiple Myeloma (POLLUX): A Randomized, Open-Label, Phase III Trial

POLLUX is a multicenter, randomized, open-label, phase 3 trial that evaluated **dexamethasone** (D-Rd) or **lenalidomide** (Rd) in patients with **relapsed/refractory multiple myeloma** on or after at least one prior line of therapy. This trial showed the addition of **daratumumab** (Darzalex) to Rd and D-Rd led to a 27% reduction in the risk of death compared with Rd alone.

Novel agents as main drivers for continued improvement in survival in Multiple Myeloma

This retrospective observational study carried out at the University Hospital in Salamanca in Spain, confirms the continuing improvement in the survival of **multiple myeloma** patients over time with the development of new treatments. The combination of novel agents like **proteasome inhibitors** and **immunomodulators** as first-line treatments appear to be the main factor driving improvement. This has resulted in overall survival of more than 12 years in patients aged ≤ 70 years, and 8 years in patients aged >70 years. Researchers concluded that multiple myeloma has become a chronic and even curable disease, in a subset of patients, with the current therapeutic approaches.

Anaveon announces first patient dosed with ANV419 in a Phase I/II Study of ANV419 in patients with multiple myeloma

Anaveon is conducting an open-label, Phase I/II study (OMNIA-2) of ANV419 with sites in Europe. This study will enroll up to 52 patients with **relapsed / refractory multiple myeloma**. The study consists of an initial 8-weeks of ANV419 monotherapy, followed by randomization of ANV419 in combination with **daratumumab** and **hyaluronidase-fihj**, or **lenalidomide** plus low dose **dexamethasone** to assess the safety, tolerability, and preliminary efficacy of ANV419.

Broadly applicable TCR-based therapy for multiple myeloma targeting the immunoglobulin J chain

A study carried out at Leiden University Medical Centre (the Netherlands) identified T cells that are specific for the immunoglobulin J chain, which is highly expressed in the majority of multiple myeloma (MM) patients. The T cell receptors (TCRs) specific for J chain peptides were cloned, sequenced, and transferred into other immune cells to test for potential anti-myeloma activity. All four TCRs demonstrated potent anti-myeloma activity, which will be further tested for clinical applications.

ORIC Pharmaceuticals announces clinical development

ORIC and Pfizer are collaborating to enhance the clinical development program for **ORIC-533, an oral small molecule inhibitor of CD73**. CD73 is a cell marker that has been shown to correlate with unfavourable clinical outcomes in **multiple myeloma** patients. Through the agreement, the parties plan to advance ORIC-533 to a Phase 2 combination study with elranatamab, Pfizer's investigational B-cell maturation antigen CD3-targeted bispecific antibody for the treatment of multiple myeloma.

CAR T-Cell Therapy With CYAD-01 Shows Efficacy in Myeloid Malignancies

Trials of the use of CYAD-01 (a CAR T-cell product) has shown promising results in patients with **relapsed/refractory acute myeloid leukemia (AML**), **myelodysplastic syndromes (MDS**), and **multiple myeloma**, including good tolerance and anti-leukemic activity. CYAD-01 is a CAR T-cell product where a patient's T cells are removed from their body and altered to specifically express a novel protein receptor fused with a T-cell activating domain.

The multi-centre THINK study was an open-label, dose-escalation, phase 1 study for patients with relapsed or refractory acute myeloid leukaemia, myelodysplastic syndromes, or multiple myeloma, after at least one previous line of therapy. Patients were recruited from five hospitals in the USA and Belgium.

Caribou gets FDA fast track for allogeneic CAR-T

The FDA has provided fast track designation to Caribou Biosciences for their product CB-011**. CB-011 is one of the products of Caribou's proprietary chRDNA (CRISPR hybrid RNA-DNA)** technology which allows for creation of genome-edited cell therapies. It is being evaluated in Phase 1 clinical trials for **relapsed or refractory multiple myeloma (r/r MM**). CB-011 itself is an allogeneic anti-BCMA CAR-T therapy intended to be an off-the-shelf treatment option for patients with r/r MM.

Novel 'Off the Shelf' CAR-T Product Shows Promise in Multiple Myeloma

Interim results from this phase 1 trial demonstrated that the use of an **allogeneic B-cell maturation antigen (BCMA)-targeting CAR T-cell therapy** was feasible, safe, and induced responses in patients with **relapsed or refractory multiple myeloma**. The overall response rate was 56% with that rate

increasing to 71% in the group treated at the optimal cell dose of CAR T cells after an intensified conditioning regimen incorporating fludarabine, cyclophosphamide, and ALLO-647.

3.3 Leukaemia

Evaluation of the association between congenital cytomegalovirus infection (cCMV) and pediatric acute lymphoblastic leukemia (ALL)

Acute lymphoblastic leukaemia (ALL) is the most prevalent form of paediatric cancer and a leading cause of death in children. This study used newborn dried blood spots from 1189 confirmed ALL cases and 4756 matched controls to investigate whether there is an association between ALL and a congenital cytomegalovirus (cCMV) – a common viral infection. The study found that overall, there was no significant association between cCMV infection and ALL. However, when considering ALL subtypes, the association of hyperdiploid ALL cases with cCMV infection was significantly greater compared with unmatched controls.

Long-term survival with oral azacitidine for patients with acute myeloid leukemia in first remission after chemotherapy: updated results from the randomized, placebo-controlled, phase 3 QUAZAR AML-001 trial

This article re-examines the outcomes of the original study into long-term survival with an oral chemotherapy, **azacytidine (Oral-AZA),** for patients with **acute myeloid leukemia (AML**). The updated findings demonstrate the feasibility and sustained long-term clinical benefit of Oral-AZA, now with more than 4 years follow-up for patients in remission after chemotherapy. The researchers suggest that patients with AML completing intensive induction and consolidation therapy should be considered for Oral-AZA maintenance, particularly those who are not eligible for haematopoietic stem cell transplantation.

Inflammation levels linked to survival in acute myeloid leukemia (healio.com)

Severe inflammation among individuals with **acute myeloid leukemia (AML**) can limit their bodies' ability to kill cancerous blood cells. In this 5-minute video, researchers from NYU Grossman School of Medicine and NYU Langone Health's Perlmutter Cancer Center explain how their "iScore" system for measuring patient inflammation can help to measure AML severity and may be a useful tool for physicians.

Synergistic effect of HDAC inhibitor Chidamide with Cladribine on cell cycle arrest and apoptosis by targeting HDAC2/c-Myc/RCC1 axis in acute myeloid leukemia - PubMed (nih.gov)

This research investigated the synergistic effect and mechanism of a **histone deacetylase inhibitor, Chidamide (CHI**), in combination with an antimetabolite drug as a targeted therapy for **acute myeloid leukemia (AML)**. Researchers used assays looking for cell growth, cell cycle arrest, and apoptosis (cell death) in AML cells to examine the effect of the drug combination.

DNA sequencing to detect residual disease in adults with acute myeloid leukemia prior to hematopoietic cell transplant

Preventing relapse for adults with **acute myeloid leukemia (AML**) in first remission is the most common indication for **allogeneic haematopoietic cell transplant**. The presence of AML measurable residual disease (MRD) has been associated with higher relapse rates, but testing is not standardized. To determine whether DNA sequencing to identify residual variants in the blood of adults with AML in first remission before allogeneic hematopoietic cell transplant identifies patients

at increased risk of relapse and poorer overall survival compared with those without these DNA variants.

Current CML guidelines overemphasize second generation TKIs: revisiting the paradigm

Current National Comprehensive Cancer Network guidelines (NCCN version 1.2023) for chronic-phase **chronic myeloid leukemia (CML**) recommend **second-generation tyrosine kinase inhibitors** (2G-TKIs) as first-line therapy for patients with intermediate or high-risk Sokal or Euro scores. This paper discusses why imatinib should be the preferred first-line drug for all risk groups.US FDA approves Shorla's oncology drug for T-cell leukaemia

The US Food and Drug Administration has granted approval for Shorla Oncology's **Nelarabine Injection**, an oncology drug, to treat both **T-cell Lymphoblastic Lymphoma** (T-LBL) and **T-cell Acute Lymphoblastic Leukemia** (T-ALL), an aggressive blood and bone marrow cancer that progresses quickly and is most common in children. It offers an alternative to a product for which there is a regular shortage and to fill the clinical need in this patient community.

The menin inhibitor revumenib in KMT2A-rearranged or NPM1-mutant leukaemia

This Phase 1 trial in the US between 2019 and 2022 of **revumenib monotherapy**, has shown early evidence of potential treatment for **advanced and treatment-resistant leukaemia**. **Revumenib**, a menin inhibitor, was tested on 60 patients, and over half experienced complete or partial remission. More than three-quarters of the latter group were still in recovery two months after remission.

Moleculin Announces Final Topline Data from Successful European Phase 1 Trial Evaluating Annamycin as Single Agent Treatment of Relapsed or Refractory Acute Myeloid Leukemia (AML)

Annamycin is a treatment for adults with relapsed or refractory **acute myeloid leukemia (AML)** developed by Moleculin Biotech Inc. It currently has Fast Track Status and Orphan Drug Designation from the US Food and Drug Administration (FDA). Results from the phase one trial show that the safety and efficacy of Annamycin aligns with the overall safety profile observed in previously completed and ongoing clinical studies of the product.

Safety and efficacy of co-administration in children with B-ALL relapse after CD19 CAR-T therapy

This study looked at the safety and efficacy of **co-administration of CD19- and CD22-targeted CAR-T** cell therapies for **B-lineage acute lymphoblastic leukemia (B-ALL)** patients who relapse after their first CD19 CAR-T treatment. Five patients who had relapsed after CD19-targeted CAR-T were recruited were given a mixed infusion of CD19- and CD22-targeted CAR-T cells. After CART2, all five patients had minimal residual disease (MRD)-negative complete remission (CR). The 6- and 12-month overall survival (OS) rates were 100%.

EP0042 wins FDA orphan drug status for acute myeloid leukemia

Ellipses Pharma ("Ellipses"), a global drug development company focused on accelerating the development of cancer medicines and treatments through an innovative drug development model, announced that the U.S. Food and Drug Administration (FDA) has granted Orphan Drug Designation (ODD) **to EP0042, a dual FLT-3 and Aurora kinase inhibitor**, for the treatment **of acute myeloid leukaemia (AML).**

The FDA grants ODD based on review of promising early clinical data from investigational treatments for rare diseases, such as AML, defined as affecting fewer than 200,000 people in the US. ODD qualifies the developer for certain incentives with the goal of accelerating drug development for

patients, including tax credits and seven years of market exclusivity in the US upon approval by the FDA. In February 2023, the FDA approved EP0042's Investigational New Drug Application, which allowed for the opening of additional trial sites in the US for this compound.

3.4 Aplastic anaemia

Hetrombopag plus porcine ATG and cyclosporine for the treatment of aplastic anaemia: early outcomes of a prospective pilot study

Hetrombopag (HPAG), a thrombopoietin-receptor agonist, has shown encouraging efficiency in immunosuppressive therapy (IST) for **severe aplastic anaemia (SAA**). This prospective pilot study from China aimed to determine the efficacy of HPAG as a first line treatment. The authors found that HPAG plus IST, compared with IST alone, was beneficial in patients with SAA and induced a higher quality and faster haematologic response without increasing adverse events. However, they note that as this was a pilot study, further trials are needed to confirm the results.

3.5 Lymphoma

FDA has granted accelerated approval to pirtobrutinib for relapsed or refractory mantle cell lymphoma

Pirtobrutinib is the first BTK inhibitor of any kind specifically approved for patients with MCL that have been previously treated with a covalent BTK inhibitor. Approval was based on data from a subset of 120 patients with MCL from the open-label, single-arm BRUIN study who had previously received a covalent BTK inhibitor and achieved a 50% overall response rate.

According to BRUIN investigators, the approval of **pirtobrutinib (Jaypirca**) represents an important advance for patients with **relapsed or refractory mantle cell lymphoma (MCL**), who currently have limited options and a poor prognosis following discontinuation of treatment with a covalent BTK inhibitor.

B cell lymphoma drug (liso-cel; Breyanzi) recommended for EU approval

The European Medicines Agency's Committee for Medicinal Products for Human Use (CHMP) has recommended the approval of **lisocabtagene maraleucel (liso-cel; Breyanzi**) for the treatment of select patients with **diffuse large B-cell lymphoma (LBCL**). If approved by the European Commission, it could provide a new standard of care for people in the European Union living with relapsed or refractory LBCL after first-line treatment, an area of critical unmet need. On June 24, 2022, the FDA approved liso-cel as second-line therapy for patients with relapsed or refractory LBCL.

Roche's CAR-T cell therapy for relapsed or refractory forms of large B-cell lymphoma is approved in Canada

Roche's CAR-T cell therapy '**Columvi'** received approval from Health Canada in March 2023 for the treatment of relapsed or refractory forms of the blood cancer **diffuse large B-cell lymphoma (DLBCL**). CAR-T therapies have changed the approach to treating rare forms of blood cancer such as DLBCL. Columvi is the first of its kind to be dosed for a fixed duration, rather than long-term which is expensive and burdensome for patients. Roche now plans to seek approval from the US FDA, with decision expected by July 2023.

Blood test predicts CAR-T response in non-Hodgkin lymphoma

Researchers from the University of Texas have developed a non-invasive blood test that uses whole-genome sequencing to assess the risk that non-Hodgkin lymphoma patients will not respond to **CD19-directed CAR-T therapy**. By stratifying patient risk before they receive CD19-directed CAR-T cells this will allow researchers to personalise therapy to improve outcomes or select other options for patients.

3.6 Thalassaemia

Saviour sibling, 2, 'cures' 6-year-old sister of thalassemia

'Saviour siblings' are conceived through IVF and subject to pre-implantation genetic screening of inherited conditions. This is then used to select for embryos that may be a transplant match for an existing child. This process was used to cure a 6-year-old in India from **thalassemia**.

3.7 Sickle Cell Disease (SCD)

Cost-effectiveness analysis of adding omega-3 or vitamin D supplementation to standard therapy in treating painful crises of pediatric sickle cell disease patients

This study found adding **omega-3 or vitamin D supplements** boosts the therapeutic effectiveness of standard therapy for **vaso-occlusive crises (VOCs)** in **paediatric sickle cell disease (SCD)** patients. VOC is a common complication of SCD, causing blocked blood flow and depriving the tissues of oxygen. Omega-3 supplements reduced the number and severity of VOCs, while vitamin D lessened their severity only. Supplementation also reduced the number of days spent in the hospital but was associated with a slight increase in medical costs.

Reduction in vaso-occlusive events following stem cell transplantation in patients with sickle cell disease

Pain is the most prominent symptom of **sickle cell disease (SCD),** caused by recurrent **acute vaso-occlusive events (VOE)** that become more frequent and severe over the lifetime of the patient. **Haematopoietic stem cell transplantation (HSCT)** is potentially curative for patients with SCD, however there is little published data on the change in VOE following HSCT. This study demonstrates a reduction in VOE after allogeneic HSCT and the researchers plan to use these results to inform the development of novel HSCT gene therapy treatments.

Motixafortide to be tested for stem cell mobilization in SCD

The safety and feasibility of using **motixafortide for stem cell mobilization** in people with **sickle cell disease (SCD)** will be tested in a Phase 1 clinical trial. Stem cell mobilization is an essential step for gene therapies, but currently used mobilization regimens can cause serious side effects in SCD patients. This Phase 1 trial aims to assess if **motixafortide**, alone or in combination with other agents, may be a potential alternative to these regimens. The ability of motixafortide to increase stem cell mobilization for collection and later use has been successfully tested in other diseases, including multiple myeloma. Its effects will be assessed when the therapy is used alone and in combination with **natalizumab**, an antibody-based therapy for multiple sclerosis sold under the brand name **Tysabri** that also has hematopoietic stem cell mobilizing capabilities.

BioLineRx, **motixafortide's** developer, and the Washington University School of Medicine in St. Louis, Missouri, will collaborate on the planned trial. Enrollment is scheduled to begin in the second half of this year.

3.8 Other blood diseases and treatments

Drug once tested for hepatitis B could help rare bone marrow syndrome (fiercebiotech.com)

Research led by Washington University School of Medicine in St. Louis has identified a possible treatment strategy for a **rare bone marrow failure syndrome that is named poikiloderma with neutropenia**. The work also may have implications for treating other bone marrow failure syndromes with similar underlying dysfunctions.

Boy with rare genetic disorder cured at BGS

A 13-year-old child was admitted to BGS Gleneagles Global Hospital in India. Following a clinical evaluation and complete assessment, indications were that he had **Fanconi anaemia** (**a rare form of aplastic anaemia affecting the bone marrow**) which had transformed to **Acute Myeloid Leukemia** (AML). A haploidentical allogeneic haemopoietic stem cell transplant (HSCT) from a parent was performed as no identical match could be found. The transplant was successful, and the boy discharged. One of the boy's doctors noted that this case serves as an illustration of how confidence in science, perseverance, and teamwork can produce valuable outcomes for patients.

Pioneering "poo transplant" trial gives hope to severely ill cancer patients

Faecal microbiota transplant (FMT) is emerging as an exciting potential treatment for a range of conditions. This is the first time FMT will be trialed in Australia in blood cancer survivors who have developed severe Graft-versus-Host-Disease (GVHD), which is caused by their lifesaving bone marrow transplant when donor immune cells attack the recipient's organs and tissues.

Waldenström macroglobulinemia treatment moves away from chemotherapy

Waldenström macroglobulinaemia is a rare cancer of the bone marrow that results in abnormally high numbers of B-cells (a type of white blood cell). Clinical trials across the US, Canada and Europe are combining **Bruton's tyrosine kinase (BTK) inhibitors** with chemotherapy or other agents to try to provide patients with faster, deeper responses, that will hopefully last longer into the future.

SYK Inhibitor Promising in Early Trial of Primary ITP

A small, randomized, Phase I/II trial carried out in China and published in the Lancet investigated the safety, tolerability, and effectiveness of **spleen tyrosine kinase (SYK)** inhibitor, **Sovleplenib**, as a treatment option for **primary immune thrombocytopenia**. Based on this, a phase 3 trial is ongoing to confirm the efficacy and safety of Sovleplenib.

4 Blood practice trends and patient blood management

4.1 Donations

An international comparison of haemoglobin prediction models for blood banking

Blood banks use a **haemoglobin (Hb) threshold** before blood donation to minimize donors' risk of **anaemia**. In this paper, researchers compared the outcome of various prediction models for haemoglobin thresholds in different settings and highlighted differences and similarities.

- Within countries, different haemoglobin deferral prediction models perform similarly well.
- The relative importance of predictor variables is very similar across countries.
- Performance of models in different settings is dependent on the deferral rate. As a result, prediction models may be of higher value in countries with higher deferral rates.

4.2 Screening and cross-matching

A report on a modified protocol for flow cytometry-based assessment of blood group erythrocyte antigens potentially suitable for analysis of weak ABO subgroups

Weaker subgroups of the ABO blood groups can cause discrepancies and diagnostic difficulties in routine blood banking. This paper describes a new method that has the potential to provide **a quick reliable test using flow cytometry**. Researchers hope that, in the future, this method will provide a quick and reliable assay useful in **transfusion medicine**, especially for an in-depth characterization of rare weak ABO variants in collaboration with traditional serological and genetic tests.

4.3 Inventory management

Managing the Lifeblood of Healthcare: A Comprehensive Analysis of the Blood Bank Information Systems Market

Allied Market Research have released a new business intelligence report on **the global Blood Bank Information Systems market**, which is expected to grow by 7.8% (CAGR – compound annual growth rate) between 2021 and 2023. Blood Bank Information Systems are software applications used by blood banks to manage the process of collecting, testing, and storing blood. It also helps in managing donors and patients, communication with clients, and integrated with other hospital management systems for easy sharing of data.

The outbreak of the COVID-19 pandemic had a negative impact on the global Blood Bank Information Systems Market. Blood banks, blood centers, and governments were compelled to adopt new policies to adapt to a decreased blood supply as well as to protect the donors from COVID-19 infection.

Top impacting factors included:

- increasing demand for blood and blood products
- advancements in technology
- stringent regulatory requirements
- increasing prevalence of chronic diseases
- aging infrastructure in many blood banks.

4.4 Transfusion

Genetics and machine learning can improve blood transfusion outcomes

This UK research project is a collaborative effort between NHS Blood and Transplant (NHSBT) and the Blood Transfusion Genomics Consortium (of which Australian Red Cross Lifeblood is a member). Current methods for extended blood group antigen typing are costly and extremely time intensive, meaning that NHSBT can only type 15% of its donors for all medically relevant antigens. This project is investigating improvements to patient care through the introduction of genomics and artificial intelligence (AI) for extended blood matching into routine care pathways.

Development and validation of a prediction model for need for massive transfusion during surgery using intraoperative haemodynamic monitoring data

This prognostic study examined the possibility of using **intraoperative haemodynamic data** to predict massive transfusion and allow for early intervention for high-risk patients. Using retrospective data, the study showed that **machine-learning-developed algorithms** can successfully

classify patients as high risk and in need of attention and intervention and explored the possibility of using an **artificial intelligence clinical decision support system (AI-CDSS)** for clinical practice. Future prospective studies are needed to determine the extent to which early intervention for patients with massive haemorrhage can improve clinical outcomes.

The Impact of Restrictive Transfusion Practices on Haemodynamically Stable Critically Ill Children Without Heart Disease: A Secondary Analysis of the Age of Blood in Children in the PICU Trial

Researchers sought to assess the clinical and economic impact of **compliance with red blood cell (RBC) transfusion guidelines through secondary analysis of data** from 50 international tertiary care centers. Guidelines recommend against RBC transfusion in haemodynamically stable (HDS) children without cardiac disease if haemoglobin is greater than or equal to 7 g/dL. They found that adherence to the guidelines is not associated with increased organ dysfunction in this population but is independently associated with increased likelihood of live ICU discharge and lower ICU costs.

Comparison of computerized provider order entry specific transfusion indications versus the use of "Other"

The purpose of this study was to examine how frequently healthcare providers were selecting "Other" when placing orders for red blood cells (RBCs), platelets and fresh frozen plasma (FFP), and to assess the free-texted reasons for these "Other" orders. The new **Computerised Provider Order Entry (CPOE) system** at the high product-ordering areas of Long Island Jewish Medical Center and Cohen's Children's Medical Center, from April to November 2021, allowed healthcare providers to select "Other" as an indication and provide reasons for transfusion outside of accepted guidelines.

The study (though limited in scope) provided indications that "Other" is often selected when there is a prepopulated alternative. The results also raised questions about the efficacy of CPOE as a means of **reducing unnecessary transfusions and potential blood overuse**. Examination of "Other" orders and the reasons for them revealed trends that could inform educational initiatives to better improve the utilization of blood products and patient outcomes.

Two-year outcomes following a randomised platelet transfusion trial in preterm infants

Fifteen million infants are born prematurely globally each year and, despite significant advances, extreme prematurity continues to be associated with long-term impairment, and a high risk of death and major brain injury. Many such infants with **thrombocytopaenia** receive platelet transfusions despite no evidence that this prevents bleeding and increasing concerns about potential harm.

The study found that a higher platelet count threshold of 50×10^9/L for prophylactic transfusion in preterm infants less than 34 weeks' gestation at birth increased the rate of death or neurodevelopmental impairment at 2 years of corrected age. There is no evidence to support benefit for high prophylactic platelet transfusion thresholds in the preterm infant. There is increasing evidence of harm persisting into childhood.

Opinion piece: Balanced transfusion: Less evidence than you might think

This opinion piece questions the evidence base for 1:1:1 red blood cell, plasma and platelet ratios for balanced transfusion in trauma and other bleeding patients. The author speculates there may be inherent bias in the evidence, given that plasma and platelets are generally given after red blood cells, therefore suggesting that patient survival rates are harder to attribute. Note: An internet search did not find any further debate.

4.5 Haemovigilance

Haemovigilance: Giving it our best SHOT!

The UK's Serious Hazards of Transfusion (SHOT) program has been in operation since 1996. In this commentary, the authors summarise some of SHOT's achievements and consider what can be learned from their experience and findings.

Haemovigilance has evolved from an initial focus on transfusion-transmitted infections (which triggered the establishment of programs globally) to a much broader approach. Haemovigilance links closely with national blood policy development, patient blood management and with changes in blood product manufacturing (from donor to recipient). It also provides a foundation for research efforts – identifying areas of need and measuring change effects, and that many gaps still exist.

Case report: Successful treatment with plasma exchange in life-threatening hyperhaemolytic syndrome unrelated to sickle cell disease

Hyperhaemolytic syndrome (HHS) is a severe form of delayed transfusion reaction primarily described in **sickle cell anemia** patients. It is characterised by a haemoglobin decrease to pre-transfusion levels or lower, often with reticulocytopenia and no evidence of auto or allo-antibodies. This report presents two cases of severe HHS in patients without sickle cell anaemia, refractory to treatment with steroids, immunoglobulins, and rituximab. In both cases, plasma exchange resulted in a profound and immediate response allowing for splenectomy and resolution of haemolysis. The study concluded that use of plasma exchange should be considered as a supportive measure by clinicians who are treating life-threatening cases of HHS.

The impact of revised definitions for transfusion-associated circulatory overload and transfusion-related acute lung injury on haemovigilance reporting

This Australian Red Cross Lifeblood study aimed to assess the impact of the new transfusion-associated circulatory overload (TACO) and transfusion-related acute lung injury (TRALI) definitions on haemovigilance reporting. This is the first study that has provided data for the revised TRALI definition, with comparison on each of the definitions available in the linked article. The study found that the revised TACO definition captured more cases than the former definition, and no significant differences were observed in the number of TRALI cases under the proposed new definition.

Transfusion related TRALI: a retrospective review of reported cases in Queensland over 20 years

Transfusion related acute lung injury (TRALI) is a rare but potentially fatal transfusion reaction. An effective haemovigilance program is important in implementing successful and targeted risk reduction strategies. The report provides a summary of TRALI cases (in Queensland over the past 20 years) referred for investigation and describes the epidemiological and laboratory features of local TRALI cases.

Management of wrong blood transfusion to an RhD negative woman in labor

This article discusses an emergency blood transfusion of a young woman during delivery and surgical removal of retained placenta. The patient was RhD negative, and the packed red blood cells (PRBCs) transfused were RhD positive. Realising the mistake, the woman's medical team managed with high dose anti-D immunoglobulin to remove the RhD positive red blood cells from the patient's circulation. Follow-up was performed by flow cytometry until RhD positive RBCs were no longer detected. Ten months after the delivery, antibody screening was negative, however there were no results to prove the procedure had prevented RhD-alloimmunisation.

Comparison of Blood Transfusion Rates Before and After Implementation of a Quality Improvement Initiative for Transfusion Safety and Appropriateness

In July 2019, the McGill University Health Center (MUHC) in Montreal implemented a requirement for all incoming resident physicians to complete a haemovigilance transfusion training module. This quality improvement study compared the blood transfusion rates before and after implementation of this training. The findings suggest that the implementation was associated with a decrease in the rate of blood transfusions, and that such an approach could be a low-cost, low-barrier intervention to improve transfusion appropriateness.

5 COVID-19

Inactivation of SARS-CoV-2 infectivity in platelet concentrates or plasma following treatment with ultraviolet C light or with methylene blue combined with visible light

COVID-19 is unlikely to be a major transfusion-transmitted pathogen. However, convalescent plasma is a treatment option used in some regions. The risk of transfusion-transmitted infections can be minimized by implementing Pathogen Inactivation (PI), such as THERAFLEX MB-plasma and THERAFLEX UV-Platelets systems. This paper explores the capability of these systems.

Two approaches to tackling COVID-19 in patients with blood cancer

Patients with blood cancer have fewer antibodies after SARS-CoV-2 vaccination — but recent work shows that these antibodies seem to bind to viral spike protein more strongly than those in matched controls. In addition, another study finds that convalescent or vaccinee plasma might improve **COVID-19** outcomes in those with blood cancer.

The authors suggest that antibody affinity maturation might be more rapid in individuals with B cell malignancies, which leads to a multitude of important mechanistic questions relevant to the understanding of B cell development and vaccine design.

Convalescent plasma (hyperimmune immunoglobulin) for COVID-19 management: An update

Convalescent plasma therapy (CPT) or hyperimmune immunoglobulin (HI) has been effectively used in the treatment of many endemic or epidemic viral infections as a part of passive immunization. This paper is a review of literature regarding trials and research work regarding CPT for the treatment of a range of diseases. This includes various research approaches, clinical trials conducted globally, and the clinical trials exploring the efficacy and safety of CPT to predict its future perspective to manage **COVID-19**. The authors conclude that CPT or HI have great potential in the future for the management of COVID-19 but requires more research and clinical evidence.

Two Case Reports of Chronic Inflammatory Demyelinating Polyneuropathy After COVID-19 Vaccination

The occurrence of chronic inflammatory demyelinating polyneuropathy (CIDP) related to coronavirus disease 2019 (COVID-19) has rarely been reported. This paper reports on two such cases and their treatment.

COVID-19 Serology Data Provide Guidance for Future Deployments of Convalescent Plasma

When COVID-19 pandemic struck the USA in spring 2020, the country responded by deploying convalescent plasma (CP) as an emergency interim therapy, resulting in treatment of >50,000

hospitalised patients. CP was deployed in the absence of specific therapies but based on historical knowledge of efficacy against prior epidemics.

The resulting serological data has now been analysed to provide learnings and insights for the next infectious disease emergency. The researchers found that measurement of antibody content and function after a viral illness is important for diagnosis and selection of the best convalescent plasma (CP) units for passive immunization.

Analysis of the COVID-19 serology data (>19,000 samples) suggest that, for the next infectious disease emergency, the best approach after quick establishment of methods for robust antibody-level stratification would be to administer CP in the top quintile of antibody content and neutralizing capacity.

6 Blood sector research and development

Ordaōs and Yatiri Bio to tackle acute myeloid leukemia through cell surface treatments

Recent advances in machine learning, mass spectrometry, bioinformatics, and ex-vivo model systems have the potential to drive a new era of precision oncology for **acute myeloid leukaemia** patients and the development of therapeutics specifically for relevant patient subsets. **Yatiri Bio's** ability to identify drug targets combined with **Ordaōs** capability in designing and creating mini proteins shows great promise in helping to discover therapeutic targets for diseases with unmet needs.

Stopping blood loss with a bandage covered in microneedles

Chemical and biomedical engineers have designed a new type of bandage that can **stop uncontrolled bleeding from a traumatic injury** almost immediately. The prototype patch uses **haemostatic microneedle technology** – biocompatible and biodegradable microneedle arrays (MNAs) – that increase its surface contact with blood to accelerate the clotting process. The patch is designed to be prefabricated and ready for immediate use – much like a typical over-the-counter adhesive bandage.

UB receives $2.1 million grant to prevent toxic side effects of leukemia treatment

The University at Buffalo in New York has received over $2 million in grant funding from the National Cancer Institute to advance the safety and effectiveness of targeted drugs to treat **acute myeloid leukemia**. The project aims to develop **antibody-drug conjugates (ADC)** – a class of drugs that target cancer cells – as well as **payload-binding selectivity enhancers (PBSE),** a class of drugs that may help prevent anti-cancer drugs from harming healthy cells.

Microfluidic study of retention and elimination of abnormal red blood cells by human spleen with implications for sickle cell disease

The spleen clears altered red blood cells (RBCs) from circulation, contributing to the balance between RBC formation and removal. This study presents a unique 'spleen-on-a-chip' platform to study splenic retention and elimination of RBCs *in vitro*. Results provide unique mechanistic insights into how the spleen maintains its homeostatic balance, and sheds light on how disruptions in this balance could lead to anaemia, splenomegaly, and acute splenic sequestration crisis (ASSC) in **sickle cell disease** and possible clinical manifestations in other haematologic diseases.

FDA clears next generation autotransfusion software from Haemonetics

FDA provided clearance for next-generation software for the **Cell Saver Elite+ autotransfusion system**. Cell Saver Elite+ allows hospitals to recover a patient's blood in surgical procedures which have the potential for medium to high blood loss, wash it and deliver it to a product bag. The system could help to avoid unnecessary allogeneic transfusions while reducing related costs.

AMLnet, A deep-learning pipeline for the differential diagnosis of acute myeloid leukemia from bone marrow smears

A group of researchers from Zhejiang University in Hangzhu, have developed and validated an automated **acute myeloid leukaemia (AML)** diagnostic system (**AMLnet**) which they say is fast, highly accurate, and universal, and that will help eliminate intra- and inter-observer variance and facilitate the early diagnosis and treatment of AML.

According to their article in Journal of Haemotology and Oncology, AMLnet is a deep-learning pipeline that utilizes a comprehensive database encompassing 8245 bone marrow smear images from 651 patients with acute myeloid leukemia (AML) based on a retrospective dual-center study between 2010 and 2021. AMLnet has shown it can discriminate not only between AML patients and healthy individuals but also accurately identify various AML subtypes. This technology has the potential to serve as a fast prescreening and decision support tool for cytomorphological pathologists, especially in areas where pathologists are overburdened by medical demands, as well as in rural areas where medical resources are scarce.

Australian Genomics pilots a whole-of-system approach to integrating genomics into healthcare

In the first five years of operation, Australian Genomics has evaluated the outcomes of genomic testing in more than 5,200 individuals across 19 rare disease and cancer flagship studies. Partners include state/territory and federal organisations.

Australian Genomics supports government-funded genomic research projects, distils research outcomes to inform policy and practice, and progresses national standards for genomic data management.

Through networking, they aim to bring together clinicians, diagnosticians, researchers, bioinformaticians, industry, policy makers, and consumers who are united in their aim to achieve equitable and appropriate applications of genomics in healthcare.

Allies or enemies – the multifaceted role of myeloid cells in tumor microenvironment

Understanding the tumor microenvironment (TME) has paved the way for novel forms of therapy which target the immune cell compartment. For example, agents activating T lymphocytes, are thought to be effective, though in a relatively small percentage of patients. This study focused on the **myeloid compartment in the TME** and describes how distinct myeloid cell types can act as enemies of cancer cells to induce or enhance existing immune response, while others act as strong allies, supporting malignant cell growth and establishing an immune evasive TME.

8 NBA - National Blood Sector Research and Development Program

The following section includes a summary of recent results from research commissioned by NBA,

Does intravenous immunoglobulin improve outcomes in chronic rejection of renal transplants?

This project from Round 2 of the NBA's grant program is now complete. This project examined the impact **of intravenous immunoglobin (IVIg) in chronic antibody mediated rejection (cAMR)** of transplanted kidneys. The study aimed to confirm if IVIg has a benefit for cAMR patients, or if it should be reserved for conditions for which it is beneficial. Results showed that patients who received IVIg had slower progression of rejection compared with a control group. The research team, led by A/Prof William Mulley at Monash University, are preparing this work for publication and will also submit the work to the Annual Scientific Meeting of the Transplant Society of Australia and New Zealand.

Prehospital administration of freeze-dried plasma for traumatic haemorrhagic shock

This seed grant from Round 5 of the NBA's grant program is now complete. The aim of this pilot trial was to assess the feasibility of transfusing freeze-dried plasma with red blood cells (RBC), using a randomised controlled design in an aeromedical pre-hospital setting. This study is the first to report that pre-hospital use of freeze-dried plasma in Australia is feasible. The research team, led by Professor Biswadev Mitra at Monash University, have submitted a manuscript on the work to Lancet Haematology.

Completed grant exploring blood quality in cardiac surgery (ID417_Simmonds)

This National Blood Sector Research and Development Program Round 4 project led by Griffith University is now complete. The study evaluated the **effect of different blood management practices on the functional properties of the blood cells and proteins utilised during cardiopulmonary bypass (CPB)**. Researchers were able to evaluate what impact the choice of anti-coagulant has on perioperative storage of blood; the effects of the CPB pump on collected blood; and the impacts of the cell salvage process. The Principal Chief Investigator, Associate Professor Michael Simmonds, received a 2021 Rising Star Award from the International Society for Clinical Haemorheology for work funded in part by this grant. There are three planned publications linked to this project which will be published on the NBA website once available. The NBA met with the research team in February to discuss the findings of this project in more detail, please contact Research@blood.gov.au if you are interested in being involved.

9 Industry, supply chains and economy

Layoffs loom as Takeda trims early-stage efforts in AAV gene therapy, rare hematology

Takeda is moving away from early-stage R&D work in adeno-associated virus-based gene therapies and **the rare haematology spaces**, with an unknown number of employees set to "transition out" of the pharma. The company has informed its team that discovery and preclinical efforts in adeno-associated virus-based (AAV) gene therapy will be discontinued, alongside research and preclinical work in rare haematology. The move is reported to allow Takeda to focus more on core therapeutic areas and late-stage clinical programs.

Takeda pledges $770M for plasma-derived therapy plant in Japan (fiercepharma.com)

Takeda revealed plans to invest about 100 billion Japanese yen ($764.6 million) to build a **new state-of-the-art production facility in Osaka** that will be operational by around 2030. The facility will not only serve more patients in Japan but will offer extra capacity for the company's overall global production network.

Rare blood disorders biotech Hemab raises $135M, begins trek into clinic

Hemab Therapeutics, a biotech company, has raised $135 million from new investors **to push its blood disorder programs into the clinic**. The biotech has a list of goals it wants to check off before then, including having five clinical candidates by 2025. Hemab have confirmed they do not plan to work on haemophilia A or B and is instead developing treatments for neglected bleeding disorders that currently have few or no approved options.

Why dynamic data feeds are critical for successful commercial machine learning models

'Data drift' is a huge challenge in the pharma industry as companies are dealing with massive volumes of complex and diverse data that are not always generated or accessible in real-time to update machine learning (ML) models. Inaccurate, outdated, or incomplete data can have a profound impact on the accuracy of predictive models and ultimately, healthcare decisions. **Predictive analytics** can be particularly helpful in identifying new opportunities by forecasting market trends and predicting future demand for specific products or treatments. For instance, these models can identify markets that are likely to experience growth based on demographic trends, emerging health risks, and regulatory changes.

10 Government, policy and regulation

Health Technology Assessment Policy and Methods Review

Under the 2022-27 Strategic Agreement with Medicines Australia (Strategic Agreement) the Department of Health and Aged Care will support and resource a Health Technology Assessment (HTA) Policy and Methods Review (Review). A public consultation on the draft Terms of Reference (ToR) for the Review will close on 20 January 2023.

MSAC - Documents for Applicants and Assessment Groups

The enhanced Medical Services Advisory Committee (MSAC) application forms are now available in the Health Products Portal (HPP) for use by applicants to lodge applications for the 24 March 2023 deadline. The MSAC application form has been enhanced to address feedback provided by MSAC applicants from the recent MSAC cycles. The enhancements will make the completion of an application in the Health Products Portal easier, and better support collaboration.

11 Global change: social, environmental and economic

Climate change and parasitic risk to the blood supply

Climate change has a range of impacts on human disease with implications for blood operators and clinicians.

A systematic review in Transfusion journal highlights the potential for climate change to impact the epidemiology of pathogenic diseases agents (including viruses, bacteria and parasites), and the flow on effects for blood transfusion safety. As global temperatures continue to increase, along with the frequency of extreme events, human migration, increases in conflict (particularly over scarce

resources) and more frequent infectious disease outbreaks. Climate change impacts local ecosystems and habitats, which has significant implications for increasing risk of human exposure to disease and emergence of new pathogens. While the paper offers not specific recommendations to blood operators, the authors urge vigilance and ongoing monitoring of impacts. This may include connecting with public health organisations and One Health initiatives that are already tracking infectious agents.

12 Other diseases

12.1 Malaria

- WHO Guidelines for Malaria
- Non-invasive malaria screening device uses light for diagnosis
- Malaria: COVID RAT-style test to expose parasite that hides in your body
- A nasal algae vaccine against malaria
- Low-dose intravenous and subcutaneous CIS43LS monoclonal antibody for protection against malaria
- Japanese firms get GHIT funding for malaria drug development
- WHO publishes recommendations on two new types of insecticide-treated nets
- Ghana first to approve Oxford's malaria vaccine

Ghana is the first country to approve a new malaria vaccine, R21, which appears to be more effective than previous ventures. The World Health Organization is also assessing the vaccine for approval. Malaria kills around 620,000 people per year.

12.2 Dengue

- Malaysia reports nearly 150% increase in dengue in 2022 - Outbreak News Today
- NEA warns of another dengue outbreak in 2023 as cases remain high in Singapore
- Malaysia dengue cases up 211% in 2023 to date
- Lab-Bred Mosquitos Could Slow the Spread of a Deadly Human Disease
- Ibiza is put on dengue fever alert after tourists catch disease on holiday island
- The resurgence of dengue epidemic and climate change in India
- More than half of children in US Virgin Islands have had dengue, making them eligible for vaccine
- Dengue Antiviral Candidate Found Efficacious and Safe

12.3 Japanese Encephalitis

- Australia: First Japanese encephalitis case of season reported in Victoria
- Mandatory reporting of Japanese encephalitis virus vaccines to the Australian Immunisation Register began on 21 December 2022

Risk of ongoing Japanese Encephalitis outbreaks in Australia

The article by Dr Sarah Allen and colleagues based at the Women's and Children's Hospital in Adelaide states that the virus is likely to persist in mainland Australia. "**Japanese Encephalitis Virus (JEV)** is known to overwinter in temperate regions and cause seasonal summer–autumn outbreaks, so there is potential that JEV might become an ongoing seasonal challenge in temperate Australia," the researchers wrote.

12.4 Haemorrhagic fevers (filoviruses e.g. Ebola)

Second outbreak of Marburg virus in Africa

Both Equatorial Guinea and now Tanzania have recently reported cases of Marburg disease (an hemorrhagic fever disease closely related to Ebola). The outbreak could mean climate change is playing a role, due to higher average temperatures leading to host animals and the viruses they carry moving to new parts of the world.

12.5 Mpox (monkeypox)

As of 28 November 2022, the WHO will begin using a new preferred term "mpox" as a synonym for monkeypox. Both names will be used simultaneously for one year while "monkeypox" is phased out.

- WHO recommends new name for monkeypox disease
- Epidemiology of Human Mpox — Worldwide, 2018–2021
- CDC panel recommends Bavarian Nordic's Mpox vaccine for all adults at risk
- CDC Offers Tentative Guidance for Severe Mpox Treatment
- Mpox is highly fatal among people with advanced HIV, study finds
- Known active ingredient as new drug candidate against mpox
- New Artificial Intelligence-Based App Detects Mpox Rashes
- Mexico reports more than 50 Mpox cases in two weeks

12.6 Bird Flu

- H5N1: Two human bird flu cases detected in China as outbreak spreads
- Global H5N1 bird flu outbreak so bad many countries are now considering vaccination
- Avian flu reappears in Cambodia, UN health agency warns

12.7 Murray Valley encephalitis

- Man in hospital with Murray Valley encephalitis, first NSW case of the virus since 2011

12.8 Zika virus

- Hungary reports two Zika virus infections in travelers to Thailand

13 In case you missed it

Blood cancer patient Nikki Wagner pays $250,000 for treatment

This story looks at the out-of-pocket treatment costs for blood cancer patients by exploring patient stories and a report from the Leukaemia Foundation.

Evaluation of maternal infection during pregnancy and childhood leukemia among offspring in Denmark

This cohort study suggests that certain types of maternal infection during pregnancy were associated with an increased risk of childhood leukemia.

First transfusion of lab grown blood cells
First HIV Remission in Patient Treated With Stem Cells From Cord Blood

Leukaemia Foundation calls for action on too many blood cancer deaths

A new report "State of the nation: Blood cancers in Australia" released by the Leukaemia Foundation states that blood cancers combined are now the second most common cause of cancer death in Australia. Key findings include lack of consistency in Australia's healthcare system impacts blood cancer patients, lack of equity in treatment access, lack of access to supportive care and the financial burden of treatment (partly due to soaring costs).