MONASH University

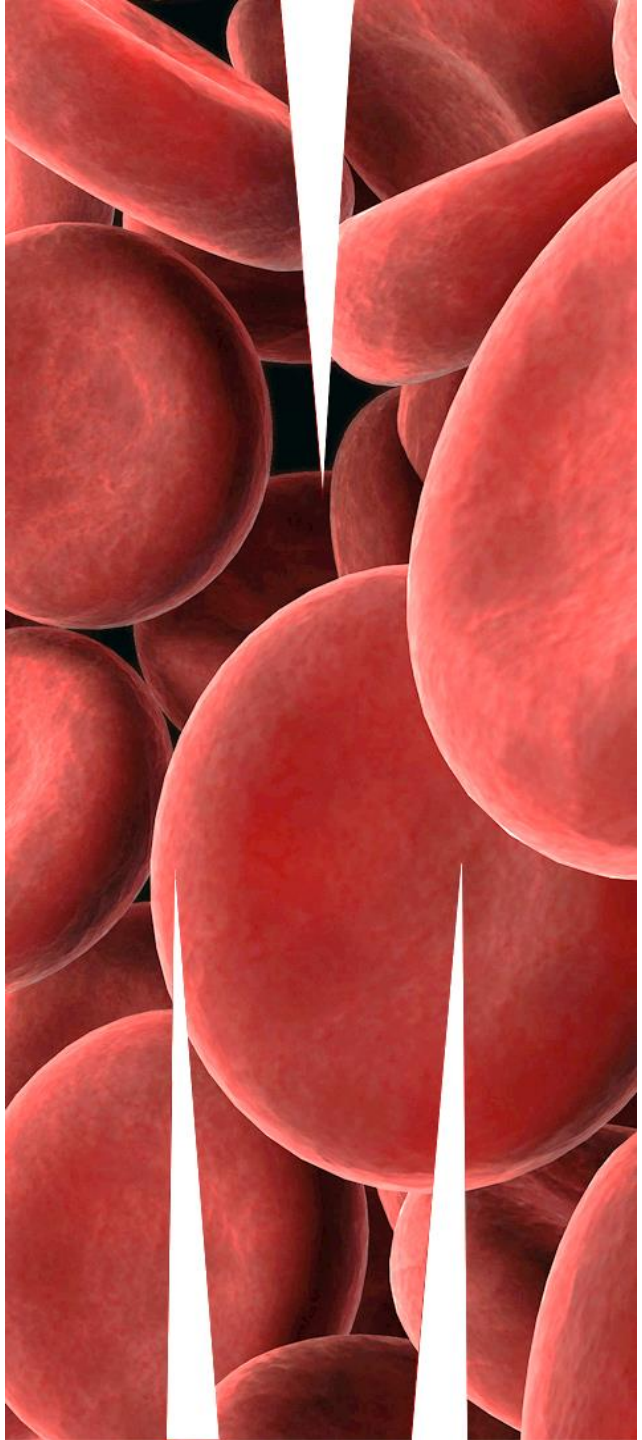
Immunoglobulin therapy in the bispecifics era

Erica Wood
Transfusion Research Unit
School of Public Health and Preventive Medicine, Monash University

Haematologist, Monash Health

Erica.wood@monash.edu

transfusion research unit

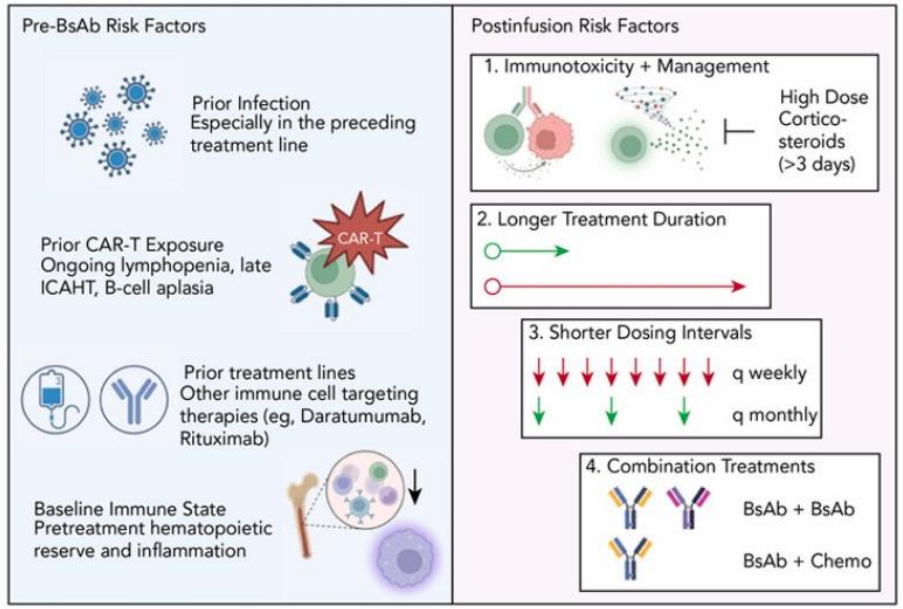


How should we use Ig for patients receiving BsAbs?

MONASH University

transfusion research unit

How I Prevent Infections in Adults Receiving Bispecific Antibody Therapies for Advanced B-Cell Malignancies



Key abbreviations: BsAb, bispecific antibody; CAR-T, chimeric antigen receptor T-cell.

Risk factors for infections	BsAb	CAR-T
Therapy target		
BCMA	++	++
CD19	+	+
CD20	+	+
GPRC5D	+	+
Initial risk factors (within first month)		
Lymphodepletion		+++
T-cell dysfunction/exhaustion	+	
Early ICAHT	+	+++
CRS	+	++
Tocilizumab and/or anakinra	+	++
Corticosteroids	+	++
Delayed risk factors (after first month)		
Repeated dosing	+++	
T-cell dysfunction	++	+
Delayed cytopenias	+	++
Infection prevention strategies (see text for details)		
Viral		
HSV and VZV prophylaxis	+++	+++
CMV monitoring	+	+
Bacterial and fungal		
Fluoroquinolones		+
PJP prophylaxis	+++	+++
Mold prophylaxis		+
IGRT based on target		
BCMA	+++	+
CD19	+	+
CD20	+	+
GPRC5D	++	+

Conclusions: **T-cell engaging bispecific antibodies have transformed the treatment landscape in non-Hodgkin lymphoma and multiple myeloma but present unique patterns of infections. Infection prevention strategies are critical to optimize outcomes and should therefore be considered essential components of treatment delivery.**

*Rejeski et al. DOI: 10.1182/**blood**.2025032298*

blood Visual Abstract

MONASH University

transfusion research unit

Hypogammaglobulinaemia and infections in patients receiving bispecific therapies

- Patients profoundly immunosuppressed (multifactorial)
- Bacterial, viral, fungal, other infections common
- Immunoglobulin replacement therapy (IgRT) widely used
- Retrospective studies, but no RCT Ig vs…
- Trial data ≠ real world data

MONASH University

transfusion research unit

Infections are common and may be severe

ORIGINAL ARTICLE

Incidence, timing, and management of infections in patients receiving teclistamab for the treatment of relapsed/refractory multiple myeloma in the MajesTEC-1 study

Ajay K. Nooka MD[1] | Cesar Rodriguez MD[2] | María Victoria Mateos MD, PhD[3] | Salomon Manier MD, PhD[4] | Katherine Chastain MD[5] | Arnob Banerjee MD, PhD[6] | Rachel Kobos MD[5] | Keqin Qi PhD[7] | Raluca Verona PhD[6] | Margaret Doyle MSc[8] | Thomas G. Martin MD[9] | Niels W. C. J. van de Donk MD, PhD[10]

Cancer. 2024;130:886–900

Infections in 80%, grade 3/4 in 55.2%:

- COVID-19 (21.2%)
- respiratory (19.4%)
- *Pneumocystis jirovecii* pneumonia (4.2%)
- viral (4.2%)
- GI infections (1.2%)

- 70.9% had 1+ IgG level <400 mg/dL
- Median 1.2m to IgG <400 (0.2–19.8)
- 46% received 1+ dose of IgG replacement
- Grade 3/4 neutropenia in 65.5% (median 2.3m to grade ≥3/febrile neutropenia [0–18.1])

MONASH University

transfusion research unit

Infections are common and may be severe

REGULAR ARTICLE

blood advances

Early mortality with bispecific antibody therapy in RRMM: an IMWG immunotherapy database real-world analysis

Carlyn Rose Tan,[1] Saad Usmani,[1] Andriy Derkach,[2] Andre de Meneze Silva Corraes,[3] Ricardo Parrondo,[4] Sikander Ailawadhi,[4] Sireesha Asoori,[5] Mrugakshi Dave,[6] Rakesh Popat,[7] Oliver Morjaria,[7] Roman Hajek,[8] Jana Mihalyova,[8] Myo Htut,[9] Murali Janakiram,[9] Alissa Visram,[10] Efstathios Kastritis,[11] Meletios A. Dimopoulos,[11] Joaquín Martínez-López,[12] Chandramouli Nagarajan,[13] Susan Bal,[14] Luciano J. Costa,[14] Hermann Einsele,[15] Torsten Steinbrunn,[15] Johannes M. Waldschmidt,[15] Christine Riedhammer,[15] Rahul Banerjee,[16] Wee Joo Chng,[17] Allison Tso,[18] Yi Lin,[3] Thomas Martin,[5] and Hira Mian[10]

12 MAY 2026 • VOLUME 10, NUMBER 9

MONASH University

transfusion research unit

Infections are common and may be severe

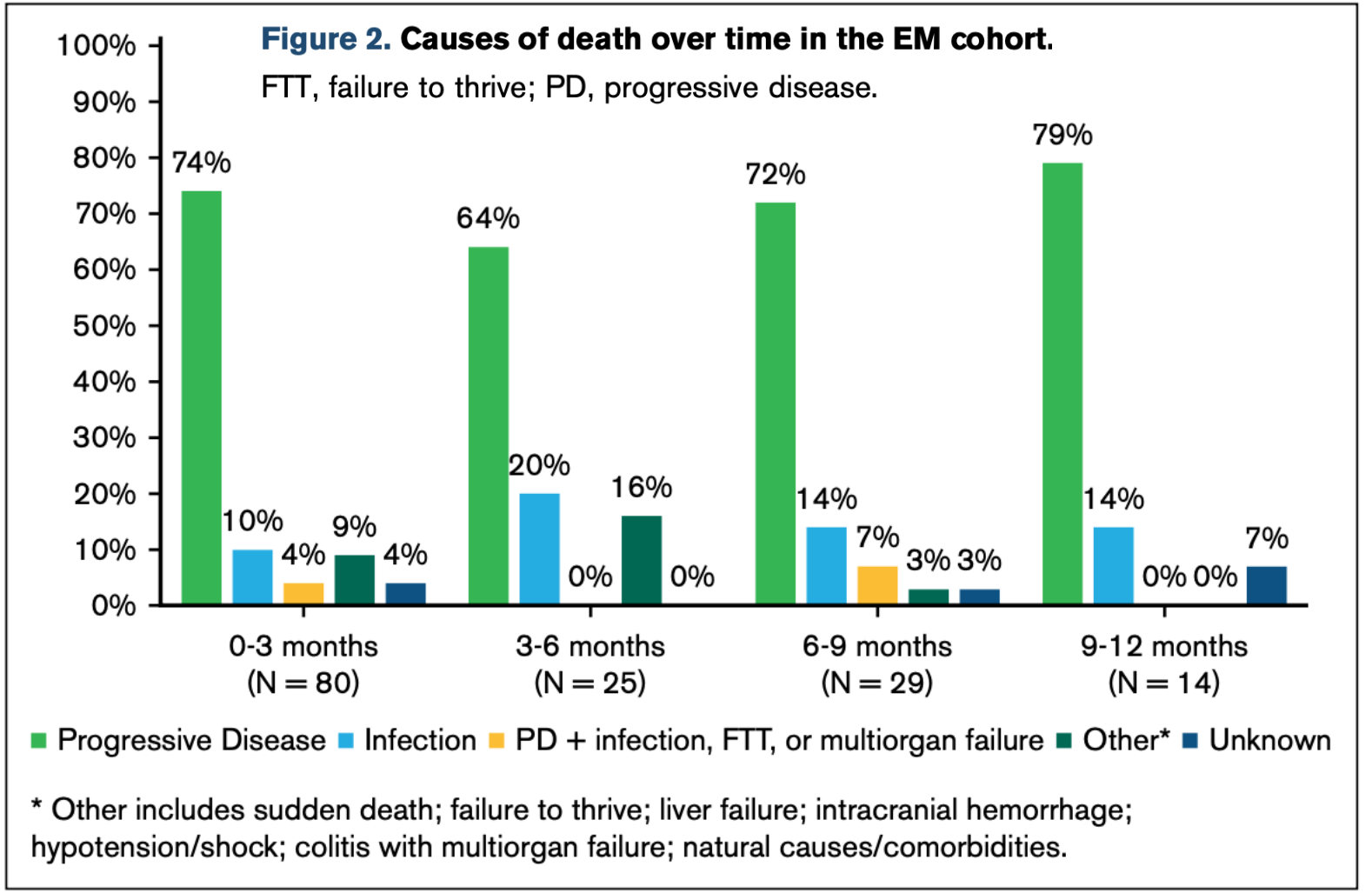


Figure 2. Causes of death over time in the EM cohort.

FTT, failure to thrive; PD, progressive disease.

* Other includes sudden death; failure to thrive; liver failure; intracranial hemorrhage; hypotension/shock; colitis with multiorgan failure; natural causes/comorbidities.

MONASH University

transfusion research unit

Infections are common and may be severe

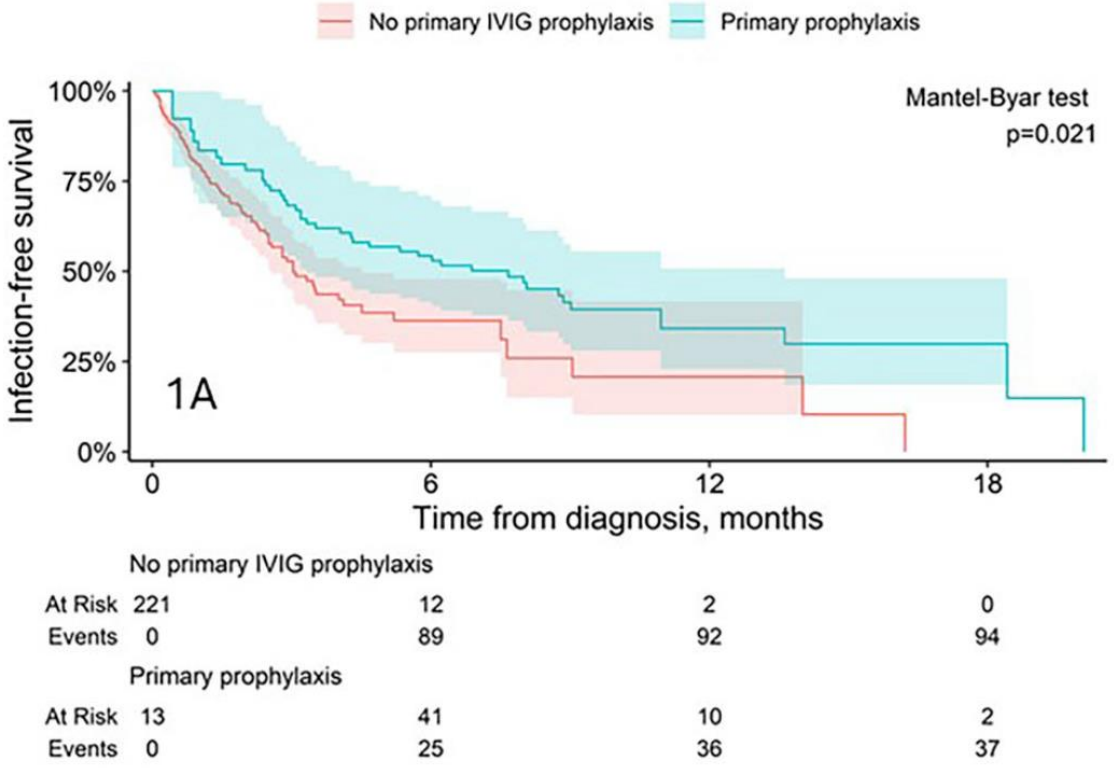
Effect of Intravenous Immunoglobulin (IVIG) Supplementation on infection-free survival in recipients of BCMA-directed bispecific antibody therapy for multiple myeloma

Meera Mohan[1]✉, Aniko Szabo[2], Heloise Cheruvalath[3], Anna Clennon[4], Vineel Bhatlapenumarthi[1], Anannya Patwari[1], Metodi Balev[5], Divaya Bhutani[5], Asis Shrestha[6], Sharmilan Thanendrarajan[6], Binod Dhakal[1], Maurizio Zangari[6], Anup Trikannad[6], Sruthi Vellanki[6], Samer Al-Hadidi[6], Suzanne Lentzsch[5], Frits van Rhee[6], Aishee Bag[7], Anita D'Souza[1], Nishi Shah[8], Rajshekhar Chakraborty[5], Mansi R. Shah[7] and Carolina Schinke[6]

Blood Cancer Journal (2025)15:74

MONASH University

transfusion research unit



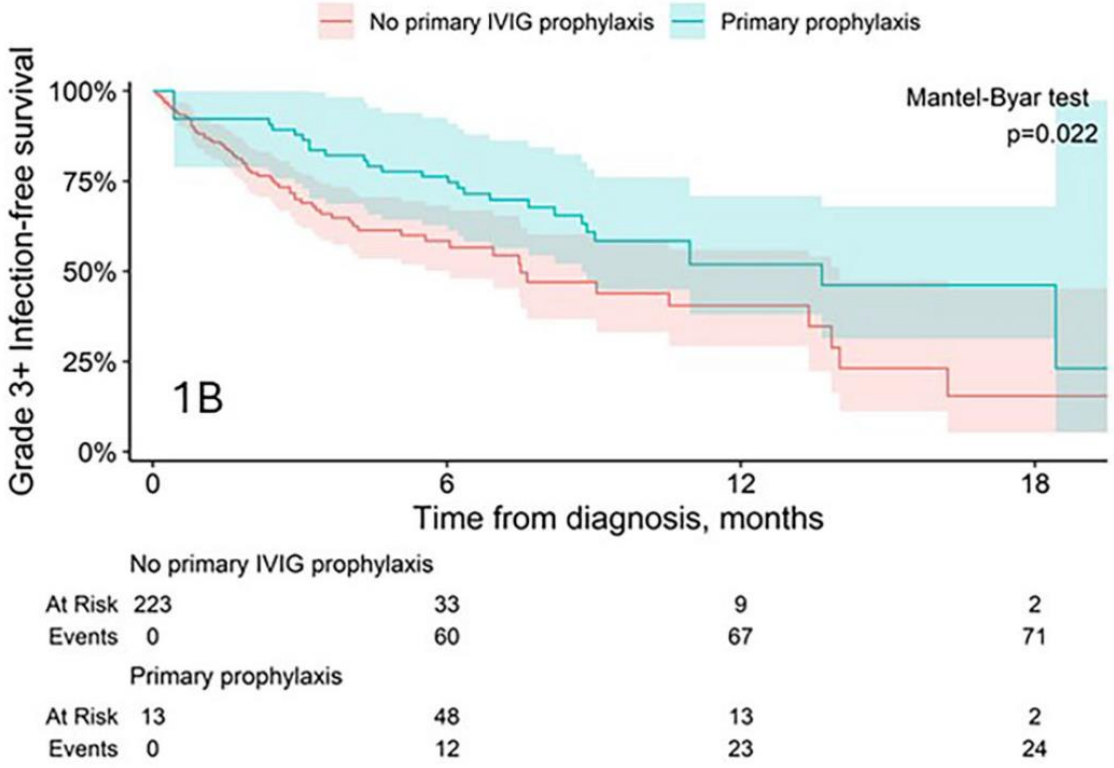


Fig. 1 Infection-free-survival. Infection-free-survival for all-grade infection (**A**) and ≥ grade 3 infection (**B**) in patients treated with and without primary IVIG.

RESEARCH LETTER

blood advances

Cytomegalovirus reactivation in patients with multiple myeloma receiving bispecific antibodies

Enric Sastre-Escolà,[1-3] Gemma K. Reynolds,[4-7] Michelle K. Yong,[4-6,8] Violet Zhu,[4-6] Simon J. Harrison,[4,6,9] Amit S. Khot,[6,9] Monica A. Slavin,[4-6,8] and Benjamin W. Teh[4-6]

[1]Infectious Diseases Department, Bellvitge University Hospital, Bellvitge Biomedical Research Institute, University of Barcelona, L'Hospitalet de Llobregat, Spain; [2]Centro de Investigación Biomédica en Red de Enfermedades Infecciosas, Instituto de Salud Carlos III, Madrid, Spain; [3]Hospital Duran i Reynals, Institut Català d'Oncologia, Barcelona, Spain; [4]National Centre for Infections in Cancer and [5]Department of Infectious Diseases, Peter MacCallum Cancer Centre, Melbourne, VIC, Australia; [6]Sir Peter MacCallum Department of Oncology, The University of Melbourne, Melbourne, VIC, Australia; [7]Department of Infectious Diseases and Immunology, Austin Health, Melbourne, VIC, Australia; [8]Victorian Infectious Diseases Service, The Royal Melbourne Hospital, Melbourne, VIC, Australia; and [9]Department of Clinical Hematology, Peter MacCallum Cancer Centre and The Royal Melbourne Hospital, Melbourne, VIC, Australia

28 JULY 2026 • VOLUME 10, NUMBER 14

MONASH University

transfusion research unit

Infection prevention, treatment, monitoring and reporting not standardised

With thanks to Manu Juneja, Zoe McQuilten and colleagues

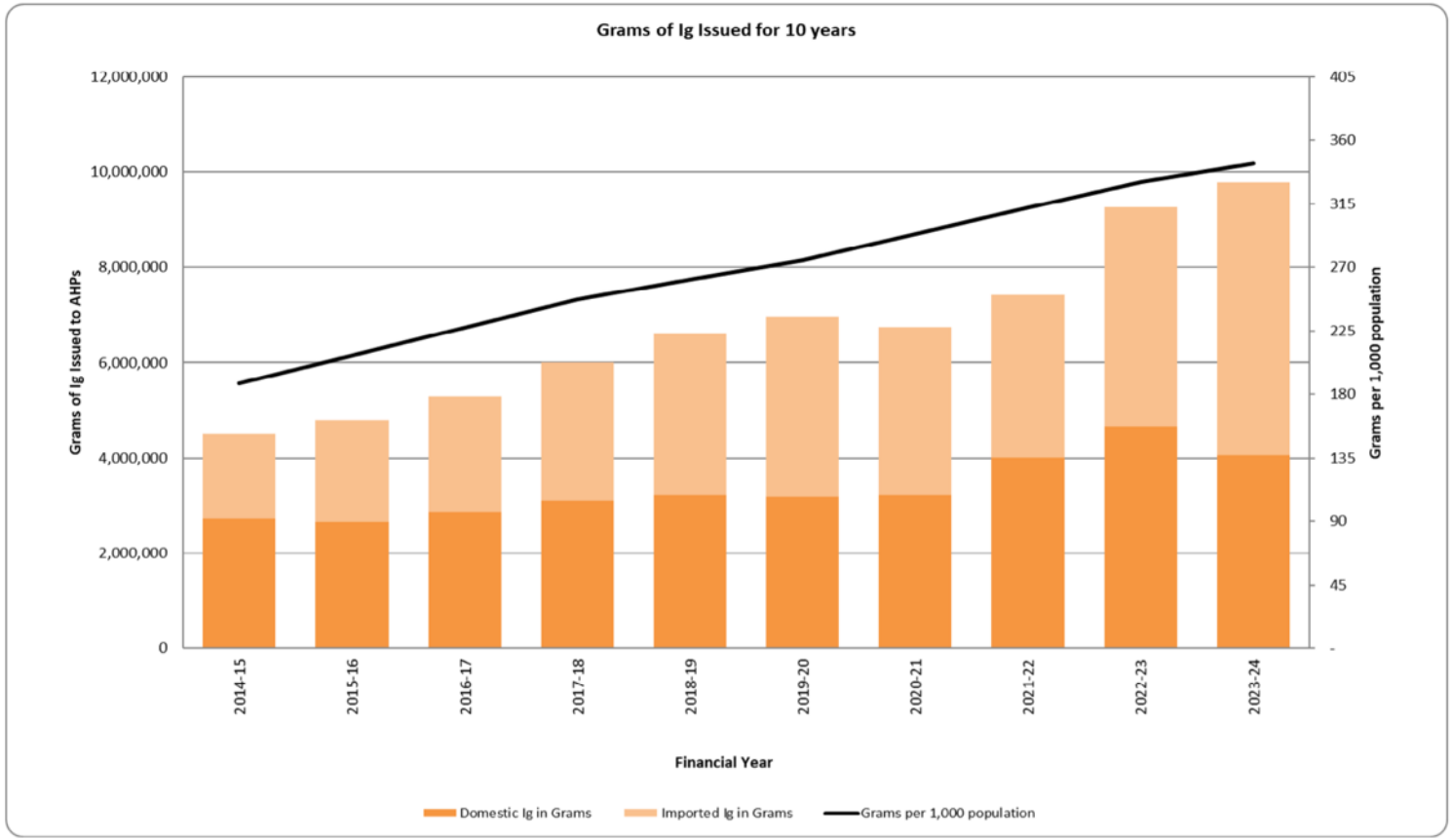
Systematic review:

- 72 eligible publications, 47 intervention cohorts, 2016-25
- CAR-T: 27/47, BsAb: 20/47
- Highly variable reporting of infection monitoring and prevention approaches, e.g.
  - Protocol-defined infection monitoring guidance reported: 4/47 (8.5%)
  - IgRT initiation criteria stated: 11/47 (23.4%)
  - Few details on many other elements of infection risk, recovery etc
- To be presented at ASH

Why focus on Ig use?

OPTIMAL
Centre of Research Excellence in improving immunoglobulin use and clinical outcomes

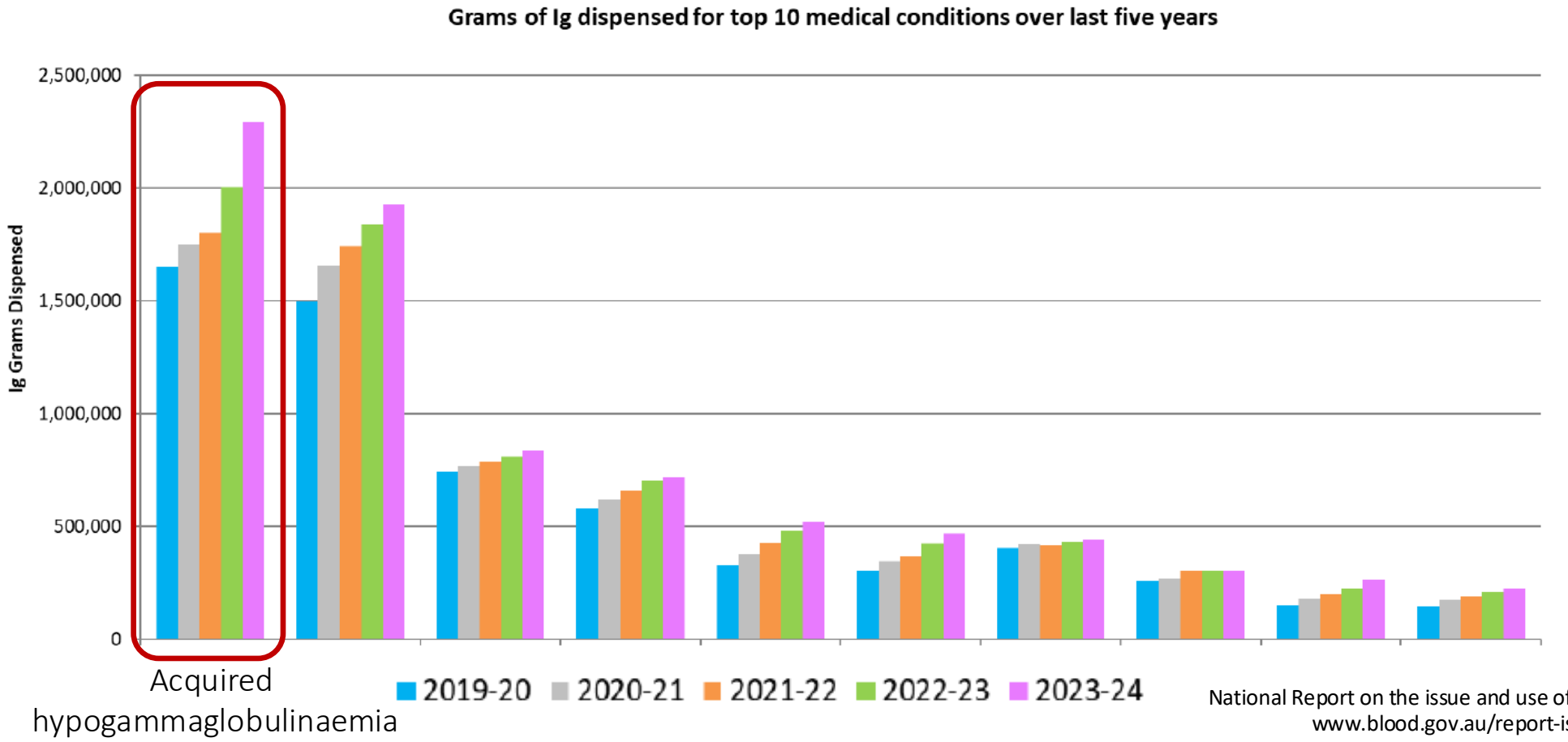
- Limited resource
- Use increasing, supply constrained
- Australia one of highest per capita users internationally
- >$1 billion/y in product costs alone
- Need to understand patient perspectives on how Ig is used
- Ensure Ig available for people who need it most



National Report on the issue and use of immunoglobulin (Ig) 2023-24
www.blood.gov.au/report-issue-and-use-immunoglobulin

Why focus on Ig use?

OPTIMAL
Centre of Research Excellence in improving immunoglobulin use and clinical outcomes



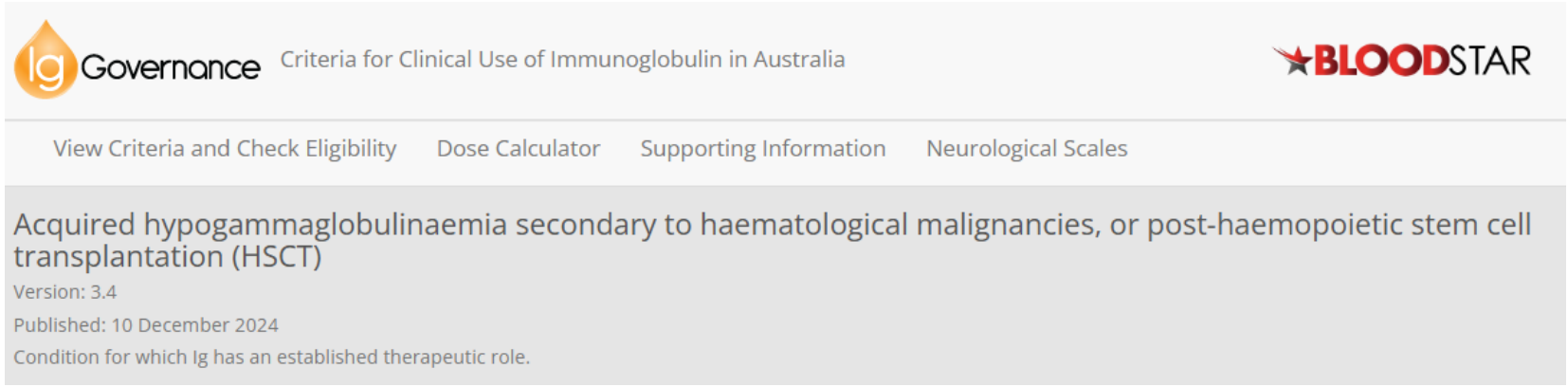
Acquired hypogammaglobulinaemia

National Report on the issue and use of immunoglobulin (Ig) 2023-24
www.blood.gov.au/report-issue-and-use-immunoglobulin

Lack of evidence to inform policy, guidelines, practice

OPTIMAL
Centre of Research Excellence in improving immunoglobulin use and clinical outcomes

- Evidence for Ig use in many conditions is limited
- Even where evidence Ig therapy has benefit, for many conditions, paucity of evidence to guide clinicians on how best to use Ig for an individual patient:
  - *When to start?*
  - *When to stop?*
  - *Optimal dose?*
  - *Schedule?*
- Effects of new Rx
- Clinical outcomes
- Adverse events
- Non-product costs



Criteria to access Ig ≠ clinical guidance on how to use Ig

Stream 1: Optimising Ig use for infection prevention in blood cancer patients

OPTIMAL
Centre of Research Excellence in improving immunoglobulin use and clinical outcomes

CORE OUTCOME DATASET

Address current evidence gaps on Ig use and outcomes by developing a core outcome dataset to be used by nurses as part of routine Ig clinical care and audit activities

RE-DESIGNING IG DELIVERY

Using co-design principles, we will explore how can we best deliver Ig, by re-designing and piloting a new and improved service delivery system

HEALTH ECONOMICS MODELLING

We will predict infection risks and clinical scenarios for which Ig treatment represents value for money to the Australian community

OPTIMISE DOSING

Leveraging our trials infrastructure, we will use biological samples to generate novel data on how to better target Ig treatment and identify patients most likely to benefit, and to dose Ig to get the most value

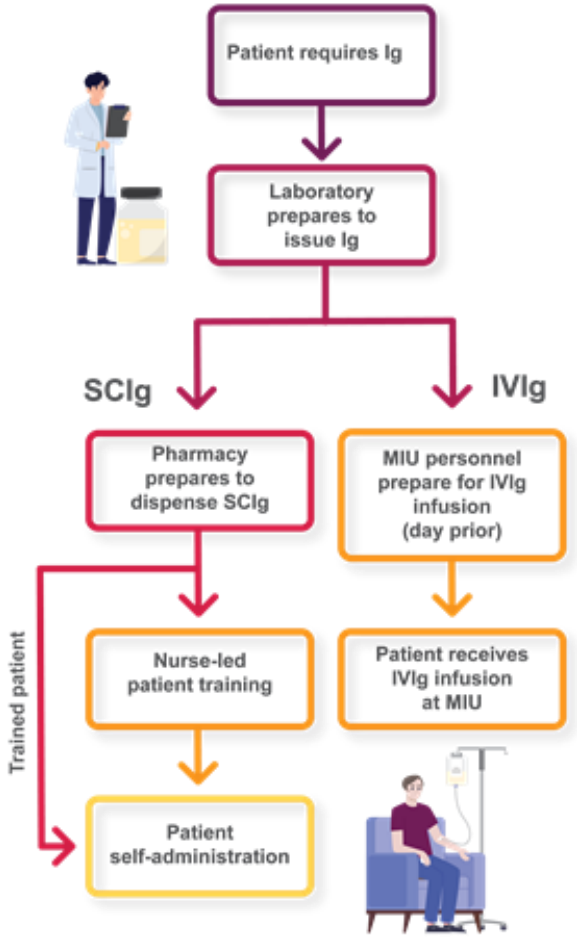
EVIDENCE-BASED GUIDELINES & DECISION SUPPORT TOOLS

We will develop evidence-based clinical practice guidelines which will ultimately reduce variation in care and ensure Ig is being used where it is needed most

Understanding the true cost of Ig therapy

OPTIMAL
Centre of Research Excellence in improving immunoglobulin use and clinical outcomes

TRUST Ig
TRUe cost of Transfusion



Supportive Care in Cancer (2026) 34:382
https://doi.org/10.1007/s00520-026-10551-y

RESEARCH

Intravenous versus subcutaneous immunoglobulin in patients with haematological malignancies: time-driven activity-based costing

Sara Carrillo de Albornoz[1,2] · Helen Haysom[1] · Allison Mo[1,3] · Jessica Guglielmino[4] · Terri Dunstan[5] · Kylie Rushford[4] · Amanda Ellison[4] · Karinna Saxby[6] · Dan Andrew[7] · Angelene Jesurajah[7] · Philomina Banahene[7] · Erin Hu[7] · Loo Sin Hoo[5] · Dennis Petrie[2] · Erica M. Wood[1,3] · Alisa M. Higgins[8] · Zoe K. McQuilten[1,3]

Received: 25 September 2025 / Accepted: 6 March 2026

Abstract

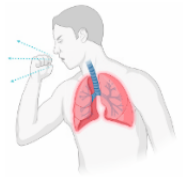
Purpose Prophylactic immunoglobulin (Ig) is used to prevent infections in patients with hypogammaglobulinaemia due to haematological malignancies (HM). Ig can be administered intravenously (IVIg) in hospital or self-administered subcutaneously (SCIg) at home, using different dosing regimens but with comparable effectiveness. In Australia, Ig product costs alone were AU$915.7 million in 2022/2023, 60% of the national blood budget. However, the total cost of IVIg and SCIg, including administration costs, remains uncertain.

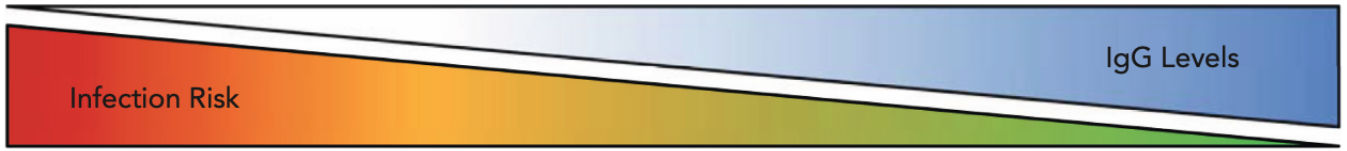
Methods We conducted a prospective, time-driven, activity-based costing study to compare the costs of providing IVIg and SCIg to patients with HM from an Australian healthcare perspective. Ig product, consumables, equipment, and in-hospital costs were included. Analyses were conducted assuming full adherence and using (1) published prices for IVIg and SCIg, which excluded plasma fractionation costs to the Australian government, and (2) equivalent average weighted price for IVIg and SCIg, including plasma fractionation costs.

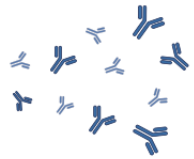
Results Annual IVIg product cost per patient was lower than that for SCIg under both costing scenarios: (1) AU$10,012 and (2) AU$5895, driven by higher SCIg doses. The costs of treating a patient with IVIg for a year were (1) AU$9936 and (2) AU$5787 lower than with SCIg, mainly due to higher SCIg product costs. When only in-hospital administration costs were considered (excluding Ig product and SCIg home consumables), SCIg treatment was AU$1019 less costly than IVIg.

Conclusion Our results indicated higher annual direct costs per patient treated with SCIg than IVIg, despite higher in-hospital costs associated with IVIg administration. Further research, including understanding costs to patients, is warranted.

Keywords Immunoglobulin · IVIg · SCIg · Haematological Malignancies · Transfusion · Cost







	Prophylactic IGRT	Pre-emptive IGRT	Rescue IGRT
	A preventive, up-front strategy — IGRT is started before infections occur.	A risk-adapted strategy — IGRT is started after early signals of immune compromise, but before recurrent infections.	A treatment-on-demand strategy — IGRT is started only after infections occur.
Patient Population	• History of infections • Multiple Myeloma > NHL • Severely Low IgG <200 mg/dl • Immunocompromised state (B-cell aplasia)	• No Infection History • Expected IgG <400 mg/dl • High Inflammatory and tumor burden markers	• Young, no comorbidities • Intact hematopoiesis • Low Inflammatory and tumor burden markers • IgG >600 mg/dl
Trigger	Initiation of therapy (or early in the course), regardless of IgG level or infection history	Declining IgG below a predefined threshold (eg, <400 mg/dL) *or* early isolated or mild harbinger infections	Hospitalization for infection, recurrent infections (≥2 bacterial infections), or proven serious infection
Rationale	Prevent immune deficiency and reduce early infectious complications	Intervene early to avoid serious clinical sequelae	Reserve IGRT for patients with demonstrated benefit

Figure 3. IGRT strategies. IgG levels shown here assume the absence of an IgG paraprotein; refer to the text for details.

OPTIMAL
Centre of Research Excellence in improving immunoglobulin use and clinical outcomes

Rejeski K, Banerjee R, Hill JA.
How I prevent infections in adults receiving bispecific antibody therapies for advanced B-cell malignancies.
Blood 2026;148(8):927-938

International Myeloma Working Group immunotherapy committee consensus guidelines and recommendations for optimal use of T-cell-engaging bispecific antibodies in multiple myeloma

*Paula Rodriguez-Otero, Saad Usmani, Adam D Cohen, Niels W C J van de Donk, Xavier Leleu, Jaime Gállego Pérez-Larraya, Salomon Manier, Ajay K Nooka, Maria Victoria Mateos, Hermann Einsele, Monique Minnema, Michele Cavo, Benjamin A Derman, Noemi Puig, Francesca Gay, P Joy Ho, Wee-Joo Chng, Efstathios Kastritis, Gösta Gahrton, Katja Weisel, Chandramouli Nagarajan, Fredik Schjesvold, Joseph Mikhael, Luciano Costa, Noopur S Raje, Elena Zamagni, Roman Hájek, Niels Weinhold, Kwee Yong, Jing Christine Ye, Surbhi Sidana, Giampaolo Merlini, Tom Martin, Yi Lin, Ajai Chari, Rakesh Popat, Jonathan L Kaufman, on behalf of the International Myeloma Working Group**

www.thelancet.com/oncology **Vol 25 May 2024**

Infection management should continue even after discontinuation of bispecific antibody therapy since the risk of infections is not immediately resolved after treatment discontinuation. Additional studies are needed to better understand the duration of immunosuppression seen with these agents and its optimal management.

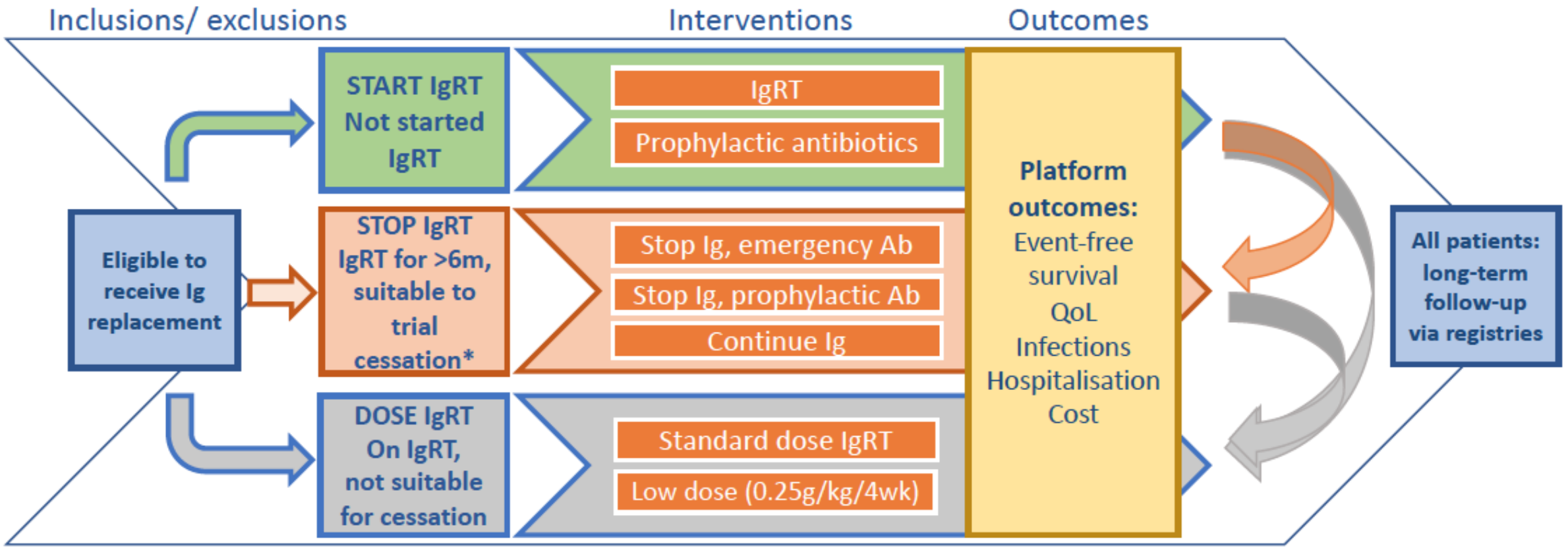
MONASH University

transfusion research unit

RATIONAL Platform Trial (NHMRC/MRFF)

Blood Synergy

rationaltrial.com



rationaltrial.com

MONASH University

ALG Australasian Leukaemia & Lymphoma Group

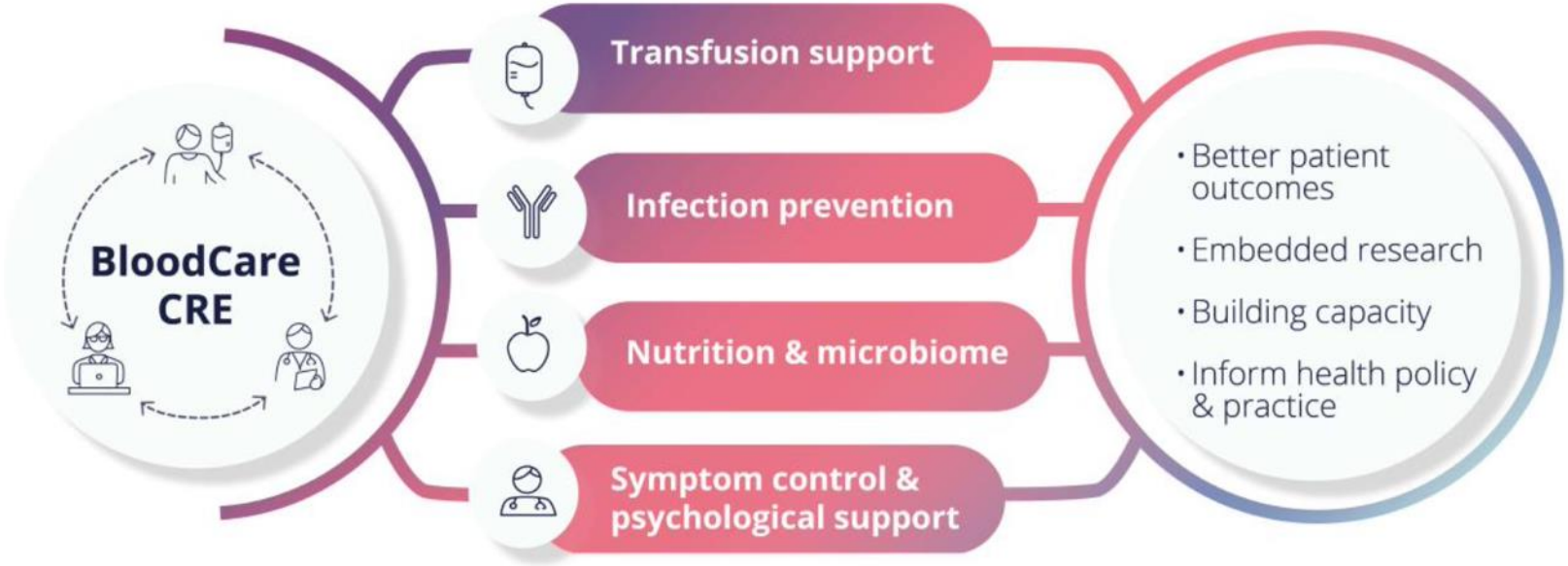
transfusion research unit

New NHMRC BloodCare CRE

Blood Care Centre of Research Excellence

CIA Prof Zoe McQuilten

- Expand and extend supportive care research for patients with blood cancers
- PhD opportunities available



MONASH University

bloodcarecre.org

transfusion research unit

PAIRS: Post-allograft immunoglobulin study

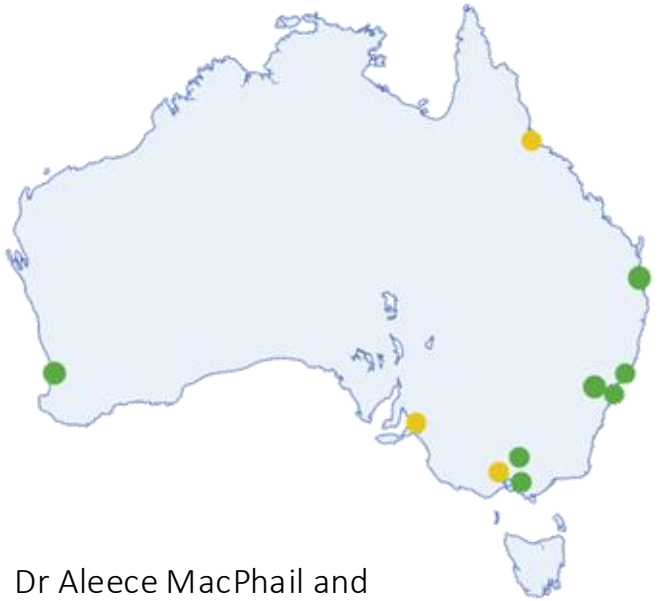
Observational cohort study of Ig, infection in alloSCT, CAR-T

Outcomes

- Hypogammaglobulinaemia, Ig replacement, infection
- Incidence and risk factors for hypogammaglobulinaemia
- Current Ig prescribing practices
- Dosing and kinetics of Ig levels after replacement

Progress:

- 10 active sites, 670 patients to date
- Aiming complete data collection end of 2026



Dr Aleece MacPhail and
OPTIMAL CRE PhD student Jamie Jackson
Funding: Blood Synergy and OPTIMAL CRE

LETTER TO THE EDITOR

blood advances

TO THE EDITOR:

Vaccination should not be forgotten in patients receiving immunoglobulin replacement therapy

Sigrun Einarsdottir,[1,2] Silvia Escribano-Serrat,[1,3] Marina Gomez-Llobell,[1] Malin Hultcrantz,[4,5] Mini Kamboj,[5,6] Miguel-Angel Perales,[1,5] Roni Shouval,[1,5] Zainab Shahid,[5,6] and Per Ljungman[7,8]

[1]Adult Bone Marrow Transplant Service, Department of Medicine, Memorial Sloan Kettering Cancer Center, New York, NY; [2]Department of Hematology, Sahlgrenska University Hospital, Gothenburg, Sweden; [3]Department of Medicine, Universitat Autonoma de Barcelona, Barcelona, Spain; [4]Myeloma Service, Department of Medicine, Memorial Sloan Kettering Cancer Center, New York, NY; [5]Department of Medicine, Weill Cornell Medical College, New York, NY; [6]Infectious Disease Service, Department of Medicine, Memorial Sloan Kettering Cancer Center, New York, NY; and [7]Department of Cellular Therapy and Allogeneic Stem Cell Transplantation and Infectious Diseases, Karolinska University Hospital, and [8] Division of Hematology, Department of Medicine Huddinge, Karolinska Institutet, Stockholm, Sweden

27 JANUARY 2026 • VOLUME 10, NUMBER 2

Acknowledgements

- Zoe McQuilten, Aleece MacPhail and all TRU colleagues
- Manu Juneja
- OPTIMAL investigators and advisory committee members
- Participating hospitals and investigators, patients and families
- Funders and collaborators

More info:
www.monash.edu/medicine/sphpm/transfusionresearch/home
Blood Synergy: bloodsynergy.org
OPTIMAL CRE: www.optimalcre.org
BloodCare CRE: bloodcarecre.org

MONASH University

transfusion research unit

Table 1. Baseline characteristics of CMV-seropositive patients with MM with 45 episodes receiving BsAbs

Characteristic	All episodes n = 45, n (%)	No CMV reactivation n = 34, n (%)	CMV reactivation n = 11, n (%)
Age, median (IQR), y	68 (57-72)	62 (57-72)	70 (64-73)
Male sex	32 (71)	25 (73.5)	7 (64)
Prior therapy lines, median (IQR)	5 (3-5)	4 (3-5)	5 (4-6)
>3	31 (69)	22 (65)	9 (82)
>5	11 (24)	7 (21)	4 (36)
Prior hematopoietic stem cell transplant			
Autologous	41 (91)	31 (91)	10 (91)
>1	18 (40)	15 (44)	3 (27)
Allogeneic	3 (7)	2 (6)	1 (9)
Prior CAR-T*	4 (9)	3 (9)	1 (9)
Neutropenia <1 neutrophil x 10^9/L	6/44 (14)	3/33 (9)	3/11 (27)
Persistent lymphopenia	32 (71)	21 (62)	10 (91)
Hypogammaglobulinemia (IgG <400 mg/dL)†	38 (84)	28 (82)	10 (91)
Cotrimoxazole prophylaxis	44 (98)	33 (97)	11 (100)
Valacyclovir prophylaxis	44 (98)	33 (97)	11 (100)
Immunoglobulin replacement†	32 (71)	23 (68)	9 (82)
Prior CMV reactivation	4 (9)	1 (3)	3 (27)

Table 2. **Clinical and microbiological features, antiviral treatment, and outcomes of CMV reactivation episodes**

Characteristic	Total n = 11, n (%)	CMV DNAemia, n = 7, n (%)	Clinically significant CMV infection, n = 4, n (%)
Positive blood CMV PCR	11 (100)	7 (100)	4 (100)
Reason for PCR performance			
Sporadic determination (asymptomatic)	4 (36)	3 (43)	1 (25)
Fever	7 (64)	4 (57)*	3 (75)
+ Gastrointestinal symptoms	3 (27)	1 (14)	2 (50)
+ Cytopenias	2 (18)	1 (14)	1 (25)
+ Liver function test abnormalities	1 (9)	0	1 (25)
CMV PCR load peak, median (IQR), IU/mL	1326 (290-2512)	789 (230-2239)	9 610 (1 215-61 270)
Time to first negative PCR, median (IQR), d	28 (15-36)	33 (15-39)	23 (22-36)
Time from BsAb start to CMVr, median (IQR), d	48 (34-78)	48 (7-72)	61.5 (39.5-163.5)
Bacterial coinfection	3 (27)	1 (14)	2 (50)