Related Donor suitability guidelines for haemopoietic progenitor cells

Background

Assessment of the suitability of allogeneic donors to donate haemopoietic progenitor cells (HPC) involves consideration of both risk to the donor from donation, as well as potential risk of the transmission of infectious and other disease to the recipient. While the ABMDR provides guidance for unrelated donor assessment, suitability criteria are often different for related donors, as there may be a higher tolerance for risk to both donor and recipient. This guideline provides consensus recommendations for related HPC donor assessment in Australia and New Zealand. Donor conditions are grouped according to relevance to either donor or recipient safety. The recommendations are based on available guidelines, which are also summarised.

It should be noted that legislation exists in each State and Territory regarding when children can and cannot act as an allogeneic HPC donor. It is essential that donor physicians are aware of relevant legislation both because this differs between jurisdictions and because it differs according to the child's capacity to understand the nature of what is being asked of them.

It is acknowledged that determination of donor suitability relies on the clinical judgement of the physician responsible for the assessment. The recommendations provided in this document serve only as a guideline to assist this process. Where donor assessment identifies circumstances not addressed in these guidelines, discussion with other practitioners involved in donor assessment, including the authors of this document, is encouraged.

Abbreviations

ABMDR	Australian Bone Marrow Donor Registry
ASA-PS	American Society of Anesthesiologists – Physical Status classification system
BCC	Basal cell carcinoma
BM	Bone marrow
B thal	Beta thalassaemia
CJD	Creutzfeldt-Jakob disease
CKD	Chronic kidney disease
DM	Diabetes mellitus
GA	General anaesthetic
GFR	Glomerular filtration rate
HbS	Sickle cell disease
MBL	Monoclonal B-cell lymphocytosis

MGUS	Monoclonal gammopathy of uncertain significance
NAFLD	Non-alcoholic fatty liver disease
NPAAC	National Pathology Accreditation Advisory Council
IDU	Injecting drug use
IST	Immunosuppression therapy
SCC	Squamous cell carcinoma
SLE	Systemic lupus erythematosus
TGA	Therapeutic Goods Administration
TGO88	Therapeutic Goods Order No. 88
WBMT	Worldwide Network for Blood and Marrow Transplantation
WMDA	World Marrow Donor Association

Definitions

Ineligible – an allogeneic cellular therapy product donor who has identified risk factor(s) for relevant communicable diseases. Such donors may be suitable to proceed with donation, at the discretion of the recipient transplant physician, who should discuss this risk with the recipient. NPAAC standards regarding management of 'non-conforming' donors and products would apply to such donors.

Policy

Related donors should be assessed by a medical practitioner who does not have primary responsibility for the recipient (third party haematologist). Final responsibility for all donor care, including follow-up of results and referral for medical care if appropriate, rests with the donor's medical team, and not with the recipient transplant physician.

It is imperative that confidentiality be maintained regarding all aspects of donor care. Where a donor is deemed unacceptable based on a medical condition, the recipient should not be informed of the reason without the donor's consent. If a donor declines to donate, the same information (e.g. "not suitable due to medical reasons") should be provided to the recipient. Where a potential communicable disease risk is identified in the donor, consent must be obtained from the donor before this can be disclosed to the recipient.

In all cases HPC donation should proceed only with the consent of the donor or, where the donor lacks legal capacity, with the consent of the donor's substitute decision-maker. Most importantly, in these situations the decision to donate should always be voluntary and not be coerced.

BMTSANZ

Conditions most relevant to donor safety

Criterion	TGO88	ABMDR (unrelated donors)	WBMT (related donors)	BMTSANZ Recommendation
Age	Need limits	18-60yr	Nil	Acceptable: 14-75, with extra criteria for minors and elderly (below).
BMI	Nil	<35 assess for fitness for GA & venous access	≤40	Acceptable ≤40; not acceptable for BM if >40.
Heart disease	Nil	Discretion of 3rd party haematologist	Use ASA-PS & other risk assessment tools. Refer to cardiologist.	Discretion of 3rd party haematologist, consider consultation with cardiologist.
Thrombosis	Nil	Nil	If anticoagulation no longer indicated.	Accept if anticoagulation no longer indicated or temporary cessation considered acceptable Consider role of prophylaxis in at-risk donors post G-CSF or BM harvest
Stroke	Nil	Permanent deferral	Discretion of 3rd party haematologist.	Generally not acceptable
Cognitive impairment	Nil	Permanent deferral	Donor advocate, consider cryopreservation.	Donor advocate involvement prior to HLA typing, consider cryopreservation.
Sickle cell disease	Nil	Permanent deferral	Avoid G-CSF in HbS, HbS/B thal.	Avoid G-CSF in sickle cell disease.
Autoimmune disease	Nil	G-CSF may be contraindicated	Defer if systemic autoimmune disease. Defer if on pred >5mg or other IST. Avoid G-CSF in inflammatory joint disease.	Avoid G-CSF in inflammatory joint disease. If systemic autoimmune disease, discuss with recipient physician. Also note possibility of disease transmission to recipient (also relevant to recipient safety).
Severe back pain, back surgery	Nil	Nil	Avoid BM harvest	Avoid BM harvest in general, discuss with anaesthetist if considering proceeding.
Gout	Nil	Nil	Avoid G-CSF	Acceptable with donor consent.
Diabetes mellitus	Nil	Nil	Assess late effects	Acceptable (but assess end organ damage).

Kidney disease	Nil	Permanent deferral for autoimmune or infectious CKD	Defer if associated with chronic infection, DM, SLE or GFR < 30.	Not acceptable if GFR < 30 (Cockroft-Gault calculation).
Epilepsy	Nil	Defer if < 3yr post seizure	Accept if allowed to drive.	Discretion of 3rd party haematologist, discuss with neurologist.
Breastfeeding	Nil	G-CSF: express & discard until 7 days post dose BM: Express & discard until 24hr post GA	Express & discard until 24 hr post G-CSF or GA.	G-CSF: express & discard until 7 days post dose BM: Express & discard until 24hr post GA.
Pregnant	Nil	Defer	Defer	Defer
Liver disease	Nil	Defer for hepatic failure.	Deranged LFT, ? cause: defer until cause known. NAFLD: suitable. Cirrhosis: not acceptable if Child-Pugh B or C.	Deranged LFT, uncertain cause: defer until cause known. NAFLD: suitable. Cirrhosis: not acceptable if Child-Pugh Score B or C.
Splenomegaly	Nil	Nil	Acceptable depending on cause. Expect 10-15% increase in spleen size.	Acceptable depending on cause. Generally, BM collection preferred. Monitor closely if G-CSF given.
Respiratory	Nil	Defer for respiratory failure.	Asthma: acceptable if not on oral steroids Cough or dyspnoea at rest: not suitable.	Discretion of 3rd party haematologist, consider consultation with respiratory physician.
Anaesthetic risk	Nil	Inform anaesthetist.	Avoid BM (GA) if >ASA P2.	Discuss with anaesthetist.

Criteria for the use of children as donors (<14 years)

1. No medically equivalent adult related donor.
2. After evaluation, staff deem a strong personal and emotionally positive relationship exists between donor and recipient.
3. Parental consent and donor assent generally required. Where required by law approval should also be sought from relevant State committee.
4. All care should be provided by a paediatric service with experience in management of HPC donors.

Criteria for the use of a minor donor (14-17yrs):

1. No medically equivalent adult related donor.
2. After evaluation, staff deem a strong personal and emotionally positive relationship exists between donor and recipient.
3. Parental consent and donor assent generally required. Where donor is deemed able to provide consent, a parent or guardian will co-sign. Where required by law approval should also be sought from relevant State committee. Discussion with a paediatric transplant physician regarding requirements for donor consent is recommended.
4. Donors being managed at adult facilities should weigh > 35kg.
5. Donors 14-17 considered to require specialised paediatric management should be referred to a paediatric service for assessment and collection. This should be considered prior to HLA typing for these donors.

Criteria for the use of an elderly donor (65 – 75yrs):

1. Must meet suitability criteria.
2. Comorbidities must be identified and a management plan identified for each.
3. Performance status must permit safe collection of cells.
4. Resources must be provided for disabilities, including visual or hearing impairments.
5. Prefer HPC-A collection over HPC-M harvest.
6. Careful consideration should be given to the possibility of inadequate mobilisation. In high risk cases, collection and cryopreservation prior to the recipient commencing chemotherapy may be considered.

Conditions most relevant to recipient safety

Criterion	**TGO88**	**ABMDR (unrelated donors)**	**WBMT (related donors)**	**BMTSANZ Recommendation**
Malignancy (excluding SCC, BCC, cervical CIN)	Nil	Accept if ≥5 years post 'cure' Permanent deferral for haem malignancy.	Accept if 5-10 years post remission. Permanent deferral for haem malignancy. Note MBL and MGUS not included.	Accept if 5 years post remission, but discuss with recipient physician if any systemic chemotherapy due to MDS/AML risk. Haem malignancy not acceptable. MBL or MGUS generally <u>not</u> acceptable.

Cytopenias (unexplained)	Nil	Nil	Accept if: Neutrophils >1.0 Lymphocytes >0.5 Platelets >100 Hb within 20 of LLN	BMAT + cytogenetics if: Neutrophils <2.0 (and not African) Platelets < 130 Consider testing for germline mutations (incl. RUNX1, CEBPA, p53), particularly if family history of AML/MDS, thrombocytopenia, BM failure or familial cancer syndromes
Drug user	Ineligible for 5 years from last injection	Permanent deferral if any prior IDU.	Permanent deferral if IDU Consider cryopreservation for others	**Ineligible** for 5 years from last injection. Consider cryopreservation for any drug user.
Prison inmate > 72 hours	Ineligible until 12 months post release	Defer until 12 months post release.	Nil	**Ineligible** until 6 months post release.
'High risk' sexual practice	Ineligible until 12 months from last contact	Defer until 12 months from last contact.	Nil	**Ineligible** until 6 months from last contact.
Needle-stick, tattoo, piercing	Ineligible until 6 months post exposure, or 4 months if HCV NAT negative	Defer until 4 months post exposure.	Nil	**Ineligible** until 4 months post exposure.
Non-human graft, history of CJD, human pituitary hormone	Permanently ineligible	Permanent deferral	Discretion of 3rd party haematologist	**Ineligible** donor, discuss with recipient physician
Corneal, organ or BM transplant	Nil	Permanent deferral	Nil	Corneal: **ineligible** BM: generally not acceptable Solid organ: generally not acceptable.
HIV or HTLV1	Permanently ineligible	Permanent deferral	Nil	Not acceptable.
Hep B, Hep C	Ineligible until non-infected state established	Notify transplant centre	Nil	**Ineligible** donor, discuss with recipient physician

History of malaria	Ineligible until negative immunological test ≥120 days post completion of therapy	Perform immunological test and notify transplant centre if <120 days post treatment.	Nil	**Ineligible** until negative immunological test ≥120 days post completion of therapy.
Travel to malaria risk area	Accept if > 12 months ago. Accept if negative immunological test ≥120 days after travel	Perform immunological test and notify transplant centre if <120 days post exposure.	Nil	Need immunological test if exposure within last 12 months. **Ineligible** until negative immunological test ≥120 days post exposure.
History of meningitis	Nil	Permanent deferral	Accept	Acceptable
Active bacterial infection	Nil	Osteomyelitis: accept if <2 years after 'cure'.	Osteomyelitis: accept if 'cured'	Acceptable if treatment completed.
History of Zika	Nil	Disclose to transplant centre if <4 months since recovery.	Nil	**Ineligible** until 4 months post recovery.
Contact with Zika	Nil	Disclose to transplant centre if sexual contact.	Nil	**Ineligible** until 6 months post exposure.
Travel to Zika risk area	Nil	Dengue/arbovirus policy applies – disclose to transplant centre if travel was less than 4 weeks prior to collection date.	Nil	**Ineligible** until 6 months post exposure.
Live attenuated vaccine (MMR, Varivax, Zostavax, BCG, oral cholera, oral typhoid fever)	Ineligible if within 4 weeks	Defer 4 weeks	Nil	**Ineligible** if within 4 weeks.

Sources

1. Therapeutic Goods Order No. 88 – Standards for donor selection, testing and minimizing infectious disease transmission via therapeutic goods that are human blood and blood products, human tissues and human cellular therapy products. Australian Government Department of Health and Aging. 20th May 2013.
2. Donor Screening Recommendations to Reduce the Risk of Transmission of Zika Virus by Human Cells, Tissues, and Cellular and Tissue-Based Products. US Department of Health and Human Services, Food and Drug Administration. March 2016.
3. Australian Bone Marrow Donor Registry Standard: Donor Health Assessment and Infectious Disease Testing (ABMDR-STD-OP-006-11), Sept 2016.
4. National Pathology Accreditation Advisory Council: Requirements for Procedures Related to the Collection, Processing, Storage and Issue of Human Haemopoietic Progenitor Cells (Fifth Edition 2015)
5. Worel N, Buser A, Greinix H, Hagglund H, Navarro W, Pulsipher M et al. Suitability Criteria for Adult Related Donors: A Consensus Statement from the Worldwide Network for Blood and Marrow Transplantation Standing Committee on Donor Issues. BBMT 2015; 21: 2052-2060.
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7. Donor Screening Recommendations to Reduce the Risk of Transmission of Zika Virus by Human Cells, Tissues, and Cellular and Tissue-Based Products. US Department of Health and Human Services, Food and Drug Administration. March 2016.