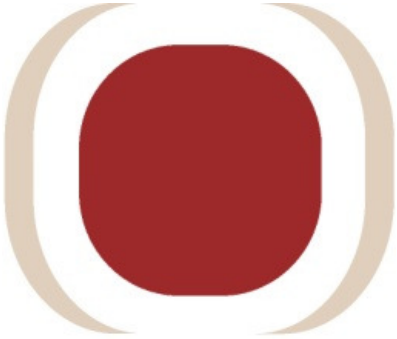

ABMTRR
Australasian
Bone Marrow Transplant
Recipient Registry

Guidelines for completing Allogeneic and 100 Day Form

Table of Contents

INTRODUCTION

This form was previously known as Form UA. It is now divided into two sections, **Allogeneic Transplant** and **100 Day** to match the pages on the ABMTRR Online database, ASTRO.

Who should use these forms?

- **Allogeneic Transplant Form** (Page 1)
  These forms should be submitted for all unrelated donor transplants from Australian centres and optional for all other allogeneic transplants
- **100 Day Report Form** (Page 2)
  This is optional for all transplants, allogeneic and autologous.
  Your centre may wish to keep record of acute post transplant events such as engraftment, best disease status achieved, acute GvHD.

When should these forms be submitted?

Submission of the Allogeneic Transplant section can be made at the same time of the Registration Form, or may be at the time of the 100 Day submission.

The forms may be submitted on the paper forms and sent to ABMTRR either by post or emailed as an attachment. Alternatively, submissions may be made online via ASTRO.

Date format: All dates are reported as dd/mm/yy

PATIENT/TRANSPLANT IDENTIFICATION

Hospital

Patient UPN

Patient name identifier

Date of Birth

Transplant date

Details given for these fields should match those provided on the Registration Form (Form A)

ALLOGENEIC TRANSPLANT FORM

1. Donor information

Number of donors

Indicate the number of donors used in this transplant

Donor sex
Male or female

If donor is female, number of pregnancies
Specify the number of pregnancies of the donor. Enter "unknown" if not known rather than leave blank. (enter as "99" in the Online Database)

Donor age
Enter age in years

2. Recipient performance status prior to transplant

Use Karnofsky (patients 16 years and older) or Lansky score (patient less than 16 years)
Use this scale to determine the score (10-100) that best represents the recipient's activity status at the requested time point.

The performance score should be documented at the time of the pre-transplant work up prior to starting conditioning treatment. If it has been recorded more than a month prior to transplant, it may be used provided the patient has not received any additional treatment and their condition is unchanged.

	Karnofsky Scale (recipient age≥16 years)	**Lansky Scale** (recipient age <16 years)
(80-100)	*Able to carry on normal activity; no special care is needed*	*Able to carry on normal activity; no special care is needed*
100	Normal, no complaints, no evidence of disease	Fully active
90	Able to carry on normal activity	Minor restriction in physically strenuous play
80	Normal activity with effort	Restricted in strenuous play, tires more easily, otherwise active
(50-70)	*Unable to work, able to live at home cares for most personal needs, a varying amount of assistance is needed*	*Mild to moderate restriction*
70	Cares for self, unable to carry on normal activity or to do active work	Both greater restrictions of, and less time spent in active play
60	Requires occasional assistance but is able to care for most needs	Ambulatory up to 50% of time, limited active play with assistance/supervision
50	Requires considerable assistance and frequent medical care	Considerable assistance required for any active play, fully able to engage in quiet play
(10-40)	*Unable to care for self, requires equivalent of institutional or hospital care, disease may be progressing rapidly*	*Moderate to severe restriction*
40	Disabled, requires special care and assistance	Able to initiate quiet activities
30	Severely disabled, hospitalization indicated, although death not imminent	Needs considerable assistance for quiet activity
20	Very sick, hospitalization necessary	Limited to very passive activity initiated by others (e.g. TV)
10	Moribund, fatal process progressing rapidly	Completely disabled, not even passive play

3. CMV Status

Report the CMV status of the recipient prior to start of conditioning therapy. Include the donor CMV status for allogeneic transplants.

Most laboratory reports a positive result as reactive and a negative result as non-reactive.

Select “unknown” only if the test results are inconclusive or reported as not known.

The “not done” option should only be used if the CMV status is not evaluated, or if the lab reports CMV testing by PCR (DNA detection), prior to commencement of conditioning. PCR testing is used to detect the presence of the CMV virus but does not test for prior exposure.

4a. CMV prophylaxis, agents used

CMV prophylaxis is the use of antiviral drugs to prevent CMV reactivation and disease. It is administered to patients who are CMV seropositive. It is usual for CMV prophylaxis to be given from the day of engraftment to 100 days post-transplant in order to prevent reactivation (positive CMV PCR or pp65 antigen) of CMV infection and CMV disease.

Prophylaxis may continue beyond this time if a patient has chronic GVHD and is "high-risk". In most centres the preference will be to use a pre-emptive strategy (see below), so primary prophylaxis for CMV is unusual.

4b. CMV Pre-emptive strategy used

A pre-emptive antiviral strategy involves giving antiviral therapy to those patients who reactivate their CMV infection. Reactivation is detected by positive CMV (Quantitative PCR or pp65 antigen) in the absence of CMV disease. The point at which reactivation occurs is the date of the first positive QPCR or pp65 result.

A reactivation of CMV would usually be treated with a course of antiviral therapy (ganciclovir, foscarnet) until the viral load has become undetectable. A clinician may use oral valganciclovir for patients with low viral copy numbers who are being managed in the outpatient setting.

5. GvHD Prophylaxis

These are immunosuppressive agents given to prevent the development of graft versus host disease and are usually planned per protocol. Agents commonly used include methotrexate and cyclosporin.

Do not report any agents used to treat GvHD. (ie. given at the onset of GvHD)

6. Disease treatment/management between diagnosis and transplant?

Indicate if the patient received any chemotherapy, radiotherapy or surgery to manage the disease (for which the transplant was indicated for) prior to the transplant.

7. Graft information

7a. Graft manipulation (ex-vivo)

Indicate if the graft was manipulated for CD34+ selection, T cell depletion or other.

Do not include RBC or plasma depletion or volume reduction.
If the product was thawed, then indicate that the cells were cryopreserved in the next question.

7b. Have cells been cryopreserved?

Do not report cryopreservation or thawing as a graft manipulation.
If the product was never cryopreserved, then select “no”

8. Cell count

Report the Nucleated cell count and CD34+ cell count.
These should be reported in the units specified ie. Nucleated cells in 10^8/kg and CD34+ cells in 10^6/kg.

Cell counts in cord blood units may need to be adjusted to be reported in the units mentioned above.

9. Unrelated Donor Information

ABMDR Recipient-ID

The identification number will be provided on the ABMDR form, usually consisting of seven digits.

Donor-ID

The donor identification code is provided on the donor form. It may consist of either the registry code followed by a donor identification number, or an identification number only.

Registry country

Indicate the country where the donor registry is based. The Registry name is not required.

Multiple Donor

Complete this section if there were more than one donor for this transplant.

10a. Second Donor information

Donor sex
Donor CMV status
Cell Source (transplant source)
Donor ID

10b. Second Donor cell count

Nucleated cells
CD34+ cells

If a third donor is used, complete the questions on a separate form regarding Multiple Donor, indicating that they are details of the third donor:

- Question 25 from the Registration Form and
- Questions 10a and 10b from the Allogeneic Transplant Form.

100 DAY REPORT

Information provided here should be within the stated time period from the date of infusion to a hundred days post transplant. Any "latest" dates of events should be as close to 100 days as possible.
If chronic Graft versus Host Disease develops during this period, it should be documented in the Annual Follow Up Form.

If another transplant occurs before the 100 days, then any events should be reported up to the day before conditioning therapy is commenced. If no preparative conditioning is planned, then the reporting period will include up to the day before the subsequent infusion date. Another Registration and 100 Day Form will then be required for the subsequent infusion. No further follow up is required for the previous transplant.

1. Survival Status

Indicate the recipient's survival status at the most recent contact or correspondence.

Last known date of contact or death date

Report the last known date that the patient was alive or the date of death.

This date is used in survival analyses and it is important to have this updated annually (for alive recipients) if known.

If the recipient has not been seen by a physician and survival status is known, this should be reported

Main cause of death

Report the underlying cause of death... the underlying cause of death is "the disease or injury that initiated the chain of events that led directly or inevitably to death." *Ref: CIBMTR Forms Manual: Recipient Death Data Form 2900 Document Number: A00564 version 1*

Examples:

- If an infection leads to heart failure, the infection should be reported as the primary cause of death.
- If the patient dies of acute renal failure which was associated with progressive myeloma, then the myeloma should be reported as the primary cause of death.

Report only one main cause of death, however contributing causes may be listed, under "Comments", if relevant. Do not report the mode of death eg cardiac or respiratory arrest.

If the recipient has recurrent/persistent/progressive disease at the time of death, consider if the disease was the primary cause of death or a contributing cause of death. One should not assume that the presence of disease indicates that the disease was the primary cause of death.
It may be reported on a post mortem as the primary cause, however, for registry reporting, use the criteria below to help determined how to report this.

- **Disease is present and progressing:**
  In the presence of clinical disease, if the disease is progressing, the main cause of death should be reported as **"Relapse/Progression/Persistent disease",** regardless of any accompanying complications or infections during the post-transplant period.
- **Disease is present and stable or improving:**
  In the presence of clinical disease, and the disease is stable or there had been an improvement after transplant, and the patient were to die of complications or infections, then the main cause of death would then be the complication or infection. The cause of death would be reported as "**Treatment related"**, then indicating all the causes as appropriate by ticking the relevant checkboxes. (see below)

Treatment related causes

☐ Transplant related (select as many as appropriate)

☐ GvHD	☐ Cardiac toxicity
☐ Infection	☐ Pulmonary toxicity
☐ Rejection/poor graft function	☐ VOD
☐ Other, specify_____	

New malignancy
If the recipient dies of a new malignancy, ensure that the details of the malignancy have been reported.

If the malignancy was diagnosed prior to the transplant, then report this under "Other"

If the malignancy is considered a progression of the disease for which the transplant was for, then the main cause of death should be reported as "Disease progression" rather than a new malignancy, eg. transplant indication was MDS, then the disease progresses to AML post transplant.

Note: Aplastic anaemia
If a recipient was transplant for aplastic anaemia and dies of relapsed disease, then the cause of death should be reported as "Rejection/poor graft failure" (under "Transplant related" causes).

Other, specify

Select this option only when the other available options are not appropriate.

2. Engraftment

2a. Neutrophil engraftment

Neutrophil engraftment is defined as an absolute neutrophil count (ANC) of 0.5 x 10^9/L or more on consecutive laboratory values on three different days. The date of recovery is the first of these three days.

For transplants using non-myeloablative or reduced intensity regimens, the neutrophil count may never drop below 0.5 x 10^9/L. Report these as "Never below 0.5 x 10^9/L"

If the neutrophil count never reaches 0.5 x 10^9/L in the 100 day period after transplant, then report as "not achieved" and enter the last date this was assessed within the 100 days.

2b. Did graft failure occur?

Graft failure includes persistent neutropenia, <5% donor chimerism, and ANC <0.5x10^9/L for three or more consecutive laboratory values.
Graft failure often requires an additional infusion of donor cells and may result from the use of specific drugs, infection (especially CMV), GVHD, as well as other causes.

2c. Platelet engraftment

This is defined as the platelet laboratory values of 20 x 10^9/L or more. The "date achieved" will the first of three consecutive days, and the patient has not received any platelet transfusions in the 7 days prior. (eg. if the last platelet transfusion was given on the 1st Feb, then the 8th Feb is the earliest date that can be reported as date of engraftment.)

For transplants using non-myeloablative or reduced intensity regimens, the platelet count may never drop below 20 x 10^9/L. Report these as "Never below 20 x 10^9/L"

If the platelet count never reaches 20 x 10^9/L in the 100 day period after transplant, then report as "Not achieved" and enter the last date this was assessed within the 100 days.

3. Best disease status achieved post transplant, prior to treatment modification

(not relevant for non-malignant diseases)

Report the recipient's best response to the planned course of the transplant. This does not include response to any treatment given for relapsed or persistent disease that was not a planned part of the transplant.

If the recipient was in complete remission at the time of transplant, then the only possible response will be "Continued complete remission".

Recipients not in complete remission at the time of transplant who achieve CRU (Complete remission unconfirmed – persistent scan abnormalities of unknown significance) should be reported as "Complete remission achieved". Include the date assessed.

Refer to the definition of Complete remission for the specific disease classification

If the recipient was not in complete remission at the time of transplant, and has persistent or residual disease during the 100 days post transplant, then select "Never in complete remission" Include the latest assessment date in the report.

4. First relapse or Progression post transplant

Only report the **first** relapse or, in the case of persistent or residual disease, the **first** indication of disease progression.

Detection methods include clinical/haematological, cytogenetic, and molecular.

Clinical assessment includes radiological and physical assessments eg. when recipient is evaluated by the physician.

Flow cytometry may be included as cytogenetic assessment.

Only the first instance of each detection method should be reported.

If relapse or progression has not occurred, then report the latest date the disease was assessed.

5. Adverse events in the first 100 days post transplant?

If any of the following occurred, include the date of onset.

Interstitial pneumonitis
May result from infectious or non-infectious causes or it may be idiopathic, where an organism has not been isolated.

Diagnosis may include radiological results, bronchoscopy (including BAL), biopsies, arterial blood gas assessments, full blood count, blood chemistries and cultures.

Veno-occlusive disease
Veno-occlusive disease or sinusoidal obstruction syndrome is a form of toxic liver injury

characterised by the development of hepatomegaly, ascites/weight gain, and jaundice. Diagnosis relies on clinical criteria, ultrasound results, central venous blood pressure and liver biopsy.

Haemorrhagic cystitis
This is characterised by bleeding and inflammation of the bladder wall. Severity may range from macroscopic to gross haematuria.

CMV reactivation
Detection by quantitative PCR and CMV-pp65 antigen test in blood.

CMV disease
Proven disease can manifest as hepatitis, pneumonitis, gastroenteritis, encephalitis, nephritis, cystitis, radiculitis, retinitis, pancreatitis. Detection of the CMV virus from the site of disease (lung, gastrointestinal tract, liver, brain tissue, kidney, bladder, heart pancreas) using culture, immunohistochemical methods or in-situ hybridisation. CMV Retinitis is diagnosed by finding characteristic retinal lesions by a specialist opthalmologist

Some centres cannot readily obtain biopsies and may treat for CMV disease in the absence of a diagnosis.

Probable disease: Initiation of CMV therapy using ganciclovir, foscarnet or cidofovir for a tissue based infection (eg gastroenteritis, pneumonitis, hepatitis) for which CMV is considered the most likely cause based on a high serum CMV viral load, and the absence of an alternative diagnosis.

ALLOGRAFT SECTION

6. Acute Graft versus Host Disease

Acute Graft versus Host Disease is caused by T lymphocytes present in the donor stem cell graft recognising the patient as foreign. Symptoms usually consist of dermatitis, hepatitis and gastroenteritis. Other organs may be involved, eg. lungs.

GvHD was originally classified as acute or chronic based on the time of onset, acute GvHD being within 100 days post transplant. Diagnosis should now be based on clinical and histological features rather than the time of onset.

Indicate if the patient developed acute GvHD. If yes, then complete the following:

Date of first incidence of acute GvHD.
Report the first incidence only

Grading and staging of acute GvHD

Based on the criteria published by Przepiorka et al, Bone Marrow Transplant 1995; 15(6):825-8

Staging of organ involvement

Stage	Skin	Liver	Gut
1	Rash on <25% of skin *1	Bilirubin 34-50 µmol/L *2	Diarrhoea volume > 500ml/day *3 or persistent nausea * 4
2	Rash on 25-50% of skin	Bilirubin 51-102 µmol/L	Diarrhoea volume > 1000 ml/day
3	Rash on >50% of skin	Bilirubin 103-255 µmol/L	Diarrhoea volume >1500 ml/day
4	Generalized erythroderma with bullous formation	Bilirubin > 255 µmol/L	Severe pain with/without ileus

*1. Use "Rule of Nines" (see below) or burn chart to determine extent of rash.

*2. Range given as total bilirubin. Downgrade one stage if an additional cause of elevated bilirubin has been documented.

*3. Volume of diarrhoea applies to adults. For paediatric patients, the volume of diarrhoea should be based on body surface area. Downgrade one stage if an additional cause of diarrhoea has been documented.

*4. Persistent nausea with histological evidence of GVHD in the stomach or duodenum.

5. Criteria for grading given as minimum degree of organ involvement required to confer that grade.

6. Grade IV may also include lesser organ involvement with an extreme decrease in performance status.

Evaluate the Maximum Grade using the table below

Grade	Skin		Liver		Gut
I	Stage 1 or 2	AND	nil	AND	nil
II	Stage 3	OR	Stage 1	OR	Stage 1
III	-		Stage 2-3	OR	Stage 2-4
IV	Stage 4	OR	Stage 4		-

RULE OF NINES

Percent body surfaces

Body area	**%**
Each arm	9
Each leg	18
Chest and abdomen	18
Back	18
Head	9
Pubis	1

7. Donor cellular infusion (DCI)

Note: If additional cells are given for failed or poor neutrophil recovery, loss of graft or late graft failure, ie. the intent is to repopulate the recipient's marrow with haematopoietic cells, then this should be reported as a transplant.

Please indicate if additional cell therapy was given.

If yes, complete the following.

First infusion date
Report the date of the first infusion only.

Cell type
Donor cell types include but not limited to:

- Lymphocytes
- Mesenchymal cells
- Dendritic cells
- Peripheral blood mononuclear cells, stimulated and unstimulated

Indication
DCI is a form of immunotherapy with cells donated from any donor. It may be used for:

- treatment of recurrent disease, by inducing a graft versus leukaemia /tumour effect
- pre-emptive treatment in cases of high risk of disease relapse
- treatment of GvHD
- promote engraftment when chimerism studies show less than 100% donor cells
- conversion of mixed chimerism to full chimerism
- treatment of infections eg. viral
- treatment of B cell lymphoproliferative disorder - PTLD or EBV lymphoma

REFERENCES

1. Instructions for Pre-Transplant Essential Data (Pre-TED) Form. Center for International Blood and Marrow Transplant Research. A00413 Version 2.3 (8/28/2012)

2. MED-AB Forms Manual. A guide to the completion of the EBMT HSCT Med-AB Forms 2010. European Group for Blood and Marrow Transplantation. (Last modified 17/07/2012)

3. CIBMTR Forms Manual: Recipient Death Data Form 2900. A00564 version 1

4. CIBMTR Forms Manual: 100 Days Post-HSCT Data Form 2100. A00531 version 1.1 (7/20/2012)

5. Definitions of Cytomegalovirus Infection and Disease in Transplant Recipients Per Ljungman,1 Paul Griffiths,2 and Carlos Paya3. Clinical Infectious Diseases 2002; 34:1094-7