HSCT Forms Guidelines

Version: June 2024

Contents

PURPOSE OF THE REGISTRY

The details on the purpose and operations of Australia and New Zealand Transplant and Cell Therapies Registry are described in the ANZTCT Registry Protocol. This is available on the ABMTRR website at: http://www.abmtrr.org/index.php/resources/data-management/

REGISTRATION REQUIREMENTS

Haematopoietic stem cell transplant information is submitted into ASTRO (Australasian Stem cell Transplant Registration Online). This is required for each transplant.
The pdf versions of the Autologous and Allogeneic Registration forms are available on the ABMTRR website: http://www.abmtrr.org/index.php/resources/data-management/

A haematopoietic stem cell transplant is defined as involving an infusion of haematopoietic stem cells with the intention of repopulating the bone marrow and hence the recovery of haematopoiesis in all lineages.

Registration of a transplant is NOT required:

- If patients were scheduled for transplant and did not receive the cells regardless of commencing conditioning chemotherapy or not.

- If infusion of cells is a Donor Cellular Infusion (DCI/DLI)
  The intention of giving a donor cellular infusion is not to restore haematopoiesis, but may be to treat infections (e.g. viral) or recurrent disease. A DCI may also be given to treat GVHD or promote engraftment when chimerism studies reveal less than 100% donor cells. Conditioning treatment is not given prior to receiving the additional donor cells since replacement of the marrow is not the goal.
  These infusions are reported in the transplant follow up if following a HCT.

- If the infusion of autologous PBPC is given as a rescue for graft failure.
  Although this may be to restore haematopoiesis, these are not required to be reported as a separate transplant.

In some cases, there may be difficulty applying these definitions e.g. with donor lymphocyte infusions, haematopoietic cells are also present. In this case the intention of the treatment should be taken into account i.e. if the intention was to repopulate the patient marrow with haematopoietic cells, then the procedure is considered a transplant. This includes additional donor cells given for failed or poor ANC recovery, loss of graft, or late graft failure.

Patient consent

Consent is required from all transplant recipients for the transfer of information describing themselves and their transplant procedures to the ANZTCT Registry. The patient consent procedure will be dependent on the individual hospital's policy.

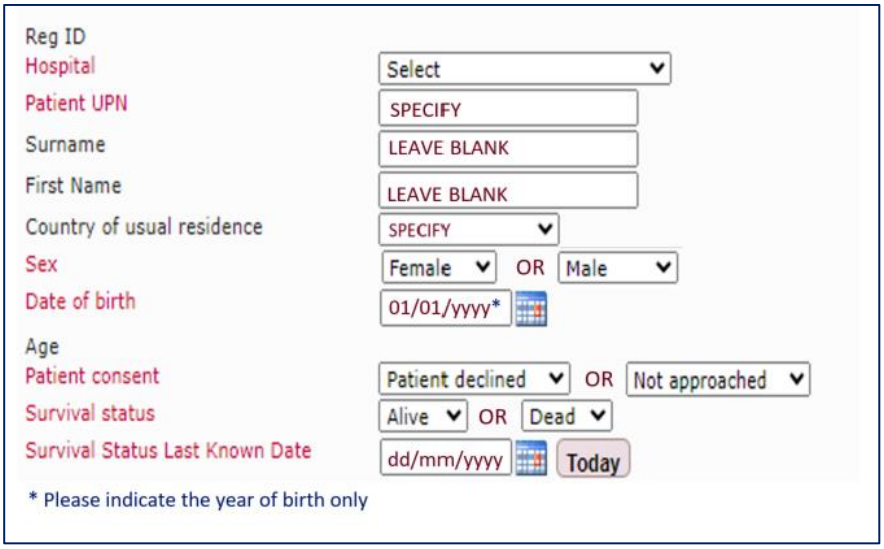
A sample patient information and consent form is available in the ANZTCT Registry Protocol for your reference.

Data for non-consented patients

Patients who have not consented to participate with sharing data with the ANZTCT Registry are still required to have their all of their data submitted to the Registry. However, the purpose of its use will be strictly used for centre activity, safety and quality purposes, such as benchmarking. The data will not be used for other projects or research.

All data fields including follow-up information are required to be completed for these patients.

Identifying details should be entered as below:



A Patient UPN should be assigned to the patient as this is the centre's reference identifier for this patient. Please refer to the description for this under Forms > Patient Details

If the Country of Residence is **Australia**, the following fields also appear:

Postcode will appear for **New Zealand** residents:

These should also be completed where possible

TRANSPLANT TYPES – DEFINITIONS

Planned multiple transplants as part of treatment protocol

These are planned as two (tandem) or more autografts or an autograft followed by an allograft. The transplants may take place at more than one transplant centre, i.e. autograft and allograft centre.

These transplants are registered as separate transplants and selecting 'Yes' for 'HSCT part of a planned multiple graft protocol?' would identify these as planned multiple infusions.

Note: the subsequent transplant is not given in response to disease relapse or progression.

Please note that the 'autologous staged' option for Transplant type should no longer be used. Each infusion is entered as a separate autologous transplant.

Infusions given over more than one day

This is regarded as one transplant using the first day of infusion as the transplant date.

Allogeneic boost

After an allograft, additional cells from the original allogeneic donor may be given in response to delayed neutrophil recovery, without conditioning treatment. This would be regarded as a separate transplant.

Autologous top up

Also known as "Autologous rescue". These are the patient's cells given to restore haematopoiesis after graft failure. These infusions do not have to be entered, however you should report the graft failure in the appropriate follow up form.

Post-Transplant Donor Cellular Infusion

These are cells obtained from an allogeneic source and used to treat the following indications:

- Suboptimal chimerism, promote engraftment or immune reconstitution
- Treat GVHD, disease or infection
- Prophylaxis of GVHD, disease or infection

This information is collected on the 100 day and 1st Annual Follow Up pages. Donor cells given for failed or poor neutrophil recovery, loss of graft or late graft failure should be reported as a subsequent transplant.

Cell Therapy without a preceding HCT

These cells may be from an autologous or allogeneic source and should be reported in the Cell Therapy forms e.g. CAR-T cell therapy.

Date format: All dates are formatted as dd/mm/yyyy

FORMS

The forms required for each transplant:

- **Transplant Registration** – includes the Patient and Transplant information pages in ASTRO. The pdf versions are available as Autologous and Allogeneic Forms. Submission should occur soon after the transplant infusion.
- **100 Day** – due after100 days post infusion.
- **Annual Follow Up** – due annually for the first 10 years, then every two years thereafter.

  If the patient receives another transplant, then the period leading up to the start of conditioning chemotherapy (or infusion if no conditioning is planned) should be reported on the Annual Follow-Up form of the previous transplant. The Follow-Up forms then come due with the most recent transplant. There should be no period overlapping on these forms.

These forms are available on the ABMTRR website http://www.abmtrr.org/index.php/resources/data-management/

PATIENT DETAILS

Patient UPN

This is the **U**nique **P**atient **N**umber that the transplant centre assigns to each patient or transplant to identify transplant recipients.

Please do not use the Hospital Medical Record Number.

Name ID

These fields are optional

This is only used to assist the transplant centre in identifying the recipient e.g. for follow up or queries. The maximum number of characters as follows: first four letters of surname and first two letters of the first name.

If the name contains ‘c’ or an apostrophe, enter as following examples: McKN enter as MCKN, O’ROU enter as OROU

Country and Place of usual residence

Enter the country, and the State if Australian.

This should be where the patient normally resides. Do not enter a temporary accommodation the patient may be residing at during the transplant.

Postcode

Enter postcode for Australian and New Zealand patients.

Sex

Date of birth

Indigenous status

This currently applies to Australians only. This information is available from the hospital medical record.

Patient consent

Consent is required from all transplant recipients for the transfer of information describing themselves and their transplant procedures to the ANZTCT Registry. The patient consent procedure will be dependent on the individual hospital's policy.

CIBMTR ID

This is the identifier assigned by CIBMTR (Centre for International Blood and Marrow Transplant Research) to recipients whose transplants are also reported to their registry.

Survival Status and Survival Status Last Known Date (Latest date patient is seen)

Please enter the latest survival status and the latest date available at the time of reporting. This date may be obtained from correspondence or pathology results etc. This date is used in survival analysis.

If the patient has died, then this will be the death date.

TRANSPLANT DETAILS

Has the patient's Address Changed?

This field is relevant for a patient receiving a subsequent transplant and the patient has moved since their previous transplant.

If the patient has moved, then enter the new place of usual residence details.

Transplant date

Enter the date of first day if the infusion is given over more than one day. It will be regarded as one transplant.

Type of transplant

Options: Allogeneic, Autologous

Do not use the 'Autologous staged' option. These should be reported as part of a planned multiple graft protocol, with each infusion listed as a separate autologous or allogeneic transplant.

HSCT part of a planned multiple graft protocol

Please indicate if the transplant is part of a planned series of autologous infusions or a tandem transplant protocol.

Transplant number

Chronological number of transplants for this patient

If more than one transplant (Paper form)

If second or subsequent transplant, was previous transplant performed at different centre? (ASTRO)

Complete the following

- Date of prior transplant
- Centre where transplant performed
- Type of previous transplant

Providing information in this section will assist the Registry in linking the transplant to an existing patient record in the database if a prior transplant has been registered separately.

If the transplant was performed at a different centre, an approximate date can be entered if this is not known.

Mobilisation

Select the agent(s) given to an autologous recipient or an allogeneic donor for the mobilisation (otherwise known as priming) of cells for this transplant.

If there are multiple collections, then include all agents used.

Transplant source (Stem cell source)

Select the cell source (or cell sources if more than one type) that are infused in this transplant.
If there are more than one donor e.g. double cord transplant, completion of the Multiple Donor section is required.

Donor-recipient relation - complete for allogeneic transplants

HLA matched other relative or **mismatched relative** includes siblings who are not HLA identical and all other blood related relatives. Adoptive or step-parents/children are reported as unrelated.

If **"…other relative"** is selected, then the following fields apply

Haploidentical

Please indicate if the donor is known to be haploidentical.

A haplotype (half of a genotype) refers to the combination of linked HLA genes transmitted on a single parental chromosome. The only way to establish whether a related donor is haploidentical is by looking at the HLA typing of the family including parents, siblings and/or children of the patient. Usually genotypic identity can only be proven if data on both parents are available. The number of mismatches cannot be used to completely identify a family donor as haploidentical, but is a good approximation is if the number of mismatches is 2 or more.

Ref: EBMT MED-AB Forms Manual 21/12/2020

Specify relation

The relationship of donor to recipient e.g. mother, sister.

HLA-Match

If the donor is unrelated or HLA-mismatched related, then complete the following table.

A	B	C	DRB1	DQB1	DPB1	
						Antigenic (serological or low resolution)
						Allelic (DNA or high resolution)

Options: matched, 1 mismatched, 2 mismatched, not done

Typing is usually performed by NGS or similar methods. These results should be entered into the Allelic fields. The Antigenic fields should be left blank however they remain in the table for results from older transplants when it was more commonly used method for tissue typing.

Were any of following components of this transplant performed substantially as outpatient procedures?

Indicate if more than half the time is spent as an outpatient during the following procedures:

- **Conditioning**
  For example, chemotherapy was administered as an outpatient on 3 days of a 5 day protocol then indicate “yes” for this field
- **Infusion**
- **Acute post-transplant period**
  This is defined as up to 30 days post-transplant.
  Answer ‘Yes’ if the patient spends less than 15 days as an inpatient. If the patient is admitted into the Hospital in the Home program (or equivalent), then this is considered as outpatient care
  If patient dies within the 15 days, then leave this blank.

Date diagnosed of primary disease for this transplant

This is the date of diagnosis of the indication for which the patient is being transplanted.

Some scenarios:

Transformed lymphoma (NHL to another NHL, or HD to NHL) – the transformed lymphoma is the indication for transplant so the diagnosis date is the date of the transformation. Richter's Syndrome (CLL to NHL), the diagnosis date is the date that the CLL transformed to NHL (this was previously noted as the diagnosis date of the CLL)

Myeloma progressed from a solitary plasmacytoma, then the date of diagnosis is the date of myeloma diagnosis.

MDS transformed to AML – diagnosis date of primary disease for the transplant would be date of transformation to AML

Main classification and Diagnosis

Refer to the Disease Classification section.

ABMTRR Diagnosis List is available on our website to help identify the Main Classification of the diagnosis.

Preparative Regimen

Was conditioning preparation intended to be myeloablative?

Complete for allogeneic transplants only

If the conditioning regimen is reduced intensity or considered non-myeloablative then the "No" should be selected for this question.

Pre-transplant conditioning

Select all agents given.

In addition:

- Indicate the dose options for Melphalan and TBI
- Indicate the source of ATG e.g. ATGAM, Thymoglobulin, Fresenius/Grafalon

Graft information

Cell count

- Nucleated cells x 10^8/kg
- CD34 cells x 10^6/kg

These are to be reported in number per kilogram recipient's weight. Please take care that you are reporting the correct units.

The cell counts reported should represent the actual number of cells infused. This would be after thawing and/or manipulation if utilised.

For cryopreserved products, if the cell count was not performed after thawing, then report the available cell count and add a note of when it was performed e.g. at time of harvest/ product arrival/ pre-cryopreservation (in the 'Prior procedure detail" field)

Do not use the value corrected for cell viability.

Graft manipulation

Allogeneic only

Indicate if the graft was manipulated for CD34+ selection, T cell depletion or other. Do not include RBC or plasma depletion or volume reduction.

Have cells been cryopreserved?

If the cells were harvested from the donor and then cryopreserved and stored for a period beforehand, please indicate here.

Recipient Performance status prior transplant

Use Karnofsky (patients 16 years and older) or Lansky score (patient less than 16 years) to determine the score (10-100) that best represents the recipient's functional status.

The performance score should be documented at the time of the pre-transplant work up prior to commencement of 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.

Performance status

	Karnofsky Scale (recipient age≥16 years)		Lansky Scale (recipient age <16 years)	
100	Able to carry on normal activity; no special care is needed	Normal, no complaints, no evidence of disease	Able to carry on normal activity; no special care is needed	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
70	Unable to work, able to live at home, cares for most personal needs, varying amount of assistance needed	Cares for self, unable to carry on normal activity or to do active work	Mild to moderate restriction	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
40	Unable to care for self, requires equivalent of institutional or hospital care, disease may be progressing rapidly	Disabled, requires special care and assistance	Moderate to severe restriction	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

Recipient CMV status

Report the CMV status of the recipient prior to start of conditioning therapy.

Most laboratory reports a positive result as reactive and a negative result as non-reactive. Select "unknown" only if the test results are inconclusive, unequivocal 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.

A positive IgM or IgG assay is considered a positive/reactive result. Any previous history of positive antibody assay can be reported as a "positive" test result.

Were any of the following used to treat or manage disease between diagnosis and transplant?

This includes chemotherapy, radiotherapy, or surgery if it was used for disease management. Details of these and extra information may be entered into the details field. Do not include previous transplants.

Allogeneic Transplant

Multiple Donors?

Complete questions 10, 11,14a, 14b and 18 on an additional paper form for each donor.
In ASTRO, select this checkbox to display the extra fields required for the additional donor.

Number of Donors

Indicate the number of donors used in this transplant.

Donor sex

Female donor, number of pregnancies

Specify the number of donor pregnancies if known.

Donor age

Enter age in years

Donor CMV status

Most laboratory reports a positive result as reactive and a negative result as non-reactive. Select "unknown" only if the test results are inconclusive, unequivocal 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.

If the cell source is from cord blood, this question is not relevant.

CMV Prophylaxis, agents used

CMV prophylaxis is the use of antiviral agents to prevent CMV reactivation and disease. It is administered to CMV seropositive patients and may be given from the day of engraftment to 100 days post-transplant to prevent reactivation (positive CMV PCR or pp65 antigen) of CMV.
In most centres the preference will be to use pre-emptive strategy (see below), so primary prophylaxis for CMV is unusual.

CMV Prophylaxis: Pre-emptive Strategy

Answer ‘yes’ to this question if the patient is regularly monitored for CMV activity using sensitive methods such as Quantitative polymerase chain reaction (PCR) or CMV pp65 antigen.

The strategy involves the surveillance of CMV activity as described above.

If there is detection of CMV viremia (reactivation*), antiviral therapy (e.g. ganciclovir, foscarnet) can then be given with the aim to suppress viral replication before the onset of clinical symptoms, until the viral load becomes undetectable.

GVHD Prophylaxis

Immunosuppressive agents are given to prevent the development of graft versus host disease. Do not report any agents used to *treat* GvHD, i.e. agents given at the onset of GvHD

Any GvHD prophylaxis agents given prior to day 0 (e.g. anti-thymocyte globulin) should be reported under the Pre-transplant Conditioning

Unrelated Donor Information

Include adoptive or step-parents/children here

ABMDR (NZBMDR) Recipient-ID

This is the recipient identification number or code provided by the Australian or New Zealand donor registries. (ABMDR/ NZBMDR).

Donor-ID

The GRID (Global Registration Identifier for Donors) coding system, a 19 digit number complying with international guidelines.

Previously, it consisted of either the registry code followed by a donor identification number, or an identification number only.

Registry country

Select the country where the donor registry is based.

Multiple Donor

The fields in this section include:

- 2nd Donor sex, number of pregnancies if female
- 2nd Donor CMV status
- 2nd Donor Cell Source
- 2ndDonor Relationship
- 2nd Donor HLA Match
- 2nd Donor ID
- 2nd Donor Registry country
- 2nd Donor Nucleated cells
- 2nd Donor CD34+ cells

This section displays in ASTRO when 2 or more is selected for Number of donors e.g. double cord transplant.

There are no provisions for the collection of data for more than 2 donors in ASTRO. The ANZTCT Registry should be contacted.

DISEASE CLASSIFICATION

ABMTRR Diagnosis List is available on the ABMTRR website to help identify which main classification a diagnosis should be reported under.

Please indicate the **most specific** disease classification using the International Classification of Diseases for Oncology (ICD-O) or the CIBMTR Form 2402 https://cibmtr.org/CIBMTR/Data-Operations/Data-Collection-Forms

Acute Leukaemia

Refer to the Diagnosis List to help classify the diagnosis and disease classification

Acute myeloid leukaemia

Report cytogenetic and molecular abnormalities

AML transformed from MDS/MPS
Complete both the Myelodysplasia / Myeloproliferative Diseases and AML sections.
The date of diagnosis of primary disease for the transplant will be the date of transformation to AML, i.e. when the AML was first diagnosed.
In ASTRO: the additional MDS fields will display when “Yes” is selected for “AML transformed from MDS/MPS”.

Was disease related to prior exposure to therapeutic drugs/radiation? (Treatment related?)
The AML may be associated with the agents given to treat a prior malignancy. The AML would then be a secondary malignancy.

Acute Lymphoblastic Leukaemia

Report cytogenetic and molecular abnormalities

Other Acute Leukaemia

E.g. Acute undifferentiated leukaemia, biphenotypic leukaemia

Report cytogenetic and molecular abnormalities

Chronic Myelogenous Leukaemia

Indicate the presence of Philadelphia chromosome t(9,22) and bcr-abl gene

Other Leukaemias

E.g. Chronic lymphocytic leukaemia (CLL), Prolymphocytic leukaemia

If the recipient has Chronic lymphocytic leukaemia which has transformed to Diffuse large B cell lymphoma (Richter's transformation), then report Non-Hodgkin Lymphoma as the indication for transplant.

Myelodysplastic/Myeloproliferative Disorders

Refer to the Diagnosis List to help classify the diagnosis and disease classification

Myelodysplastic Syndromes (MDS)

Myeloproliferative Neoplasms (MPN)

- primary myelofibrosis, Polycythaemia Vera

Combined Myelodysplastic/Myeloproliferative Disease

- CMML, JMML

Therapy related

Indicate if the MDS/MPD was related to prior exposure to therapeutic drugs or radiation

Transformed to AML

If the MDS/MPN has transformed into AML, then the AML is the indication for transplant. Complete **both sections for MDS/MPD and AML** on the paper form. Date of diagnosis (of primary disease for this transplant) will be the transformation date.
In addition, the Date of MDS/MPN diagnosis should be given.
In ASTRO, the additional fields will display when "AML transformed from MDS/MPS" checkbox is selected.

Lymphoma

Refer to the Diagnosis List to classify the diagnosis and disease classification

Hodgkin Lymphoma

Non-Hodgkin Lymphoma

- B-cell neoplasms
- T-Cell & NK-cell neoplasms

If the lymphoma transforms from one subtype to another prior to transplant, report the most current subtype at the time of transplant. Then report the original lymphoma subtype under **Lymphoma histology at diagnosis** (**Prior histology if transformed** in the paper forms)

HL and NHL can occur at the same time. It should be determined which is the main indication for transplant as only one should be reported.

"B-cell lymphoma, unclassifiable, with features intermediate between DLBCL and classical Hodgkin lymphoma" should be reported under Non-Hodgkin Lymphoma, "Other B cell lymphoma, specify"

Richter's transformation - CLL transformed into Diffuse large B-cell lymphoma is reported under Non-Hodgkin Lymphoma. Indicate CLL as the prior histology on the paper form or "Richter's transformation" as the "Lymphoma Histology at Diagnosis" in ASTRO.

Precursor T- and Precursor B-cell lymphoblastic lymphoma (or lymphoma/leukaemia) should be reported as acute lymphoblastic leukaemia (T-cell lymphoblastic leukaemia/lymphoma or B-cell ALL).

Plasma Cell Disorders

E.g. Myeloma, Plasma cell leukaemia, Primary amyloidosis

Multiple Myeloma

Specify monoclonal protein type: IgG, IgA, IgD, IgE, IgM (not Waldenstrom macroglobulinemia)
Light chain type: kappa, lambda
Or
Light chain only – indicate which light chain type i.e. kappa or lambda
Non-secretory – kappa/lambda light chains are not detected

Stage at Diagnosis: Indicate which staging system is used, Durie-Salmon or ISS

I.S.S. System

Stage I	β2 microglobulin < 3.5 mg/L, albumin ≥ 35 g/L
Stage II	β2 microglobulin < 3.5 mg/L and albumin <35 g/L or β2 microglobulin 3.5 to < 5.5 mg/L irrespective of albumin
Stage III	β2 microglobulin ≥ 5.5 mg/L irrespective of albumin

Durie-Salmon System

Stage I	All of the following: • Haemoglobin >99 g/L • Serum calcium <2.65mmol/L • No lytic lesions or one single minor lesion • Monoclonal IgG < 50g/L or IgA <30 g/L (for `common' type myeloma), Or light chains in urine <4 g/24 hrs (for light chain myeloma)
Stage II	Neither stage I or III
Stage III	One or more of the following: • Haemoglobin < 85 g/L • Serum calcium > 2.65mmol/L • Monoclonal IgG >70 g/L, IgA >50 g/L ('common' type) or light chains in urine > 12 g/24 hrs • Multiple skeletal lesions and/or pathologic fractures
Sub-classification	
A	Relatively normal renal function (serum creatinine < 180µmol/L)
B	Abnormal renal function (serum creatinine ≥ 180µmol/L)

Solid Tumours

Refer to the Diagnosis List to help classify the diagnosis and disease classification

The 'Disease status at transplant' is no longer required for solid tumours.

Non Malignant Diseases

Refer to the Diagnosis List to help classify the diagnosis and disease classification

Bone Marrow Failure Syndromes e.g. aplastic anaemia

Haemoglobinopathy

Histiocytic Disorders

Inherited Disorders

- **Disorders of metabolism / Osteopetrosis**
- **Immune Deficiencies**
- **Platelet Disorders**

Autoimmune Disorders

- **Connective Tissue Disease** e.g. scleroderma (Systemic sclerosis)

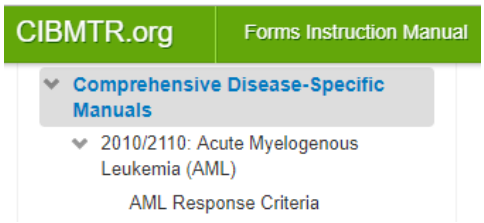
- **Vasculitis** e.g. Wegener granulomatosis, Behçet's Syndrome
- **Arthritis** e.g. Rheumatoid arthritis, Stills disease
- **Multiple sclerosis**
- **Other Neurological Autoimmune Disease**
- **Haematological Autoimmune Disease**
- **Bowel Disease**

Other disease, specify

Use this option only if the disease does not belong to any of the previous categories.

Disease Status at Transplant

Refer to the Response criteria of the specific disease for the definitions in the CIBMTR Forms Instruction Manual. These are located in the Comprehensive Disease-Specific Manuals: https://www.manula.com/manuals/cibmtr/fim/1/en/topic/none



Disease classification	Disease Status at Transplant
Acute Leukaemia	Never Treated Primary Induction Failure (PIF) Complete Remission - specify number of CR Relapse - specify number of relapse If a partial response is achieved, then report as PIF or relapse
CML	Chronic Phase – haematological, cytogenetic, molecular remission achieved? Accelerated Phase Blast Crisis specify the number of Chronic Phase, Accelerated Phase or Blast Crisis
CLL, PLL	Never Treated Complete Remission (CR)

	Partial Remission (PR) No Response/Stable Disease (NR/SD) Progression Relapse (untreated)
MDS/MPN/CMML (not required for JMML)	Complete Remission (CR) Improvement, but no CR (Haematological Improvement- HI) No response (NR) /Stable disease Progressive/Worse from Haem Improvement Relapsed after CR * Indicate Number of relapse Supportive care or treatment without chemotherapy (Never treated)
Lymphoma	Never Treated Primary Refractory (less than PR to initial therapy)/PIF res Partial Response/remission* Complete Remission* Relapse * Progression * specify Number of PR, CR, or Relapse (Do not include PRs when calculating the CR number) For relapse only - indicate if disease is sensitive to chemotherapy Sensitivity is measured based on the last chemotherapy given within the six months prior to transplant. • Sensitive: ≥ 50% reduction in the bi-dimensional diameter of all disease sites with no new sites of disease • Resistant: < 50% reduction in the diameter of all disease sites or development of new disease sites • Untreated: no chemotherapy was given within the six months prior to the pre-transplant conditioning. • Unknown: not assessed or not available
Multiple Myeloma and Solitary plasmacytoma	Never Treated Stringent Complete Remission (sCR) Complete Remission Very Good Partial Response (VGPR) Partial Response (PR) Stable Disease (SD) Progressive Disease (PD) Relapse from CR (untreated)
Solid Tumour	Not required

FOLLOW UP REPORTING

Follow up is due at:

- 100 days - captures information during the acute post-transplant phase
- Annual up to 10 years, and then every second year thereafter.

The 100 day and First Annual Follow Up is particularly important for quality analysis and survival.

It is not necessary to catch up on completing all past annual follow up forms if these have not been reported. Completing only the latest annual follow up is recommended, unless otherwise requested by the Registry.

Subsequent transplant reporting

If another transplant is given during a follow up period, 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 form and the associated follow up will then be required for the subsequent transplant. No further follow up will be required for the previous transplant.

Lost to follow up

If the centre has completely lost contact with the patient, the patient will remain “Alive” with the last date known alive entered.

There are no provisions to enter ‘lost to follow up’ into the database, however a brief note (e.g. lost to follow up/ patient moved to …) may be added to the ‘Patient Comments’ which will display on the follow up lists to identify these patients.

Centre transfer for follow up

If a patient is being followed up at another transplant centre, the Registry should be contacted to arrange transfer of the patient’s record to the other reporting centre with the centre’s permission.

When a patient is transferred from one transplant centre to another transplant centre, the information entered into ASTRO should include the period whilst under their care.

If the patient no longer visits the transplant centre for follow up care, the transplant centre should continue to update ASTRO using correspondence from a specialist or GP. A pathology report can also be used to update the latest contact date.

100 DAY

Apart from the "Survival Status Last Known Date", all other information provided here should be within the hundred days post-transplant. Any "latest" dates of events should be as close to 100 days as possible (e.g. latest dates of assessment.) However, if Acute Graft versus Host Disease (aGVHD) develops beyond 100 days, the date of first incidence of aGVHD should still be reported here.
If chronic Graft versus Host Disease develops within the 100 days, it should be documented in the 1st Annual Follow-Up Form.

If another transplant occurs before the 100 days, then events should be reported up to the day prior commencement of conditioning therapy. If no preparative conditioning is planned, then the reporting period will include up to the day before the subsequent infusion date. Another Transplant Registration and the associated follow up will then be required for the subsequent infusion.

Survival

Survival Status

Indicate the recipient's latest known survival status.

Last known date of contact, or death date

Report the last known date the patient was known alive or the date of death. A date from correspondence or pathology report etc. may be used.

Primary cause of death

Report only one main cause of death. However, if it the cause was transplant related, then select all the contributing causes.
Primary cause of death, options:

- Relapse progression/persistent disease
- Transplant related
- New malignancy
- Other, specify
- Unknown

Report the underlying cause of death which is defined as "the disease or injury that initiated the chain of events that led directly or inevitably to death."

Ref: CIBMTR Forms Instruction Manual: 2900, Question 4

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". Do not report the mode of death e.g. 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. It should not be assumed 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 "**Transplant related"**. Select as many contributing causes as relevant. E.g. Infection, GVHD, pulmonary toxicity

Transplant related causes:

Cardiac toxicity- includes heart failure, congestive heart failure, non-infectious pericarditis, and/ or cardiac tamponade.

Pulmonary toxicity – includes non-infectious lung failure, which can include ARDS, pulmonary haemorrhage, radiation pneumonia, etc. If bronchiolitis obliterans is a part of chronic GVHD, it can also be reported here

Rejection/ poor graft function – this is defined as ANC < 0.5×10^9/L and bone marrow biopsy with < 5% cellularity either after engraftment is achieved of after day 28 post-transplant.

Veno-occlusive disease (hepatic sinusoidal obstruction syndrome) – defined as having at least two of the following features

- Jaundice (bilirubin > 34 µmol/L)
- Hepatomegaly with right upper quadrant pain
- Ascites and/or weight gain (> 5% over baseline, as generally accepted)

Ref: McDonald GB, et al. *Hepatology* 1984; 4:116-22. Jones RJ, et al. *Transplantation* 1987; 44:778-83

New malignancy
If a new malignancy has contributed to the death, then the diagnosis of the malignancy should be reported under New Malignancies.

Please note:

- If the cause of death was due to a malignancy diagnosed before the transplant, then report the cause as a prior malignancy under "Other"
- If the malignancy is considered a progression of the disease for which the transplant was for (e.g. MDS to AML), then the main cause of death should be reported as "Disease progression" rather than a new malignancy.

Aplastic anaemia – graft failure

If a recipient was transplanted 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.

Engraftment

Neutrophil engraftment

This 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.
Do not start counting ANC values ≥ 0.5 x 10^9/L until after the ANC has dropped to the lowest level (nadir) post day 0.
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"

Did graft failure occur?

This is primary graft failure with 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.

Platelet engraftment

This is defined as the platelet laboratory values of 20 x 10^9/L or more. The "date achieved" will be the first of three consecutive days, and the patient has not received any platelet transfusions in the 7 days prior. (e.g. 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 platelet 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"

In some situations, the patient may be discharged before their platelet count has reached 20 x 10^9/L or is discharged within seven days following a platelet transfusion. The date with available platelet count should be used as the platelet engraftment date instead of an estimated date unless the available platelet count is too far away from the estimated date.

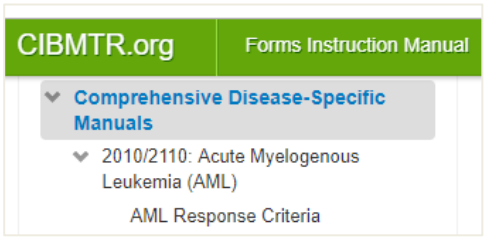
Example: if a platelet count is available within 7 days from the estimated date of platelet engraftment, then use actual platelet count date as the platelet engraftment date.

If a platelet count is 7 or more days from the estimated platelet count date, then use the estimated date as long as there was evidence the platelet count was on the rise.

Disease assessments

Please refer to the appropriate disease response criteria in the CIBMTR Forms Instruction Manualhttps://www.manula.com/manuals/cibmtr/fim/1/en/topic/none

e.g.



Best disease status achieved post transplant, prior to treatment modification

(Malignant diseases only)

Responses entered into ASTRO for this section will copy to the other follow up pages where this question appears as this is a once only event.

Report the recipient's best response to the planned course of the transplant. Do 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 post transplant, then select "Never in complete remission" Include the latest assessment date in the report.
The best response is usually achieved within the 100 days however it may occur beyond this for some diagnoses e.g. Myeloma and CLL.

Relapse or Progression post transplant

Responses entered into ASTRO for this section will copy to the other follow up pages where this question appears as this is a once only event.

Report the **date of first detection** of relapse (or disease progression for persistent or residual disease) after transplant.

Detection methods include clinical/haematological.

Cytogenetic and Molecular detection methods are relevant for leukaemia only.

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

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 under "If no, date last assessed".

Adverse events in the first 100 days post transplant

Report the following events, and 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

CMV reactivation is detected by positive CMV (Quantitative PCR or pp65 antigen) in the absence of CMV disease.

CMV disease

Indicate if there is probable or proven evidence of CMV disease

References:

1. Definitions of Cytomegalovirus Infection and Disease in Transplant Patients for Use in Clinical Trials.Ljungman P et al; Disease Definitions Working Group of the Cytomegalovirus Drug Development Forum. Clinical Infectious Diseases2017; Jan 1;64(1):87-91. Epub 2016 Sep 28

2. 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

Was anti-CMV therapy given

This refers to any anti-viral medication that was given to treat CMV infection in the first 100 days. Do not include any agents given for prophylaxis.

Acute Graft versus Host Disease

Complete for allogeneic transplants only.

GvHD was originally classified as acute or chronic based on the time of onset, where acute GvHD occurred within 100 days post transplant. The diagnosis of acute and chronic GVHD is now based on clinical and histological features and may be diagnosed outside of these parameters. For example, symptoms/signs consistent with acute GVHD may be diagnosed at day 140, however for reporting purposes, it should be reported on the 100 Day form under Acute GVHD

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

Date of first incidence of acute GvHD

Report the first incidence only

Grading and staging of acute GvHD

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

Przepiorka et al, Bone Marrow Transplant 1995; 15(6):825-8

*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.

RULE OF NINES
Percent body surfaces

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

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		-

Donor cellular infusion (DCI)

DCI is a form of immunotherapy with cells donated from an individual other than the recipient. These cells are given post transplant for the treatment of disease or infection, or mixed chimerism, with the aim to create an immune effect within the patient. It is not an intent to repopulate the recipient's marrow with haematopoietic cells.

Donor cells given for failed or poor neutrophil recovery, loss of graft or late graft failure should be reported as a subsequent transplant.

First infusion date

Report the date of the first infusion

Cell type

Donor cell types include but are not limited to:

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

Indication

Include but are not limited to:

- 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 e.g. viral
- treatment of PTLD or EBV lymphoma

ANNUAL FOLLOW-UP

The information provided should be within the follow up period, including events **since the last report** for the following fields:

- Last known disease status
- Did graft failure occur
- Performance status
- Chronic GVHD

Any assessment dates (e.g. latest assessment of disease or performance status) should be as close to the anniversary date as possible.

It is not so important to report the **once only events** in the correct follow up period as the information in these fields are copied to show in all Annual Follow Up pages. These include:

- First Relapse or Progression post transplant fields
- Best disease status achieved post transplant
- Date of first incidence of chronic GvHD
- New malignancy (displays in Patient Details and Annual Follow Up pages)

Survival Status, Last known date of contact

Refer to these questions mentioned under 100 Day.

Disease assessments

Last known disease status

Completing this section allows more accurate analysis of patient status, when assessing patient outcome or survival.

Assessment of the disease status may be from a clinical assessment, correspondence from a physician, radiological, or laboratory test (FBE, biochemistry, cytogenetic, flow cytometry, molecular)

The “Date assessed” may not be the same as the “Last known date of contact”.

Please note: in ASTRO, the data in the “Last known disease status” and associated ”Date assessed” are overwritten with the latest reporting in subsequent Annual Follow Up forms.

Best disease status achieved post transplant, prior to treatment modification

Refer to 100 day section.

Responses entered into 100 Day page in ASTRO for this section will copy to the Annual Follow Up pages where this question appears as this is a once only event.

Did graft failure occur?

Late or secondary graft failure may occur when the recipient meets criteria for engraftment but later develops the loss of chimerism (<5%) and/or persistent neutropenia.

First Relapse/Progression post transplant

Responses entered into ASTRO for this section will copy to the other follow up pages where this question appears as this is a once only event.

Refer to 100 Day section.

New malignancy, lymphoproliferative or myeloproliferative disorder post transplant

Include:

- Skin cancers
- Post transplant lymphoproliferative disorders
- Benign conditions, with the potential of developing into a malignancy e.g. CIN (early stages), pleomorphic adenoma

Do not report:

- transformation of the primary disease (the indication for the transplant)
- progression of the primary disease e.g. plasmacytoma develops into myeloma, MDS into AML.
- recurrence of a prior malignancy, (malignancy reported in the pre-transplant history)

Performance Status at this year's follow-up

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

Audit status: Estimate or documented?

Indicate if the Performance Score has been documented in the recipient's notes or correspondence (documented) or derived from the notes or correspondence (estimated)

Chronic Graft Versus Host Disease

Complete for allogeneic transplants only.

The diagnosis of acute and chronic GVHD is based on clinical and histological features previously it had been based on the time of onset i.e. before or after 100 days. For example, if cGVHD is diagnosed at d+85, then this should still be entered on the 1st Annual Follow Up form.

Is patient currently on immunosuppression?

Indicate whether the recipient is taking systemic steroids (e.g. prednisone) or non-steroidal immunosuppressive agents (e.g. cyclosporine, mycophenolate) to treat or prevent GVHD within this reporting period.

Options: Yes/No/Not applicable/Unknown

Immunosuppression date ceased

Report the date within this reporting period

Was Chronic GvHD present during this period?

Indicate if the patient developed chronic GvHD within the reporting period. If "Yes" is selected in ASTRO, the associated fields display.

Date of first incidence of chronic GvHD

Report the first incidence only

The response entered into ASTRO for this question will copy to the other Annual Follow Up pages where this question appears as this is a once only event.

Maximum grade of chronic GVHD during this period (NIH criteria)

Category	Number of affected organs or sites	Maximum severity score in affected organs or sites
Mild	1 – 2 organs (excluding lung)	1
Moderate	3 or more organs	1
	Any organ	2 (or lung score of 1)
Severe	Any organ	3 (or lung score 2 or 3)

Maximum grade is based on the following: NIH Consensus Criteria 2014
www.ncbi.nlm.nih.gov/pmc/articles/PMC4329079

Options: Mild/Moderate/Severe/unknown

Maximum extent of chronic GvHD

Indicate the maximum extent of chronic GvHD during this reporting period using following criteria (Sullivan KM, Blood 1981: 57:267)

Limited: Localised skin involvement resembling localised scleroderma with or without liver involvement No other organ involvement
Extensive: Generalised skin and/or multiple organ involvement

Organs affected

Tick as many checkboxes as applicable to include all the organs that were affected during the follow up period.

Data entered in this section should be relevant for this follow up period only. The follow up period will commence from the previous year's report up to the next anniversary of the transplant.

Donor cellular infusion

Complete for Allogeneic transplants only.

Report donor cellular infusions given to the recipient up to the first year post transplant. Infusions given after this period are not required to be reported.

Refer to 100 Day section for details.

REFERENCES

1. Center for International Blood & Marrow Transplant Research (CIBMTR) Forms Manuals https://www.cibmtr.org/manuals/fim

2. MED-AB Forms Manual. A guide to the completion of the EBMT HSCT Med-AB Forms https://www.ebmt.org/registry/ebmt-data-collection