Cell Therapy Data Collection Guidelines for DISEASE FORMS

Contents

INTRODUCTION

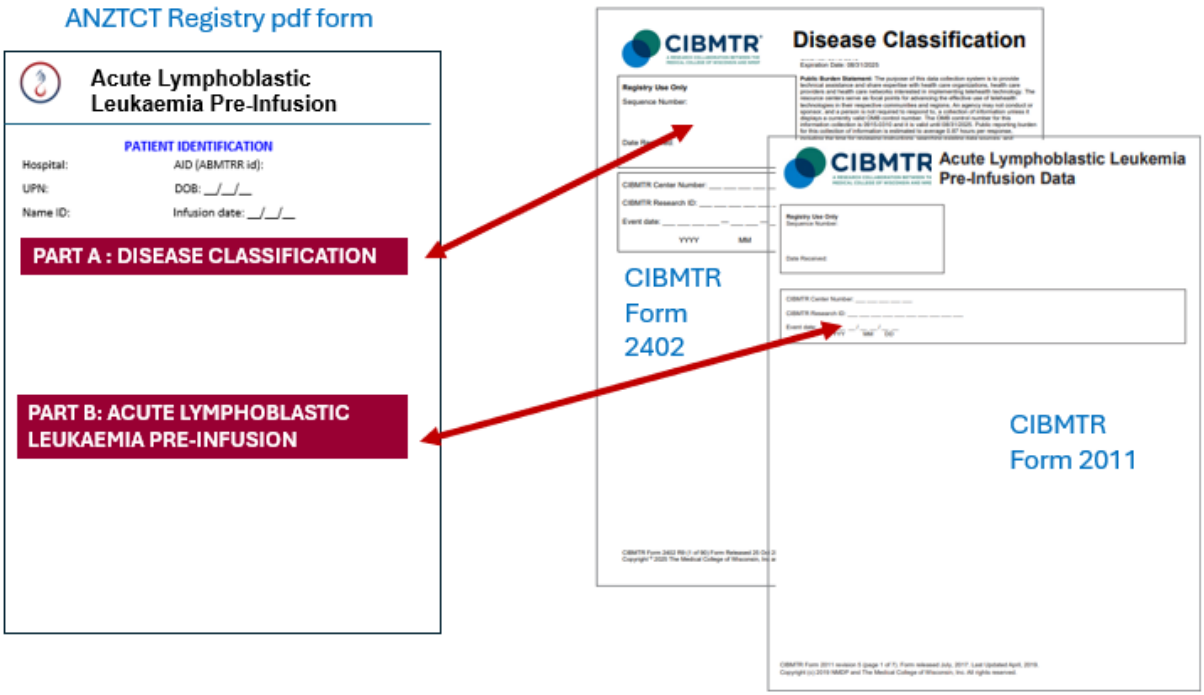
These guidelines refer to the Disease Classification and Disease specific forms and are intended to accompany the CORE Forms guidelines.

FORMS REQUIRED AT REGISTRATION

The questions relating to the diagnosis, disease characteristics and the disease response (prior to the infusion) are captured on two forms in REDCap to align with the CIBMTR forms:

- **Part A**: Disease Classification Form (*CIBMTR Form 2402*)
- **Part B**: Disease Specific Forms:
    - ALL Pre-Infusion (*CIBMTR Form 2011*)
    - Lymphoma Pre-Infusion (*CIBMTR Form 2018*)
    - Myeloma Pre-Infusion (*CIBMTR Forms 2016*)
    - CLL (*CIBMTR 2013*) to come

Please note that the pdf version of the ANZTCT disease forms contain content from Disease Classification (Part A) and the Disease Specific Form (Part B) on the same form to assist with streamlining data collection processes. These pertain to the disease prior to the cell infusion.



FORMS REQUIRED AT FOLLOW UP

These are required at 30 days, 100 days, 6 months, and then annually thereafter.

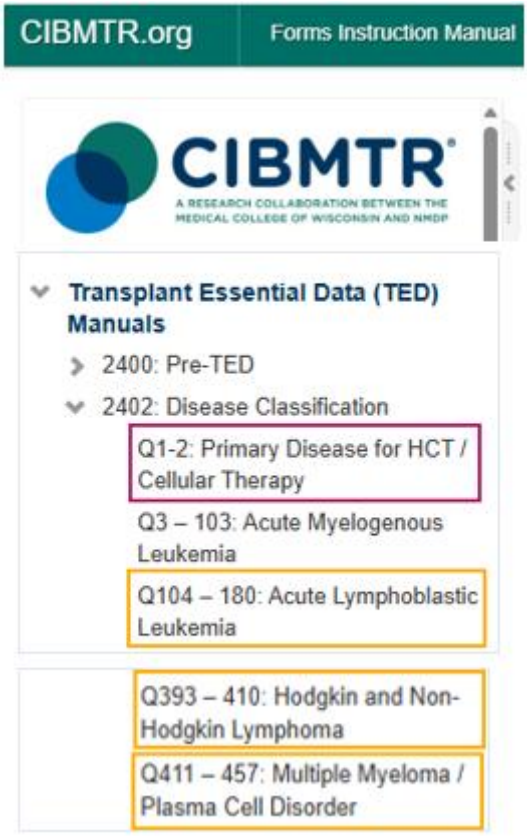
- ALL (Acute Lymphoblastic Leukaemia) Post Infusion
- Lymphoma Post Infusion
- Myeloma Post Infusion

These capture the best disease response to the cell therapy and any relapses or disease progression along with associated disease management.

In these guidelines, the explanation or definition of every field may not be included if they seem self-explanatory. For the comprehensive guidelines and definitions please refer to the CIBMTR Instruction Manual website: www.cibmtr.org/manuals/fim (as described below)

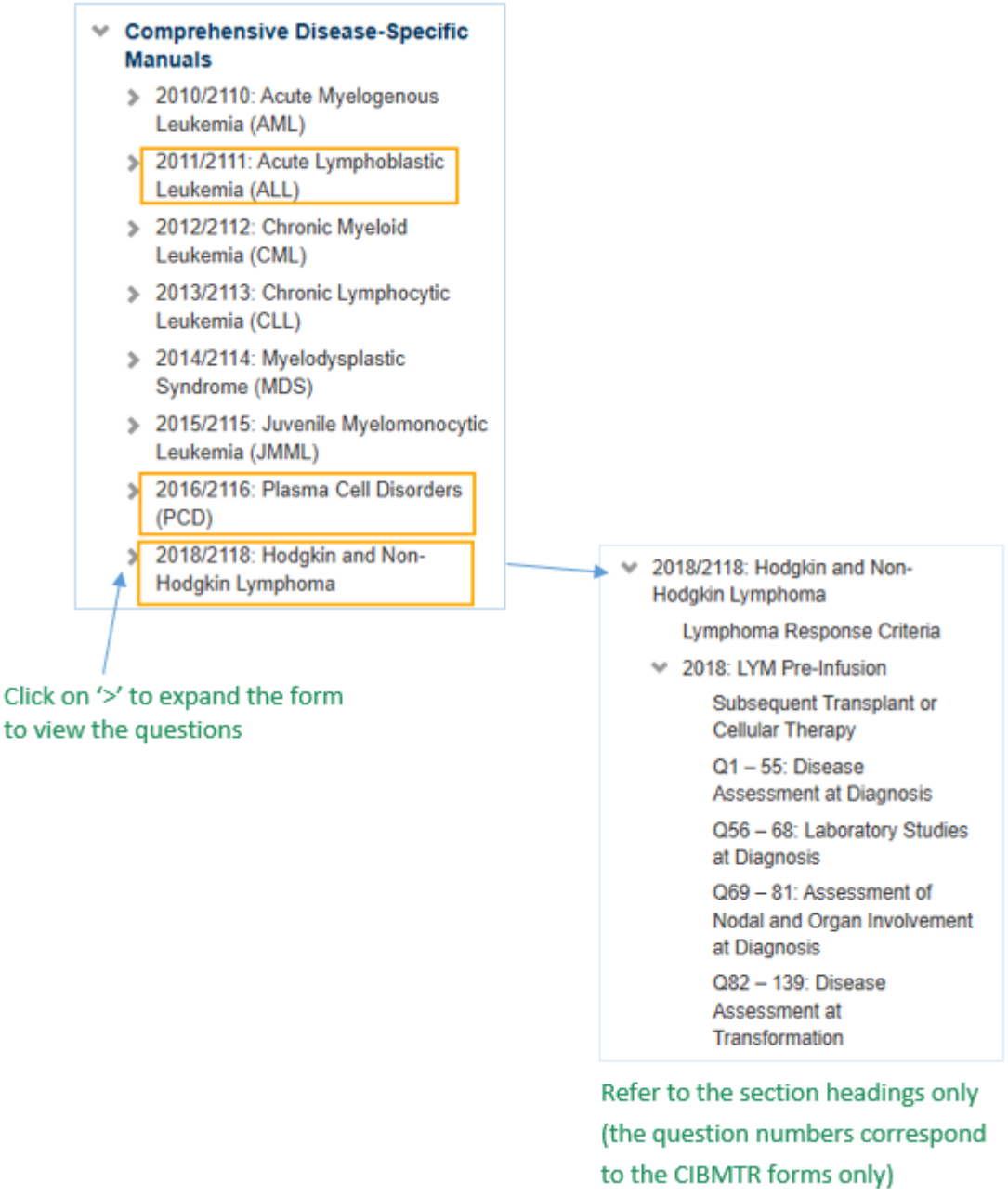
Part A: Disease Classification Forms (*CIBMTR Form 2402*) as shown on the CIBMTR website

Link to: 2402: Disease Classification - Forms Instruction Manual - 1



Part B: Disease Specific Forms:

Link to: [Comprehensive Disease-Specific Manuals - Forms Instruction Manual - 1]



Note:

- Forms 2011, 2016, 2018 represent the pre-infusion forms
- Forms 2111, 2116, 2118 represent the post infusions forms

GENERAL GUIDELINES FOR COMPLETING FORMS

The pdf versions of the forms are available at: https://anztct.org.au/registry/data-management-resources/

These may be used as a guide to assist with the data collection. Please note that not all options to the questions (as they appear in REDCap) are shown on these forms.

Guide for entering data

Date fields

Dates are entered as: dd/mm/yyyy

Please do not leave these blank if an estimate can be entered, using the following guidelines:

- only the month and year is known - enter as 15/mm/yyyy
- only the year is known - enter as 01/07/yyyy

In some cases, this rule may not make sense e.g., the diagnosis is in May and it is known that treatment was started on a given date in mid-May, then the diagnosis date may be entered as the 1st May.

Reporting lab values <, > and range of numbers.

Fields that are set as accepting numbers only will not accept '<' or '>' characters. Please report these results as described below:

- For < Less Than values: n – 1
- For > Greater Than values: n + 1
- When a value is reported as a range of numbers, report the median value of the range

Examples:

- Reporting <5% blasts in the bone marrow should be reported as 4% blasts
- Chimerism results indicating >95% donor cells should be reported as 96% donor cells
- 60-70% blasts in the bone marrow should be reported as 65% blasts

A fraction is given as 45-50%. If required to report a whole number, the median value is 47.5%, then apply rounding to give a value of 48%

DISEASE CLASSIFICATION FORM (PART A)

Reporting Subsequent Infusions

If this form has been submitted to the ANZTCT Registry for a previous cell therapy infusion for the same indication, only report assessments that have occurred since that infusion.

If the subsequent infusion is given for relapse or progression of the same indication, then report the assessments at the time of relapse/progression as the in between timepoint.

DIAGNOSIS

Date of diagnosis

This is the date of diagnosis of the indication for the cell infusion, e.g., if the CAR-T is given for diffuse large B cell lymphoma which had transformed, then this is the date of the DLBCL diagnosis i.e., the date of transformation.

Primary Disease for HCT / Cell Therapy

Associated questions will display when the **Primary Disease for HCT / Cell Therapy** is selected as follows:

ACUTE LYMPHOBLASTIC LEUKAEMIA

ALL CLASSIFICATION

Report cytogenetic or molecular abnormalities at diagnosis where possible. Only select 'ALL NOS' if no information is known.

Did recipient have predisposing condition

Tyrosine kinase inhibitors given any time prior to preparative regimen/infusion

DISEASE ASSESSMENTS

Report assessments at three time points prior to the infusion, where available

- at diagnosis, before any treatment
- between diagnosis and latest prior to infusion
- latest assessments prior to infusion, within 30 days of lymphodepletion/infusion

Assessments include cytogenetic (karyotyping and FISH) and molecular testing.

CNS disease - at any time prior to the infusion.

DISEASE STATUS AT INFUSION AND THE DATE ASSESSED.

Refer to the ALL Response criteria in the appendix (or CIBMTR Instruction Manual)

If complete remission was achieved, the following question(s) are relevant:

Number of cycles of induction to achieve CR1 (incl CRi)

Methods used to assess MRD at infusion

MRD was detected (by the method indicated in the preceding question)

If in relapse, then the following question displays

Date of most recent relapse

Also complete the Acute Lymphoblastic Leukaemia (ALL) Pre-Infusion Form

NON-HODGKIN LYMPHOMA

LYMPHOMA HISTOLOGY

Report the lymphoma histology at the time of the cell therapy infusion.
Select a diagnosis from one of these categories: NHL B cell, NHL T cell or PTLD classification
If the lymphoma has transformed, the prior histology is reported in the subsequent questions.

DLBCL subtype was based on

This question will display if the diagnosis is Diffuse large B-cell lymphoma is selected.

TRANSFORMATION

Transformed from CLL

17p abnormality detected

Transformed from different lymphoma histology (non CLL)

Prior histology

Date of original diagnosis

A transformation may occur after or at the same time as the initial lymphoma diagnosis.

IMAGING

PET (or PET/CT) scan performed - prior to start of preparative regimen/infusion
This is the latest scan performed within three months before commencement of the lymphodepletion /cell therapy infusion, regardless of any additional therapy given after this scan

PET (or PET/CT) scan positive

Date PET (or PET/CT) scan

Deauville (five-point) score - report the highest score if there are multiple values.

LYMPHOMA DISEASE STATUS PRIOR INFUSION

Refer to the Lymphoma Response Criteria in the appendix (or CIBMTR Forms Instruction Manual)
Use the metabolic (PET) criteria where possible to assess the disease status. If the PET scan is not available or is non-PET avid disease, then the radiographic criteria can be used.

- Compare the assessments at baseline (at diagnosis) and immediately prior to the cell therapy to determine the disease status.
- If this is a subsequent infusion treating disease relapse or progression, then the baseline is at time of relapse or progression.
- If a transformation has occurred, then count the response number (e.g., CR1, CR2) for the transformed histology only.

Date assessed (disease status)

Number of lines of therapy received: (between diagnosis and infusion)

Therapies/agents given during the same period with the same intent is considered one therapy line. If the patient does not achieve adequate response, they may be given different agents which would then be reported as a separate therapy line.

Count number of lines given after the original lymphoma diagnosis up to the cell therapy infusion.
This includes the lines given prior to any disease transformation including follicular lymphoma and CLL and also including bridging therapy.

Also Complete the Lymphoma Pre-Infusion Form

MULTIPLE MYELOMA / PLASMA CELL DISORDER

DIAGNOSIS

Multiple Myeloma / Plasma Cell Disorder

Specify the myeloma diagnosis based on the WHO classification from the dropdown options.

Heavy chain type e.g. IgG, IgA

Light chain type – lambda or kappa

Recipient has preceding or concurrent plasma cell disorder

Indicate if the recipient had a concurrent or preceding plasma cell disorder. The recipient may progress to symptomatic myeloma from a preceding condition or have concurrent plasma cell disorder

Date of diagnosis, preceding/concurrent disorder

Is this the patient's first cell therapy infusion for this diagnosis?

Response to this question will determine the assessments required to be reported.
If this is a subsequent infusion, then the assessments at diagnosis would already have been submitted with the first infusion. In this case, only the assessments at the last evaluation is required.

ASSESSMENTS AT DIAGNOSIS

Report these assessments if this is the patient's first cell therapy infusion for this diagnosis and skip the assessments at last evaluation.

Serum calcium

Serum creatinine

Haemoglobin

LDH and Upper limit of normal

Serum albumin

Serum B2-microglobulin

Plasma cells in blood

- **morphological assessment - absolute value x10^6/L**
- **morphological assessment - %**
- **flow cytometry - %**

Staging at diagnosis

- **R-ISS -** complete if the cytogenetic abnormalities by FISH and LDH are known
- **ISS -** complete if the cytogenetic abnormalities by FISH and LDH are not known
- **Durie-Salmon stage -** complete if both ISS or R-ISS are unknown

Cytogenetics tested

- **FISH/Karyotyping**

- **Specify abnormalities**

ASSESSMENTS AT LAST EVALUATION PRIOR TO PREPARATIVE TREATMENT/ INFUSION

Report these assessments only if this is a subsequent cell therapy infusion for this diagnosis

Serum creatinine
Haemoglobin
Plasma cells in blood
- **morphological assessment - absolute value x10^6/L**
- **morphological assessment - %**
- **flow cytometry - %**

Cytogenetics tested
- **FISH/Karyotyping**
- Specify abnormalities

DISEASE STATUS PRIOR AT INFUSION

Disease status at infusion

Please refer to the appendix for the criteria in determining the disease status.

Date assessed

Also complete the Myeloma Pre-Infusion form

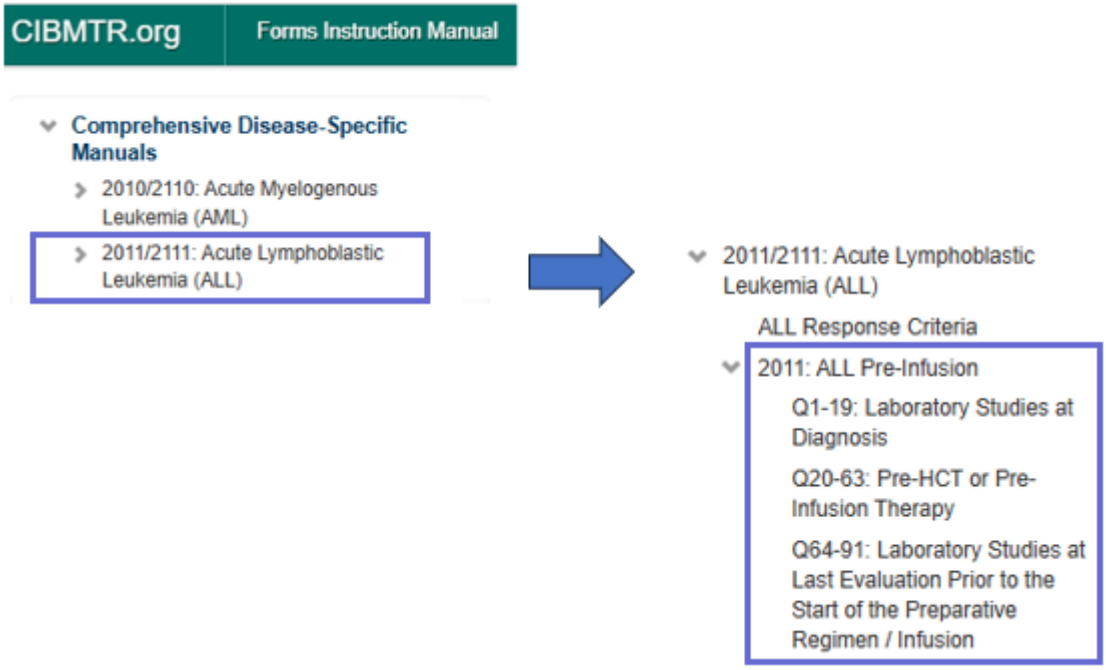
DISEASE SPECIFIC FORMS (PART B)

ALL (Acute Lymphoblastic Leukaemia) PRE-INFUSION

Please ensure that the Acute Lymphoblastic Leukaemia section has been completed in the Disease Classification Form (Part A).

Please refer to the CIBMTR guidelines for a comprehensive explanation of how to complete these questions.

2011: ALL Pre-Infusion - Forms Instruction Manual - 1



If this form has been completed for a previous cell therapy infusion, go directly to Section 2 - Disease Prophylaxis prior Preparative regimen/Infusion.

1. ASSESSMENTS AT DIAGNOSIS

Please ensure that the values are reported by the units indicated

WBC x10^9/L

% blasts blood

% blasts in BM

Extramedullary disease, indicate sites

2. DISEASE PROPHYLAXIS PRIOR PREPARATIVE REGIMEN OR INFUSION

Indicate if CNS prophylaxis given e.g., cranial irradiation, intrathecal therapy

3. DISEASE TREATMENT PRIOR PREPARATIVE REGIMEN OR INFUSION

Report treatment given between the ALL diagnosis and start of preparative treatment/infusion.

If no treatment was given, go directly to Section 4.

Therapies/agents given during the same period with the same intent e.g., induction, is considered one line of treatment. Additional courses of the induction therapy may be given. These are reported as an additional cycle within the same treatment line. If the patient does not achieve adequate response, they may be given different agents which would then be reported as a separate treatment line.

Do not report a prior HCT alone as a line of treatment.

Treatment 1 given

Selecting 'Yes' will display the following associated fields:

Therapy type

Therapy type (or purpose) is dependent on the disease status at the time:

- Induction – to achieve complete remission (CR)
- Consolidation - once achieving CR; given either as part of a protocol or to achieve a deeper response, removing any minimal residual disease.
- Maintenance – after receiving induction and consolidation, extended low dose therapy to maintain CR.
- Relapse treatment – given to achieve a further CR after disease recurrence

Intrathecal therapy: Y | N

Agents given by lumbar puncture, directly to the cerebrospinal fluid to treat or prevent CNS disease.

Systemic therapy

Dates started and ended

Number of cycles

Specify systemic agents

Radiation therapy

Date started and ended

Radiation site

Best response to line of therapy

Date assessed

Refer to the ALL Response (Acute Lymphoblastic Leukaemia) criteria in the appendix

MRD negative following this line of therapy: Y | N

This should be based on results performed within 30 days after therapy was completed for this treatment line and before a new line commences.

Recipient relapsed following this line of therapy: Y | N

Date relapsed

Site of relapse

Complete this section as many times as required for multiple lines of therapy

4. EVALUATIONS PRIOR TO START OF PREPARATIVE REGIMEN OR INFUSION

Values should be within approximately 30 days prior to preparative regimen/infusion, but after completion of any treatment. If this is not available, then report as unknown.

Values and date of sample for the following:

WBC x10^9/L

% blasts blood

% blasts in BM

Flow cytometry performed

Report the percent of disease detected by flow cytometry in blood and bone marrow if performed and the date of the sample

Extramedullary disease present

Report sites of disease involvement other than in the blood or bone marrow

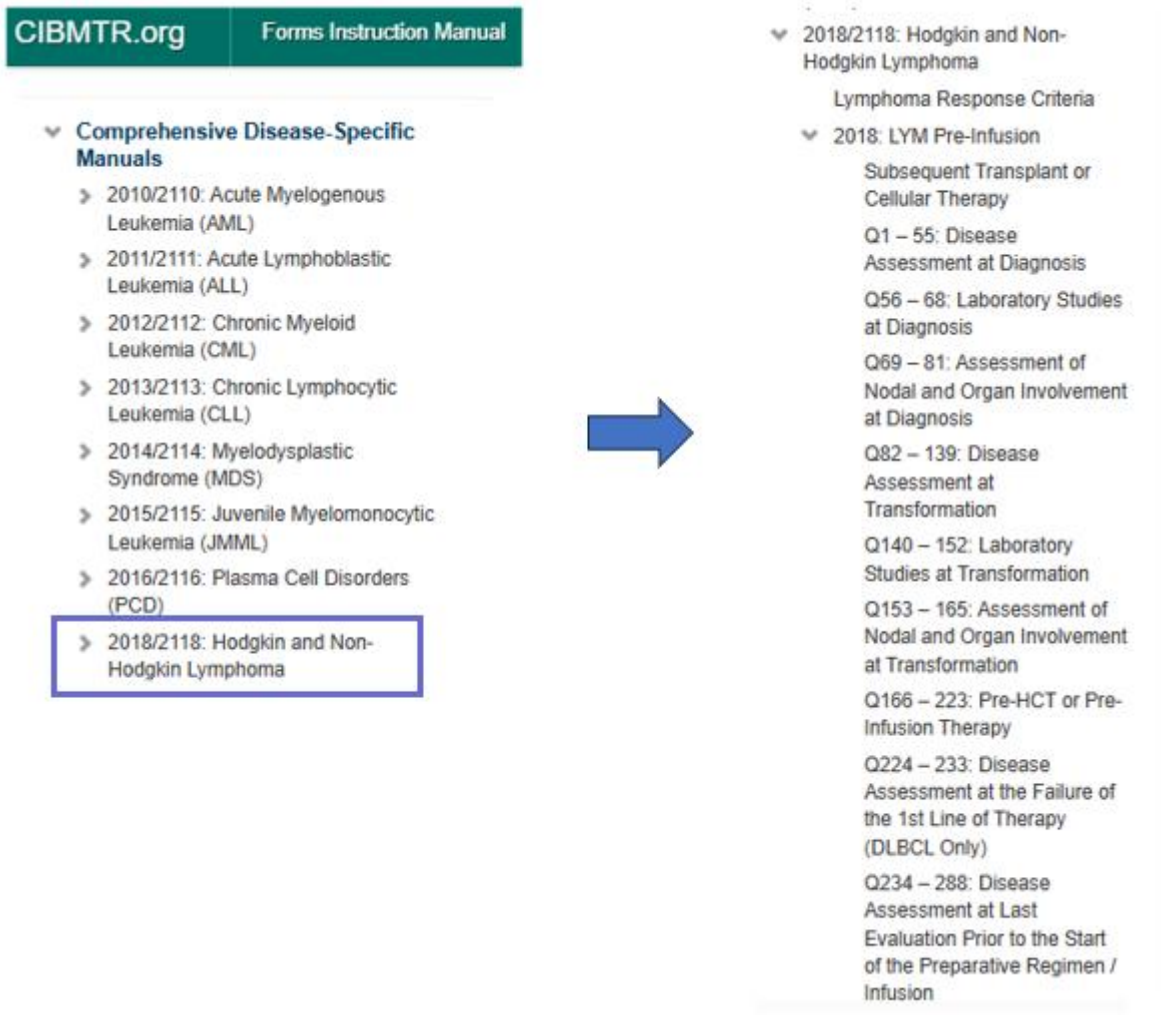
LYMPHOMA PRE-INFUSION

PART B of the Lymphoma Pre-Infusion Form pdf version.

Please ensure that the Lymphoma section has been completed in the Disease Classification Form (Part A).

Please refer to the CIBMTR guidelines for a comprehensive explanation of how to complete these questions.

2018: LYM Pre-Infusion - Forms Instruction Manual - 1



If this form has been completed for a previous cell therapy infusion, then skip the questions at the time of diagnosis and go directly to Section 4 - Disease Transformation

1. DIAGNOSIS (PRIOR TO ANY TRANSFORMATION)

Lymphoma histology at diagnosis

If the diagnosis is transformed from CLL to Lymphoma, then report the lymphoma here.

If the diagnosis is more than one type of lymphoma or has transformed, then report the least aggressive lymphoma here, and the most aggressive lymphoma as the transformed histology in Section 4.

Immunohistochemical stains performed

If the percent is documented as a range, then report the average. If documented as less than a certain percentage, then report as less one, e.g., report <10% as 9%.

Were cytogenetics performed

Report any abnormalities by FISH or karyotyping

2. LABORATORY VALUES AT DIAGNOSIS

Please ensure that the values are reported by the units indicated.

LDH and Upper limit of normal

Mantle cell also requires **WBC**

Follicular also requires **Hb**

Hodgkins Lymphoma also requires **WBC, Hb, Absolute lymphocyte count, % lymphocytes, and Se albumin**

3. NODAL AND ORGAN INVOLVEMENT AT DIAGNOSIS

Values reported here should be within 30 days of the lymphoma diagnosis and before any treatment is given. If tests were performed outside of this period, 'Unknown' should be reported.

PET (or PET/CT) positive: Y | N | ND

Known nodal involvement

Nodal involvement can be found by clinical assessment, biopsy or PET/CT imaging. Complete the following if there was involvement

Total number nodal regions involved

This question appears twice with different options to select depending if is follicular or non-follicular lymphoma

Largest nodal mass

Report the largest two dimensions in cm

Extranodal or splenic involvement

Report any involvement outside of the lymph nodes e.g., spleen, bone, GIT, skin

Stage of organ involvement

B symptoms present

ECOG score

Performance scores should be documented in the patient's notes rather than derived retrospectively.

4. DISEASE TRANSFORMATION

The first two questions have also been included in Part A

Transformation from CLL? Y | N

If yes, then skip the remaining transformation sections and go to Section 7 Disease Treatment

Transformation occurred (non CLL)

If no transformation has occurred, go to directly to Section 7 - Disease Treatment

Specify the histology – this is the histology after the transformation has occurred.

Transformation pathology submitted to Registry

Transformation date same as diagnosis date

This question establishes if the histology information has already been captured in earlier sections

- Yes (concurrent diagnosis) - go to Section 7 Disease Treatment
- No , report Date of transformation

Complete the rest of this section and sections 5 and 6

Immunohistochemical stains performed

Indicate if the listed markers were positive/negative or unknown

Were cytogenetics tested

Report any abnormalities by FISH or karyotyping

5. LABORATORY VALUES AT TRANSFORMATION

Values reported here should be within 30 days of the transformation and before any treatment is given. If tests were performed outside of this period, 'Unknown' should be reported.

Please ensure that the values are reported by the units indicated

LDH and Upper limit of normal

Mantle cell also requires **WBC**

Follicular also requires **Hb**

Hodgkins Lymphoma also requires **WBC, Hb, Absolute lymphocyte count, % lymphocytes, and Se albumin**

6. NODAL, ORGAN INVOLVEMENT AT TRANSFORMATION

Results reported here should be within 30 days of the transformation reported in the prior section and performed before any treatment is given. If tests were performed outside of this period, 'Unknown' should be reported.

Refer to Section 3 for the guidelines to the questions below

PET (or PET/CT) positive

Known nodal involvement

Total number nodal regions involved

Largest nodal mass (max dimensions)

Extranodal / splenic involvement?

Stage of organ involvement

B symptoms present 6months prior transform

ECOG score

7. DISEASE TREATMENT

Report treatment given between the lymphoma diagnosis and the start of preparative treatment or infusion.

If there was a lymphoma transformation, report all treatment given starting from the original lymphoma diagnosis.

Therapies/agents given during the same period with the same intent is considered one therapy line. If the patient does not achieve adequate response, they may be given different agents which would then be reported as a separate therapy line.

If this is a subsequent infusion and the treatment lines have been previously reported with an earlier cell therapy infusion, only report treatment lines given after the prior cell therapy infusion.

Treatment was given after diagnosis: Y | N

Systemic therapy: Y | N

- **Date started and stopped**
- **Number of cycles**
- **Specify regimen/agents**
- **This therapy line given to mobilised cells: Y | N**

Intrathecal therapy: Y | N

- **Indicate if given for prophylaxis or treatment of CNS disease or unknown.**
- **Date started and stopped**
- **Specify agent given**

Intraocular therapy: Y | N

- **Indicate if given for prophylaxis or treatment of CNS disease or unknown.**

Date started and stopped
Specify agent given

Radiation therapy: Y | N
Date started and stopped
Extent of radiation field
Radiation sites
Radiation dose
Technique - e.g. Electron beam, Proton or specify other

Surgery Y | N
Date of surgery
Splenectomy, and other site(s)

Photopheresis: Y | N

Cell therapy: Y | N – this question is no longer required to be reported as a line of therapy

Best response to line of therapy: (Radiographic criteria)

CR |PR | NR/SD | PD |Not done Date assessed

Best response to line of therapy: (Metabolic criteria)

CR |PR | NR/SD | PD |Not done Date assessed

Refer to the CIBMTR Lymphoma Response Criteria in the appendix

This therapy given as maintenance / consolidation: Y| N

Definitions for consolidation and maintenance as follows:

- Consolidation – given after achieving CR; either as part of a protocol or to achieve a deeper response.
- Maintenance – given after induction and consolidation, extended low dose therapy to maintain CR.

This line of therapy given as bridging to cell infusion

Please ensure that the date of treatment commencement is the same as the date reported on the Cell Therapy Pre-Infusion form (section 8 Bridging therapy)

Relapse/progression occurred after this therapy line

If yes, report the date relapse/progression

Complete this section as many times as required for multiple lines of therapy

8. DIFFUSE LARGE B-CELL LYMPHOMA ONLY

Achieved CR after 1st line of therapy?

If yes, go directly to Section 9

If no, then follow questions will show

LDH and the lab's upper normal limit of LDH

Stage of organ involvement

ECOG score

Extranodal or splenic involvement

Refer to Section 3 for the guidelines

These assessments should be between the first and second treatment lines. If a second line is not given, then report the assessments prior to preparative therapy/infusion, using the most recent if assessed more than once.

9. DISEASE ASSESSMENT AT LAST EVALUATION - PRIOR TO PREPARATIVE REGIMEN / INFUSION

Results reported here should be within approximately 30 days prior to starting preparative therapy/infusion, but after the latest treatment line if applicable. If tests were performed outside of this period, 'Unknown' should be reported.

Were cytogenetics performed

Report any abnormalities by FISH or karyotyping

Laboratory values

Provide values for the lymphoma types (as specified in the NHL, B-cell classification question)

Haemoglobin – Follicular and Hodgkins only

Absolute lymphocyte count – Hodgkins only

Minimal residual disease

Report if any of the following assessments were positive for detecting minimal residual disease.

Flow cytometry

PCR

NGS, 3rd gen (Next Generation Sequencing)

If positive:

Date of sample

Sample source - e.g. blood, bone marrow

Pathology report(s) submitted to Registry: Y | N

Refer to Section 3 for the guidelines to the questions below

Known nodal involvement

Total number nodal regions involved - report for Follicular only

Largest nodal mass (maximum dimensions)

Extranodal or splenic involvement

Report the sites involved

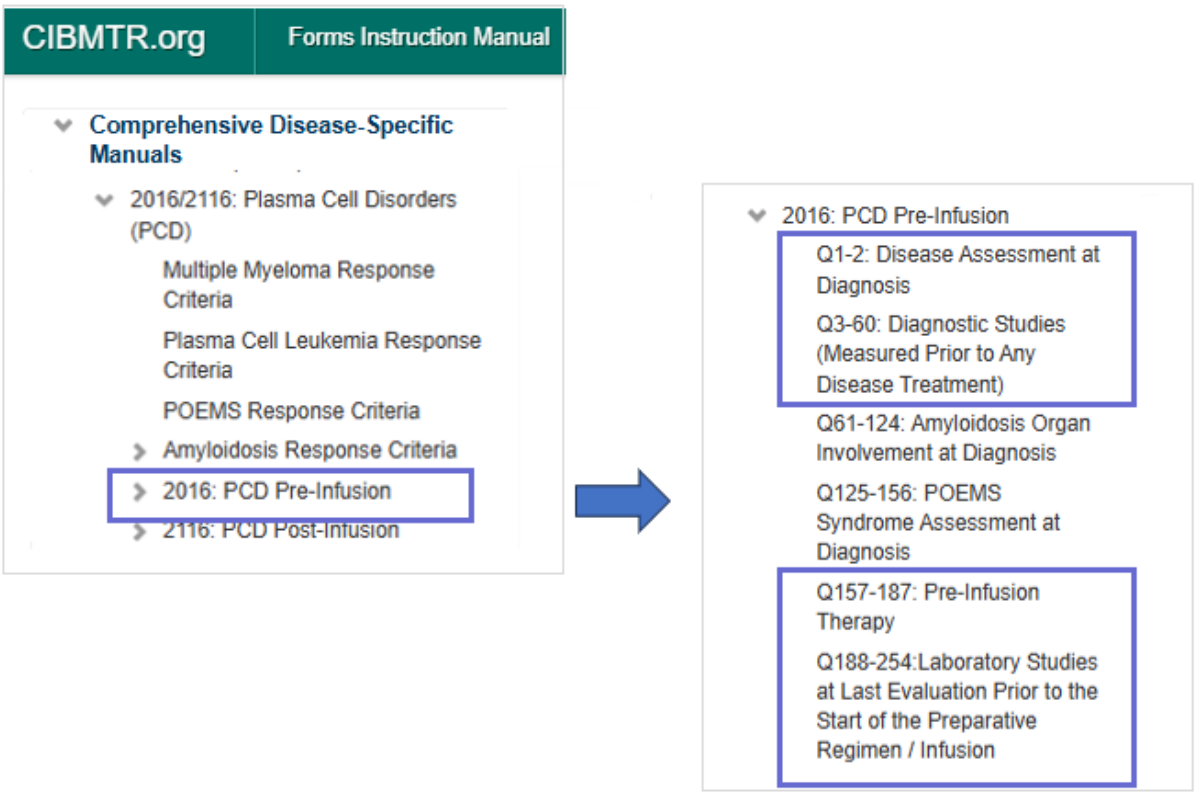
MYELOMA PRE-INFUSION

PART B of the Myeloma Pre-Infusion Form pdf version.

Please ensure that the Myeloma section has been completed in the Disease Classification Form.

Please refer to the CIBMTR guidelines for a comprehensive explanation of how to complete these questions.

2016: PCD Pre-Infusion - Forms Instruction Manual - 1



If this is the first cell therapy infusion for myeloma, then all questions are relevant.

If this is a subsequent infusion for myeloma and the assessments at diagnosis were reported with the previous infusion, then skip Section 1 (assessments at diagnosis) and continue with the Disease treatment and latest disease assessments.

1. DISEASE ASSESSMENTS AT DIAGNOSIS

Only complete the assessments at diagnosis if this is the first cell therapy infusion. If this form is being completed for a subsequent infusion, then complete the assessments at the last evaluation.

The values reported here should be prior to the first treatment given for myeloma.

The assessments include:

- **Serum monoclonal protein (M-spike),** only from electrophoresis
- **Serum immunofixation**: heavy chain, light chain. (NA for non-secretory myeloma)
- **Serum free light chains**: kappa and lambda values and ULN (lab's upper limit of normal)
- **Serum quantitative immunoglobulins**:
    - IgG, IgA, IgM, IgD, IgE and their associated ULN
- Urinary assessments
    - **Urinary monoclonal protein (M-spike) / 24 hours**
    - **Urinary light chain:** lambda or kappa
    - **Total urinary protein in 24 hours**
    - **Urinary albumin / creatinine ratio**
    - **Urinary protein / creatinine ratio**
- **Plasma cells in bone marrow:**
    - BM aspirate by flow cytometry %
    - BM aspirate Morphologic (%)
    - BM biopsy (%)
- **Immunohistochemical stains** performed for CD138, CD38
- **Gene expression profile performed**: Y/N
    - **Considered high-risk myeloma**: Y/N
- **Was imaging/scan performed?**
    - Type of imaging/scan (CT, PET/CT, MRI)
    - Date of scan

- Positive areas of involvement

2. LAST EVALUATION PRIOR TO LYMPHODEPLETION/ INFUSION

If testing is performed multiple times prior to the start of the preparative regimen, report the last test before the start of the preparative regimen.

The assessments include:

- **Serum β2 – macroglobulin**
- **Plasma cells in blood**
  - flow cytometry - %
  - morphological assessment - absolute value $x10^6/L$
  - morphological assessment - %
- **Serum albumin**
- **Serum monoclonal protein (M-spike),** only from electrophoresis
- **Serum immunofixation**, specify the bands present
  - Original monoclonal/New (oligoclonal) bands
- **Serum free light chains**
  - **kappa and lambda** values and ULN (lab's upper limit of normal)
- Urinary assessments
  - **Urinary monoclonal protein (M-spike) / 24 hours**
  - **Urinary immunofixation**, specify the bands present
    - Original monoclonal/New (oligoclonal) bands
  - **Total urinary protein in 24 hours**
  - **Urinary albumin / creatinine ratio**
  - **Urinary protein / creatinine ratio**
- **Minimal residual disease (MRD),** report only bone marrow or blood results
  - **Next generation sequencing (NGS) and Next generation flow (NGF)**
    - Report if positive, negative or unknown
    - sample source
    - sensitivity of the test
- **Plasma cells in blood**
  - morphological assessment - %

- flow cytometry - %
- bone marrow biopsy - %

- **Cytogenetics tested**
  - Specify any abnormalities detected by FISH/Karyotyping
- **Recipient received dialysis:**
  - Yes/No, Date of dialysis
- **Was imaging/scan performed?**
  - Indicate the Type of imaging/scan (CT, PET/CT, MRI)
  - Date of scan
  - Positive areas of involvement

3. PRE-INFUSION THERAPY

Was any therapy given to treat disease in this reporting period? Y/N

Total number of lines of therapy given prior to cell therapy

For a subsequent infusion, do not report lines of therapy that have already been reported with the previous infusion.

Systemic therapy

Start date and stop date

Please enter estimated dates if exact dates are unknown. Refer to guidelines for examples

Reason systemic therapy stopped

Drug regimen

Report other drugs if not listed in the regimen dropdown list

This line of therapy given for stem cell mobilization: Y/N

Radiation therapy

Start date and stop date

Please enter estimated dates if exact dates are unknown. Refer to the general guidelines (pg 6) for examples

Total radiation dose

Best haematologic response to line of therapy

Refer to the Myeloma Response criteria in the appendix

Date haematologic response to line of therapy

Disease relapsed/progressed following this line of therapy: Yes/No

Date of relapse/progression

Complete this section as many times as required for multiple lines of therapy

DISEASE SPECIFIC POST INFUSION FORMS

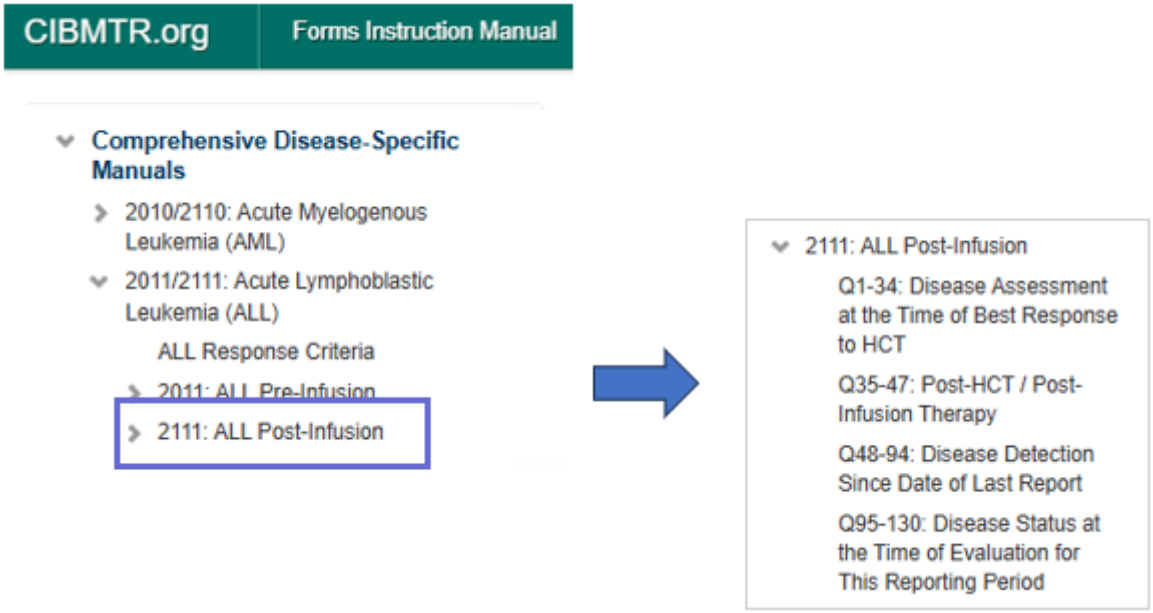
ALL (Acute Lymphoblastic Leukaemia) POST INFUSION

Follow up period

- 30 day
- 100 day
- 6 months
- Annual thereafter

Please refer to the CIBMTR guidelines for a comprehensive explanation of how to complete these questions.

2111: ALL Post-Infusion - Forms Instruction Manual - 1



1. BEST RESPONSE TO HCT OR CELLULAR THERAPY

Best response to (HCT or) cellular therapy

This is the **best response achieved from the CAR-T therapy**.

Any disease relapse that occurs afterwards does NOT change the best response.

For example, if complete remission is achieved as a response to the CAR-T and the disease later relapses, then the best response is still the complete remission. Relapse is reported in Section 3

The option 'Continued complete remission' should only be selected if the disease status prior to the infusion is Complete remission.

If in Continued CR or Date of best response previously reported, go directly to Post Infusion Therapy section.

Do not include the response to therapy given for relapse / persistent / progressive disease

Date of best response

Report the earliest date that the best response was first documented e.g. date of bone marrow/biopsy sample. If this is not available, the date of review if the response was assessed clinically may be used.

Tests performed at time of best response

These questions will display if this is the first time reporting the best response to cell therapy, i.e. reporting the date of best response for the first time (otherwise report 'previously reported')

The assessments should be within the time frame as follows:

Follow up period	Approximate time range
30 day	+/- 7 days of best response date
100 day, 6 months	+/- 15 days of the best response date
Annual	+/- 30 days of the best response date

Molecular testing performed? (Positive/Negative/not done)

- **BCR/ABL**
- **TEL-AML/AML1**
- **Other markers**

Flow cytometry performed

- **Disease detected in blood/bone marrow**
- **Date of sample**
- **Percentage disease detected**

Were cytogenetics tested

- **FISH/Karyotyping**
- **Specify abnormalities**

Disease status by another method

- **Date assessed**
- **Disease detected**

2. POST INFUSION THERAPY

Therapy given since last report

Therapy given as prophylaxis, maintenance or consolidation is reported here. This maybe planned as part of the cell therapy protocol.

Please note that therapy given for relapse/progression or persistent disease (including treatment for minimal residual disease) is reported in Section 4

CNS irradiation

Cranial or craniospinal

Intrathecal therapy

Systemic therapy – date started and agents

Cell therapy - do not report HCT here

Other therapy - specify

3. DISEASE DETECTION SINCE LAST REPORT

This section is intended to capture information only on recipients who relapse, have persistent or minimal residual disease in this reporting period.

Disease was detected by any assessment method

Answer 'No' if there is no relapse or persistent disease in this reporting period and continue to Section 4.

Answer 'Yes' if disease has relapsed, or persistent or minimal residual disease is present and complete the following where appropriate

Report the earliest date of disease detection for each method performed.

Molecular testing (Positive/Negative/not done)

- **Date of sample**
- **BCR/ABL**
- **TEL-AML/AML1**
- **Other markers**

Flow cytometry

- **Disease detected in blood/bone marrow**

- **Date of sample**
- **Percent disease detected**

Cytogenetic testing

- **FISH/Karyotyping**
- **Date of sample and specify abnormalities**

Clinical /haematological assessment

Date assessed and sites involved

Disease status by another method

- **Date assessed and specify method**

4. THERAPY GIVEN TO TREAT RELAPSED, PERSISTENT OR MINIMAL RESIDUAL DISEASE

Treatment given post-infusion for minimal residual disease, persistent disease, or relapse since the date of last report is reported in this section

Therapy was given to treat disease

Reason therapy given

Report the scenario that applies

- **Minimal Residual Disease:** Recipient is in haematologic CR, but has evidence of disease detectable by more sensitive assessments e.g. molecular, flow cytometry or cytogenetics.
- **Persistent Disease:** The recipient was in primary induction failure or relapse at the time of infusion and has not achieved a haematologic CR post-infusion.
- **Relapsed Disease:** The recipient was either in CR at the time of infusion or had achieved a CR post-infusion, relapsing post infusion.

CNS irradiation

Intrathecal therapy

Systemic therapy

Date first started and agents given

Cell therapy

Subsequent HCT

If 'Yes' to either of these, an additional cell therapy or transplant form is required.

Accelerated withdrawal of immunosuppression in response to disease

Indicate if the immunosuppression was withdrawn to promote graft versus leukaemia effect.

Other therapy - specify

Complete this section as many times as required for multiple lines of therapy

5. DISEASE EVALUATION FOR THIS REPORTING PERIOD

This section is intended to capture further assessments if the disease status has changed since the assessments in Section 3 (Disease Detection since last report).

The Latest disease status is same as reported in Section 3, without subsequent treatment (as reflected by the assessments reported in Section 3)

Yes – go directly to Section 6

Choose this option if:

- disease was detected in this reporting period and no therapy was given between dates in section 3 and the latest date of contact for this report
- disease was detected and reported in section 3, treatment was given but no assessments performed before the latest date of contact.

No – complete this section

Choose this option if:

- disease was not detected during this reporting period. Enter assessment results here as no results were entered in section 3
- disease was detected and reported in Section 3, treatment was given and disease was re-assessed.

N/A, disease not assessed – end of form

- Only choose this option if there were no assessments performed, including clinical assessments.

Molecular testing performed

- **BCR/ABL**
- **TEL-AML/AML1**
- **Other markers**

Flow cytometry performed

- **Disease detected in blood/bone marrow**
- **Date of sample, percentage disease detected**

Were cytogenetics tested

- **FISH/Karyotyping**
- **Specify abnormalities**

Clinical /haematological assessment

- **Date assessed**
- **Disease detected**

Disease status by another method

- **Date assessed**
- **Disease detected**

6. CURRENT DISEASE STATUS

This is the haematologic disease status at the latest disease assessment in this reporting period. Refer to the ALL Response Criteria in the appendix.

Current disease status

Complete remission or No complete remission

Date assessed

This date should be the approximately within 30 days from the date of contact.

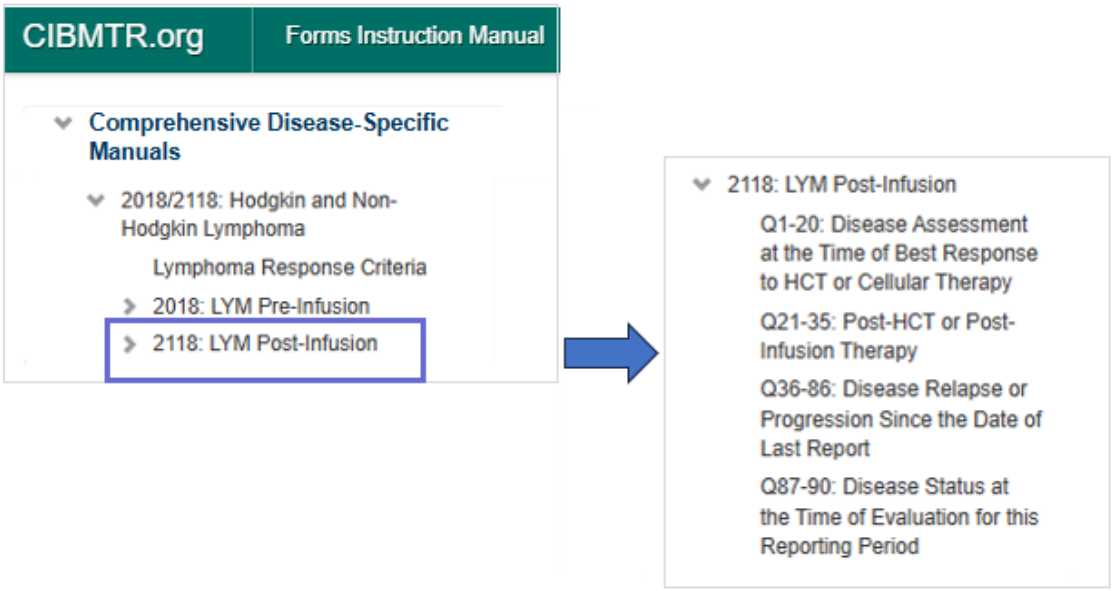
LYMPHOMA POST INFUSION

Follow up period

- 30 day
- 100 day
- 6 months
- Annual thereafter

Please refer to the CIBMTR guidelines for a comprehensive explanation of how to complete these questions.

2118: LYM Post-Infusion - Forms Instruction Manual - 1



1. BEST RESPONSE TO CELL INFUSION SINCE LAST REPORT

This is the best response achieved from the CAR-T therapy.

Any disease relapse that occurs afterwards does NOT change the best response.

For example, there is a complete or partial response to CAR-T and the disease progresses, then the best response is still the complete or partial response. Disease progression is reported in Section 3.

Best response by CT (radiologic) criteria since last report

Best response by PET (metabolic) criteria since last report

Include the response to therapy given for post cell infusion maintenance, consolidation or persistent disease as the best response. Do not include response to any therapy given for disease relapse or progression post-infusion.

To determine the best response, compare the post-infusion disease status to the disease status immediately prior to the lymphodepletion.

The option 'Continued complete remission' should only be selected if the disease status prior to the infusion is Complete remission.

Refer to the Lymphoma Response Criteria in the appendix (or CIBMTR Instruction Manual)

Date assessed

Report the earliest date that the best disease status achieved was obtained or tick the 'previously reported' checkbox if this is not the first follow up reporting this date.

The assessments should be within the time frame as follows:

Follow up period	Approximate time range
30 day	+/- 7 days of best response date
100 day, 6 months	+/- 15 days of the best response date
Annual	+/- 30 days of the best response date

Minimal Residual Disease assessed at time of best response

If the response to the above questions are 'Continued CR' or 'Not assessed', skip these questions and go to Section 2.

Flow cytometry

PCR

Next generation sequencing

Sample Source and date sample collected for the assessments above

2. POST HCT / INFUSION THERAPY

Report therapy given for maintenance, consolidation, and persistent disease (including MRD) since last report.

Do NOT include therapy for relapse or progressive disease.

Therapy given since last report

Systemic therapy

Date stated and stopped,

Specify agent

Reason therapy stopped

Part of clinical trial, trial id

Radiation therapy

Cellular therapy – additional cell therapy forms required

Other therapy, specify

If multiple lines of therapy were given in this reporting period, duplicate sections are available to capture each therapy line.

3. DISEASE RELAPSE OR PROGRESSION SINCE LAST REPORT

If relapse or progression occurred, complete the following

Relapse or progression occurred

Molecular testing

Date sample

Cytogenetic testing

FISH/Karyotyping

Date sample

Radiological assessment

Date assessed

Clinical/haematologic assessment

Date assessed

Nodal involvement

Extranodal or splenic involvement and sites

If a recipient 'relapses' post-infusion with a less severe type of lymphoma (i.e. received an infusion for DLBCL, with or without a history of follicular lymphoma, and relapses with follicular lymphoma). Then the relapse of the 'less severe lymphoma' should be reported as a relapse in the follow up forms.

4. THERAPY FOR RELAPSE OR PROGRESSION

Therapy given for relapsed, progressive or minimal residual disease

Report any treatment was given for relapsed or disease progression.

Treatment may also be given for minimal residual disease (MRD), but **only report this if the MRD is new**. Do not include here if it was existing at the time of cell therapy as this is reported in Section 2.

Reason therapy given

Report the scenario that applies

- **Relapsed Disease**: The recipient was either in CR at the time of infusion or had achieved a CR post-infusion, then relapsed post infusion.
- **Progressive Disease**: Disease progressed following a period of stable disease or after achieving a partial remission.
- **Minimal Residual Disease**: Recipient is in haematologic CR, but has evidence of disease relapse detectable by more sensitive assessments e.g. molecular, flow cytometry or cytogenetics. Do not report MRD that has persisted from prior to the infusion.

Systemic therapy

Date started and stopped

Specify agents given

Therapy part of clinical trial, Trial ID

Intrathecal therapy

Date started and stopped

Therapy

Intraocular therapy

Date started and stopped

Therapy

Radiation therapy

Cell therapy

complete new Cell Therapy Forms

Other therapy – specify therapy

Best response to line of therapy by CT (radiologic) criteria

Date assessed

Best response to line of therapy by PET (metabolic) criteria

Date assessed

Refer to the Lymphoma Response Criteria in the appendix.

If multiple lines of therapy were given for relapse or progression in this reporting period, duplicate sections are available for reporting each line.

5. DISEASE STATUS AT TIME OF EVALUATION FOR THIS REPORTING PERIOD

This is the disease status at the latest disease assessment in this reporting period.

Current disease status by CT (radiologic) criteria

Date assessed

Current disease status by PET (metabolic) criteria

Date assessed

Disease specific assessments (CT or PET scans) do not need to be repeated at each reporting period to report the current disease status.

Once a particular disease status is achieved, this disease status can continue to be reported again until there is evidence of relapse or progression.

Report "Not assessed" only when the recipient relapses or progresses and receives treatment for the relapse / progression, and an additional CT scan was not performed post therapy to assess the disease status.

Deauville Score

This is captured prior to the infusion on the Disease Classification form and at 12 months post infusion. This is a five-point score obtained from the PET report.

Date assessed

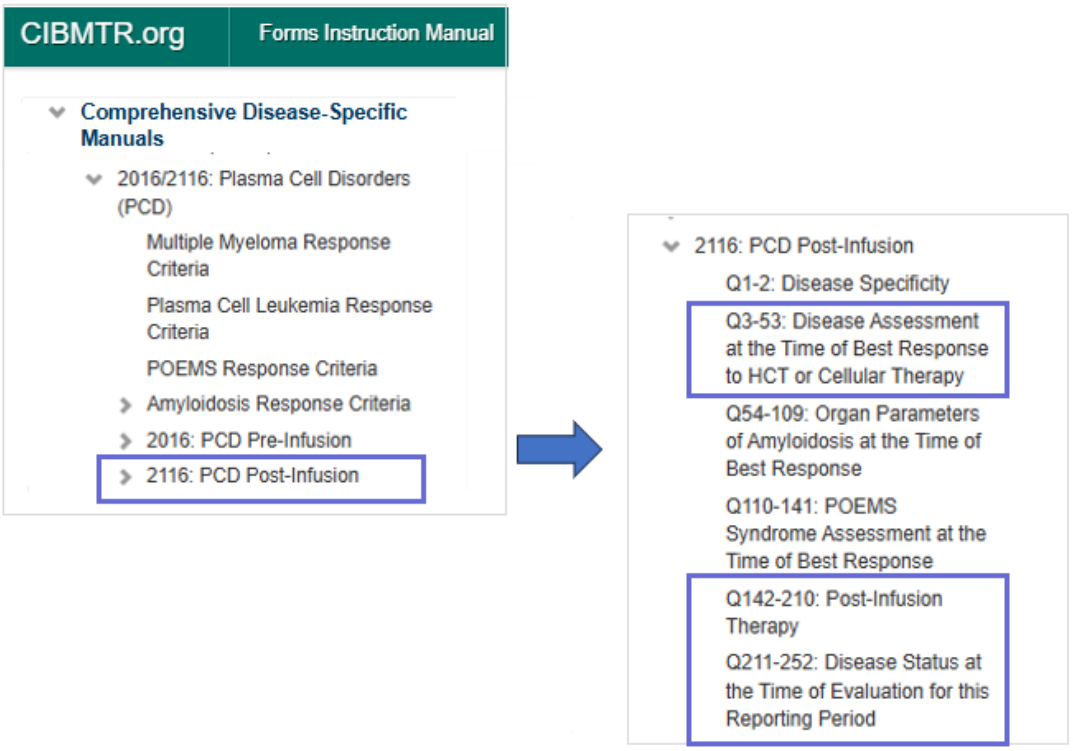
MYELOMA POST INFUSION

Follow up period

- 30 day
- 100 day
- 6 months
- Annual thereafter

Please refer to the CIBMTR guidelines for a comprehensive explanation of how to complete these questions.

2116: PCD Post-Infusion - Forms Instruction Manual - 1



1. BEST HAEMATOLOGIC RESPONSE TO CELL THERAPY SINCE LAST REPORT

This is the best response achieved following the infusion including the response to any planned treatment (e.g. maintenance, consolidation or persistent disease treatment) post infusion as part of the cell therapy.

Do not include response to treatment given for relapsed or progressive disease.

Best haematologic response to Cell Therapy since last report

Date of best response was previously reported? Yes/No

If no, Date of best response

If the date of response was previously reported, then the assessments at the time of best response has already been reported in a prior follow up. Go directly to section 3, Disease Relapse/Progression

2. ASSESSMENTS AT THE TIME OF BEST RESPONSE

Report assessments performed closest to the date of best response and within the approximate time ranges, as below

Follow up period	Approximate time range
30 day	+/- 7 days of best response date
100 day, 6 months	+/- 15 days of the best response date
Annual	+/- 30 days of the best response date

- **Serum creatinine** and ULN (lab's upper limit of normal)
- **Serum monoclonal protein (M-spike),** only from electrophoresis
- **Serum immunofixation**, specify the bands present
    - Original monoclonal/New (oligoclonal) bands
- **Serum free light chains**
    - **kappa and lambda** values and ULN (lab's upper limit of normal)
- Urinary assessments
    - **Urinary monoclonal protein (M-spike) / 24 hours**
    - **Urinary immunofixation, specify the bands present**
        - Original monoclonal/New (oligoclonal) bands
    - **Total urinary protein in 24 hours**
    - **Urinary albumin / creatinine ratio**
    - **Urinary protein / creatinine ratio**
- **Minimal residual disease (MRD),** report only bone marrow or blood results
    - **Next generation sequencing (NGS) and Next generation flow (NGF)**
        - Report if positive, negative or unknown
        - sample source
        - sensitivity of the test
- **Plasma cells in bone marrow**
    - Plasma cells in BM aspirate, flow cytometry - %
    - Plasma cells in BM aspirate, morphologic - %
    - Plasma cells in BM biopsy - %
- **Was imaging/scan performed**?
    - Indicate the Type of imaging/scan (CT, PET/CT, MRI)
    - Date of scan
    - Positive areas of involvement

3. RELAPSE/DISEASE PROGRESSION

Relapse or progression since the last report

Relapse/progress date

4. ASSESSMENTS AT THIS REPORTING PERIOD

If there were multiple assessments performed in this period, report the latest assessments.

Were disease assessments performed in this reporting period? Y/N

If there were no assessments performed in this reporting period, go directly to section 5, Current disease status.

- **Serum creatinine** and ULN (lab's upper limit of normal)
- **Serum monoclonal protein (M-spike),** only from electrophoresis
- **Serum immunofixation,** specify the M-spike type

  e.g. IgG, IgA, IgM, IgD, IgE, lamba, kappa

  specify the bands present: original monoclonal/new (oligoclonal) bands
- **Serum free light chains**
  - **kappa and lambda** values and ULN (lab's upper limit of normal)
- Urinary assessments
  - **Urinary monoclonal protein (M-spike) / 24 hours**
  - **Urinary immunofixation,** specify the bands present
    - Original monoclonal/New (oligoclonal) bands
  - **Total urinary protein in 24 hours**
  - **Urinary albumin / creatinine ratio**
  - **Urinary protein / creatinine ratio**
- **Plasma cells in bone marrow**
  - Plasma cells in BM aspirate, flow cytometry - %
  - Plasma cells in BM aspirate, morphologic - %
  - Plasma cells in BM biopsy - %
- **Recipient received dialysis**: Y/N, date of dialysis
- **Was imaging/scan performed?**
  - Indicate the Type of imaging/scan (CT, PET/CT, MRI)

- Date of scan
- Positive areas of involvement

5. CURRENT DISEASE STATUS

Refer to the Multiple Myeloma Response Criteria in the appendix.

All of the disease-specific assessments (biopsies, scans, labs) do not need to be repeated at each reporting period in order to complete current disease status data fields. Once a particular disease status is achieved, that disease status can continued to be reported (based on labs / clinical assessments) until there is evidence of relapse / progression.

Haematologic Disease Status

Date assessed

6. POST INFUSION THERAPY

Purpose of this Treatment line

- Maintenance/Consolidation/treat persistent disease

  The therapy is given as prophylaxis or maintenance for recipients in CR, or as pre-emptive therapy for recipients with minimal residual disease
- Treatment of relapse/progression

  The myeloma has relapsed or progressed
- Maintenance following treatment of relapse/progression

Systemic therapy

Start date and stop date

Please enter estimated dates if exact dates are unknown. Refer to the general guidelines (see page 6) for examples

Reason systemic therapy stopped

Drug regimen

Other systemic drugs given

Radiation therapy

Start and stop date

Total radiation dose

Cellular therapy e.g. CAR-T cells

Best haematologic response to line of therapy

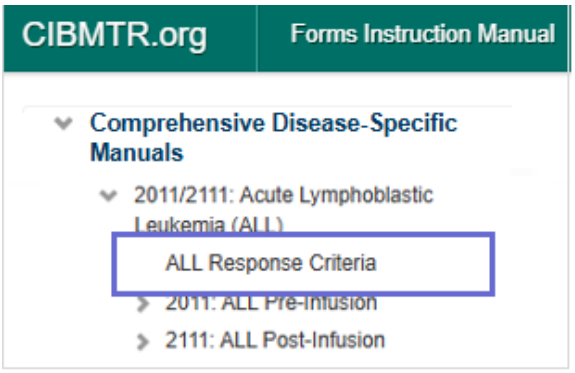
Date of response

Complete these questions for each line of therapy given during the reporting period by adding an additional instance (creating a new Post Infusion Form) in REDCap.

APPENDIX

Please refer to the CIBMTR guidelines for a comprehensive explanation to determining the disease response.

ALL Response Criteria - Forms Instruction Manual - 1



ALL RESPONSE CRITERIA

Complete Remission (CR)

Haematologic CR is defined as meeting all of the following criteria for at least four weeks.

- < 5% blasts in the bone marrow
- Normal maturation of all cellular components in the bone marrow
- No extramedullary disease (e.g., CNS, soft tissue disease)
- Neutrophils ≥ 1.0 x 10^9/L
- Platelets ≥ 100 x 10^9/L
- Transfusion independent

If there has not been a four-week interval between completion of therapy and the pre-transplant disease assessment, then CR may be reported as the status at transplant, since it represents the “best assessment” prior to HCT.

Include recipients who are MRD positive/unknown. MRD assessments include cytogenetic, flow cytometry, and molecular methods.

Alternative, post-transplant CR criteria are accepted in the setting of paediatric ALL when the centre does not routinely perform bone marrow biopsies post-transplant and the patient was in CR pre-transplant. These criteria are not used for pre-transplant ALL disease status. The criteria are as follows:

- Complete donor chimerism (≥ 95% donor chimerism without recipient cells detected)
- No extramedullary disease (e.g., CNS, soft tissue disease)
- Neutrophils ≥ 1.0 x 10^9/L

- Platelets ≥ 100 x 10^9/L
- Transfusion independent (a minimum of four weeks without platelet or RBC transfusion)

The number of this complete remission can be determined by using the following guidelines:

- 1st CR: no prior relapse
- 2nd CR: one prior relapse
- 3rd or higher: two or more prior relapses

Complete Remission with Incomplete Hematologic Recovery (CRi)

Haematologic CRi is defined as meeting all of the following criteria for at least four weeks:

- < 5% blasts in the bone marrow
- Normal maturation of all cellular components in the bone marrow
- No extramedullary disease (e.g., CNS, soft tissue disease)
- Transfusion independent (a minimum of four weeks without platelet or RBC transfusion) (Please note, if the physician documents transfusion dependence related to treatment and not the patient's underlying ALL, then CR should be reported)

Primary Induction Failure (PIF)

The patient received treatment for ALL but never achieved CR or CRi at anytime. PIF is not limited by the number of unsuccessful treatments; this disease status only applies to recipients who have never been in CR or CRi.

Relapse (REL)

Relapse is defined as the recurrence of disease after CR, meeting at least one of the following criteria:

- ≥ 5% blasts in the marrow or peripheral blood
- Extramedullary disease
- Disease presence determined by a physician upon clinical assessment

Do not include disease detected by MRD or other methods of assessment (i.e., molecular, cytogenetics, flow cytometry)

The number of this relapse can be determined by using the following guidelines:

- 1st relapse: one prior CR
- 2nd relapse: two prior CRs
- 3rd or higher: three or more CRs

Do not include a partial response (PR) when determining number of relapse. Recipients who achieve a PR to treatment should be classified as either PIF or relapse; PR in ALL is generally of short duration and is unlikely to predict clinical benefit.

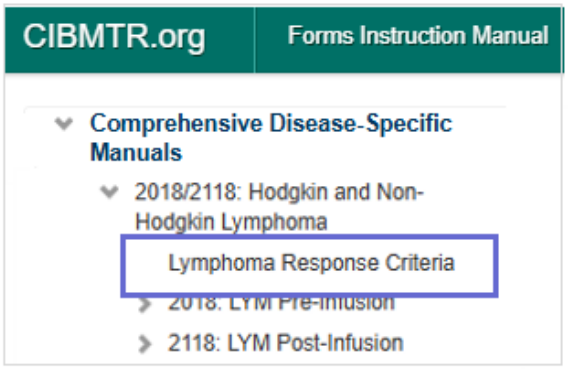
No Treatment

The recipient was diagnosed with acute leukemia and never received therapeutic agents. Include patients who have received only supportive therapy, including growth factors and/or blood transfusions.

LYMPHOMA RESPONSE CRITERIA

Please refer to the CIBMTR guidelines for a comprehensive explanation to determining the disease response.

Lymphoma Response Criteria - Forms Instruction Manual - 1



Metabolic Criteria

Complete Remission (CR)

Requires all of the following:

- A score of 1, 2, or 3 with or without a residual mass on a PET 5 point scale; and
- Disappearance of any previously non-measured lesions; and
- No new lesions; and
- No evidence of FDG-avid disease in the marrow.

Partial Remission

Requires all of the following:

- Score 4 or 5 on a PET 5 point scale with reduced uptake compared with baseline; and
- No new lesions.

Stable Disease

Does not meet metabolic criteria for complete remission, partial remission, or progressive disease.

Progressive Disease (after Partial Remission, Stable Disease), **Relapsed Disease** (after Complete Remission)

Requires at least one of the following:

- Score 4 or 5 on a PET 5 point scale with increased uptake compared with baseline; or
- Any new FDG-avid foci consistent with lymphoma; or
- New or recurrent FDG avid foci in the bone marrow.

Radiographic Response Criteria

For recipients with CNS lymphoma, an MRI may be used in place of the CT for the radiographic response criteria.

Complete Remission (CR)

Requires all of the following:

- All target nodes / nodal masses must have regressed as measured by CT to ≤ 1.5 cm in longest diameter; and
- Disappearance of any previously non-measured lesions; and
- No extralymphatic sites of disease; and
- No organomegaly.

Normal morphology of bone marrow is also required for a complete radiological remission if the marrow was an involved site. Immunohistochemical stains must be negative if morphology is indeterminate.

Partial Remission

Requires all of the following:

- ≥ 50% decrease in the SPD of up to 6 target measurable nodes and extranodal sites*; and
- No increase in the size of previously non-measurable lesions; and
- No new lesions.
  If splenomegaly is present, a > 50% decrease in spleen length is also required to report a partial radiological remission

*For lesions too small to measure on CT, assign 5mm x 5mm as the default value and then 0 mm x 0 mm when the lesion is no longer visible. For a node >5 mm x 5 mm, but smaller than normal, use the actual measurement of the node for calculations.

Stable Disease

Does not meet radiographic criteria for complete remission, partial remission, or progressive disease.

Progressive Disease (after Partial Remission, Stable Disease)**, Relapsed Disease** (after Complete Remission)

Requires at least one of the following:

- An individual node must be abnormal with:
  - LDi >1.5 cm; and
  - ≥ 50% increase from nadir in the PPD; or
- An increase in LDi or SDi from nadir
  - ≥ 0.5 cm increase in LDi or SDi from nadir for any lesion ≤ 2cm; or
  - ≥ 1.0 cm increase in LDi or SDi from nadir for any lesion > 2 cm; or
- A 50% increase in spleen length compared to its prior increase beyond baseline; or
- New or recurrent splenomegaly; or

- Clear progression of pre-existing non-measured lesions; or
- Regrowth of any previously resolved lesions; or
- A new node > 1.5 cm in any axis; or
- A new extranodal site > 1.0 cm in any axis or if < 1.0 cm in any axis, its presence must be unequivocally attributable to lymphoma; or
- Assessable disease of any size unequivocally attributable to lymphoma; or
- New or recurrent involvement of the bone marrow.

LDi: longest transverse diameter of a lesion

SDi: shortest axis perpendicular to the LDi

SPD: sum of the product of the perpendicular diameters for multiple lesions

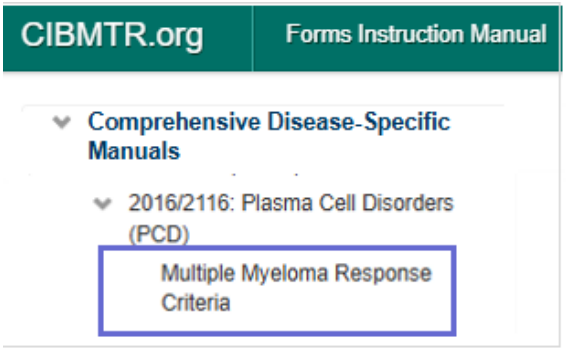
PPD: cross product of the LDi and perpendicular diameter

Adapted from: Cheson, B. D., Fisher, R. I., Barrington, S. F., Cavalli, F., Schwartz, L. H., Zucca, E., & Lister, T. A. (2014). Recommendations for Initial Evaluation, Staging, and Response Assessment of Hodgkin and Non-Hodgkin Lymphoma: The Lugano Classification. Journal of Clinical Oncology, 32(27), 3059-3067. doi:10.1200/jco.2013.54.8800

MULTIPLE MYELOMA RESPONSE CRITERIA

Please refer to the CIBMTR guidelines for a comprehensive explanation to determining the disease response.

Multiple Myeloma Response Criteria - Forms Instruction Manual - 1



Confirmatory testing

For **sCR, CR, VGPR, PR and SD,** these responses require two consecutive assessments (by the same method) made at any time before starting new therapy. If radiographic studies were performed, there must be no known evidence of new or progressive bone lesions. Radiographic studies are not required for confirmation.

CR does not require two consecutive assessments by each method. The method of the two consecutive assessments may be any of the biochemical tests (urine/serum testing) listed in the disease status criteria.

Urine Studies: Never Done or Diagnosis Only (and positive)

VGPR and PR may still be reported even if urine studies were never obtained or were only obtained at diagnosis and positive.

PD requires two consecutive assessments (by the same method) made at any time before classification as disease progression, and/or the start of any new therapy.

Relapse requires two consecutive assessments (by the same method) and/or the start of any new therapy to be classified as relapse.

Stringent Complete Response (sCR)

Follows criteria for CR, plus all of the following:

- Normal free light chain ratio, see note [1]

- Absence of clonal cells in the BM by immunohistochemistry or immunofluorescence (repeat BM biopsy confirmation not needed).

[1] Free Light Chain Ratios

Normal kappa / lambda ratio range of 0.26 – 1.65. Recipients with renal failure, normal ratio range is 0.37 – 3.1.

Complete Response (CR)

Measurable and Non-Measurable Multiple Myeloma

All the following:

- Negative immunofixation on serum and urine samples, see note [2]
- Disappearance of any soft tissue plasmacytomas
- < 5% plasma cells in the bone marrow (repeat confirmatory BM biopsy not needed)

[2] the sample for the urine immunofixation and electrophoresis criteria must be a 24-hour urine and not a random urine.

Light Chain Only Myeloma

All the following:

- Normal serum free light chain ratio [1]
- Negative immunofixation on serum and urine samples
- Disappearance of any soft tissue plasmacytomas
- < 5% plasma cells in the bone marrow (confirmation with repeat bone marrow biopsy not needed)

[1] the normal kappa / lambda ratio range is 0.26 – 1.65. For recipients with renal failure (serum creatinine > 2 mg / dL), the normal kappa / lambda ratio range is 0.37 – 3.1; any value within this range should be considered within normal limits.

Non-Secretory Myeloma

All the following:

- Disappearance of all soft tissue plasmacytomas
- < 5% plasma cells in the bone marrow (confirmation with repeat bone marrow biopsy not needed)

Very Good Partial Response (VGPR)

Measurable Myeloma

One or more of the following:

- Heavy Chain Myeloma
  - Serum and urine M-protein detectable by immunofixation but not on electrophoresis
  - ≥ 90% reduction in serum M-protein and urine M-protein level < 100 mg/24 hours
- Light Chain Only Myeloma
  - Serum and urine M-protein detectable by immunofixation but not on electrophoresis
  - ≥ 90% reduction in serum M-protein and urine M-protein < 100 mg/24 hours
  - ≥ 90% decrease in the difference between involved and uninvolved free light chain levels

Non-Measurable Myeloma

If the serum and urine M-protein are not measurable (i.e. do not meet the following criteria at the time of diagnosis):

- Serum M-protein ≥ 1 g/dL
- Urine M-protein ≥ 200 mg/24 hours

then a ≥ 90% decrease in the difference between involved and uninvolved free light chain levels is required in place of the M-protein criteria (provided the serum free light chain assay shows involved > 100 mg/L and the serum free light chain ratio is abnormal).

VGPR cannot be reported for recipients with non-secretory myeloma

Partial Response (PR)

Measurable Myeloma

One or more of the following:

- Heavy Chain Myeloma
  - ≥ 50% reduction in serum M-protein
  - Reduction in 24-hour urinary M-protein by ≥ 90% or to < 200 mg/24 hours
- Light Chain Only Myeloma
  - ≥ 50% reduction in serum M-protein
  - Reduction in 24-hour urinary M-protein by ≥ 90% or to < 200 mg/24 hours
  - ≥ 50% decrease in the difference between involved and uninvolved free light chain levels

Non-Measurable Myeloma

If serum and urine M-protein are not measurable (i.e. Serum M-protein ≥ 1 g/dL, Urine M-protein ≥ 200 mg/24 hours)

- ≥ 50% decrease in the difference between involved and uninvolved free light chain levels is required in place of the M-protein criteria (provided the serum free light chain assay shows involved level > 100 mg/L and the serum free light chain is abnormal).

Non-Secretory Myeloma

- ≥ 50% reduction in bone marrow plasma cells is required in place of M-protein (provided the baseline bone marrow plasma cell percentage was ≥ 30%)
- recipients who had soft tissue plasmacytoma(s) present at baseline, a ≥ 50% reduction in their size is also required.

Stable Disease (SD)

Does not meet the criteria for CR, VGPR, PR, or PD.

Progressive Disease (PD)

Measurable Myeloma

At least one of the following:

Heavy Chain Myeloma

- Increase of ≥ 25% from the lowest response value achieved in at least one of the following:
  - Serum M-protein with an absolute increase ≥ 0.5 g/dL (for progressive disease, serum M-protein increases of ≥ 1 g/dL are sufficient if the starting M-protein is ≥ 5 g/dL)
  - Urine M-protein with an absolute increase ≥ 200 mg/24 hours
  - Bone marrow plasma cell percentage with an absolute increase of at least 10% plasma cells
- Definite development of new bone lesions or soft tissue plasmacytomas, or definite increase in the size of any existing bone lesions or soft tissue plasmacytomas (≥ 50% increase from nadir in size of > 1 lesion, or a ≥ 50% increase in the longest diameter of a previous lesion > 1 cm in short axis); and/or
- ≥ 50% increase in circulating plasma cells (minimum of 200 cells per µL) if this is the only measure of disease

Light Chain Only Myeloma

- Increase of ≥ 25% from the lowest response value achieved in one or more of the following:
  - Urine M-protein with an absolute increase of ≥ 200 mg/24 hours
  - The difference between involved and uninvolved free light chain levels with an absolute increase > 10 mg/dL (> 100 mg/L) (applicable to Light Chain Only Myeloma)
  - Bone marrow plasma cell percentage with an absolute increase of at least 10% plasma cells

- Definite development of new bone lesions or soft tissue plasmacytomas, or definite increase in the size of any existing bone lesions or soft tissue plasmacytomas (≥ 50% increase from nadir in size of >1 lesion, or a ≥ 50%
- ≥ 50% increase in circulating plasma cells (minimum of 200 cells per μL) if this is the only measure of disease

Non-Measurable Myeloma

At least one of the following:

- Increase of ≥ 25% from the lowest response value achieved in one or more of the following:
    - The difference between involved and uninvolved free light chain levels with an absolute increase > 10 mg/dL (> 100 mg/L)
    - Bone marrow plasma cell percentage with an absolute increase of at least 10% plasma cells
- Definite development of new bone lesions or soft tissue plasmacytomas, or definite increase in the size of any existing bone lesions or soft tissue plasmacytomas (≥ 50% increase from nadir in size of >1 lesion, or a ≥ 50% increase in the longest diameter of a previous lesion >1 cm in short axis); and/or
- ≥ 50% increase in circulating plasma cells (minimum of 200 cells per μL) if this is the only measure of disease

Non-Secretory Myeloma

At least one of the following:

- Increase of ≥ 25% from the lowest response value achieved in one or more of the following:
    - Bone marrow plasma cell percentage (irrespective of baselines status) with an absolute increase of at least 10% plasma cells
- Definite development of new bone lesions or soft tissue plasmacytomas, or definite increase in the size of any existing bone lesions or soft tissue plasmacytomas (≥ 50% increase from nadir in size of >1 lesion, or a ≥ 50% increase in the longest diameter of a previous lesion >1 cm in short axis); and/or
- ≥ 50% increase in circulating plasma cells (minimum of 200 cells per μL) if this is the only measure of disease

Relapse from CR

At least one of the following:

- Reappearance of serum or urine M-protein by immunofixation or electrophoresis; and/or
- Development of ≥ 5% plasma cells in the bone marrow; and/or
- Appearance of any other sign of progression such as:
    - Development of new soft tissue plasmacytomas or bone lesions (osteoporotic fractures do not constitute progression)

    - Hypercalcemia (> 11mg/dL)
    - Decrease in haemoglobin of ≥ 2 g/dL not related to therapy or other non-myeloma-related conditions
    - Rise in serum creatinine by 2 mg/dL or more from the start of therapy and attributable to myeloma
    - Hyperviscosity related to serum paraprotein
- Abnormal free light chain ratio (recipients with light chain only myeloma)
    - Recipient with normal creatinine (i.e., < 2 mg / dL): Kappa / lambda ratio is outside the normal range of 0.26 – 1.65
    - Recipient with elevated creatinine (i.e., ≥ 2 mg / dL): Kappa / lambda ratio is outside the range of 0.37 – 3.1