

# Lymphomas

## Guide to the completion of the EBMT data collection form: Lymphomas\_v2.1

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**EBMT Registry**

EBMT Clinical Research & Registry Department



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## Table of Contents

Introduction.....	4
Lymphomas.....	4
Disease.....	5
Date of diagnosis.....	5
Classification.....	5
Lymphomas: B-cell lymphoma (including Hodkin and Non-Hodgkin lymphoma).....	6
Disease.....	6
Transformation of indolent B-cell lymphoma.....	6
Parameters for international prognostic indices.....	6
Age at diagnosis.....	6
LDH levels elevated.....	6
Ann Arbor staging.....	6
ECOG performance status.....	8
> 1 extranodal site involved.....	8
> 4 nodal sites involved.....	8
Haemoglobin < 120g/L.....	9
White Blood Cell count.....	9
CNS involvement.....	9
Final score.....	9
Chromosome Analysis.....	9
Chromosome analysis done before HCT/CT treatment.....	9
Extended dataset.....	10
Method of analysis used.....	10
What were the results?.....	10
Date of chromosome analysis.....	10
Chromosome analysis details.....	10
Molecular Marker Analysis.....	11
Molecular marker analysis done before HCT/CT treatment.....	11
Date of molecular marker analysis (if tested).....	11
Molecular marker analysis details.....	11
Immunophenotyping.....	12
Immunophenotyping done before HCT/CT treatment.....	12
Date of immunophenotyping (if tested).....	12
Immunophenotyping details.....	12
Lymphomas: T-cell non-Hodgkin lymphoma (NHL).....	13
Disease.....	13
Sub-Classification: Mature T-cell & NK-cell Neoplasms.....	13
Lymphomas: Immunodeficiency-associated lymphoproliferative disorders (incl. PTLD).....	13
Disease.....	13
Sub-Classification: Immunodeficiency-associated lymphoproliferative disorders (incl. PTLD).....	13
Post-transplant lymphoproliferative disorder (PTLD).....	13

Non-destructive PTLD.....	14
Monomorphic PTLD.....	14
Did the disease result from a previous solid organ transplant?.....	14
Date of transplant.....	14
Type of transplant.....	14
Lymphomas.....	14
Previous therapies (between diagnosis and HCT/CT).....	14
Bibliography.....	15

## Introduction

Please make sure you have already checked the **Introduction to the EBMT Registry Completion Guidelines** document latest version available under *Manuals and Reference Documents* section on [EBMT website](#).

## Lymphomas

Lymphomas are malignant neoplasms of the lymphatic system, which includes lymph nodes, spleen, thymus, Waldeyer's ring, appendix, and Peyer's patches.

Lymphomas are divided into 3 subgroups: B-cell Lymphomas (including Hodgkin lymphoma (HL)), T-cell lymphomas (NHL), and **Immunodeficiency-associated lymphoproliferative disorders**.

### B-cell Lymphomas

B-cell lymphomas are malignancies of B lymphocytes and their precursors at various stages of the differentiation. Very immature B-cell precursor malignancies are usually not included but are discussed at acute leukemias. The very immature are subject of the acute leukaemia working party.

Very mature B-cell malignancies as chronic lymphocytic leukaemia and multiple myeloma are also not subsumed on this definition and are subject to the work of the chronic malignancies working party. The very immature are subject of the acute leukaemia working party.

Non-Hodgkin lymphomas have the tendency to grow discontinuously in the lymphatic system and they can involve the extralymphatic system more often than HL. Thus, the gastrointestinal tract, the liver, the bone marrow, and the peripheral blood are affected much more often than in Hodgkin's disease. Ratio male:female = 1.5:1. About 2/3 of the patients with NHL are between 50 and 80 years old. Patients with AIDS have a 1000 times higher incidence of NHL. Typical symptoms are: swelling of lymph nodes, fever, night sweats, weight loss, and skin affection. The bone marrow is affected in 50% of cases, thus, the laboratory results often show anaemia, thrombocytopenia, and leukocytopenia. In Non Hodgkin's lymphoma either B or T lymphocytes can be involved.

Hodgkin lymphoma has a monoclonal origin with B-lymphocytes being involved in most cases. At an early stage, only lymph nodes are affected, at an advanced stage, it is a systemic disease that might as well affect extralymphatic organs (bone marrow, liver). Ratio male:female is 3 to 2. In Europe and the USA, there are two age peaks: one around 30 and one above 60 years old. It is assumed that there is a connection in some cases between EBV infection and the pathogenesis of Hodgkin lymphoma. Typical symptoms are: swelling of lymph nodes without pain (60% cervical, 30% mediastinal, 20% axillar, 15%

both abdominal or inguinal) - few patients describe painful lymph nodes after consumption of alcohol; fever, night sweats, weight loss, and hepatosplenomegaly. The laboratory results often show elevated ESR and LDH values, anaemia, and typical lymphocytopenia.

### **T-cell lymphomas (NHL)**

T cell lymphomas are malignancies of T lymphocytes at various stages of the differentiation. Very immature T-cell precursor malignancies are subsumed of the Acute Leukaemia Working Party.

**Immunodeficiency-associated lymphoproliferative disorders** are pathologically and clinically heterogeneous. In many instances, similar features are shared by a spectrum of immunodeficiency-associated lymphoproliferative disorders in clinically diverse settings. However, the World Health Organization (WHO) classifies them by their immunodeficiency setting largely according to the paradigm of posttransplant lymphoproliferative disorders.

## Disease

### Date of diagnosis

Report the date of the first pathological diagnosis of the disease. Add the date when the sample was collected for examination or (in its absence) the date indicated by a physician within the patient's medical record.

### Classification

Select the relevant class for the type of lymphoma that was diagnosed.

- B-cell lymphoma (including Hodgkin and Non-Hodgkin lymphoma)
- T-cell non-Hodgkin lymphoma (NHL)
- Immunodeficiency-associated lymphoproliferative disorder (incl. PTLD)

## Lymphomas: B-cell lymphoma (including Hodgkin and Non-Hodgkin lymphoma)

### Disease

#### Sub-Classification: Mature B-cell neoplasms

Select the subclass that is appropriate for mature B-cell neoplasm by checking the box next to it. The classifications are based on the 2022 WHO classifications (1).

#### Transformation of indolent B-cell lymphoma

Please indicate if patients with low-grade (clinically indolent) lymphomas or high-grade (clinically aggressive) lymphoma undergo transformation.

#### Parameters for international prognostic indices

##### Age at diagnosis

Indicate the patient's age at diagnosis in years. The web application will automatically complete this item.

##### LDH levels elevated

Indicate if serum lactate dehydrogenase (LDH) level is elevated as per the reference laboratory's ranges (answer **Yes**), not elevated (answer **No**) or it was **Not evaluated** by clicking the correspondent answer box.

##### Ann Arbor staging

The Ann Arbor staging system is widely used for anatomic staging of lymphoma, both Hodgkin and non-Hodgkin. The definition of these stages can be found in the AJCC Cancer Staging Manual (7th edition) or Union for International Cancer Control (UICC) staging manual (2). Check the box **Not evaluated** if it was not assessed.

Stage	Definition
I	Involvement of a single lymph node region (I), or localized involvement of a single extralymphatic organ or site in the absence of any lymph node involvement (IE).
II	Involvement of two or more lymph node regions on the same side of the diaphragm (II), or localized involvement of a single extralymphatic organ or site in association with regional lymph node involvement with or without the involvement of other lymph node regions on the same side of the diaphragm (IIE). The number of regions involved may be indicated by a subscript, for example, II3.
III	Involvement of lymph node regions on both sides of the diaphragm (III), which also may be accompanied by extralymphatic extension in association with adjacent lymph node involvement (IIIE) or by the involvement of the spleen (IIIS) or both (IIIE,S).
IV	Diffuse or disseminated involvement of one or more extralymphatic organs, with or without associated lymph node involvement; or isolated extralymphatic organ involvement in the absence of adjacent regional lymph node involvement, but in conjunction with the disease in distant site(s). Any involvement of the liver or bone marrow or nodular involvement of the lung(s) is always Stage IV. The location of Stage IV disease is identified further by specifying the site according to the notations listed for Stage III

Table 1. Ann Arbor stage definitions (1,2).

## ECOG performance status

The ECOG performance status scale describes a patient's level of functioning in terms of their ability to care for themselves, daily activity, and physical ability (walking, working, etc.). It is published [here](#). Check the box **Not evaluated** if it was not assessed.

Grade	ECOG performance status
0	Fully active, able to carry on all pre-disease performance without restriction
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light housework, office work
2	Ambulatory and capable of all self-care but unable to carry out any work activities; up and about more than 50% of waking hours
3	Capable of only limited self-care; confined to bed or chair more than 50% of waking hours
4	Completely disabled; cannot carry on any self-care; totally confined to bed or chair

Table 2. Definitions of ECOG scores (3).

### > 1 extranodal site involved

Indicate if more than 1 extranodal site (area or organ outside of the lymph nodes, spleen, thymus, and the pharyngeal lymphatic ring) was involved at the time of diagnosis. Check the box **Not evaluated** if the index was not assessed.

### > 4 nodal sites involved

Indicate if more than 4 nodal sites were involved at the time of diagnosis. Check the box **Not evaluated** if the index was not assessed.



### Haemoglobin < 120g/L

Indicate if the haemoglobin (haemoglobin) level was lower than 120g/L at the time of diagnosis. Check the box Not evaluated if the haemoglobin level was not assessed.

### White Blood Cell count

Indicate the number of white blood cells x 10<sup>9</sup> cells/L at the time of diagnosis or make a corresponding mark if it was Not evaluated.

### CNS involvement

Indicate whether the CNS was involved or not, please select unknown or not evaluated when appropriate.

### Final score

If the separate items to calculate the prognostic scores are not available, complete the **final score**. This should be completed for LBCL, mantle cell lymphoma, follicular lymphoma or Waldenstrom macroglobulinaemia only.

- For LBCL, please complete the final score according to the **IPI score** is applicable for all “Large B-cell lymphomas (LBCL)” except for “Primary large B-cell lymphoma of immune-privileged sites”. IPI is also applicable for “Follicular Large B cell lymphoma (FLBL)” that is now treated as LBCL .
- For mantle cell lymphoma, please complete the final score according to the **MIPI score**.
- For follicular lymphoma, please complete the final score according to the **FLIPI score**; except for “Follicular Large B cell lymphoma (FLBL)” for which IPI is more appropriate.
- For Waldenstrom macroglobulinaemia, please complete the final score according to the **ISSWM score**.

For other lymphoma, final score is not applicable.

## Chromosome Analysis

This section only needs to be completed for patients with the following types of B-cell NHL:

- Mantle cell lymphoma
- Waldenstrom macroglobulinaemia (LPL with monoclonal IgM)
- Burkitt lymphoma or Intermediate DLBCL/ BL (and all LBCL)

### Chromosome analysis done before HCT/CT treatment

Indicate if chromosome analysis was done or not before the HCT/CT treatment. Check **Unknown** if it is not known whether it was performed.

If **Yes**, report the results of the most recent complete analysis.

### *Extended dataset*

#### Method of analysis used

If chromosome analysis was performed, indicate which method was used. And select all that apply.

### What were the results?

**Normal** - the chromosome analysis has been performed and the results have been found normal

**Abnormal** - the chromosome analysis has been performed and abnormalities have been found. In addition, indicate the total number of different abnormalities present (**number of abnormalities present**).

**Failed** - the chromosome analysis was done but failed

### Date of chromosome analysis

Indicate the date of the chromosome analysis.

### Chromosome analysis details

See the cytogenetics form or ask the cytogenetics team and consult your physician.

If chromosome analysis was performed, indicate for each abnormality in the table whether it was **Absent** or **Present** for the respective diagnosis. If a chromosome abnormality was not evaluated, report **Not evaluated**. Please note that the cytogenetics abnormalities are requested according to the subclassification

Please see the list of the most relevant cytogenetics abnormalities according to the diagnosis sub-classification. If a cytogenetics was analysed by different methods, please indicate the results of the most sensitive method.

For abnormal results, indicate below whether the abnormalities were absent, present or not evaluated (*according to the type of lymphoma diagnosed*).

Mantle cell lymphoma or Waldenstrom macroglobulinaemia	<b>del(17p)</b>	<input type="checkbox"/> Absent	<input type="checkbox"/> Present	<input type="checkbox"/> Not evaluated
	<b>FISH used:</b>	<input type="checkbox"/> No	<input type="checkbox"/> Yes	
Burkitt lymphoma or all LBCL	<b>t(2;8)</b>	<input type="checkbox"/> Absent	<input type="checkbox"/> Present	<input type="checkbox"/> Not evaluated
	<b>t(8;14)</b>	<input type="checkbox"/> Absent	<input type="checkbox"/> Present	<input type="checkbox"/> Not evaluated
	<b>t(8;22)</b>	<input type="checkbox"/> Absent	<input type="checkbox"/> Present	<input type="checkbox"/> Not evaluated
	<b>t(14;18)</b>	<input type="checkbox"/> Absent	<input type="checkbox"/> Present	<input type="checkbox"/> Not evaluated
All above mentioned B-cell lymphomas	<b>Other chromosome abnormalities; specify:</b> _____	<input type="checkbox"/> Absent	<input type="checkbox"/> Present	

If a chromosome abnormality was checked, but not listed as an option in the table, select **Other** and **specify** the abnormality and mark whether it was **Absent** or **Present**.

## Molecular Marker Analysis

This section only needs to be completed for patients with the following types of B-cell NHL:

- Mantle cell lymphoma
- Burkitt lymphoma or Intermediate DLBCL/ BL (and all LBCL)

### Molecular marker analysis done before HCT/CT treatment

Indicate whether molecular biology studies have been done to identify molecular markers. If they have been done, select **Yes**. If no molecular biology has been done, please check **No**. Select **Unknown** if it is unknown whether the analysis of the molecular markers has been done or not.

If **Yes**, report the results of the most recent complete analysis.

### Date of molecular marker analysis (if tested)

Indicate the date of the molecular marker analysis.

If the molecular marker analysis was not done/failed or it is unknown if it was performed, leave the field blank.

### Molecular marker analysis details

If molecular marker analysis was performed, indicate for each marker in the table whether it was **Absent** or **Present**. If a molecular marker was not evaluated, report **Not evaluated**.

If a molecular marker was evaluated, but not listed as an option in the table, select **Other** and specify the marker, indicating whether it was **Absent** or **Present**.

Please see the list of the most relevant molecular markers according to the diagnosis sub-classification.

*Indicate below whether the markers were absent, present or not evaluated, according to the type of lymphoma diagnosed.*

Mantle cell lymphoma	<b>TP53 mutation</b>	<input type="checkbox"/> Absent	<input type="checkbox"/> Present	<input type="checkbox"/> Not evaluated
Burkitt lymphoma or all LBCL	<b>MYC rearrangement</b>	<input type="checkbox"/> Absent	<input type="checkbox"/> Present	<input type="checkbox"/> Not evaluated
All LBCL	<b>BCL2 rearrangement</b>	<input type="checkbox"/> Absent	<input type="checkbox"/> Present	<input type="checkbox"/> Not evaluated
	<b>BCL6 rearrangement</b>	<input type="checkbox"/> Absent	<input type="checkbox"/> Present	<input type="checkbox"/> Not evaluated
All above mentioned B-cell lymphomas	<b>Other molecular markers; specify:</b> _____	<input type="checkbox"/> Absent	<input type="checkbox"/> Present	

## Immunophenotyping

This section only needs to be completed for patients with the following types of B-cell NHL:

- Mantle cell lymphoma
- Burkitt lymphoma or Intermediate DLBCL/ BL (and all LBCL)

### Immunophenotyping done before HCT/CT treatment

Indicate whether immunophenotyping studies have been done or not. If they have been done, select **Yes**. If no immunophenotyping has been done, please check **No**. Select **Unknown** if it is unknown whether the analysis has been done or not.

If **Yes**, report the results of the most recent complete analysis.

### Date of immunophenotyping (if tested)

Indicate the date of immunophenotyping.

If immunophenotyping was not done/failed or it is unknown if it was performed, leave the field blank.

### Immunophenotyping details

If immunophenotyping was performed, indicate for each immunophenotype in the table whether it was **Absent** or **Present**. If an immunophenotype was not evaluated, report **Not evaluated**.

If an immunophenotype is detected, but not listed as an option in the table, select **Other** and specify the immunophenotype and mark whether it was **Absent** or **Present**.

Please see the list of the most relevant immunophenotyping according to the diagnosis sub-classification.

Indicate below whether the immunophenotypes were absent, present or not evaluated, according to the type of lymphoma diagnosed.

Mantle cell lymphoma	<b>SOX 11</b>	<input type="checkbox"/> Absent <input type="checkbox"/> Present <input type="checkbox"/> Not evaluated
Burkitt lymphoma or all LBCL	<b>MYC</b>	<input type="checkbox"/> Absent <input type="checkbox"/> Present <input type="checkbox"/> Not evaluated
LBCL	<b>BCL2/IgH</b>	<input type="checkbox"/> Absent <input type="checkbox"/> Present <input type="checkbox"/> Not evaluated
	<b>BCL6</b>	<input type="checkbox"/> Absent <input type="checkbox"/> Present <input type="checkbox"/> Not evaluated
All above mentioned B-cell lymphomas	<b>Other immunophenotype; specify: _____</b>	<input type="checkbox"/> Absent <input type="checkbox"/> Present

## Lymphomas: T-cell non-Hodgkin lymphoma (NHL)

### Disease

#### Sub-Classification: Mature T-cell & NK-cell Neoplasms

Select the sub-class that is relevant for mature T-cell & NK-cell Neoplasms by checking the box next to it (1), please note that the classification used is the WHO 2022 classification.

## Lymphomas: Immunodeficiency-associated lymphoproliferative disorders (incl. PTLD)

### Disease

#### Sub-Classification: Immunodeficiency-associated lymphoproliferative disorders (incl. PTLD)

Select the sub-class that is appropriate for Immunodeficiency-associated lymphoproliferative disorders (incl. PTLD) by checking the box next to it (1).

For **Other iatrogenic immunodeficiency-associated lymphoproliferative disorder**, check the corresponding box.

#### Post-transplant lymphoproliferative disorder (PTLD)

For Post-transplant lymphoproliferative disorder (PTLD), specify the type.

### *Non-destructive PTLD*

Specify the type of non-destructive PTLD.

### *Monomorphic PTLD*

Specify the type of monomorphic PTLD.

### Did the disease result from a previous solid organ transplant?

Indicate if the immunodeficiency-associated lymphoproliferative disorder (incl. PTLD) is a result of a previous solid organ transplant. Check the **Unknown** box if it is unknown whether the disease resulted from a previous solid organ transplant.

### Date of transplant

If the disorder was the result of a previous solid organ transplant, indicate the date of the transplant.

### Type of transplant

If the disorder was the result of a previous solid organ transplant, select the type of transplant. If the transplant type is not **Renal**, **Cardiac**, or **Pulmonary**, select **Other** and specify the type of transplant in the textbox in English.

## Lymphomas

### Previous therapies (between diagnosis and HCT/CT)

Previous therapy lines before the HCT/CT:

If the patient received previous lines of treatment before the HCT/CT, select **Yes** and complete the corresponding **Treatment non-HCT/CT/GT/IST form**. Otherwise, select **No**. If this information is unavailable, select **Unknown**.

## Bibliography

1. Alaggio R, Amador C, Anagnostopoulos I, Attygalle AD, de Oliveira Araujo IB, Berti E, et al. Correction: “the 5th edition of the world health organization classification of haematolymphoid tumours: Lymphoid neoplasms” leukemia. 2022 Jul;36(7):1720-1748. *Leukemia* [Internet]. 2023;37(9):1944–51. Available from: <http://dx.doi.org/10.1038/s41375-023-01962-5>
2. [Table], Table 4. Ann Arbor Staging Classification for Hodgkin Lymphoma. 2023 Mar 24 [cited 2023 May 23]; Available from: [https://www.ncbi.nlm.nih.gov/books/NBK65726/table/CDR0000062933\\_\\_557/](https://www.ncbi.nlm.nih.gov/books/NBK65726/table/CDR0000062933__557/)
3. Oken MM, Creech RH, Tormey DC, Horton J, Davis TE, McFadden ET, et al. Toxicity and response criteria of the Eastern Cooperative Oncology Group. *Am J Clin Oncol*. 1982 Dec;5(6):649–55.