Lymphomas

Guide to the completion of the EBMT data collection form: Lymphomas_v1.0

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EBMT Registry

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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 two subgroups: Hodgkin lymphoma (HL) and Non-Hodgkin lymphomas (NHL).

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.

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.

Diagnosis

1. 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.

2. Lymphomas Classification:

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

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

3. B-Cell Non-Hodgkin Lymphomas Subclassification (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 2017 WHO classifications (1). If the subclass is not listed, check the box **Other B-cell lymphoma**.

3.1. Other B-cell lymphoma; specify

If the B-cell lymphoma (non-Hodgkin) subclass is not available in the list, specify the diagnosis in the textbox in English.

3.2. Waldenstrom macroglobulinemia

For Lymphoplasmacytic lymphoma (LPL), indicate if it is Waldenstrom macroglobulinaemia (LPL with monoclonal IgM).

3.4. Follicular lymphoma grading

Indicate the grade of follicular lymphoma according to the WHO (2017) grading system as listed in table 1 (1).

Grade	Description	Centroblasts, %
Grade I	follicular small cleaved	0 – 5 centroblasts/HPF
Grade II	follicular mixed	6 – 15 centroblasts/HPF
Grade IIIa	follicular large cell	> 15 centroblasts/HPF centrocytes present
Grade IIIb		> 15 centroblasts/HPF solid sheets of centroblasts

Table 1, follicular lymphoma grading (1)

If the grade of follicular lymphoma was not assessed during the pathology examination, select **Not evaluated**.

3.5. Mantle cell lymphoma grading

Mantle cell lymphoma has traditionally been considered a very aggressive and incurable lymphoma, but there are now recognized **indolent** variants, as the classical MCL. **Classical** MCL is usually composed of IGHV-unmutated or minimally mutated B cells that usually express SOX11 and typically involves lymph nodes and other extranodal sites. It is a monomorphic lymphoid proliferation with a vaguely nodular, diffuse, mantle zone, or rarely follicular growth pattern.

However, there are also morphological aggressive variants including **Blastoid** variants (cells resemble lymphoblasts with dispersed chromatin and a high mitotic rate (usually ⩾20–30 mitoses per 10 high-power fields)) and **pleomorphic** variants (cells are pleomorphic, but many are large with oval to irregular nuclear contours, generally pale cytoplasm, and often prominent nucleoli in at least some of the cells) (1).

If the morphological variant of mantle cell lymphoma was not assessed during the pathology examination, select **Not evaluated**.

3.6. KI-67

If requested, complete the KI-67 proliferation index (percentage positive cells). The PDF form illustrates for which diagnoses the KI-67 needs to be completed. If the index was not assessed, select **Not evaluated**.

4. High-grade transformation of indolent B-cell lymphoma?

Indicate if B-Cell Non-Hodgkin Lymphoma transformed from another type of lymphoma before this main treatment. Check the box **Unknown** if the answer is unknown. If the answer is **Yes**, complete the non-indication diagnosis form to report the indolent B-cell lymphoma.

5. Parameters for international prognostic indices

5.1. Age at diagnosis

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

5.2. 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.

5.3. 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 2, Ann Arbor stage definitions (1,2)

5.4. ECOG performance status

The ECOG performance status scale describes a patient's level of functioning in terms of their ability to care for themself, 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 3, definitions of ECOG scores (3)

5.5. > 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.

5.6. > 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.

5.7. Hemoglobin < 120g/L

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

5.8. White Blood Cell count

Indicate the number of white blood cells x 109 cells/L at the time of diagnosis or make a corresponding mark if it was Not evaluated.

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

6. Chromosome analysis done before main treatment (all methods including FISH)

In this section describe the results of the most recent complete chromosome analysis (performed after diagnosis but before the treatment).

Not done or failed - the chromosome analysis has not been done or failed;

Yes, abnormal results - the chromosome analysis has been performed and at least one of the results has been found to be abnormal. In addition, indicate the number of abnormalities present in the most recent analysis with abnormal results (**number of abnormalities present**).

Yes, normal results - the chromosome analysis has been performed and all the results have been found normal;

Unknown - it is unknown whether the chromosome analysis has been done or not.

If more than one analysis has been done since diagnosis but before treatment, indicate **Yes, abnormal results** if at least one analysis has been found to be abnormal. In this case,

describe the results of the most recent analysis with abnormal results.

6.1. Date of chromosome analysis (if tested)

Indicate the date of the chromosome analysis.

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

6.2. 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**.

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
- Waldenstrom macroglobulinaemia (LPL with monoclonal IgM)
- Burkitt lymphoma or Intermediate DLBCL/ BL

7. Molecular marker analysis done before main 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.

7.1. 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.

7.2. 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**.

Immunophenotyping

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.

8. Immunophenotyping done before main 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.

8.1. 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.

8.2. 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.**

T-Cell Non-Hodgkin Lymphomas (NHL)

9. T-Cell Non-Hodgkin Lymphomas 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). If the sub-class is not listed, check the box **Other T-cell lymphoma**.

Other T-cell lymphoma; specify:

If the T-cell lymphoma (non-Hodgkin) subclass is not available in the list, specify the diagnosis in the textbox in English.

Hodgkin Lymphomas

10. Hodgkin Lymphomas Sub-Classification

Select the sub-class that is appropriate for Hodgkin Lymphomas by checking the box next to it. If the sub-class is not listed, check the box **Other Hodgkin lymphoma**.

Other Hodgkin lymphoma; specify:

If the Hodgkin lymphoma subclass is not available in the list, specify the diagnosis in the textbox in English.

Immunodeficiency-associated lymphoproliferative disorders (incl. PTLD)

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

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.

11.1. Post-transplant lymphoproliferative disorder type

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

11.2. Non-destructive PTLD

Specify the type of non-destructive PTLD.

11.3. Monomorphic PTLD

Specify the type of monomorphic PTLD.

12. 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.

12.1. Date of transplant

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

12.2. 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 before HCT/CT

13. Previous therapies

List all previous lines of treatment before the main treatment, indicating for each of them:

- **Regimen used**: select the appropriate chemotherapy regimen the patient received from the list. If the regimen is not available, select **Other** and report the generic drug or regimen name(s) in the textbox in English.
- **Treatment start date**: report the date the chemotherapy regimen was initiated. This is the first day a drug of the regimen was administered.
- **Response to this line of treatment**: select the response to the chemotherapy regimen:
    - **Complete remission (CR)**
    - **Partial remission (PR)**
    - **Stable disease**
    - **Chemorefractory relapse or progression incl. primary refractory disease**
    - **Unknown**
- **Response assessment date**: report the date the response was observed.

Please consult the **LIST OF CHEMOTHERAPY DRUGS/AGENTS AND REGIMENS** on the EBMT website for drugs/regimens names. This document provides alternative names for many of the drugs/regimens. Once you have found the drug/regimen of interest on the list, add its database name to the table.

Bibliography

1. Campo E, Harris NL, Pileri SA, Jaffe ES, Stein H, Thiele J. WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues. IARC Who Classification of Tum; 2017. 586 p.
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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.