Acute leukemias

Guide to the completion of the EBMT data collection form:
Acute_Leukemias_v1.0

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EBMT Registry

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Acute leukemias

Acute leukaemia is a malignant disease that originates either in a lymphopoietic stem cell (Precursor lymphoid neoplasms (PLN), previously ALL) or in a hematopoietic stem cell or progenitor cell (acute myeloid leukaemia, AML

Disease

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. Acute leukaemias main classification

Select the main class that is appropriate for acute leukaemia and check the box next to it.

There are distinguished 3 main classes of acute leukaemia, which are

- Acute myeloid leukaemia (AML): characterised by disordered differentiation and proliferation of hematopoietic stem cells or progenitor cells into myeloblasts in acute myeloid leukaemia.
- Precursor lymphoid neoplasms (PLN, previously ALL) characterised by disordered differentiation and proliferation of lymphopoietic cells into lymphoblasts in precursor lymphoid neoplasms.
- Other acute leukaemia

Acute myeloid leukaemias (AML) classification

3. AML with myelodysplasia related changes?

In most cases, this classification applies to AML where an MDS or an MDS/MPN has been diagnosed beforehand. In a few cases, it applies to what looks as a de novo AML at the time of diagnosis, but which after further analysis of the bone marrow or after treatment for the AML, there is a suggestion that there could have been an undetected history of myelodysplastic syndrome (MDS).

Indicate whether AML with myelodysplasia related changes was diagnosed or not, tick the box **Unknown** if it is not known. If the answer is **Yes**, specify also:

3.1. Was there a previous diagnosis of MDS , MPN or MDS/MPN?

If the patient had a previous diagnosis of MDS, MPN or MDS/MPN, answer **Yes** and fill-in and submit respective indication diagnosis form in addition to the current form; otherwise, answer **No**. If it is unknown whether or not the patient had a previous diagnosis of MDS or MDS/MPN, check **Unknown**.

Note: *For AML with myelodysplasia related changes, if MDS, MPN or MDS/MPN was previously diagnosed, besides the Acute leukaemia form the corresponding indication diagnosis form for MDS, MPN or MDS/MPN must be filled in as well.*

4. Therapy-related myeloid neoplasia

Indicate whether therapy-related myeloid neoplasia (therapy-related myeloid neoplasms or t-MN) was diagnosed or not, tick the box **Unknown** if it is not known.

Therapy-related myeloid neoplasia arises as a late-effect of cytotoxic and/or radiation therapy for a primary condition. Answer **Yes** if it is related to prior treatment, but not after a previous diagnosis of MDS, MPN or MDS/MPN.

5. Chromosome analysis at diagnosis (all methods including FISH):

In this section describe the results of the most complete chromosome analysis performed around the time of diagnosis.

Choose the answer based on the following:

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.

Yes, normal results - the chromosome analysis has been performed and all the results have been found normal (46,XY or 46,XX).

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

If the results were **abnormal**, indicate the following:

5.1. Complex karyotype

Indicate whether the karyotype is complex or not, check the corresponding **Unknown** box if it is not known. The definition of a complex karyotype is 3 or more cytogenetics abnormalities being present.

5.2. Number of abnormalities

Indicate the number of abnormalities present in the most complete analysis with abnormal results

5.3. Monosomal karyotype

Indicate whether it is monosomal karyotype. A monosomal karyotype is defined by ≥2 autosomal monosomies; or 1 autosomal monosomy and at least 1 structural abnormality.

6. 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**. 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, marking whether it was **Absent** or **Present**.

If **11q23, 3q26 (EVI1), abn 5 or abn 7 type** abnormality was present, mark for each subtype abnormality if it was **Absent**, **Present** or **Not evaluated**.

6.1. Transcribe the complete karyotype

Report the chromosome analysis results as per abnormalities table.

7. Molecular marker analysis at diagnosis:

Molecular markers are specific genetic sequences that are associated with the recipient's primary disease. These markers are determined by molecular biology laboratories that have expertise in this field. They are used for diagnosis and sometimes to follow up on the disease after 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.

7.2. 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**.

7.2.1. MLL-rearrangement/mutation

If **MLL** rearrangement/mutation was present, specify for each of its subtypes in the table if it was **Absent**, **Present** or **Not evaluated**; if there were checked other subtypes that are not mentioned in the table, specify the rearrangement/mutation in the **Other MLL-rearrangement** text field and if it was **Absent** or **Present**.

7.2.2. FLT3 punctual mutation

For **FLT3 punctual mutation**, if present, specify the position of the amino-acid that is affected by the mutation; e.g. the "common" answers could be:

- FLT3-D835 (or with more details D835Y, D835V, D835H, D835E, and D835N)
- FLT3-TKD
- FLT3-I836

8. Other AML classification:

If applicable select the corresponding WHO classification of other AML diagnosis (1):

- Acute panmyelosis with myelofibrosis
- Myeloid sarcoma (granulocytic sarcoma)
- Myeloid proliferations related to Down syndrome
- Blastic plasmacytoid dendritic cell neoplasm (BPDCN)

9. FAB classification of AML

If available, indicate the appropriate FAB class.

The French-American-British (FAB) classification for acute leukaemias is a classification system that relies on how the cells appear under a microscope. The following AML classes are distinguished (2):

FAB subtype	**Name**
M0	AML with minimal differentiation
M1	AML without maturation
M2	AML with maturation
M3	Acute promyelocytic leukaemia
M4	Acute myelomonocytic leukaemia
M5	Acute monoblastic and monocytic leukaemia

M6	Acute erythroid leukaemia
M7	Acute megakaryoblastic leukaemia

Table 1, FAB classification of AML (2)

10. Involvement at time of diagnosis

Indicate if the AML has medullary, extramedullary involvement or both, mark if it is unknown. Extramedullary involvement (EMI) refers to leukemic cells found in organs or tissue outside the blood or bone marrow. The most common sites of extramedullary disease are the central nervous system (CNS), skin and ovaries/testes.

11. Organs involved at time of diagnosis

Indicate per each organ in the list if leukaemic cells were found there (answer **Yes**) or not (answer **No**), or if it was **Not evaluated** at time of diagnosis. If there were checked organs other than from the list, check the **Other** box and specify the organ, indicating if it is involved (select **Yes**) or not (select **No**).

Precursor lymphoid neoplasms classification (ALL)

12. Precursor lymphoid neoplasms classification

Select the class that is appropriate for the precursor lymphoid neoplasm (PLN) and check the box next to it. If the class is not listed, check the box **Other precursor lymphoid neoplasm** and specify it in the textbox.

13. Secondary origin: is this PLN related to prior exposure to therapeutic drugs or radiation?

Indicate if this PLN is related to prior exposure to therapeutic drugs or radiation, i.e. has a **secondary origin**. If the answer is **Yes**, indicate also:

13.1. Due to exposure to:

Select what the patient was exposed to, that caused PLN. Check the respective check box if it was chemotherapy/radiotherapy treated disease or immune suppression, otherwise check the **Other** box and specify. Select **Unknown** if PLN is considered to be of secondary origin but the exact reason cannot be identified.

14. Chromosome analysis at diagnosis (all methods including FISH):

In this section describe the results of the most complete chromosome analysis performed around the time of diagnosis.

Choose the answer based on the following:

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.
Yes, normal results - the chromosome analysis has been performed and all the results have been found normal (46,XY or 46,XX);
Unknown - it is unknown whether the chromosome analysis has been done or not.

If the results were **abnormal**, indicate:

14.1. Complex karyotype

Indicate whether it is a complex karyotype or not, check the corresponding **Unknown** box if it is not known.

14.2. Number of abnormalities

Indicate the number of abnormalities present in the most recent analysis with abnormal results

15. 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**. 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, marking whether it was **Absent** or **Present**.

If **11q23** abnormality was present, specify also if t(4;11) was **Absent**, **Present** or **Not evaluated.** If another 11q23 sub-type was checked, specify it in the **Other abn(11q23)** text field and mark if it was **Absent** or **Present**.

If **hyperdiploidy (>46 chromosomes)** is present, specify also the following:

- If 51-67 chromosomes were **Absent**, **Present** or **Not evaluated** in the chromosome analysis
- In case of trisomy; specify the extra chromosome name and if it was **Absent**, **Present** or **Not evaluated.**
- If **other hyperdiploid karyotype**; specify the number of chromosomes in the textbox and if they were **Absent** or **Present**.

For hypodiploidy (<46 chromosomes), specify the number of missing chromosomes by marking if low hypodiploid (32 - 39) chromosomes and near haploid (24-31 chromosomes), monosomy (specify details of monosomy in the text field) were **Absent**, **Present** or **Not evaluated** in the chromosome analysis.

In case of other chromosome abnormality, specify the number of chromosomes in **Other; number of chromosomes** field and mark if they were **Absent** or **Present.**

15.1. Transcribe the complete karyotype

If it is not possible to report the chromosome analysis results as per abnormalities table.

16. Molecular marker analysis at diagnosis

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.

17. Ph-like ALL

Indicate if Philadelphia chromosome (Ph)-like acute lymphoblastic leukemia (ALL) was analysed by answering **No** (in case it was not checked), **Yes** (to mark it was investigated) or **Unknown** (if it is not known whether such investigation was done or not). If the answer is Yes, complete the table and mark per each rearrangement (alteration) if it was **Absent**, **Present** or **Not evaluated**.

18. 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**.

For **MLL** (KMT2A) rearrangement/mutation, if it was present, specify for each subtype in the table if it was **Absent**, **Present** or **Not evaluated**; if there were checked other subtypes that are not mentioned in the table, specify the rearrangement/mutation in the **Other MLL** (KMT2A)**-rearrangement** text field and if it was **Absent** or **Present**.

19. Involvement at time of diagnosis:

Indicate if the PLN has medullary, extramedullary involvement or both, mark if it is **Unknown**.

20. Organs involved at time of diagnosis:

Indicate per each organ in the list if leukaemic cells were found there (answer **Yes**) or not (answer **No**), or if it was **Not evaluated** at time of diagnosis. If there were checked organs other

than from the list, check the **Other** box and specify the organ, indicating if it is involved (select **Yes**) or not (select **No**).

Other acute leukaemias

21. Acute leukaemias of ambiguous lineage classification

Acute leukaemias of ambiguous lineage may be divided into acute undifferentiated leukaemia (AUL) and mixed-phenotype acute leukaemias (MPALs). AULs are leukaemias with very primitive phenotypes with little evidence of lineage commitment. MPAL is a heterogeneous category that encompasses rare blastic hematopoietic cell neoplasms that express a mixture of myeloid and lymphoid (B- or T-lineage) antigens.

Indicate the class that is appropriate for acute leukaemia of ambiguous lineage. If the class is not listed, tick the box **Other** and specify.

22. Secondary origin: is this other acute leukaemia related to prior exposure to therapeutic drugs or radiation?

Indicate if this acute leukaemia is related to prior exposure to therapeutic drugs or radiation, i.e. has a secondary origin. If the answer is **Yes**, indicate also:

22.1. Due to exposure to:

What the patient was exposed to, that caused this acute leukaemia. Check the respective check box if it was chemotherapy/radiotherapy treated disease or immune suppression, otherwise check the **Other** box and specify. Select **Unknown** if this acute leukaemia is considered to be of secondary origin but the exact reason cannot be identified.

Note: *If not reported yet, complete and submit the respective non-indication diagnosis form in addition to the current form to report the diagnosis in regard to which drugs/therapy that caused acute leukaemia were applied.*

23. Chromosome analysis at diagnosis (all methods including FISH):

In this section describe the results of the most complete chromosome analysis performed around the time of diagnosis.

Choose the answer based on the following:

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;

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 the results were **abnormal**, indicate:

23.1. Complex karyotype

Indicate whether it is a complex karyotype or not, check the corresponding **Unknown** box if it is not known.

23.2. Number of abnormalities

Indicate the number of abnormalities present in the most recent analysis with abnormal results.

23.3. Transcribe the complete karyotype

In case of abnormal results, transcribe the complete karyotype.

24. Involvement at time of diagnosis:

Indicate if other acute leukaemia has medullary, extramedullary involvement or both, mark if it is **Unknown**.

25. Organs involved at time of diagnosis:

Indicate per each organ in the list if leukaemic cells were found there (mark **Yes**) or not (mark **No**), indicate if it was **Not evaluated** at time of diagnosis. If there were checked organs other than from the list, check the **Other** box and specify the organ, indicating if it is involved ((mark **Yes**) or not ((mark **No**).

Bibliography

1. International Agency for Research on Cancer. WHO classification of tumours of haematopoietic and lymphoid tissues: Vol. 2. 4th ed. Swerdlow SH, editor. IARC; 2017.
2. Neame PB, Soamboonsrup P, Browman GP, Meyer RM, Benger A, Wilson WE, et al. Classifying acute leukemia by immunophenotyping: a combined FAB- immunologic classification of AML. Blood [Internet]. 1986;68(6):1355–62. Available from: http://dx.doi.org/10.1182/blood.v68.6.1355.1355