Acute leukemias

Guide to the completion v2.4 of the EBMT data collection form:

Acute_Leukemias_Core_Extended_v2.4

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EBMT Registry

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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.

Acute leukaemias

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). Other Acute Leukaemias such as ambiguous lineage, undifferentiated lineage, NK cell or other rare type can be reported with this form.

Complete this form only if this diagnosis was the indication for a HCT/CT/GT or if it was specifically requested.

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.

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.
    - Acute Promyelocytic Leukaemia (APL, APML), Acute panmyelosis with myelofibrosis, Myeloid sarcoma (granulocytic sarcoma), Myeloid proliferations related to Down syndrome, Blastic plasmacytoid dendritic cell neoplasm (BPDCN), are acute myeloid leukaemia and should be reported in the AML section
    - Secondary acute myeloid leukaemia must be reported as AML, details on the type (transform from MDS, MDS/MPN overlap syndrome or for therapy related will be collected in the AML section

- **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 undifferentiated leukaemia, Mixed phenotype, Natural killer (NK) - cell lymphoblastic leukaemia/lymphoma or Other leukaemia.

Haematological values

Peripheral blood

Report the White Blood cells (WBC) count number at time of diagnosis and as a percentage or mark it as **Not evaluated** or **Unknown**.

White Blood cell count (10^9 cells/L)

Indicate the absolute number of white blood cells at diagnosis or mark it as **Not evaluated** or **Unknown**.

Please, pay attention to the units for the number of WBC reported at diagnosis: 10^9 cells/L is the same as 10^6cells/ml or 10^3cells/µl. If the WBC count is given in mm^3 then it should be transformed and reported in 10^9 cells/L: 300.000mm^3 is equal to 300 x10^9 cells/L.

% of blasts

Indicate only the exact percentage value of blasts in peripheral blood at diagnosis. The percentage of blasts can be found in the white blood cell count.

In the case an exact % is not available please provide the range

If the exact percentage is not available and reported as a range, indicate the upper and lower limit of the range.

In case neither exact percentage nor the range is available mark it as **Not evaluated** or **Unknown**.

Bone marrow

% of blasts

Indicate the percentage of blasts in bone marrow at diagnosis. If this data is not available, mark it as **Not evaluated** or **Unknown,** whatever is more appropriate.

Acute myeloid leukaemias (AML)

Disease

Classification

AML with myelodysplasia related changes?

In most cases, this classification applies to AML where an MDS, MPN 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 if the patient was previously diagnosed with MDS or MDS/MPN in the subquestion.

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, MPN 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.*

Therapy-related Acute Myeloid Leukemia (old "secondary acute leukaemia")

Indicate whether therapy-related AMLwas diagnosed or not, tick the box **Unknown** if it is not known.

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

- If the patient has therapy-related AML and did not undergo HCT/CT for the previous diagnosis, please complete the *non-indication diagnosis* form to record the previous diagnosis.
- If the patient has AML related to HCT/CT therapy treatment for the previous diagnosis, please complete the appropriate *indication diagnosis* form for this previous diagnosis.

Donor cell Leukaemia:

For Therapy-related Acute Myeloid Leukemia, please specify whether this leukaemia is on Donor cell of the previous Allogeneic transplantation or not, by answering the question "Is this a donor cell leukaemia?". It is also possible to mark this field **Not applicable** (in case patient did not have any previous allo HCT) or as **Unknown.**

Chromosome analysis

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

Chromosome analysis done at diagnosis

Report if the chromosome analysis has been done around the time of diagnosis or not. Choose the answer based on the following:

No - the chromosome analysis has not been done;

Yes - the chromosome analysis has been performed for diagnosis, specify also the **Output of analysis**: if it is **Separate abnormalities** or **Full karyotype**; The question is mainly a visibility condition. The full karyotyping is preferred as result.

Unknown - it is unknown whether the chromosome analysis has been done or not. This case may happen when the diagnosis is not performed in the transplant centre.

Failed - There were not enough dividing cells for analysis

Extended dataset

Date of chromosome analysis

If chromosome analyses was done around the time of diagnosis, please specify the date of the chromosome analyses or mark it as **Unknown**.

What were the results?

Indicate the results of the chromosome analysis you are reporting and choose the answer based on the following:

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

Abnormal results - the chromosome analysis has been performed and at least one of the results has been found to be abnormal. Provide further details on abnormal results in the sub questions below.

Extended dataset

Number of abnormalities

If the results were **abnormal**, indicate the number of abnormalities present in the most complete analysis with abnormal results.

Complex karyotype

A complex karyotype is defined by ≥3 unrelated chromosome abnormalities; excludes hyperdiploid karyotypes with three or more trisomies (or polysomies) without structural abnormalities.

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

Monosomal karyotype

A monosomal karyotype is defined by the presence of two or more distinct monosomies (excluding loss of X or Y), or one single autosomal monosomy in combination with at least one structural chromosome abnormality (excluding core-binding factor AML).

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

Multiple trisomies

If there is more than one trisomy please answer **Yes**, otherwise answer **No.** Check the corresponding **Unknown** box if it is not known.

Transcribe the complete karyotype

Please transcribe the full karyotyping. If you want also to report FISH results, please copy past the full result after the karyotyping. If the full karyotype is not available, please report using the question below.

Chromosome analysis details

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

If chromosome analysis was performed and had abnormal results, indicate for each abnormality listed in the table whether it was **Absent** or **Present**. If a chromosome abnormality was not evaluated, report **Not evaluated**. It is also mark a chromosome abnormality as **Unknown**, if it is not known whether it was evaluated or not.

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 type** or **abn 7 type** abnormality was present, mark for each subtype abnormality if it was **Absent**, **Present** , **Not evaluated** or **Unknown**. If the subtype is not listed, please use corresponding Other option and specify it in the textfield and report if it was **Absent** or **Present**.

Please find below the minimum list of requested cytogenetics abnormalities according to the WHO classification 2022:

- t(15;17)
- t(8;21)
- inv(16)/ t(16;16)
- 11q23 abnormality type, if a 11q23 abnormality is present:
    - t(9;11)
    - t(11;19)
    - t(10;11)
    - t(6;11)
    - Other abn(11q23); specify.
- 3q26 (EVI1) abnormality type, if a 3q26 abnormality is present:
    - inv(3) / t(3;3)
    - t(2;3)(p21;q26)
    - Other (3q26)/EVI1 rearrangement; specify.
- t(6;9)
- abn 5 type, if an abn 5 is present:
    - del (5q)
    - monosomy 5
    - add(5q)
    - Other abn(5q); specify.
- abn 7 type, if an abn 7 is present:
    - del(7q)

  - monosomy 7
  - add(7q)
  - Other abn(7q); specify.
- Monosomy 17
- abn(17p)
- t(1;22)
- Trisomy 8
- t(9;22)
- t(8;16)
- Other; specify.

Molecular marker analysis

Molecular marker analysis at diagnosis

Molecular markers are specific genetic sequences that are associated with the recipient's primary disease. Molecular marker analysis can be done by PCR, flow-cytometry or NGS. 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 around the time of diagnosis 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.

Extended dataset

Date of molecular markers analysis

Please specify the date of the molecular markers analysis which results will be reported below. Select **Unknown** if the date is unavailable.

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**. Select **Unknown** if it is unknown whether the analysis of the molecular marker has been done or not.

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**.

See the list below:

- AML1::ETO (RUNX1::RUNX1T1) (formerly AML1-ETO (RUNX1/RUNXT1)) Molecular product of t(8;21)
- CBFB::MYH11 (formerly CBFB-MYH11) Molecular product of inv(16)(p13.1;q22) or (16;16)(p13.1;q22)
- PML::RARA (formerly PML-RAR) Molecular product of t(15;17)
- KMT2A (former MLL)-rearrangement/mutation:
    - KMT2A::MLLT3 (former MLLT3(AF9)-MLL) Molecular product of t(9;11)(p22;q23)
    - KMT2A-PTD (former MLL-PTD) (partial tandem duplication)
    - KMT2A::AFDN (former MLLT4(AF6)-MLL) Molecular product of t(6;11)(q27;q23)
    - KMT2A::ELL (former ELL-MLL) Molecular product of t(11;19)(q23;p13.1)
    - KMT2A::MLLT1 (former MLLT1(ENL)-MLL) Molecular product of t(11;19)(q23;p13.3)
    - KMT2A::MLLT10 (former MLLT10(AF10)-MLL) Molecular product of t(10;11)(p12;q23)
    - Other KMT2A(MLL)-rearrangement; specify
- DEK::NUP214 (former DEK-NUP214(CAN)) Molecular product of translocation t(6;9)(p23;q34)
- RPN1::MECOM (former RPN1-EVI1) Molecular product of inv(3)(q21q26.2) or t(3;3)(q21q26.2)

- RBM15::MRTFA (former RBM15::MKL1) Molecular product of translocation t(1;22)(p13;q13)

- NPM1 mutation
- c-KIT
- DNMT3A
- ASXL1
- TP53
- RUNX1
- IDH2
- IDH1
- BRAT
- SRSF2
- SF3B1
- CEBPA: if CEBPA present, specify also whether or not there was bZIP mutation (answer yes, no, unknown) and if the mutation is biallelic (answer yes, no, unknown).
- FLT3-ITD (internal tandem duplication)
- FLT3-TKD
- BCR::ABL1 (former BCR-ABL)

- GATA2
- MECOM(EVI1)
- KAT6A::CREBBP (former KAT6A-CREBBP)
- BCOR
- EZH2
- STAG2
- U2AF1
- ZRSR2
- Other; specify.

If KMT2A (former **MLL)** rearrangement/mutation was present, specify for each of its subtypes in the table if it was **Absent**, **Present** ,**Not evaluated** or **Unknown**; 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**.

For **CEBPA mutation**, if present, please specify if

- there is a mutation in the CEBPA bZIP?

- the mutation is biallelic (either in bZIP or other mutation in the CEBPA gene) .

Next generation sequencing (NGS) performed at diagnosis

If NGS was done at diagnosis, select **Yes**. Otherwise, please check **No**. Select **Unknown** if it is unknown whether the NGS has been done or not.

Disease

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)

FAB classification of AML

If available, indicate the appropriate FAB class. If not evaluated, mark as **Not evaluated.**

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)

Involvement at time of diagnosis

Medullary involvement

If the AML, indicate whether the Marrow / Blood was involved answering **yes**, **no** or **unknown**. Please be aware that although the vast majority of acute leukaemias involve the invasion of the bone marrow by blasts, there are cases where blast invasion is only found in organs other than the bone marrow (e.g. choromas).

Extramedullary involvement

Extramedullary involvement 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; other organs can be involved.

Please indicate if any other organ(s) than the Marrow or Blood were involved at diagnosis, by reporting extramedullary involvement and answering **yes**, **no** or **unknown.**

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**).

See the list below:

- Skin:
- CNS:
- Testes/Ovaries:
- Other; specify.

Precursor lymphoid neoplasms (previously ALL)

Disease

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. Select from the following answer options:

- B lymphoblastic leukaemia/lymphoma
- T lymphoblastic leukaemia/lymphoma

- Other precursor lymphoid neoplasm; specify. This group should be selected if the lineage of the lymphoblast is not identifiable.

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

Indicate if this precursor lymphoid neoplasm is related to prior exposure to therapeutic drugs or radiation, i.e. has a **secondary origin** answering **yes, no** or **unknown**. If the answer is **Yes**, indicate also:

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
- Immune suppression
- Other; specify _____
- Unknown: if PLN is considered to be of secondary origin but the exact reason cannot be identified.

If the PLN is related to prior exposure to therapeutic drugs or radiation, please make sure that the diagnosis of the prior treatment is reported in the registry:

- if no HCT/CT was done for this previous diagnosis, please use a ***Non-Indication Diagnosis*** form, or
- if the patient had HCT/CT for the previous diagnosis, use the appropriate indication **diagnosis** form to report it, unless already registered in EBMT Registry.

Is this a donor cell Leukaemia :

For PLN(ALL) related to prior exposure to therapeutic drugs or radiation, please specify whether this leukaemia is on Donor cell of the previous Allogeneic transplantation or not, by answering the question "Is this a donor cell leukaemia?". It is also possible to mark this field **Not applicable** (in case patient did not have any previous allo HCT) or as **Unknown.**

Chromosome analysis

Chromosome analysis done at diagnosis

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:

No - the chromosome analysis has not been done.

Yes - the chromosome analysis has been performed for diagnosis.

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

Extended dataset

Date of chromosome analysis

If chromosome analysis was performed, please specify the date of the chromosome analysis around the time of diagnosis, which results will be reported. Mark this field as **unknown** if the date is not available.

What were the results?

Indicate the results of the chromosome analysis you are reporting and choose the answer based on the following:

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

Abnormal results - the chromosome analysis has been performed and at least one of the results has been found to be abnormal.

Failed - the chromosome analysis has failed.

Extended dataset

Number of abnormalities

- If the results of the chromosome analysis were **abnormal**, indicate the number of abnormalities present in the most complete analysis with abnormal results

Complex karyotype

A complex karyotype is defined by ≥3 unrelated chromosome abnormalities in the absence of other class-defining recurrent genetic abnormalities; excludes hyperdiploid karyotypes with three or more trisomies (or polysomies) without structural abnormalities.

If the results of the chromosome analysis were **abnormal**, indicate whether the karyotype is complex or not, check the corresponding **Unknown** box if it is not known.

Transcribe the complete karyotype

Please transcribe the full karyotyping. If you want also to report FISH results, please copy past the full result after the karyotyping. If the full karyotype is not available, please report using the question below.

Chromosome analysis details

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

If chromosome analysis was performed and had abnormal results, indicate for each abnormality listed in the table whether it was **Absent** or **Present**. If a chromosome abnormality was not evaluated, report **Not evaluated**. Select **Unknown** if it is not known whether the abnormality was evaluated or not.

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

For hypodiploidy (<=45 chromosomes), if hypodiploidy is present, answer subquestions to 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, Not evaluated** or **Unknown** 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.**

Molecular marker analysis

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.

Extended dataset

Date of molecular markers analysis

If molecular biology has been done, report the date of the molecular marker analysis. Select **Unknown** if the date is unavailable.

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**. Select **Unknown** if it is not known whether the molecular marker was evaluated or not.

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 , Not evaluated** or **Unknown**; 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**.

Please see the list of molecular markers requested for PLN:

- BCR::ABL1 (former BCR-ABL) Molecular product of t(9;22)(q34;q11.2)
- PML-RAR Molecular product of t(15;17)
- KMT2A (former MLL)-rearrangement/mutation:
    - KMT2A::AFF1 (former AFF1(AF4)-MLL) Molecular product of t(4;11)(q21;q23)
    - KMT2A::MLLT1 (former MLLT1(ENL)-MLL) Molecular product of t(11;19)(q23;p13.3)
    - KMT2A::MLLT3 (former MLLT3(AF9)-MLL) Molecular product of t(9;11)(p22;q23)
    - Other KMT2A (former MLL)-rearrangement;specify
- ETV6::RUNX1 (former known as TEL::AML1) Molecular product of t(12;21)(p13;q22)

- IGH::IL3 (former IL3-IGH) Molecular product of translocation t(5;14)(q31;q32)
- TCF3::PBX1 (former TCF3-PBX1) Molecular product of translocation (1;19)(q23;p13.3)
- TCF3::HLF Molecular product of translocation (17;19)
- IKZF1 (IKAROS) deletion or mutation
    - IKZF1 mutation (other than deletion)
    - IKZF1 deletion
- Mutation of NOTCH1 and FBWX7 (former NOTCH1 /FBWX7)
- PAX5 mutation
- KRAS mutation
- NRAS mutation
- PTEN mutation
- FLT3 mutation
- PTPN11 mutation
- BCL/MYC-rearranged
- TP53 mutation
    - Type of TP53 mutation: Somatic or Germline, Unknown accepted
- Other; specify.

Ph-like ALL?

Philadelphia (Ph)-like acute lymphoblastic leukemia (ALL) is a high-risk subtype of B-precursor ALL (B-ALL) characterised by a gene-expression profile similar to Ph^+ ALL but lacking the specific *BCR-ABL1* fusion gene. They could be treated by TKIs.

These alterations can be subdivided into 5 distinct subgroups based on the type of cytokine receptor or kinase fusion present:

(1) rearrangements of *CRLF*2: ex: *P2RY8-CRLF2* rearrangements, *IGH@-CRLF2.*

(2) ABL-class gene rearrangements, such as *ABL1*, *ABL2*, *PDGFRB*, and *CSF1R*

(3) *JAK2* and *EPOR* rearrangements.

(4) sequence mutations or deletions activating JAK-STAT- or MAPK signalling pathways. For example: mutations of *IL7R*, *FLT3*, and *IL2RB, mutations of JAK1 and JAK3, mutation of SH2B3.*

(5) other rare kinase alterations (ex: *mutations of NRAS, KRAS, PTPN11, and NF1).*

In case Ph is negative, please indicate if Philadelphia chromosome (Ph)-like acute lymphoblastic leukaemia (ALL) was analysed or not by answering:

- **No** in case it was not checked (skip the table below),
- **Yes** to mark it was investigated (proceed to report its results in the table below), or
- **Not evaluated** if it was not evaluated.

If the (Ph)-like acute lymphoblastic leukaemia (ALL) was analysed, complete the table with alterations and mark per each rearrangement (alteration) if it was **Absent**, **Present, Not evaluated** or **Unknown**.

Please see the list of molecular marker of interest for Ph-like:

- CRFL2 rearrangement
    - P2RY8::CRLF2 (former CRFL2-P2RY8)
    - IGH::CRLF2
    - Other CRFL2 rearrangement; specify.
- ABL1 rearrangement:
    - ETV6::ABL1 (former ABL1-ETV6)
    - NUP214::ABL1 (former ABL1-NUP214)
    - Other ABL1 rearrangement; specify.
- ABL2 rearrangement:
    - RCSD1::ABL2 (former ABL2-RCSD1)
    - Other ABL2 rearrangement; specify.
- JAK2 rearrangement:
    - PAX5::JAK2 (former JAK2-PAX5)
    - JAK2-BCR
    - Other JAK2 rearrangement; specify.
- EPOR rearrangement:
    - IGH::EPOR (former EPOR-IGH)
    - Other EPOR rearrangement; specify.

Next generation sequencing (NGS) performed at diagnosis

If NGS was done at time of diagnosis, select **Yes**. Otherwise, please check **No**. Select **Unknown** if it is unknown whether the NGS has been done or not.

Disease

Involvement at time of diagnosis

Medullary involvement

Indicate whether the Marrow / Blood was involved answering **yes**, **no** or **unknown**. Please be aware that although the vast majority of acute leukaemias involve the invasion of the bone marrow by blasts, there are cases where blast invasion is only found in organs other than the bone marrow (e.g. choromas).

Extramedullary involvement

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.

Please indicate if any other organ(s) than the Marrow or Blood were involved at diagnosis, by reporting extramedullary involvement and answering **yes**, **no** or **unknown.**

Organs involved at time of diagnosis

Indicate per each organ in the list if leukemic 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**).

See the list below:

- Skin;
- CNS;
- Testes/Ovaries;
- Other; specify.

Extended dataset

Next Generation Sequencing (NGS)

For AML and PLN

Complete this form only if NGS was performed at diagnosis.

Next-generation sequencing (NGS) is a molecular methodology that allows the rapid sequencing of thousands to millions of DNA or RNA molecules simultaneously, by determining the unique and specific order of nucleic acid bases. This tool therefore allows the sequencing of several genes and several individuals simultaneously, by comparing the patient's sequence to a reference sequence. This method to

screen for targetable genomic alterations (panel) is now widely available and has become part of routine practice for Acute Leukaemia, and has an impact on treatment selection. In short, it is a way to check a patient’s DNA or RNA for mutations that might play a role in acute leukaemia.

The report of NGS analysis contains the list of genes tested (called panel) and details on genes mutated (called variant) like the modification at DNA level, the modification at the protein level, the exon where the modification is located and the frequency of the variant.

Date NGS performed

If NGS studies have been done around the time of diagnosis to identify genomic alterations, please specify the **date of the NGS swab** whose results will be reported below.

Please specify the **panel** *(list of genes tested)* used for the analysis:

For each of the options of the list, select **Mutation present** if the gene mutation was present. Otherwise, please select **Mutation absent**.

Refer the list from appendix 1 (List of genes).

If there were other genes which were checked that are not mentioned in the table, specify the name in the **Other, specify** text field and check the option **Mutation present** or **Mutation absent**.

OR

Transcribe the NGS panel: please copy past the list of Genes for which DNA mutations have been evaluated, with separator between genes (space, point, coma, etc.)

For each gene, specify per mutation

For each variant (gene where genomic alteration has been detected) please provide from the report , information related to mutation at DNA level, the mutation at the protein level, the exon where the mutation is located and the frequency of the variant

DNA mutation:

please indicate the nucleotide change, DNA base change and location

Protein mutation:

please indicate the protein change, amino acid change and location

Exon:

if known please indicate the exon were the mutation is located otherwise tike Unknown

Frequency (VAF):

please indicate variant allele frequency or mark it as **Unknown**.

Clinical impact of the mutation:

Please indicate the clinical impact of the mutation, if not known select **Unknown.**

Examples:

Gene	***DNA mutation***	***Protein mutation***	***Exon***	***Frequency (VAF)***
TET2	*c.3578G>A (DNA base G located in position 3578 is replace by the DNA base A at DNA level)*	*p.Cys1193Tyr (Cysteine located on position 1193 is replace by Tyrosine in the protein TET2)*	*5*	*46%*
RUNX1	*c.488T>C*	*p.Phe163Ser*		*45%*
NRAS	*c.34G>T*	*p.Gly12Cys*	*2, 3*	*38%*
NPM1	*c.860_863dupTCTG*	*p.Trp288Cysfs*12*	*10, 11*	*20%*

Other acute leukaemias

Disease

Classification

Acute leukaemias of ambiguous lineage may be divided into:

Acute undifferentiated leukaemia (AUL). AULs are leukaemias with very primitive phenotypes with little evidence of lineage commitment.

Mixed-phenotype acute leukaemias (MPALs). 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.

Natural killer (NK) - cell lymphoblastic leukaemia/lymphoma.

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

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 by answering **yes** (i.e. has a secondary origin), **no** or **unknown**. If the answer is **Yes**, indicate also:

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.*

Is this a donor cell Leukaemia :

For other acute leukemia related to prior exposure to therapeutic drugs or radiation, please specify whether this leukaemia is on Donor cell of the previous Allogeneic transplantation or not, by answering the question “Is this a donor cell leukaemia?”. It is also possible to mark this field **Not applicable** (in case patient did not have any previous allo HCT) or as **Unknown.**

Chromosome analysis

Chromosome analysis at diagnosis

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:

No - the chromosome analysis has not been done.

Yes - the chromosome analysis has been performed for diagnosis.

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

Extended dataset

Date of chromosome analysis

If chromosome analysis was performed around the time of diagnosis, please specify the date of the chromosome analysis or mark it as **Unknown**.

What were the results?

Indicate the results of the chromosome analysis you are reporting and choose the answer based on the following:

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

Abnormal results - the chromosome analysis has been performed and at least one of the results has been found to be abnormal.

Failed - the chromosome analysis has failed.

Number of abnormalities

If the results were **abnormal**, indicate the number of abnormalities present in the most complete analysis with abnormal results.

Complex karyotype

A complex karyotype is defined by ≥3 unrelated chromosome abnormalities in the absence of other class-defining recurrent genetic abnormalities; excludes hyperdiploid karyotypes with three or more trisomies (or polysomies) without structural abnormalities.

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

Chromosomal abnormalities

If the results of the chromosome analysis were **abnormal**, specify the chromosome abnormalities in the text field and mark whether they were **Absent** or **Present**.

Transcribe the complete karyotype

If it is not possible to report the chromosome analysis results as per abnormalities table above, please report the full complete karyotype.

Involvement at time of diagnosis

Medullary involvement

Indicate whether the Marrow / Blood was involved answering **yes**, **no** or **unknown**. Please be aware that although the vast majority of acute leukaemias involve the invasion of the bone marrow by blasts, there are cases where blast invasion is only found in organs other than the bone marrow (e.g. choromas).

Extramedullary involvement

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.

Please indicate if any other organ(s) than the Marrow or Blood were involved at diagnosis, by reporting extramedullary involvement and answering **yes**, **no** or **unknown.**

Disease

Organs involved at time of diagnosis

Indicate per each organ in the list if leukemic 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**).

See the list below:

- Skin;
- CNS;
- Testes/Ovaries;
- Other; specify.

Extended dataset

Acute leukaemias

First line therapies(from diagnosis to 1st HCT/CT)

First lines of therapy before the HCT/CT:

Indicate if the patient receives first line therapy related to Acute leukaemia before the HCT/CT treatment. If answered **Yes**, complete the "Treatment non-HCT/CT/GT/IST" form. If the patient does not receive first line therapy, answer **NO**. If this information is not available, mark **Unknown**.

Appendix 1

List of genes

Genes		
ABL1	FGFR2	PDGFRA
ALK	FLT3	PDGFRB
ANKRD26	FUS	PHF6
ASXL1	GATA1	PRPF8
ASXL2	GATA2	PTEN
ATM	GNAS	PTPN11
ATRX	HMGA2	RAD21
BAALC	HRAS	RARA
BCL2	IDH1	RB1
BCOR	IDH2	RBM15
BCORL1	IKZF1	RUNX1
BRAF	JAK2	SETBP1
CALR	KDM6A	SF3B1
CBL	KIT	SH2B3
CCND1	KMT2A	SMC1A
CDKN2A	KRAS	SMC3
CEBPA	MECOM	SRSF2
CREBBP	MET	STAG2
CSF3R	MPL	TCF3
CUX1	MYBL1	TET2
DDX41	MYC	TFE3
DNMT3A	MYD88	TP53
EGFR	MUH11	U2AF1
ETNK1	NOTCH1	WT1
ETV6	NPM1	ZRSR2
EZH2	NRAS	Other, specify:
FBXW7	NTRK3	
FGFR1	NUP214	

Bibliography

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