



Acute myeloid leukaemia (AML)

The "AML" NGS panel includes the analysis of 41 genes:

ASXL1 / BCOR / BCORL1 / BRAF / CALR / CBL / CEBPA / CSF3R / DNMT3A / ETNK1 / ETV6 / EZH2 / FLT3 / GATA2 / GNB1 / HRAS / IDH1 / IDH2 / JAK2 / KIT / KMT2A-MLL / KRAS / MPL / NF1 / NPM1 / NRAS / PHF6 / PPM1D / PRPF8 / PTPN11 / RUNX1 / SETBP1 / SF3B1 / SRSF2 / STAG2 / TET2 / TP53 / UBA1 / U2AF1 / WT1 / ZRSR2.

It can be used in the three areas of **diagnosis**, **prognosis** and **theranostics** and must be associated with a cytogenetic study to classify an AML and define its prognosis.

► Two classifications exist for an AML **diagnosis** with mutational data: the WHO 2024 classification and the ICC/ELN 2022 classification.

- WHO 2024: the *NPM1* and *CEBPA* mutational status is used to define 2 entities of "AML with defining genetic abnormalities".

Rq : for *CEBPA*, the concepts of biallelic mutations (whatever the type of mutation) (biCEBPA) or a monoallelic mutation of the bZIP domain (smbZIP-CEBPA) are retained.

- ICC/ELN 2022: the *NPM1*, *CEBPA* and *TP53* mutational status is used to define 3 entities of "AML with defining genetic abnormalities".

Rq : for *CEBPA*, it is exclusively a bZIP domain mutation (monoallelic or biallelic).

For both classifications, in the context of "AML with defining genetic abnormalities", 10% of blasts are sufficient (and no longer 20%) to make the diagnosis of AML (exception: for WHO 2024: 20% for *CEBPA* and *BCR::ABL1* and whatever the percentage of blasts for *NPM1* - for ICC/ELN 2022: 20% for *TP53* and *BCR::ABL1*).

For the entity "AML, myelodysplasia-related", in addition to the search for defined cytogenetic abnormalities, analysis of mutations in the following 8 genes must be performed according to WHO 2024: *ASXL1*, *BCOR*, *EZH2*, *STAG2*, *SF3B1*, *SRSF2*, *U2AF1* and *ZRSR2*. The ICC/ELN 2022 also includes a 9th gene: *RUNX1*.

- ▶ The AML NGS panel also provides **prognostic** support (ICC/ELN 2022 recommendations) by allowing the definition of molecular factors for a favorable, intermediate or unfavorable prognosis:
 - **Favorable:**
 - ▶ *NPM1* mutation without *FLT3-ITD* mutation
 - ▶ monoallelic or biallelic mutation of the bZIP domain of *CEBPA*
 - **Intermediate:**
 - ▶ *FLT3-ITD* mutation with or without *NPM1* mutation.
 - **Unfavorable:**
 - ▶ *TP53* mutation (VAF of at least 10%), frequently associated with a complex karyotype.
 - ▶ *ASXL1*, *BCOR*, *EZH2*, *RUNX1*, *SF3B1*, *SRSF2*, *STAG2*, *U2AF1* or *ZRSR2* mutations. These markers should not be used as an adverse prognostic marker if they co-occur with favorable-risk AML subtypes.
- ▶ In **theranostic**, testing for *FLT3* mutation is already a prerequisite for a targeted treatment. *IDH1*, *IDH2* and *TP53* mutations may also represent therapeutic targets.

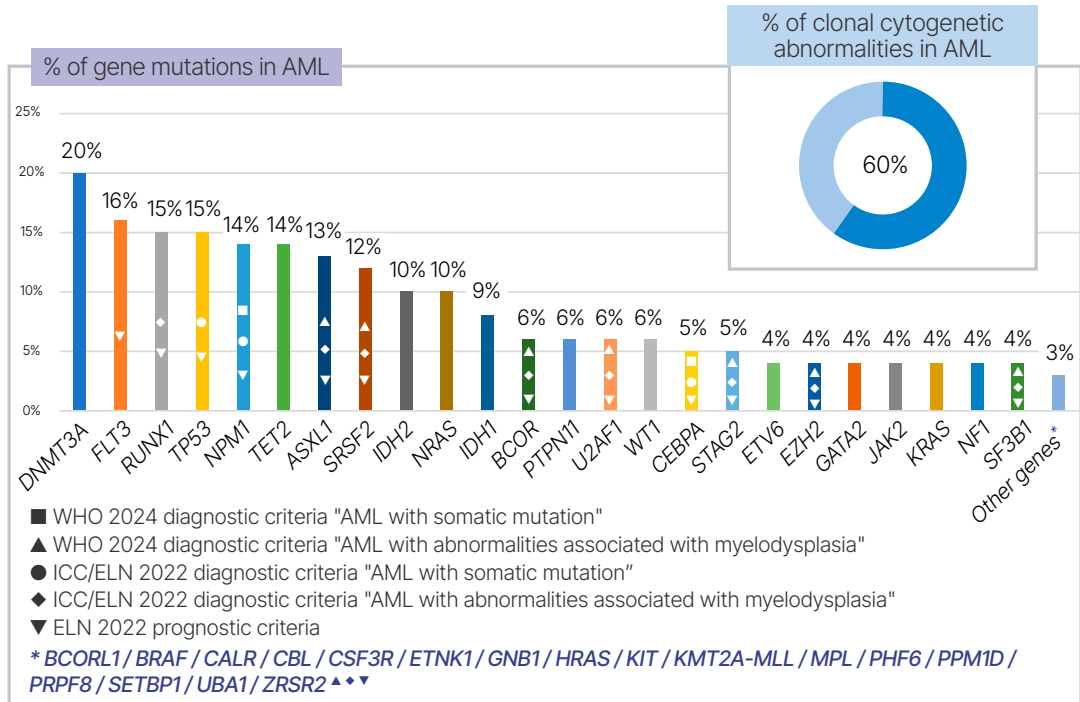
NB: A pharmacogenetic test may be required as part of the treatment of acute leukaemia, particularly to anticipate the response to thiopurines and certain supportive care. A detailed explanatory text is available at the end of the brochure.

The "AML" NGS panel therefore allows exhaustive analysis of somatic mutations reported in AML. It is not suitable for searching for germline mutations or monitoring residual disease.

As a reminder, cellular haematology, cytogenetic and molecular biology data must be compared for a diagnosis and/or prognosis of haematological malignancy

As part of the new ELN 2024 recommendations, a new design for our NGS panel is currently being developed to determine *DDX41* status and may be available before the end of 2025.

Gene mutations and clonal cytogenetic abnormalities in AML



Source: www.mycancergenome.org

"AML" NGS Panel - Targeted genes

Gene	Transcript	Exon rank	Gene	Transcript	Exon rank
ASXL1	NM_015338	Full coding region	KRAS	NM_033360	Full coding region
BCOR	NM_017745	Full coding region	MPL	NM_005373	Full coding region
BCORL1	NM_021946	Full coding region	NF1	NM_000267	Full coding region
BRAF	NM_004333	Full coding region	NPM1	NM_002520	Full coding region
CALR	NM_004343	Full coding region	NRAS	NM_002524	Full coding region
CBL	NM_005188	Full coding region	PHF6	NM_032458	Full coding region
CEBPA	NM_004364	Full coding region	PPM1D	NM_003620	Full coding region
CSF3R	NM_000760	Full coding region	PRPF8	NM_006445	Full coding region
DNMT3A	NM_022552	Full coding region	PTPN11	NM_002834	Full coding region
ETNK1	NM_018638	Full coding region	RUNX1	NM_001754	Full coding region
ETV6	NM_001987	Full coding region	SETBP1	NM_015559	Full coding region
EZH2	NM_004456	Full coding region	SF3B1	NM_012433	Full coding region
FLT3	NM_004119	Full coding region	SRSF2	NM_003016	Full coding region
GATA2	NM_032638	Full coding region	STAG2	NM_001042749	Full coding region
GNB1	NM_002074	Full coding region	TET2	NM_001127208	Full coding region
HRAS	NM_176795	Full coding region	TP53	NM_000546	Full coding region
IDH1	NM_005896	Full coding region	U2AF1	NM_006758	Full coding region
IDH2	NM_002168	Full coding region	UBA1	NM_003334.4	Full coding region
JAK2	NM_004972	Full coding region	WT1	NM_024426	Full coding region
KIT	NM_000222	Full coding region	ZRSR2	NM_005089	Full coding region
KMT2A MLL	NM_001197104	Full coding region			

Test code: MYSLA

Pre-analytical requirements: EDTA whole blood or bone marrow

Turnaround time: 10 days (Results may require an extended turnaround time of one week, depending on the confirmation tests required by Sanger sequencing).

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References

WHO: World Health Organization

ICC: Internal Consensual Classification

ELN: European Leukemia Net

WHO Classification of Tumours Editorial Board. Haematolymphoid tumours. Lyon (France): International Agency for Research on Cancer; 2024. (WHO classification of tumours series, 5th ed.; vol. 11). <https://publications.iarc.who.int/637>.

The 5th edition of the World Health Organization Classification of Haematolymphoid Tumours: Myeloid and Histiocytic/Dendritic Neoplasms. Khoury JD et al, *Leukemia*. 2022 Jul;36(7):1703-1719. PMID: 35732831

International Consensus Classification of Myeloid Neoplasms and Acute Leukemias: integrating morphologic, clinical, and genomic data. Arber DA et al, *Blood*. 2022 Sep 15;140(11):1200-1228. PMID: 35767897

Diagnosis and management of AML in adults: 2022 recommendations from an international expert panel on behalf of the ELN. Döhner H et al, *Blood*. 2022 Sep 22;140(12):1345-1377. PMID: 35797463

Targeted high-throughput sequencing of gene panels in pharmacogenetics of oncology treatments and supportive care of acute leukemia

In its July 2025 guideline, the French National Authority for Health (HAS) considers that targeted high-throughput sequencing of gene panels is justified in the following situations:

- **Institution of thiopurine therapy, in the context of a confirmed diagnosis of acute leukemia:**

Analysis of a targeted gene panel **should be performed** pre-therapeutically, in the post-induction phase in patients requiring thiopurine therapy as part of consolidation or maintenance chemotherapy. The two genes concerned are *TPMT* and *NUDT15*: for treatment with mercaptopurine (adult and pediatric populations) and thioguanine (pediatric populations only).

This list of genes is subject to change based on future HAS assessments.

- **Implementation of supportive care in the context of a confirmed diagnosis of acute leukemia:**

Analysis of a targeted gene panel for supportive care may be performed optionally:

before treatment initiation

or

after treatment initiation

particularly in cases of a history or occurrence of unusual toxicity (grade I to III) following the use of the supportive medication in question.

The genes and medications concerned, as well as the corresponding populations, are as follows:

- ▶ *CYP2D6* for treatment with codeine and tramadol (adult and pediatric populations);
- ▶ *CYP2D6* for treatment with ondansetron and tropisetron (adult populations only);
- ▶ *CYP2C19* for treatment with proton pump inhibitors (PPIs) (adult and pediatric populations);
- ▶ *CYP2C9* for treatment with nonsteroidal anti-inflammatory drugs (NSAIDs) (adult population only).

This list of genes is subject to change based on future HAS assessments.

Note: Pharmacogenetic testing requires a prior medical prescription as well as a certificate of consultation and consent.

Test code : EPGX

Pre-analytical requirements : EDTA whole blood

Turnaround time : 4 weeks

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References

Avis n°2025.0031/DC/SEAP du 17 juillet 2025 du collège de la Haute Autorité de santé relatif à l'inscription sur la liste des actes et prestations mentionnée à l'article L. 162-1-7 du code de la sécurité sociale, de l'acte de séquençage haut débit ciblé des panels de gènes en pharmacogénétique des traitements d'oncologie et des soins de support des leucémies aiguës