



## 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 2022 classification and the ICC/ELN 2022 classification.

- WHO 2022: 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 2022: 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 2022: *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 :

- *NMP1* mutation without *FLT3-ITD* mutation
- monoallelic or biallelic mutation of the bZIP domain of *CEBPA*

Intermediate :

- *FLT3-ITD* mutation (irrespective of allelic ratio) 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.

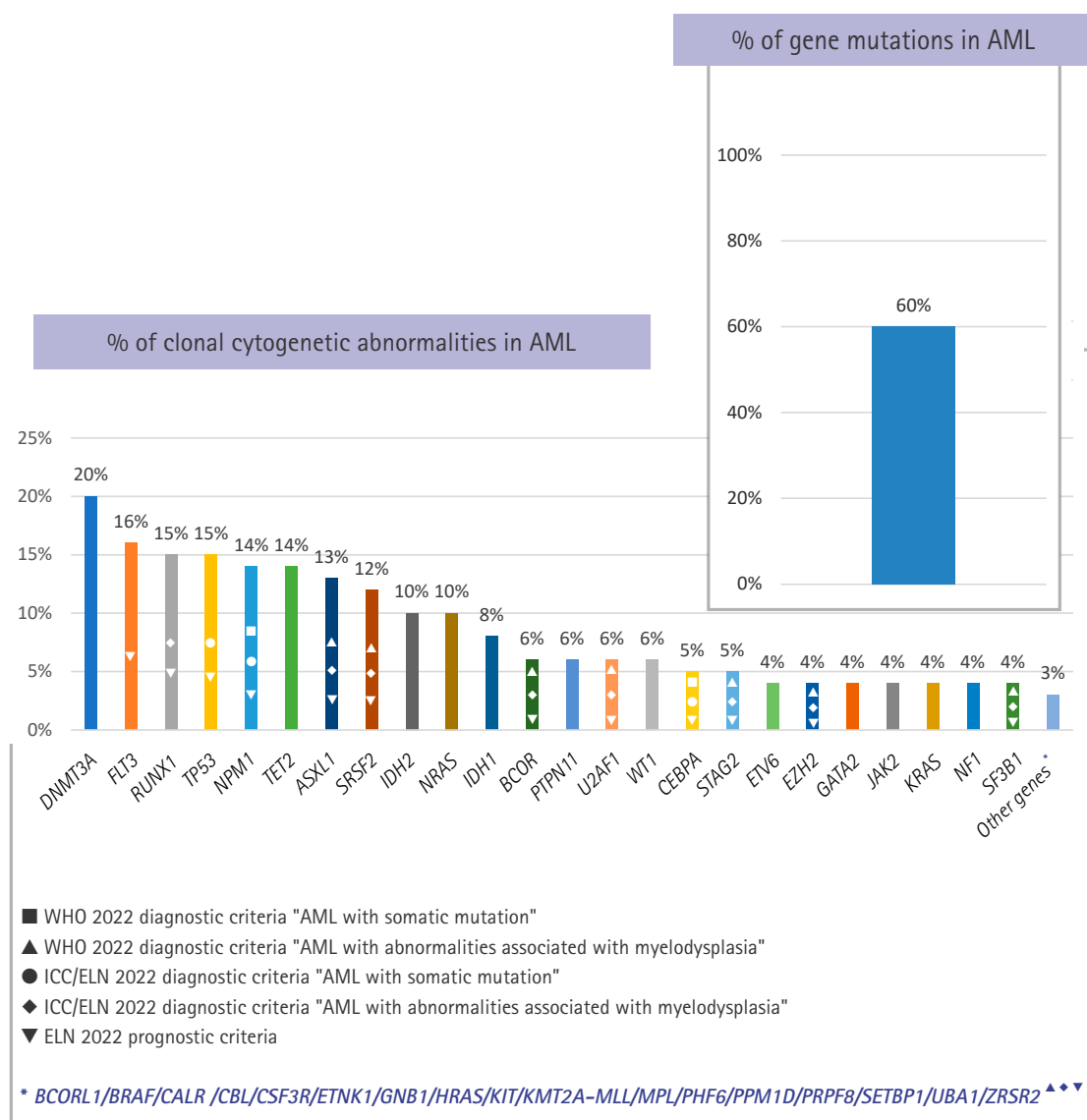
**Rq** : *FLT3-ITD/FLT3wt* ratio is no longer used.

- In **theranostic**, testing for *FLT3* mutation is already a prerequisite for a targeted treatment. *IDH1*, *IDH2* and *TP53* mutations may also represent therapeutic targets.

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

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

## Gene mutations and clonal cytogenetic abnormalities in AML



Source : [www.mycancergenome.org](http://www.mycancergenome.org)

## “AML” NGS Panel –Targeted genes

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

**Test code :** MYSLA

**Pre-analytical requirements :** EDTA whole blood or bone marrow

**Turnaround time :** 13 days (Results may require an extended turnaround time of one week, depending on the confirmation tests required by Sanger sequencing).

## Contact

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## References

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