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# Chronic Myelomonocytic Leukaemia (CMML)

The “ CMML” NGS panel includes the analysis of 23 genes: *ASXL1/BCOR/CALR/CBL/DNMT3A/EZH2/FLT3/IDH1/IDH2/JAK2/KRAS/MPL/NF1/NPM1/NRAS/RUNX1/SETBP1/SF3B1/SRSF2/TET2/TP53/U2AF1/ZRSR2.*

It can be used in the three areas of diagnosis, prognosis and theranostics. It must be associated with a bone marrow cytogenetic analysis.

- The panel is most widely appreciated for it prognostic value, as it is used to calculate the CMML CPSS-Mol prognostic score. This score is calculated from clinico-biological data, i.e., transfusion requirements, CBC-platelet data (WBC count), percentage of bone marrow blasts. It also includes cytogenetic data and the presence or absence of mutations in the *ASXL1, NRAS, RUNX1* and *SETBP1* genes. This score classifies a patient as being at "low", "intermediate-1", "intermediate-2" or "high" risk. The four aforementioned mutations are considered "high risk" according to the ELN 2018. The ICC 2022 also assigns a pejorative prognostic value to *NPM1* mutations in CMML with a high risk of acutisation. *NPM1* and *FLT3* mutations are therefore also analysed, because even though they are reported in less than 5% of CMMLs, the presence of mutations in these two genes should also lead to the diagnosis of M4-M5 AML being reconsidered.

- This NGS panel also provides diagnostic support for the cytological diagnosis of CMML in blood and bone marrow. The association of *TET2* and *SRSF2* mutations is highly suggestive of CMML. New 2022 data from the World Health Organization (WHO) on the redefinition of the diagnostic threshold for monocyte count ($\geq 0.5.10^9$/L) will reinforce the diagnostic aid of NGS in the management of CMML, in the same way as immunophenotyping of blood monocytes.

  The NGS panel can also help to differentiate between the myeloproliferative (MP-CMML) and myelodysplastic (MD-CMML) forms of CMML. Mutations in the RAS (*NRAS, KRAS* and *CBL*), *JAK2* and *SETBP1* pathways point towards the myeloproliferative form, which has a poor prognosis.

- The theranostic impact is also addressed with this panel (potential therapeutic targets: *IDH1, IDH2* and *FLT3*).

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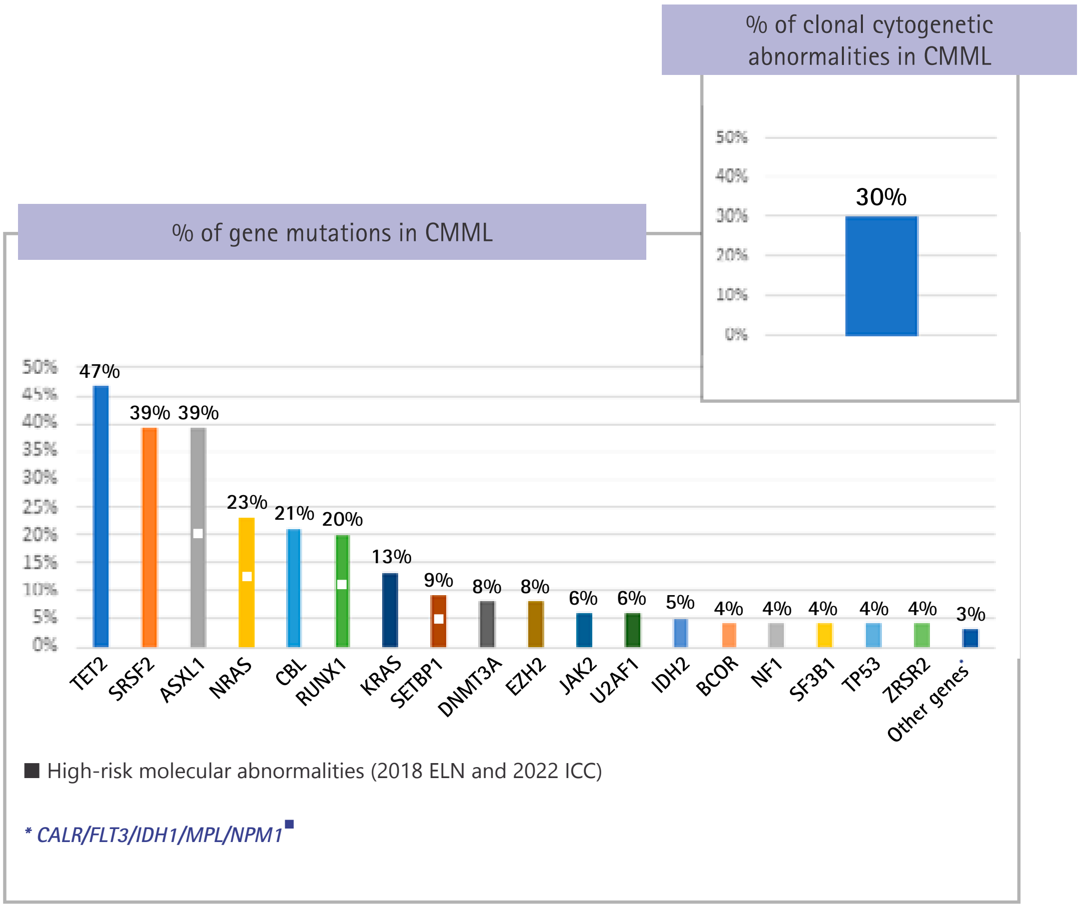
The "CMML" NGS panel therefore allows exhaustive analysis of somatic mutations reported in CMML. It is not suitable for germline mutation research.

**Note :** BCR::ABL1 fusion transcript, *PDGFRA*, *PDGFRB*, *FGFR1*, *JAK2*, *FLT3* and *ETV6* rearrangements cannot be performed by this NGS analysis (gDNA analysis). Complementary techniques are available at the Eurofins Biomnis laboratory for these gene abnormalities, which must be investigated and excluded according to the WHO and ICC 2022 diagnostic criteria of the CMML.

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

## Gene mutations and clonal cytogenetic abnormalities in CMML



Source : www.mycancergenome.org

## “CMML” NGS panel – Targeted genes

| Gene | Transcript | Exon rank |
|---|---|---|
| *ASXL1* | NM_015338 | Full coding region |
| *BCOR* | NM_017745 | Full coding region |
| *CALR* | NM_004343 | Full coding region |
| *CBL* | NM_005188 | Full coding region |
| *DNMT3A* | NM_022552 | Full coding region |
| *EZH2* | NM_004456 | Full coding region |
| *FLT3* | NM_004119 | Full coding region |
| *IDH1* | NM_005896 | Full coding region |
| *IDH2* | NM_002168 | Full coding region |
| *JAK2* | NM_004972 | Full coding region |
| *KRAS* | NM_033360 | Full coding region |
| *MPL* | NM_005373 | Full coding region |
| *NF1* | NM_000267 | Full coding region |
| *NPM1* | NM_002520 | Full coding region |
| *NRAS* | NM_002524 | Full coding region |
| *RUNX1* | NM_001754 | Full coding region |
| *SETBP1* | NM_015559 | Full coding region |
| *SF3B1* | NM_012433 | Full coding region |
| *SRSF2* | NM_003016 | Full coding region |
| *TET2* | NM_001127208 | Full coding region |
| *TP53* | NM_000546 | Full coding region |
| *U2AF1* | NM_006758 | Full coding region |
| *ZRSR2* | NM_005089 | Full coding region |

## Test code : MYSMO

## Pre-analytical requirements : Blood or marrow EDTA

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

## Contact

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## References

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