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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 genes are considered "high risk" according to the ELN and ASXL1 mutations are also included into the GFM and Mayo Molecular prognostic scores. 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* or *ASXL1* with *SRSF2* mutations is highly suggestive of CMML. Moreover, clonality is a minor WHO criteria allowing for a CMML diagnosis starting from $0.5.10^9$/L monocytes (threshold redefined in 2022) if a medullar dysplasia is present, and of clonal monocytosis of unknown significance in its absence.

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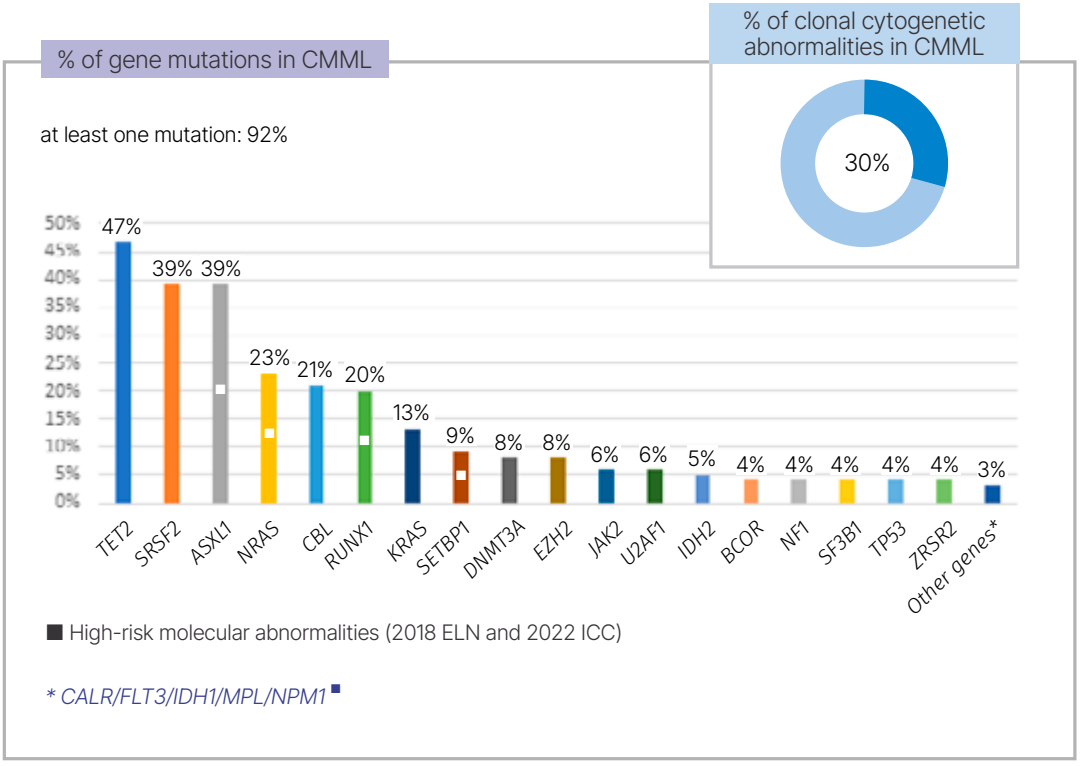
The "CMML" NGS panel therefore allows exhaustive analysis of somatic mutations reported in CMML.
It is not suitable for germline mutation research.

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. In particular, more than 94% classical monocytes on a monocyte-specific flow cytometry is a minor WHO criteria for the CMML diagnosis, starting from 1.10^9/L monocytes, even without medullar dysplasia or clonality.

Gene mutations and clonal cytogenetic abnormalities in CMML



Source : www.mycancergenome.org

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“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

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Test code: MYSMO

Pre-analytical requirements: Blood or marrow EDTA

Turnaround time: 10 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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Références

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