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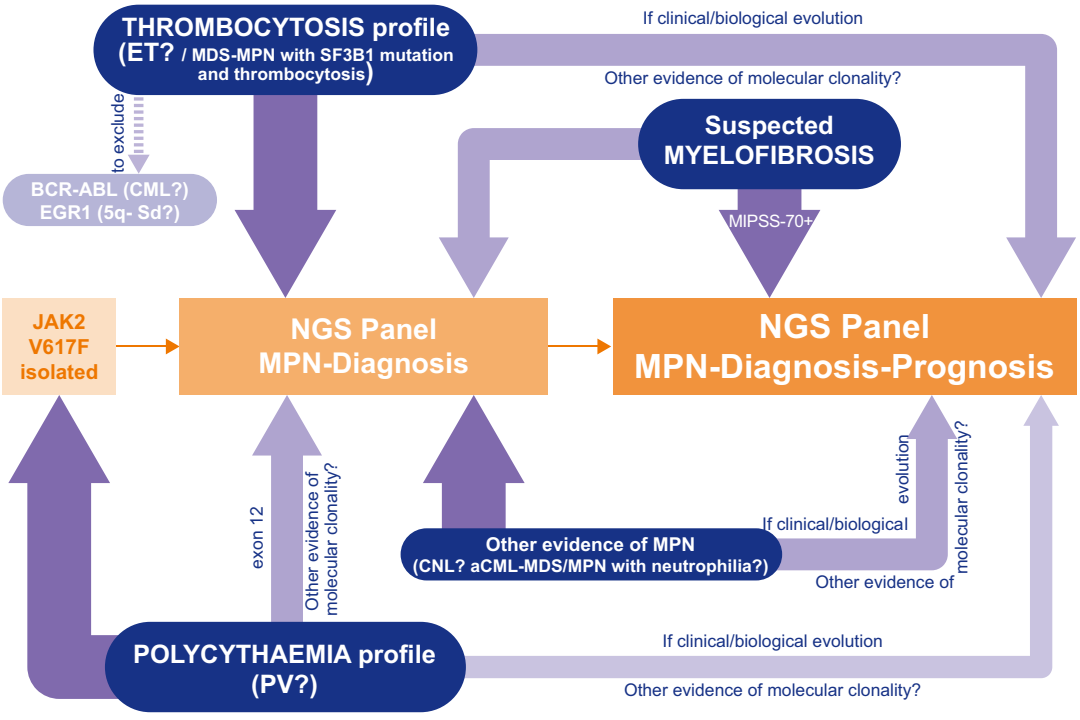
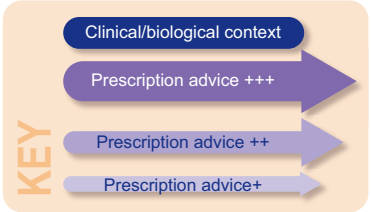
Myeloproliferative neoplasms (MPN)

Prescription advice for suspected MPN or an MPN follow-up





aCML: atypical Chronic Myeloid Leukaemia
CNL: Chronic Neutrophilic Leukaemia
ET: Essential Thrombocythaemia
MDS/MPN with neutrophilia : Myelodysplastic syndrome / Myeloproliferative neoplasm with neutrophilia
MDS-MPN with SF3B1 mutation and thrombocytosis: Myelodysplastic syndrome - Myeloproliferative neoplasm with SF3B1 mutation and thrombocytosis
PV: Polycythaemia Vera

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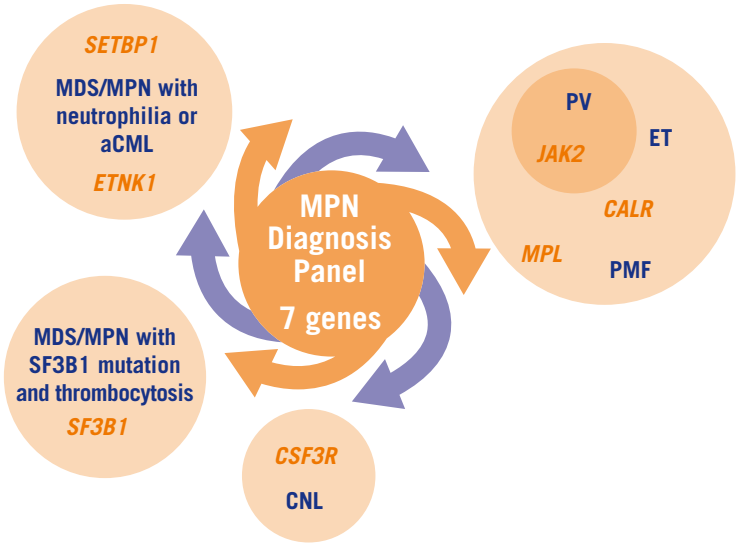
“MPN Diagnosis” NGS panel

The NGS panel «NMP-Diagnostic» consists of an analysis of the *JAK2*, *CALR*, *MPL*, *CSF3R*, *SF3B1*, *SETBP1* and *ETNK*1 genes.

According to the WHO/ICC 2022, the mutation status of the *JAK2*, *CALR*, *MPL*, *CSF3R* and *SF3B1* genes contributes to the diagnostic criteria for the following myeloproliferative neoplasias (MPN) and MDS/MPN:

- Polycythaemia vera (*JAK2* exon 14 and 12 mutations),
- Essential thrombocythemia (*JAK2*, *CALR*, *MPL* mutations)
- Primitive myelofibrosis (*JAK2*, *CALR*, *MPL* mutations),
- Chronic Neutrophilic Leukaemia (*CSF3R* mutation).
- Myelodysplastic/myeloproliferative neoplasm with *SF3B1* mutation and thrombocytosis



The presence of a *SETBP1* or *ETNK1* mutation provides diagnostic support for the WHO 2022 Myelodysplastic/myeloproliferative neoplasm with neutrophilia (or atypical CML according to ICC 2022).

Panel NGS “NMP diagnostic”- Gènes concernés

Gene	Transcript	Exon rank
CALR	NM_004343	Full coding region
CSF3R	NM_000760	Full coding region
ETNK1	NM_018638	Full coding region
JAK2	NM_004972	Full coding region

Gene	Transcript	Exon rank
MPL	NM_005373	Full coding region
SETBP1	NM_015559	Full coding region
SF3B1	NM_012433	Full coding region

Test code : MYSDG

Note : If mastocytosis is suspected, an isolated analysis of the KIT gene is proposed to the laboratory (code MYSKT).

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“MPN Diagnosis - Prognosis” NGS panel

The NGS panel “**MPN – DP (Diagnosis / Prognosis)**” consists of an analysis of 27 genes: *ASXL1/CALR/CBL/CSF3R/DNMT3A/ETNK1/ETV6/EZH2/GATA2/IDH1/IDH2/JAK2/KIT/KRAS/MPL/NPM1/NRAS/PTPN11/RUNX1/ SETBP1/SF3B1/SRSF2/STAG2/TET2/TP53/U2AF1/ZRSR2.*

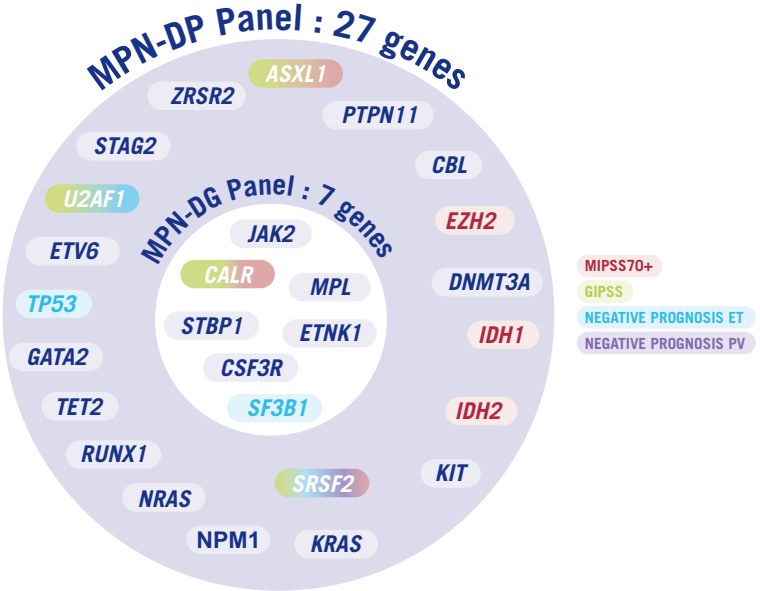
The panel can be prescribed for **diagnostic** purposes and complements the molecular analysis of the NGS “MPN Diagnosis” panel. Other mutations may also be identified, indicating molecular clonality, in particular in the context of triple-negative MPN (e.g. *TET2*, *ASXL1* or *DNMT3A*) or CNL (e.g. *SETBP1*, *ASXL1* or *SRSF2*) or MDS/MPN with neutrophilia or atypical CML (*ASXL1*, *SETBP1*, *ETNK1* and *EZH2*). The notion of CHIP (age-related clonal haematopoiesis of undetermined significance) must be discussed.

But its interest is essentially for **prognostic** purposes: in the context of primary myelofibrosis, this NGS panel can help clinicians make the right choice between an allogeneic transplant decision and simple clinico-biological monitoring by calculating the MIPSS70+ score (including *CALR* type 1/1like status and mutations with an unfavourable prognosis: *ASXL1*, *SRSF2*, *EZH2*, *IDH1* and *IDH2*) or the GIPSS score (including CALR type 1/1like status and mutations with an unfavourable prognosis: *ASXL1*, *SRSF2* and *U2AF1*). Other genes also have an unfavourable prognostic value in MF (in particular *TP53*).

In Essential Thrombocythemia, the presence of mutations in spliceosome genes (*SF3B1*, *SRSF2* and *U2AF1*) is associated with poor prognosis and mutations in the mutations in the *TP53* gene are predictive of an ultimate diagnosis of acute leukaemia.

In Polycythaemia vera, the presence of a mutation in the *SRSF2* gene is associated with poor prognosis.

For MDS/MPN with neutrophilia or atypical CML, mutations in *TET2*, *SRSF2* and *SETBP1* are associated with a favourable prognosis, whereas mutations in *RUNX1* or *NRAS* are associated with an unfavourable prognosis.



Note : The MPN-DP panel therefore allows exhaustive analysis of somatic mutations reported in MPNs. It is not suitable for searching for germline mutations.

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“MPN Diagnosis” NGS panel – Targeted genes

Gene	Transcript	Exon rank
ASXL1	NM_015338	Full coding region
CALR	NM_004343	Full coding region
CBL	NM_005188	Full coding region
CSF3R	NM_000760	Full coding region
DNMT3A	NM_022552	Full coding region
ETNK1	NM_018638	Full coding region
ETV6	NM_001987	Full coding region
EZH2	NM_004456	Full coding region
GATA2	NM_032638	Full coding region
IDH1	NM_005896	Full coding region
IDH2	NM_002168	Full coding region
JAK2	NM_004972	Full coding region
KIT	NM_000222	Full coding region
KRAS	NM_033360	Full coding region
MPL	NM_005373	Full coding region
NPM1	NM_002520	Full coding region
NRAS	NM_002524	Full coding region
PTPN11	NM_002834	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
STAG2	NM_001042749	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 : MYSDP

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.

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

WHO/ICC 2022 classification of MPN and MDS/MPN (partial data)

MPN	SMD/NMP
Chronic myeloid leukaemia (CML)	Chronic myelomonocytic leukaemia (CMML)
Polycythaemia vera (PV)	Myelodysplastic/myeloproliferative neoplasm with neutrophilia (WHO 2022) – Atypical chronic myeloid leukaemia (ICC 2022)
Essential thrombocythaemia (ET)	Myelodysplastic/myeloproliferative neoplasm with SF3B1 mutation and thrombocytosis
Primary myelofibrosis (PMF)	
Chronic neutrophilic leukaemia (CNL)	
Chronic eosinophilic leukaemia (CEL)	
Juvenile myelomonocytic leukaemia (JMML)	

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Pre-analytical requirements : Blood or marrow EDTA

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

Contact

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References

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