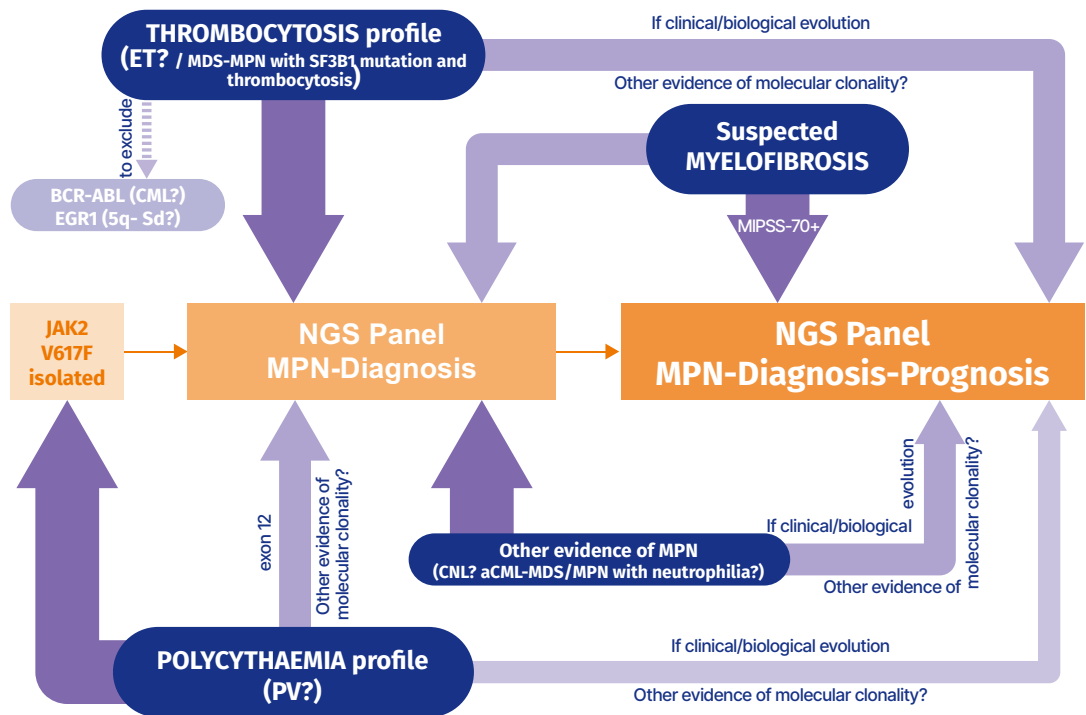




Myeloproliferative neoplasms (MPN)

Prescription advice for suspected MPN or an MPN follow-up



aCML (ICC 2022): atypical Chronic Myeloid Leukaemia
 CNL: Chronic Neutrophilic Leukaemia
 ET: Essential Thrombocythaemia
 MDS/MPN with neutrophilia (OMS 2024): 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

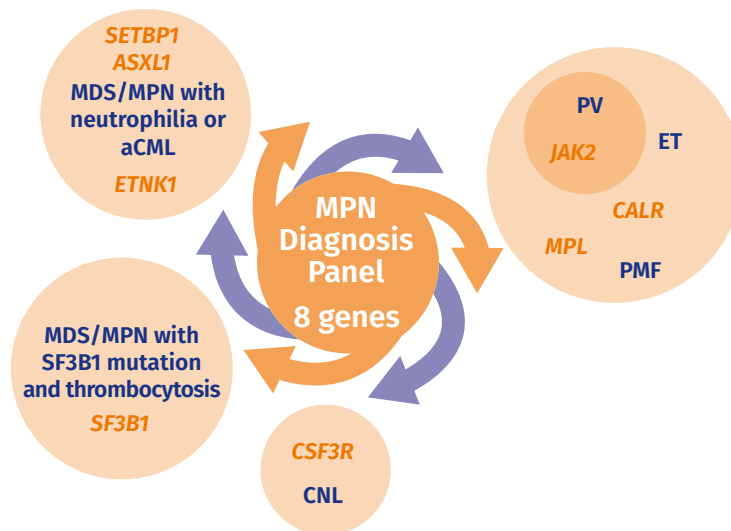


“MPN Diagnosis” NGS panel

The NGS panel "**NMP-Diagnostic**" consists of an analysis of the *JAK2* / *CALR* / *MPL* / *CSF3R* / *SF3B1* / *SETBP1* / *ETNK1* and *ASXL1* genes.

According to the WHO 2024/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 one or more mutations in *SETBP1*, *ASXL1* or *ETNK1* genes provides **diagnostic support** for the WHO 2024 Myelodysplastic/myeloproliferative neoplasm with neutrophilia (or atypical CML according to ICC 2022).

NGS analysis allows full detection of these mutations necessary for diagnosis in a single step.

"NMP diagnosis" panel - Gene list

Gene	Transcript	Exon rank
<i>CALR</i>	NM_004343	Full coding region
<i>CSF3R</i>	NM_000760	Full coding region
<i>ETNK1</i>	NM_018638	Full coding region
<i>JAK2</i>	NM_004972	Full coding region

Gene	Transcript	Exon rank
<i>MPL</i>	NM_005373	Full coding region
<i>SETBP1</i>	NM_015559	Full coding region
<i>SF3B1</i>	NM_012433	Full coding region
<i>ASXL1</i>	NM_015338	Full coding region

Test code : MYSDG

The NGS panel “**MYSKT (Diagnostic / Prognostic)**” includes the analysis of four genes: *KIT / ASXL1 / SRSF2 / RUNX1*.

In the context of mastocytosis, the KIT D816V mutation is decisive for diagnosis. The presence of one or more additional mutations associated with this hotspot carries an adverse prognostic impact.

“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.

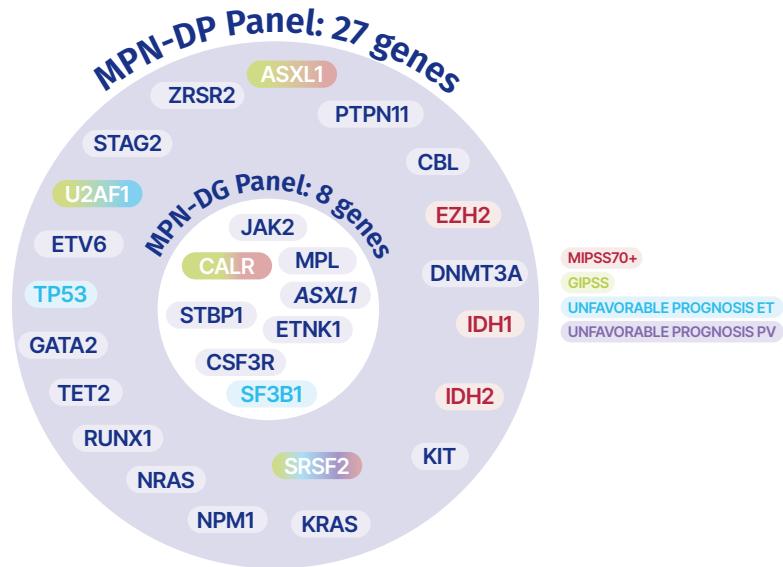
In the context of primary myelofibrosis, this NGS panel can help clinicians make the right choice between an allogeneic transplant decision and simple clinico-biological monitoring by calculating the MIPSS70+ score (including *CALR* type 1/1like status and mutations with an unfavourable prognosis: *ASXL1*, *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*). Furthermore, mutations in the RAS and CBL genes are associated with reduced efficacy of ruxolitinib treatment.

In Essential Thrombocythemia, the MIPSS-ET score includes mutations in *SF3B1*, *SRSF2*, *U2AF1* and *TP53* genes. Mutations of *SF3B1* and *SRSF2* are associated with an unfavorable prognosis, while mutations of *SF3B1* and *U2AF1* are associated with a stronger risk of secondary myelofibrosis. Moreover, *TP53* mutations are predictive of an AML transformation. On the other hand, the IPSET-thrombosis score considers *JAK2 V617F* mutation to be an independent risk factor for thrombosis.

In Polycythaemia vera, the IPSS-PV score includes *SRSF2* mutations, associated with an unfavorable 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.

In Chronic Neutrophilic Leukemia, the presence of a *ASXL1* mutation is associated with an unfavorable prognosis.



Molecular scores for MPN

Score	Disease	Negative impact mutation
MIPSS-70+ v2.0	Primary myelofibrosis (< 70 years)	ASXL1, SRSF2, EZH2, IDH1/2, absence of CALR type I or I-like mutations
GIPSS	Primary myelofibrosis	ASXL1, SRSF2, U2AF1, absence of CALR type I or I-like mutations
MIPSS-ET	Essential thrombocythemia	SF3B1, SRSF2, U2AF1, TP53
IPSET-thrombosis	Essential thrombocythemia	JAK2 V617F
MIPSS-PV	Polycythemia vera	SRSF2

“MPN Diagnosis” NGS panel – Targeted genes

Gene	Transcript	Exon rank	Gene	Transcript	Exon rank
ASXL1	NM_015338	Full coding region	MPL	NM_005373	Full coding region
CALR	NM_004343	Full coding region	NPM1	NM_002520	Full coding region
CBL	NM_005188	Full coding region	NRAS	NM_002524	Full coding region
CSF3R	NM_000760	Full coding region	PTPN11	NM_002834	Full coding region
DNMT3A	NM_022552	Full coding region	RUNX1	NM_001754	Full coding region
ETNK1	NM_018638	Full coding region	SETBP1	NM_015559	Full coding region
ETV6	NM_001987	Full coding region	SF3B1	NM_012433	Full coding region
EZH2	NM_004456	Full coding region	SRSF2	NM_003016	Full coding region
GATA2	NM_032638	Full coding region	STAG2	NM_001042749	Full coding region
IDH1	NM_005896	Full coding region	TET2	NM_001127208	Full coding region
IDH2	NM_002168	Full coding region	TP53	NM_000546	Full coding region
JAK2	NM_004972	Full coding region	U2AF1	NM_006758	Full coding region
KIT	NM_000222	Full coding region	ZRSR2	NM_005089	Full coding region
KRAS	NM_033360	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.

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

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 2024/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 2024) – 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)	

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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