



Myelodysplastic syndromes (MDS)

The "MDS" 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/KMT2/AMLL/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 bone marrow cytogenetic analysis.

- ▶ Its **prognostic** value is predominant, as it is used to calculate the M-IPSS molecular score. This score is calculated on the basis of clinico-biological data: patient age, CBC/platelet data (hemoglobin level, absolute neutrophil and platelet count) and percentage of bone marrow blasts. It also includes the R-IPSS cytogenetic score and the presence or absence of mutations in two groups of genes: a first group of 16 "main" genes: *TP53, KMT2A-MLL, FLT3, ASXL1, CBL, DNMT3A, ETV6, EZH2, IDH2, KRAS, NPM1, NRAS, RUNX1, SF3B1, SRSF2, U2AF1* and a second group of 15 so-called "secondary" genes: *BCOR, BCORL1, CEBPA, ETNK1, GATA2, GNB1, IDH1, NF1, PHF6, PPM1D, PRPF8, PTPN11, SETBP1, STAG2* and *WT1*. This score classifies a patient as being at "very low", "low", "moderate low", "moderate high", "high" and "very high" risk. The score can therefore be used to guide treatment strategy. It is also worth noting the negative impact of a *TP53* mutation in 5q- syndrome treated with lenalidomide (treatment resistance factor).
- ▶ From a **diagnostic** point of view, the search for *TP53* and *SF3B1* mutations makes it possible to define 2 new WHO and ICC 2022 entities:
 - "MDS with low blasts and SF3B1 mutation" (MDS-SF3B1). The presence of an SF3B1 mutation is associated with a favorable prognosis in MDS. The absence of a *TP53* or *RUNX1* mutation must be verified to define this entity.
 - MDS with *TP53* inactivation of poor prognosis. This entity is established on the basis of 2 *TP53* mutations (VAF \geq 10%) or a *TP53* mutation associated with (1) a del(17p) deletion demonstrated by cytogenetics (2) a VAF > 50%, (3) a LOH at the *TP53* locus.

This MDS panel also provides diagnostic support in cases of suspected MDS with no suggestive bone marrow cytology (bone marrow with no sign of dysmyelopoiesis) and no clonal cytogenetic abnormality suggestive of MDS, if one or more mutations reported in MDS are observed. The notion of CHIP (age-related clonal hematopoiesis of indeterminate potential) must then be discussed.

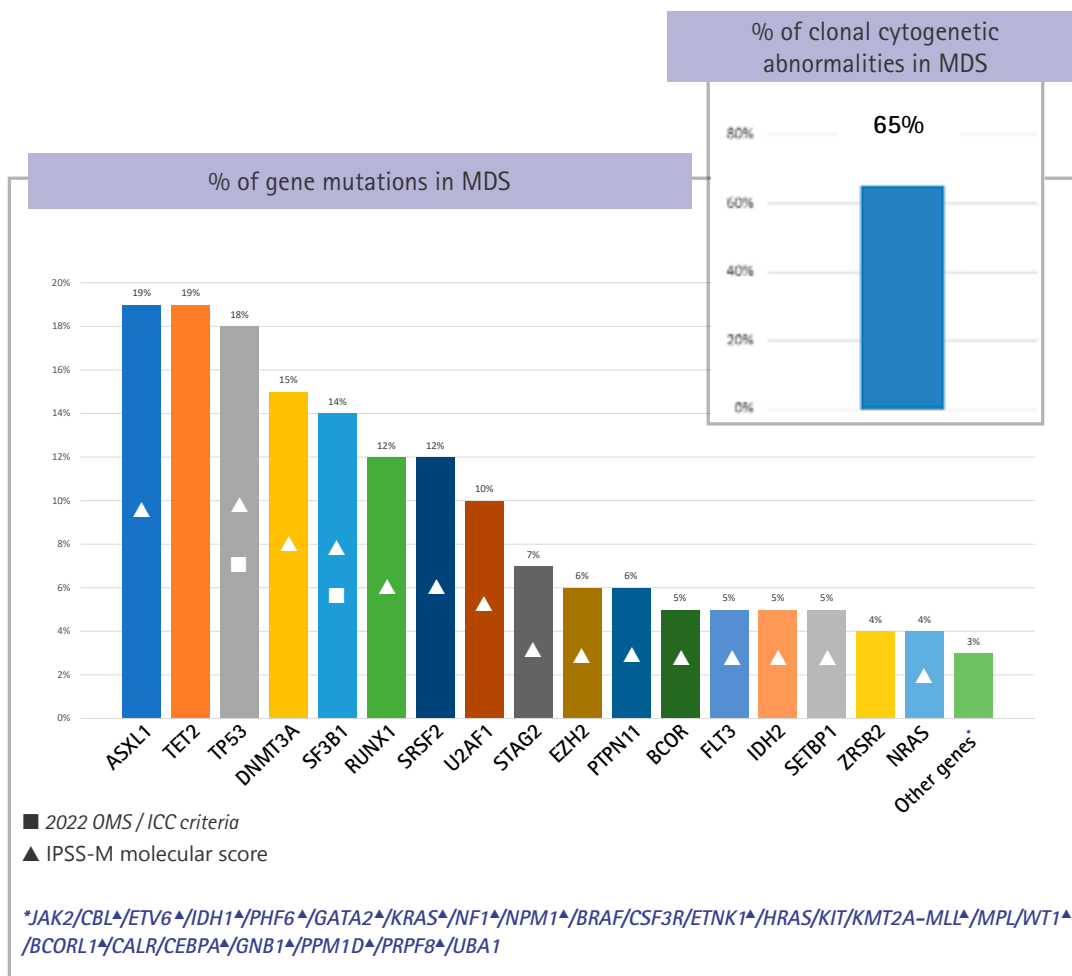
- The **theranostic** impact can also be addressed with this panel (*IDH1*, *IDH2*, *FLT3*, *TP53* therapeutic targets).

Finally, the MDS NGS panel also offers mutational analysis of the *UBA1* gene associated with the VEXAS syndrome (Vacuoles, E1 enzyme, X-linked, Autoinflammatory, Somatic) in which myelodysplastic syndromes are reported.

The "MDS" NGS panel therefore provides an exhaustive analysis of somatic mutations reported in MDS. It is not available for searching for germline mutations.

As a reminder, data from cellular haematology, histology (bone marrow trephine biopsy), cytogenetics and molecular biology must be compared in order to diagnose and/or prognose of haematological malignancy.

Gene mutations and clonal cytogenetic abnormalities in MDS



Source: www.mycancergenome.org

“MDS” NGS Panel – Targeted genes

Gene	Transcript	Exon rank	Gene	Transcript	Exon rank
<i>ASXL1</i>	NM_015338	Full coding region	<i>KRAS</i>	NM_033360	Full coding region
<i>BCOR</i>	NM_017745	Full coding region	<i>MPL</i>	NM_005373	Full coding region
<i>BCORL1</i>	NM_021946	Full coding region	<i>NF1</i>	NM_000267	Full coding region
<i>BRAF</i>	NM_004333	Full coding region	<i>NPM1</i>	NM_002520	Full coding region
<i>CALR</i>	NM_004343	Full coding region	<i>NRAS</i>	NM_002524	Full coding region
<i>CBL</i>	NM_005188	Full coding region	<i>PHF6</i>	NM_032458	Full coding region
<i>CEBPA</i>	NM_004364	Full coding region	<i>PPM1D</i>	NM_003620	Full coding region
<i>CSF3R</i>	NM_000760	Full coding region	<i>PRPF8</i>	NM_006445	Full coding region
<i>DNMT3A</i>	NM_022552	Full coding region	<i>PTPN11</i>	NM_002834	Full coding region
<i>ETNK1</i>	NM_018638	Full coding region	<i>RUNX1</i>	NM_001754	Full coding region
<i>ETV6</i>	NM_001987	Full coding region	<i>SETBP1</i>	NM_015559	Full coding region
<i>EZH2</i>	NM_004456	Full coding region	<i>SF3B1</i>	NM_012433	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>JAK2</i>	NM_004972	Full coding region	<i>WT1</i>	NM_024426	Full coding region
<i>KIT</i>	NM_000222	Full coding region	<i>ZRSR2</i>	NM_005089	Full coding region
<i>KMT2A</i> <i>MLL</i>	NM_001197104	Full coding region			

Test code : MYSMD

Pre-analytical requirements : Blood or marrow EDTA

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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