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# 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≥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.

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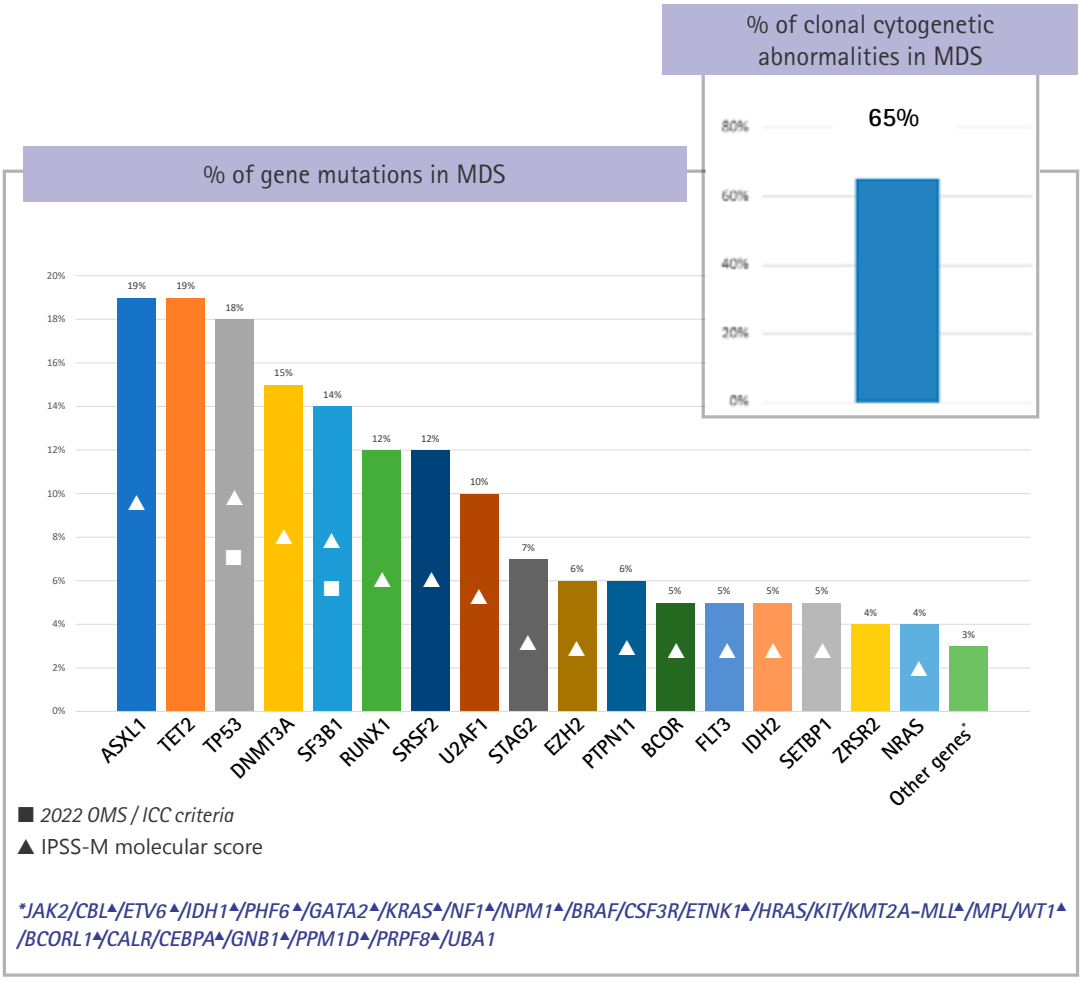
- The theranostic impact can also be addressed with this panel (*IDH1*, *IDH2*, *FLT3*, *TP53* therapeutic targets).

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



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## “MDS” NGS Panel – Targeted genes

| Gene | Transcript | Exon rank |
|---|---|---|
| *ASXL1* | NM_015338 | Full coding region |
| *BCOR* | NM_017745 | Full coding region |
| *BCORL1* | NM_021946 | Full coding region |
| *BRAF* | NM_004333 | Full coding region |
| *CALR* | NM_004343 | Full coding region |
| *CBL* | NM_005188 | Full coding region |
| *CEBPA* | NM_004364 | 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 |
| *FLT3* | NM_004119 | Full coding region |
| *GATA2* | NM_032638 | Full coding region |
| *GNB1* | NM_002074 | Full coding region |
| *HRAS* | NM_176795 | 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 |
| *KMT2A MLL* | NM_001197104 | Full coding region |

| Gene | Transcript | Exon rank |
|---|---|---|
| *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 |
| *PHF6* | NM_032458 | Full coding region |
| *PPM1D* | NM_003620 | Full coding region |
| *PRPF8* | NM_006445 | 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 |
| *UBA1* | NM_003334.4 | Full coding region |
| *WT1* | NM_024426 | Full coding region |
| *ZRSR2* | NM_005089 | Full coding region |

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## Test code : MYSMD

## Pre-analytical requirements : Blood or marrow EDTA

## Turnaround time : 10 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

The 5th edition of the World Health Organization Classification of Haematolymphoid Tumours: Myeloid and Histiocytic/Dendritic Neoplasms. Khoury JD et al, Leukemia. 2022 Jul;36(7):1703-1719. PMID: 35732831

International Consensus Classification of Myeloid Neoplasms and Acute Leukemias: integrating morphologic, clinical, and genomic data. Arber DA et al, Blood. 2022 Sep 15;140(11):1200-1228. PMID: 35767897

The Molecular International Prognostic Scoring System for risk stratification in myelodysplastic syndromes. Bernard E, Tuechler H, Greenberg PI, et al, NEJM Evid 2022;1(7) doi: 10.1056/EVIDoa2200008 / https://mds-risk-model.com/

Somatic Mutations in UBA1 and Severe Adult-Onset Autoinflammatory Disease. Beck D et al, N Engl J Med. 2020 Dec 31;383(27):2628-2638. PMID: 33108101

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