

Myelodysplastic Syndrome Panel by FISH

Indications for Ordering

- Aid in diagnosis and risk stratification of myelodysplastic syndrome (MDS) in conjunction with cytogenetics
 - Most useful at diagnosis following a failed or suboptimal standard cytogenetic study (<20 metaphases available)
- May aid in identifying individuals with MDS who could benefit from lenalidomide
 - With abnormal karyotype involving chromosome 5 and corresponding morphologic features

Test Description

Fluorescence in situ hybridization

- Performed on bone marrow (BM) cells using unstimulated cultures either from direct harvest or 24-hour culture
 - Peripheral blood can be used but is not preferred due to lowered clinical sensitivity
- Probes
 - del(5q)
 - -7/del(7q)
 - +8
 - del(20q)
- Each probe can be run as part of the panel or individually

Tests to Consider

Primary test

[Myelodysplastic Syndrome \(MDS\) Panel by FISH 2002709](#)

- Use in conjunction with conventional cytogenetics for diagnosis, prognosis and monitoring of MDS
 - Most useful at diagnosis following a failed or suboptimal standard cytogenetic study (<20 metaphases available)
 - Includes four probes – del(5q), -7/del(7q), +8, and del(20q)

Related tests

[Chromosome Analysis, Bone Marrow 2002292](#)

- Diagnosis, prognosis, and monitoring of MDS

[Chromosome Analysis, Bone Marrow with Reflex to Genomic Microarray 2007130](#)

- Diagnosis, prognosis, and monitoring of MDS
- If chromosome analysis is “normal” or “no growth,” then genomic microarray testing will be added

[Cytogenomic SNP Microarray – Oncology 2006325](#)

- Detects genomic abnormalities that may have diagnostic, prognostic, and/or therapeutic significance in leukemias/lymphomas and solid tumors, including
 - Loss/gain of DNA
 - Loss of heterozygosity (LOH)
- Cannot detect balanced chromosomal rearrangements (translocations and inversions)
- May be performed on BM, peripheral blood, or solid tumor tissues

[Myeloid Malignancies Somatic Mutation and Copy Number Analysis Panel 2012182](#)

- Includes both Cytogenomic SNP Microarray and Myeloid Malignancies Mutation Panel by Next Generation Sequencing
- Detects genetic and genomic abnormalities in myeloid disease that may have diagnostic, prognostic, and/or therapeutic significance, including
 - Loss/gain of DNA
 - Loss of heterozygosity (LOH)
 - Single gene mutations (substitutions, small insertions and deletions)
- May be performed on BM or peripheral blood

[Chromosome FISH, Interphase 2002298](#)

- Diagnosis, prognosis, and monitoring of MRD in MDS
- Specific FISH probes must be requested and include
 - del(5q)
 - -7/del(7q)
 - +8
 - del(20q)
 - 11q23 *KMT2A(MLL)* rearrangement
 - inv(3) or t(3;3) *RPN1-MECOM(EVI1)* fusion
 - 21q22 *RUNX1* loss/gain/rearrangement

[Acute Myelogenous Leukemia \(AML\) with Myelodysplastic Syndrome \(MDS\) or Therapy-Related AML, by FISH 2002653](#)

- Use in conjunction with conventional cytogenetics for diagnosis, prognosis, and monitoring in therapy-related MDS or AML associated with MDS
- Probes
 - del(5q)
 - -7/del(7q)
 - 11q23 *KMT2A(MLL)* rearrangement

[Myeloid Malignancies Mutation Panel by Next Generation Sequencing 2011117](#)

- Assess for single-gene mutations, including substitutions and insertions and deletions that may have diagnostic, prognostic, and/or therapeutic significance
- May be performed on BM or peripheral blood

Disease Overview

Diagnostic criteria (WHO 2008; International Working Group, 2007)

- Peripheral blood findings – cytopenia (hemoglobin <10g/dL, ANC <1.8X10⁹/L, platelets <100X10⁹/L), variable presence of blasts <20%, Auer rods ±, monocytes <1x10⁹/L, platelets low, normal, or increased
- BM findings – dysplasia ≥10% in one or more myeloid lineage, blast count <20%, Auer rods ±, presence of ring sideroblasts ± and % defines subtypes, presence of specific cytogenetic abnormalities (a subset is considered presumptive evidence in absence of definitive morphologic criteria)
- Diagnosis of presumptive MDS is allowed in individuals with refractory cytopenia(s) who lack definitive morphologic criteria if specific cytogenetic abnormalities are detected
 - Some clonal cytogenetic abnormalities are not included (eg, -Y, +8 or del(20q) as the sole abnormality)
- Exclusion of other disorders as etiology for dysplasia and/or cytopenia

Diagnostic issues

- Diagnosis of MDS is often difficult and may require combination testing (eg, cytogenetics, FISH, microarray and/or mutation testing)
- FISH
 - Aids in classification of disease risk in MDS for therapy decisions
 - See Revised International Prognostic Scoring System (IPSS-R) (Greenberg, Blood 2012) below for cytogenetic risk stratification
 - Aids in monitoring for MRD

- May detect specific genomic aberrations not detected by cytogenetics (eg, cryptic rearrangements)
- Has limited clinical utility following a normal 20-cell CC study

Test Interpretation

Analytical sensitivity/specificity – >95%

- Limit of detection is probe dependent – ~1-5% in interphase nuclei

Results

- Normal
 - No evidence of del(5q), -7/del(7q), +8, or del(20q)
- Abnormal – genetic abnormality detected
 - del(5q)
 - Good prognostic subgroup when isolated or combined with any other single abnormality except -7 (WHO update in progress)
 - Defines a unique MDS subtype with corresponding morphologic features
 - Presumptive evidence of MDS in the absence of definitive morphologic criteria
 - -7/del(7q)
 - -7
 - Poor prognostic subgroup when isolated or combined with any other single abnormality
 - del(7q)
 - Intermediate prognostic subgroup when isolated
 - Poor prognostic subgroup when combined with any other single abnormality
 - Presumptive evidence of MDS in the absence of definitive morphologic criteria
 - +8
 - Intermediate prognostic subgroup when isolated or combined with any other single abnormality
 - del(20q)
 - Good prognostic subgroup when isolated

Limitations

Panel detects only the specific aberrations targeted by the probes

Cytogenetic Prognostic Scoring System Used in IPSS-R			
Prognostic subgroup	Cytogenetic Abnormality		
	Single	Double	Complex
Very good	del(11q); -Y	-----	-----
Good	Normal; del(5q); del(12p); del(20q)	del(5q) combined with another abnormality	-----
Intermediate	del(7q); +8; i(17q); +19; +21; any other independent clones	Any other abnormality in combination	-----
Poor	inv(3)/t(3q)/del(3q); -7	-7/del(7q) combined with another abnormality	3 abnormalities
Very poor	-----	-----	>3 abnormalities