TRICORE

MYELOID DISORDER MUTATION PANEL

TriCore Reference Laboratories' Myeloid Disorder Mutation Panel by next generation sequencing (NGS) is a cost-effective and comprehensive way to detect key mutations associated with myeloid neoplasms. To assist pathologists and clinicians in using this sophisticated genetic information, each case will be accompanied by a global interpretive comment, crafted by our expert team of hematopathologists and molecular genetic pathologists, that synthesizes the clinical, morphologic, cytogenetic, and molecular genetic findings for optimal patient care. When combined with our interpretive guidance and our accessibility for consultation and discussion, TriCore's myeloid NGS panel will become an indispensable part of your workup.

GENES ANALYZED				
ASXL1	*CSF3R*	*IDH2*	*NPM1*	*SRSF2*
BRAF	*DNMT3A*	*JAK2*	*NRAS*	*TET2*
CALR	*EZH2*	*KIT*	*RUNX1*	*TP53*
CBL	*FLT3**	*KRAS*	*SETBP1*	*U2AF1*
*CEBPA**	*IDH1*	*MPL**	*SF3B1*	*WT1*

** In cases of acute myeloid leukemia, the NGS testing is supplemented by CEBPA analysis by Sanger sequencing and FLT3-ITD testing by capillary electrophoresis. In cases of myeloproliferative neoplasms, the NGS analysis is supplemented by pyrosequencing of MPL.*

INDICATIONS

Myeloid neoplasms are a heterogeneous group of entities with distinct molecular profiles, and the utility of the panel differs depending on the specific diagnosis or clinical setting. Testing may be indicated in the following diagnoses:

Acute Myeloid Leukemia

New Diagnosis (Age >18 years):

- Panel should be run in all cases, can be run on either blood or bone marrow depending on specimen availability and blast count
- Panels includes: *FLT3*, *NPM1*, *CEBPA*, *KIT*, *RUNX1*, *ASXL1*, and *TP53*, permitting complete risk stratification as recommended by NCCN and European LeukemiaNet Guidelines
- Panel allows complete and final subclassification of AML according to the WHO 2016 Classification
- FDA-approved targeted therapies are available for some cases with mutations detected in *FLT3* and *IDH1*, and *IDH2*
- Includes many other genes with evidence of prognostic significance such as *EZH2*, *NRAS*, *KRAS*, and *KIT*

Relapsed/Refractory Disease (after completion of consolidation):

- Comprehensive molecular profiling by myeloid gene panel is suggested at each relapse or progression

Residual Disease Monitoring

- Testing with myeloid gene panel is not recommended as the detection level (analytic sensitivity) is 3%

Myelodysplastic Syndrome

New diagnosis (cytopenias and suspicion of myelodysplasia):

- Genetic testing for somatic mutations in genes associated with MDS is highly recommended as part of initial evaluation per NCCN Guidelines Version 2.2021
- Panel detects mutations associated with better (*SF3B1*) and worse (*SRSF2*, *DNMT3A*, *U2AF1*, *CBL*, *NRAS*, *KRAS*) prognosis per NCCN
- Also includes a set of genes (*TP53*, *EZH2*, *ETV6*, *RUNX1*, *ASXL1*) that identifies cases with overall survival more similar to that of patients in the next higher R-IPSS risk group

- over -

MYELOID DISORDER MUTATION PANEL, continued

Persistent, Unexplained Cytopenias

- Consider testing in patients >50 years of age with 3-6 months of sustained cytopenia (1 or more lineages) without identifiable secondary etiology (for example, nutritional deficiency, medication effect, anemia of chronic disease)
  - Although no formal guidelines exist, myeloid gene panel may be considered as part of comprehensive work-up for etiology.
- If MDS or other myeloid neoplasia is not established:
  - Panel identifies patients with "clonal cytopenia of undetermined significance" (CCUS), including a specific subset at significantly higher risk of progression to an overt myeloid neoplasm
- If a negative result is obtained using this panel, its relatively high negative predictive value (>89%) for myeloid neoplasia indicates MDS is less likely and may prompt renewed consideration of a reactive etiology

Myeloproliferative Neoplasms and MDS/MPN

New diagnosis:

- Consider panel in all new diagnoses
  - NCCN guidelines indicate that NGS panels are useful to establish clonality and identify prognostically significant mutations
- Panel includes *JAK2* V617F and exon 12, *CALR*, and *MPL*
- Includes genes (*ASXL1*, *SRSF2*, *IDH1*, *IDH2*, *TP53*, *EZH2*, *U2AF1*, *SF3B1*, *TET2*) recommended by NCCN guidelines for identifying higher risk cases of polycythemia vera, essential thrombocythemia, and primary myelofibrosis
- For chronic myelomonocytic leukemia (CMML), the panel includes the mutations cited in the WHO 2016 Classification (*TET2*, *SRSF2*, *ASXL1*, *SETBP1*) as supportive evidence for establishing the proper diagnosis. It also identifies *NPM1* mutations, a high risk finding in this disease setting.

Evaluation for disease progression:

- NCCN guidelines recommend testing for mutations with prognostic significance. In particular, AML associated mutations should be assessed in patients with evidence of disease progression.

MYELOID DISORDERS MUTATIONS PANEL

Test Code.....MDMYE	Testing Initiated.....Tuesday	
CPT Code.....81450; G0452-26	Methodology.....Genomic Sequencing	Reported.....Reported within 14-21 days

COLLECTION	
Specimen	Preferred: Whole Blood or Bone Marrow
Collection Containers	Preferred: Lavender (EDTA) Acceptable: Pink(EDTA) Acceptable: Yellow (ACD) Acceptable: Green (NaHeparin)
Collection Amount	Preferred volume: 5.0mL Minimum volume: 1.0mL
SHIPPING/TRANSPORT AND STORAGE	
Stabilities/Storage: (*Collection to initiation of testing*)	**Temperature** **Stability** Ambient: 5 days Refrigerated: 5 days Frozen: Unacceptable
Shipping Instructions	Ship ambient and overnight for Monday-Saturday receipt.