HEMATOLOGIC MALIGNANCIES

IntelliGEN® Myeloid

Providing diagnostic, prognostic, and predictive information for patients with myeloid malignancies

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IntelliGEN® Myeloid is a next-generation sequencing (NGS) test developed by Labcorp that evaluates 50 clinically relevant genes known to provide diagnostic, prognostic, and therapy selection information for your patients with myeloid malignancies.

Pioneering scientific breakthroughs

Why choose IntelliGEN Myeloid?

Acute Myeloid Leukemia (AML)

Leading clinical practice guidelines recommend multigene panels for assessment of additional mutations to guide therapy and determine eligibility for clinical trials.[1]

- Mutations in *FLT3*, *IDH1*, and *IDH2* are specifically used to predict response to novel treatments.[2-5]
- Mutations in *NPM1*, *CEBPA*, *RUNX1* can define disease subtypes based on WHO classifications.[1]
- Mutations in *ASXL1*, *CEBPA*, *DNMT3A*, *FLT3*, *IDH1*, *IDH2*, *KIT*, *KMT2A*, *NPM1*, *RUNX1*, *TET2*, *TP53*, and *WT1* are important prognostic indicators for AML.[1]

Myelodysplastic Syndrome (MDS)

Leading clinical practice guidelines cite 27 genes included in this panel as being mutated in MDS. Clinical guidelines also recommend genetic testing for somatic mutations in genes associated with MDS and do not list FISH in recommendations for initial evaluation.[1]

Myeloproliferative Neoplasm (MPN)

Leading clinical practice guidelines recognize the clinical utility of detecting mutations in *JAK2*, *CALR*, and *MPL* in the diagnosis of MPN. Additional genes have been identified as having prognostic significance in triple-negative patients and in combination with *JAK2*, *CALR*, or *MPL* mutations.[1,6]

When to consider IntelliGEN Myeloid:

- When guidelines recommend broad genomic analysis of multiple genes with clinical evidence and therapeutic recommendations or when standard biomarker evaluation is uninformative.
- When mutations in specific genes can define disease subtypes to better inform prognosis and treatment.
- When relapse or disease progression has occurred after prior therapies.
- When your patient presents with a cytopenia and MDS is suspected.

How to order

- **As a standalone test**
  Specimen types include bone marrow and peripheral blood. Additionally, if Labcorp already has the patient sample, IntelliGEN Myeloid can be easily added.
- **As part of our Comprehensive Hematopathology Analysis service**
  Based on medical necessity and available clinical information, a Labcorp hematopathologist will select testing using a suite of technologies, resulting in an easy-to-read final report that summarizes all the findings, in addition to the individual test reports.

Powering better decisions

Clear, easy-to-follow clinical report

SUMMARY

At least one variant of **strong** clinical significance (Tier I) was detected.

Gene	Variant Detected	Amino Acid Change	Variant Frequency (%)	Clinical Impact
IDH2	c.419G>A	p.Arg140Gln	48	Tier I

See additional details below

Summary of variants detected with tiered impact based on clinical significance.

Therapeutic Implications

Gene	Amino Acid Change	FDA Approved Therapies	FDA Approved Therapies for Other Indications	Possible Drug Resistance	Clinical Trials
IDH2	p.Arg140Gln	Enasidenib	None	IFNA2, PEG-Interferon Alfa-2A	NCT03013998, NCT03953898, NCT03881735, NCT03683433, NCT03825796

Therapeutic implications with FDA approved therapies, possible drug resistance and clinical trials.

INTERPRETATION

IDH2 c.419G>A (p.R140Q) is located in exon 4 of transcript NM_002168.3 for the gene IDH2 on chromosome 15. Other variants in IDH2 have been reported to lead to disease by causing a gain-of-function in the encoded protein. The current variant results in a conservative amino acid change located in the substrate binding region (UniProt) of the encoded protein sequence. Publications reported experimental evidence evaluating an impact on protein function, and demonstrated that the variant results in neomorphic enzyme activity leading to increased levels of beta-hydroxyglutarate, in addition in mice engrafted with IDH2-R140Q-transduced stem/progenitor cells the variant was sufficient to initiate hematological malignancies of myeloid and lymphoid origin.

Prognostic Significance: Evidence for the prognostic significance of this or similar variants in this exon for AML is conflicting, with different sources describing an unfavorable or favorable prognostic effect. Therapeutic Significance: Multiple sources, including at least one drug label, suggest that this or similar variants in this gene indicate responsiveness of AML to enasidenib and Enasidenib or low-intensity therapy (azacitidine, decitabine), especially in patients >60 years and in patients with relapsed or refractory AML. At least one clinical trial for patients with AML lists this or similar variants in this gene as an inclusion criterion. Based on these data, the variant is considered to be clinically significant.

Personalized interpretation for each variant detected along with the diagnostic, prognostic, and therapeutic significance.

This patient may be eligible for the following clinical trials via the ClinicalTrials.gov site:

Gene	Clinical Trial Title	Phase	Clinical Trial #	Location
IDH2	A Master Protocol for Biomarker-Based Treatment of AML (The Beat AML Trial)	1/2	NCT03013998	CA,FL,GA,IL,KS,MD,MN,NC,NY,OH,OR,PA,TX,UT
	The PRIME Trial: PARP Inhibition in IDH Mutant Effectiveness Trial. A Phase II Study of Olaparib in Isocitrate Dehydrogenase (IDH) Mutant Relapsed/Refractory Acute Myeloid Leukemia and Myelodysplastic Syndrome	2	NCT03953898	CA,CT,NC
	A Phase II Study of Intensive Salvage Therapy Followed by Enasidenib for Patients With AML Harboring Mutations in IDH2 Who Have Failed or Been Refractory to One Prior Line of Therapy	2	NCT03881735	NY
	Phase II Study of the Targeted Mutant IDH2 Inhibitor Enasidenib in Combination With Azacitidine for Relapsed/Refractory AML	2	NCT03683433	TX
	CPX-351 Plus Enasidenib for Relapsed Acute Myelogenous Leukemia Characterized by the IDH2 Mutation	2	NCT03825796	CA

Clinical trial information is included for each variant to provide you and your patient with easy access to available trials.

IntelliGEN Myeloid Panel Genes

Gene*	Association		
	MDS	AML	MPN
ABL1[7]		●	●
ASXL1	●	●	●
BCOR	●	●	●
BCORL1		●	
BRAF[8]			●
CALR	●		●
CBL	●		●
CDKN2A	●	●	
CEBPA		●	
CSF3R		●	●
CUX1	●	●	
DNMT3A	●	●	●
ETV6	●	●	●
EZH2	●	●	●

Gene*	Association		
	MDS	AML	MPN
FBXW7			
FLT3[2,3]	●	●	
GATA1		●	
GATA2	●	●	
IDH1[4]	●	●	●
IDH2[5]	●	●	●
IKZF1		●	●
JAK2	●		●
JAK3		●	
KDM6A	●	●	●
KIT[7]		●	
KMT2A		●	
KRAS[9]		●	
MPL	●		●

Gene*	Association		
	MDS	AML	MPN
NF1	●	●	
NOTCH1			
NPM1		●	
NRAS	●	●	
PDGFRA[7]		●	
PHF6	●	●	
PML		●	
PTEN		●	
PTPN11		●	
RAD21		●	
RUNX1	●	●	●
SETBP1	●	●	●
SF3B1	●	●	●
SMC1A	●	●	

Gene*	Association		
	MDS	AML	MPN
SMC3	●	●	
SRSF2	●		●
STAG2	●	●	
TET2	●	●	●
TP53	●	●	
U2AF1	●	●	
WT1	●	●	
ZRSR2	●		●

Genes associated with FDA approved therapies

- ● Diagnostic and/or prognostic significance in MDS
- ● Diagnostic and/or prognostic significance in AML
- ● Diagnostic and/or prognostic significance in MPN

*Identification of mutations should always be used within the context of clinical findings and bone marrow evaluation

Technical information

IntelliGEN Myeloid utilizes next-generation sequencing to target single nucleotide variants and insertions/deletions in 50 genes and also detects whole-gene copy number alterations in *KMT2A*. Alterations outside the targeted regions will not be detected. Variants are categorized into Tiers based on their clinical impact, following a joint consensus recommendation from the AMP, ASCO, and CAP.

Specimen requirements	
Specimen	Bone marrow, whole blood, extracted DNA, or cell pellets (from whole blood or bone marrow)
Volume	1-2 mL bone marrow, 3-5 mL whole blood
Container	Lavender-top (EDTA) tube or green-top (sodium heparin) tube

Patient responsibility

Patient responsibility is determined by amount billed to patients after insurance provider has been billed, including copay, coinsurance, deductible, or coverage denials.

Based on managed care claim data* of over 889 patients in 2020:

82% paid $0

(32% insurance paid in full / 51% no patient responsibility for non-covered and coverage-related reasons)

90% had patient responsibility of $100 or less†
91% had patient responsibility of 200 or less†
9% had patient responsibility of over $200†

*Based on internal Labcorp billing data (2019)
† Includes claims adjudicated as non-covered and for which there was no patient responsibility indicated by the payer. The explanation of benefits (EOB) from the insurance company explains in detail the services that were either paid or denied. If a claim is denied, the patient is responsible for the amount indicated on the EOB the patient receives from the insurer. If further assistance is needed in determining the reason(s) why the insurance company did not pay for testing, patients should contact their insurance carrier directly. A listing of insurance plans billed by Labcorp Oncology and Labcorp can be found at **oncology.labcorp.com** and www.**labcorp.com**, respectively.

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For more information about IntelliGEN® Myeloid visit **oncology.labcorp.com**, or contact your Labcorp Oncology sales representative.

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