HEMATOLOGIC MALIGNANCIES

Labcorp NGS Panels

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

labcorp | Oncology

Behind every cancer test is an opportunity to find actionable answers

Three next-generation sequencing (NGS) tests that evaluate clinically relevant genes to deliver diagnoses and risk stratification for complex hematologic malignancies.

Pioneering scientific breakthroughs

Labcorp Myeloid NGS Panel
To aid in diagnosis, prognostic risk assessment, and therapeutic selection in myeloid malignancies, including acute myeloid leukemia (AML), myelodysplastic syndrome (MDS) and myeloproliferative neoplasms (MPN)

Labcorp Lymphoid NGS Panel
To aid in diagnosis, prognostic risk assessment, and therapeutic selection in lymphoid malignancies, including lymphoblastic leukemias (B-ALL/T-ALL), CLL (chronic lymphocytic leukemia), DLBCL, mantle cell lymphoma, follicular lymphoma, T cell lymphoma, hairy cell leukemia and other lymphoma subtypes

Labcorp Pan-Heme NGS Panel
To aid in diagnosis, prognostic risk assessment, and therapeutic selection in various myeloid and lymphoid malignancies

When to consider Labcorp NGS Panels:

- 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

How to order

- **As a standalone test**
  Specimen types include bone marrow aspirate, peripheral blood, and cell suspension from fresh tissue. Additionally, if Labcorp already has the patient sample, and if sufficient sample remains, these panels can be added
- **As part of Labcorp HemePath CASE (Comprehensive Analysis Services & Expertise)**
  Based on medical necessity and available clinical information, a Labcorp hematopathologist will select testing using a suite of technologies. This results 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
FLT3	c.FLT3_ITD	p.Y597_E598insDEYFYVDFREY	16	Tier I
NPM1	c.860_863dupTCTG	p.W288CfsX12	8	Tier I

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	Available Clinical Trials*
FLT3	p.Y597_E598insDEYFYVDFREY	gilteritinib, midostaurin + cytarabine + daunorubicin, quizartinib, sorafenib +/- (azacitidine or decitabine)	None	None	8
NPM1	p.W288CfsX12	None	None	None	6
KIT	D816V Not Detected	Imatinib	None	None	None

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

Interpretation

FLT3 Y597_E598insDEYFYVDFREY results in the insertion of 11 amino acids in the juxtamembrane domain of the Flt3 protein between amino acids 597 and 598 (http://www.ncbi.nlm.nih.gov/pubmed/14759363). Y597_E598insDEYFYVDFREY has not been biochemically characterized, but can be predicted to lead to activation of Flt3 based on the effects of other Flt3 internal tandem duplication (ITD) mutations (http://www.ncbi.nlm.nih.gov/pubmed/12970773, http://www.ncbi.nlm.nih.gov/pubmed/9737679, http://www.ncbi.nlm.nih.gov/pubmed/11090077)

FLT3, fms related receptor tyrosine kinase 3, activates Akt, Ras, and Erk pathways to regulate differentiation, proliferation, and survival of hematopoietic progenitor cells (http://www.ncbi.nlm.nih.gov/pubmed/29316714, http://www.ncbi.nlm.nih.gov/pubmed/28538663). Activating mutations of FLT3 are common in hematologic tumors (http://www.ncbi.nlm.nih.gov/pubmed/19467916) and the internal tandem duplication (ITD) mutation is commonly observed in acute myeloid leukemia (http://www.ncbi.nlm.nih.gov/pubmed/30181385, http://www.ncbi.nlm.nih.gov/pubmed/32241850)

Diagnostic Significance

1. Myeloid Neoplasm — FLT3 mutations have been identified in various myeloid neoplasms: acute myeloid leukemia (AML) and myelodysplastic syndromes (MDS). Identification of FLT3-ITD mutations in more than 10% of blasts (with cup-like nuclear morphology) is highly specific for AML with NPM1 mutation. Most AML cases with NUP98-NSD1 rearrangement harbor FLT3-ITD at frequencies ranging from 67-91%. In mixed lineage neoplasms, FLT3 rearrangements and mutations are found in mixed-phenotype acute leukemia (MPAL). FLT3 rearrangement defines a subtype of myeloid/lymphoid neoplasms

Prognostic Significance

1. Myelodysplastic Syndromes — FLT3 ITD or D835 missense mutations are associated with a poor prognosis in MDS.

Therapeutic Significance

1. midostaurin + cytarabine + daunorubicin — FDA approved for adults with newly diagnosed AML who are FLT3 mutation-positive, with standard cytarabine and daunorubicin induction and cytarabine consolidation. NCCN recommended as Category 1 for induction therapy and Category 2A for consolidation therapy. Also NCCN recommended for maintenance therapy as single agent (Category 2B).

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

Gene	Clinical Trial Title	Phase	Clinical Trial #	Locations
FLT3	Total Marrow and Lymphoid Irradiation, Fludarabine, and Melphalan Before Donor Stem Cell Transplant in Treating Participants With High-Risk Acute Leukemia or Myelodysplastic Syndrome	1	NCT003494569	Duarte, CA
	Orca-T Following Chemotherapy and Total Marrow and Lymphoid Irradiation for the Treatment of Acute Myeloid Leukemia, Acute Lymphoblastic Leukemia or Myelodysplastic Syndrome"	1	NCT06195891	Duarte, CA
	225Ac-DOTA-Anti-CD38 Daratumumab Monoclonal Antibody With Fludarabine, Melphalan and Total Marrow and Lymphoid Irradiation as Conditioning Treatment for Donor Stem Cell Transplant in Patients With High-Risk Acute Myeloid Leukemia, Acute Lymphoblastic Leukemia and Myelodysplastic Syndrome	1	NCT06287944	Duarte, CA
	A Study of Gilteritinib, Venetoclax and Azacitidine as a Combined Treatment for People Newly Diagnosed With Acute Myeloid Leukemia	1/2	NCT05520567	Irvine, CA Duarte, CA Los Angeles, CA
	Expanded Access Study of Gilteritinib (ASP2215) in Patients With FMS-like Tyrosine Kinase 3 (FLT3) Mutated Relapsed or Refractory Acute Myeloid Leukemia (AML) or FLT3-Mutated AML in Complete Remission (CR) With Minimal Residual Disease (MRD)		NCT03070093	Los Angeles, CA
	Study of Biomarker-Based Treatment of Acute Myeloid Leukemia	1/2	NCT03013998	Los Angeles, CA
	MYELOMATCH: A Screening Study to Assign People With Myeloid Cancer to a Treatment Study or Standard of Care Treatment Within myeloMATCH (MyeloMATCH Screening Trial)	2	NCT05564390	Los Angeles, CA

Clinical trial information is included for each variant to provide you and your patient with easy access to trials within a 200 mile radius. A full list of clinical trials is also available in the Appendix.

Technical information

These panels utilize capture-based next-generation sequencing of whole genomic DNA libraries to identify gene alterations that have diagnostic, prognostic and therapeutic significance in hematologic malignancies. Somatic mutations in the genes analyzed include single nucleotide variants (SNVs), insertions and deletions (indels), whole gene copy number variants (CNVs) in a subset of genes and sub-gene (exon level) genes in a subset of genes (see gene list for specific genes).

The sensitivity of this assay is 3% variant allele fraction (VAF) for single nucleotide variants (SNV), 5% for insertions/deletions (indels) <25 base pairs (bp) and 15% indels ≥25 bp. Sensitivity for CNVs with size ≥2 contiguous exons (subset) to whole gene is copy number ≤0.85 for deletions and ≥1.15 for gains. Multiple clinically actionable hotspots have increased VAF sensitivity and include FLT3-ITDs down to 1% VAF, as well as Indel hotspots in CALR (chr19:13054563-13054625) and CEBPA (chr19:33,792,224- 33,793,340) with VAF sensitivity >= 5% for indels regardless of length. Insertions and deletions of any length are detected when at least one breakpoint is contained within a sequence read. Insertions up to 162 bp and deletions up to 95 bp have been detected in clinical specimens. Mutations outside the targeted regions and gene rearrangements will not be detected.

Variants are categorized into Tiers (1-4) based on their clinical impact, following a joint consensus recommendation from AMP, ASCO and CAP. Clinical and experimental evidence grouped into four levels (A-D) based on significance in clinical decision making (therapeutic, diagnosis, prognosis) is assigned to variants to determine their clinical significance.

Specimen requirements	
Specimen	Bone marrow aspirate, peripheral blood, and cell suspension from fresh tissue
Volume	1-2 mL bone marrow, 3-5 mL whole blood
Container	Lavender-top (EDTA) tube or green-top (sodium heparin) tube

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