Patient Report

labcorp

Specimen ID: 046-225-9994-0
Control ID:

SAMPLE REPORT, 485140

Acct #: 90001325 **Phone:** (919) 361-7217 **Rte:** 99
Labcorp Of America
CMBP
1912 TW Alexander Dr
Durham NC 27709

Patient Details
DOB:
Age(y/m/d): 000/00/00
Gender: N
Patient ID:

Specimen Details
Date collected: 02/14/2022 0000 Local
Date received: 02/15/2022
Date entered: 02/15/2022
Date reported: 02/15/2022 1508 ET

Physician Details
Ordering:
Referring:
ID:
NPI:

Ordered Items
KIT (D816V) Digital PCR, SpTst

TESTS	RESULT	FLAG	UNITS	REFERENCE INTERVAL	LAB
KIT (D816V) Digital PCR, SpTst					
CKIT Result [A]	Positive				01
The KIT D816V mutation was detected. Results should be interpreted in conjunction with all other clinical, molecular, and cytogenetic findings for the most accurate interpretation. For serial monitoring of transcript levels, consider resubmitting a specimen using KIT (D816V) Digital PCR test. (Labcorp test code 485126).					
CKIT Quant Value	2.32		%		01
Specimen Type	Blood				01
Background					01

Systemic mastocytosis (SM) is a hematopoietic neoplasm characterized by an abnormal growth of clonal mast cells in bone marrow and other extracutaneous organs.
KIT is a receptor tyrosine kinase involved in proliferation of mast cells, melanocytes, germ cells, and hematopoietic stem cells. Activation of KIT occurs upon binding of the stem cell factor ligand, which triggers autophosphorylation and dimerization of KIT. Activated KIT signals downstream protein kinase pathways which induces cell proliferation and survival.
The vast majority (>90%) of SM cases have a somatic A to T missense mutation at position 2447 in exon 17 of the KIT gene. This KIT D816V mutation (c.2447 A>T, p.D816V) results in the substitution of aspartate (D) to valine (V) at codon 816 in the kinase activation loop domain of the protein causing a conformational change in the receptor. This conformational change results in ligand-independent constitutive activation of KIT and leads to increased cell proliferation and accumulation in various organs, and a reduction in cell death. The detection of KIT D816V is one of the minor diagnostic criteria for SM per the WHO system. KIT mutation detection is correlated with the proportion of lesional cells in the sample as well as the sensitivity of the detection method employed.
Quantitative detection using digital PCR of the KIT D816V mutation may aid physicians in diagnosis and therapeutic monitoring of patients with SM. The reported values will allow clinicians to predict disease severity and/or monitor the effectiveness of treatment protocols and to detect increasing mutation levels that may be indicative of patient relapse. An effect of mutational dose on disease phenotype may also prove significant.

TESTS	RESULT	FLAG	UNITS	REFERENCE INTERVAL	LAB
Method/Extraction					02

Nanoplate Digital PCR (dPCR)
Total genomic DNA is extracted and amplified using a multiplex digital PCR using wild-type and mutant-specific probes.
The assay is designed to detect the KIT D816V (KITc.2447A>T) mutation. Results are reported as percent mutated alleles. The mutation can be detected down to 0.03% mutated alleles.

References 01

Akin C, Fumo G, Yavuz AS, Lipsky PE, Neckers L, Metcalfe DD. A novel form of mastocytosis associated with a transmembrane c-kit mutation and response to imatinib. Blood. 2004;103(8):3222-3225.
Alvarez-Twose I, Gonz alez P, Morgado JM, et al. Complete response after imatinib mesylate therapy in a patient with well-differentiated systemic mastocytosis. J Clin Oncol. 2012;30(12):e126-e129.
Alvarez-Twose I, Matito A, Morgado JM, et al. Imatinib in systemic mastocytosis: a phase IV clinical trial in patients lacking exon 17 KIT mutations and review of the literature. Oncotarget. 2016;8(40): 68950-68963.
DeAngelo DJ, Radia DH, George TI, Robinson WA, Quiery AT, Drummond MW, Bose P, Hexner EO, Winton EF, Horny HP, Tugnait M, Schmidt-Kittler O, Evans EK, Lin HM, Mar BG, Verstovsek S, Deininger MW, Gotlib J. Safety and efficacy of avapritinib in advanced systemic mastocytosis: the phase 1 EXPLORER trial. Nat Med. 2021 Dec;27(12):2183-2191. doi: 10.1038/s41591-021-01538-9. Epub 2021 Dec 6. PMID: 34873347; PMCID: PMC8674134.
Gotlib J, Kluin-Nelemans HC, George TI, et al. Efficacy and safety of midostaurin in advanced systemic mastocytosis. N Engl J Med. 2016; 374(26):2530-2541.
Gotlib J, Gerds AT, Bose P, Castells MC, Deininger MW, Gojo I, Gundabolu K, Hobbs G, Jamieson C, McMahon B, Mohan SR, Oehler V, Oh S, Padron E, Pancari P, Papadantonakis N, Pardanani A, Podoltsev N, Rampal R, Ranheim E, Rein L, Snyder DS, Stein BL, Talpaz M, Thota S, Wadleigh M, Walsh K, Bergman MA, Sundar H. Systemic Mastocytosis, Version 2.2019, NCCN Clinical Practice Guidelines in Oncology. J Natl Compr Canc Netw. 2018 Dec;16(12):1500-1537. doi: 10.6004/jnccn.2018.0088. PMID: 30545997.
Gotlib J, Reiter A, Radia DH, Deininger MW, George TI, Panse J, Vannucchi AM, Platzbecker U, Alvarez-Twose I, Mital A, Hermine O, Dybedal I, Hexner EO, Hicks LK, Span L, Mesa R, Bose P, Pettit KM, Heaney ML, Oh ST, Sen J, Lin HM, Mar BG, DeAngelo DJ. Efficacy and safety of avapritinib in advanced systemic mastocytosis: interim analysis of the phase 2 PATHFINDER trial. Nat Med. 2021 Dec;27 (12):2192-2199. doi: 10.1038/s41591-021-01539-8. Epub 2021 Dec 6. PMID: 34873345; PMCID: PMC8674139.
Greiner G, et al. 2018. Digital PCR: A Sensitive and Precise Method for KIT D816V Quantification in Mastocytosis. Clin Chem. March 01; 64(3): 547-555.
Kristensen T, Vestergaard H, Moller MB. Improved detection of the kit d816v mutation in patients with systemic mastocytosis using a quantitative and highly sensitive real-time qpcr assay. The Journal of Molecular Diagnostics. 2011;13(2):180-188.

TESTS	RESULT	FLAG	UNITS	REFERENCE INTERVAL	LAB

Reiter A, George TI, Gotlib J. New developments in diagnosis, prognostication, and treatment of advanced systemic mastocytosis. Blood. 2020 Apr 16;135(16):1365-1376. doi: 10.1182/blood.2019000932. PMID: 32106312

Ustun C, Arock M, Kluin-Nelemans HC, et al. Advanced systemic mastocytosis: from molecular and genetic progress to clinical Haematologica. 2016;101(10):1133-1143.

Valent P, Akin C, Metcalfe DD. Mastocytosis: 2016 updated WHO classification and novel emerging treatment concepts. Blood. 2017 Mar 16;129(11):1420-1427. doi: 10.1182/blood-2016-09-731893. Epub 2016 Dec 28. PMID: 28031180; PMCID: PMC5356454.

Verstovsek S. 2012. Advanced systemic mastocytosis: the impact of KIT mutation in diagnosis, treatment, and progression. Eur J Haematology 90 (89-98).

Intake Review	Completed				01
Director Review					
	Dan Wang, PhD, FACMG Director, Molecular Oncology LabCorp Center for Molecular Biology and Pathology Research Triangle Park, NC 27709 1-800-533-0567				01

Comments:

A This test was developed and its performance characteristics determined by Labcorp. It has not been cleared or approved by the Food and Drug Administration.

01	YU	Labcorp RTP 1904 TW Alexander Drive Ste C, RTP, NC 27709-0153	Dir: Anjen Chenn, MDPhD
02	TG	Labcorp RTP 1912 TW Alexander Drive, RTP, NC 27709-0150	Dir: Anjen Chenn, MDPhD

For inquiries, the physician may contact **Branch: 800-762-4344 Lab: 800-735-4087**