Test Definition: BRAFB

Cell-Free DNA BRAF V600, Blood

Overview

Useful For

An alternative to invasive tissue biopsies for the determination of *BRAF* V600E and V600K alterations

Identification of patients with cancer who are most likely to benefit from targeted therapies

This test is **not intended for** serial monitoring of patients with cancer or as a screening test to identify cancer.

Genetics Test Information

This test evaluates cell-free DNA (cfDNA) in the peripheral blood for the presence of *BRAF* V600E or V600K alterations in patients with cancer and can be used to determine if these patients are candidates for targeted therapies.

Highlights

This test evaluates peripheral blood for *BRAF* alterations in cell-free DNA.

Detection of *BRAF* alterations in melanoma patients can be used as an alternative for *BRAF* analysis of tissue.

Current data suggests that the efficacy of *BRAF*-targeted therapy and anti-*MEK* therapy in melanoma is limited to patients whose tumors harbor a V600E or V600K alteration.

Method Name

Digital Droplet Polymerase Chain Reaction (ddPCR)

NY State Available

Yes

Specimen

Specimen Type

Whole blood

Ordering Guidance

This test is **not** a prenatal screening test.

Shipping Instructions

Specimens must be transported at ambient temperature or refrigerated (4 degrees C).

Specimen Required

Supplies: Streck Black/Tan Top Tube Kit (T715)
Container/Tube: Streck Cell-Free DNA blood collection kit
Specimen Volume: Two 10-mL Streck Cell-Free DNA blood collection tubes
Additional Information: Only blood collected in Streck Cell-Free DNA tubes will be accepted for analysis. Whole blood

will be processed to produce platelet-poor plasma before cfDNA isolation.

Forms
If not ordering electronically, complete, print, and send an Oncology Test Request (T729) with the specimen.

Specimen Minimum Volume
One 10 mL Streck cell-free DNA blood collection tube

Reject Due To
All specimens will be evaluated at Mayo Clinic Laboratories for test suitability.

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Whole blood	Ambient (preferred)	7 days	
	Refrigerated	7 days	

Clinical & Interpretive

Clinical Information
This test uses DNA extracted from the peripheral blood to evaluate for the presence of *BRAF* c.1799T>A (V600E) and c.1798_1799delGTinsAA (V600K) alterations. The *BRAF* gene is a member of the mitogen-activated protein/extracellular signal-regulated (MAP/ERK) kinase pathway, which plays a role in cell proliferation and differentiation. Dysregulation of this pathway is a key factor in tumor progression and *BRAF* alterations occur frequently in many different tumor types. *BRAF* variant analysis aids in the diagnosis of cancer types including anaplastic and papillary thyroid carcinoma, hairy cell leukemia, and papillary craniopharyngioma.

BRAF V600E and V600K alterations are associated with response or resistance to specific targeted therapies in cancer. Targeted cancer therapies are defined as antibody or small molecule drugs that block the growth and spread of cancer by interfering with specific cell molecules involved in tumor growth and progression. Multiple targeted therapies have been approved by the US Food and Drug Administration for treatment of specific cancers. Molecular genetic profiling is often needed to identify targets amenable to targeted therapies and to minimize treatment costs and therapy-associated risks.

Reference Values
An interpretive report will be provided.

Interpretation
The interpretation of molecular biomarker analysis includes an overview of the results and the associated diagnostic, prognostic, and therapeutic implications.

Cautions
Patients with a negative test result may still harbor a V600E or V600K alteration. Variant testing of a tissue specimen for *BRAF* alterations should be considered for patients with a negative result with this test.

This assay detects BRAF V600E and V600K mutations at or above approximately 0.1% variant allele fraction in plasma, depending on the fraction of circulating tumor DNA present. This is a biological variable that cannot be controlled.

This assay is designed to detect BRAF V600E (c.1799T>A) and V600K (c.1798_1799delGTinsAA) mutations. Other variants at or adjacent to codon 600 may yield indeterminate results due to probe cross-hybridization. Additionally, rare polymorphisms in the target region for this assay could lead to false-negative or false-positive results.

This test has not been clinically validated for use as a tool to monitor response to therapy or for early detection of tumors.

This test cannot differentiate between somatic and germline alterations. Additional testing may be necessary to clarify the significance of results if there is a potential hereditary risk.

Supportive Data

This test has been evaluated by our laboratory as an alternative to assessing paraffin embedded tumor specimens for BRAF alterations in patients with advanced melanoma. Those studies revealed that this assay has a high positive predictive value (100% in our study) for the presence of a BRAF V600 alteration in a patient's tumor and high concordance between the specific alteration type observed in the patient's plasma and tumor.

While the positive predictive value of this assay was very high, the negative predictive value of the assay in this study (using BRAF tissue result as the gold standard) is approximately 71%.

Clinical Reference

1. Sanmamed MJ, Fernandez-Landazuri S, Rodriguez C, et al: Quantitative cell-free circulating BRAFV600E mutation analysis by use of droplet digital PCR in the follow-up of patients with melanoma being treated with BRAF inhibitors. Clin Chem. 2015;61(1):297-304
2. Schwarzenbach H, Hoon DS, Pantel K. Cell-free nucleic acids as biomarkers in cancer patients. Nat Rev Cancer. 2011;11(6):426-437
3. Johnson DB, Sosman JA. Update on the targeted therapy of melanoma. Curr Treat Options Oncol. 2013;(2):280-292
4. McArthur GA, Chapman PB, Robert C, et al. Safety and efficacy of vemurafenib in BRAF (V600E) and BRAF (V600K) mutation-positive melanoma (BRIM-3): extended follow-up of a phase 3, randomized, open-label study. Lancet Oncol. 2014;15(3):323-332

Performance

Method Description

Blood samples are collected in Streck Cell-Free DNA blood collection tubes. Cell-free DNA (cfDNA) is isolated from double-centrifuged plasma and assessed for the presence of the *BRAF* V600E and *BRAF* V600K alterations using digital droplet polymerase chain reaction.(Unpublished Mayo method)

PDF Report

No

Day(s) Performed

Varies

Report Available
5 to 10 days

Specimen Retention Time
Whole blood: 2 weeks (if available); Extracted DNA: 3 months

Performing Laboratory Location
Mayo Clinic Laboratories - Rochester Main Campus

Fees & Codes

Fees
- Authorized users can sign in to Test Prices for detailed fee information.
- Clients without access to Test Prices can contact Customer Service 24 hours a day, seven days a week.
- Prospective clients should contact their account representative. For assistance, contact Customer Service.

Test Classification
This test was developed and its performance characteristics determined by Mayo Clinic in a manner consistent with CLIA requirements. It has not been cleared or approved by the US Food and Drug Administration.

CPT Code Information
81210

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
BRAFB	cfDNA BRAF V600 Test, Blood	93690-6

Result ID	Test Result Name	Result LOINC® Value
48044	Result Summary	50397-9
48045	Result	93690-6
48046	Interpretation	69047-9
48047	Additional Information	48767-8
48048	Specimen	31208-2
48049	Source	31208-2
48050	Released By	18771-6
606201	Method	85069-3
606202	Disclaimer	62364-5