

Mutation-Specific Therapy Selection

Expanded Panel

BRAF V600E/K/D in MELANOMA

Identify 10-15% More Patients Who May Respond to Vemurafenib

Our BRAF V600E/K/D Mutation Test identifies up to 65% of melanomas as potentially responsive to BRAF-inhibitor therapy.

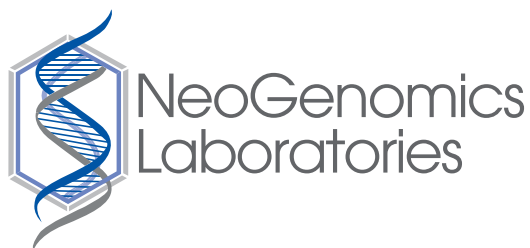
Melanoma treatment advanced significantly in August 2011 with the FDA's approval of ZELBORAF® (vemurafenib) for patients with metastatic or inoperable tumors that carry the BRAF-activating V600E mutation. Patients carrying the V600K mutation have also shown response to vemurafenib,¹ and pre-clinical studies demonstrate effect against the V600D mutation in vitro.² V600E occurs in ~50% of melanomas, V600K in at least 10%, and V600D in <5%.³

NeoGenomics provides rapid diagnostic testing in paraffin-embedded melanoma tumors for all three activating mutations to identify more patients for whom vemurafenib therapy can be considered.

- **Testing these additional mutations increases identification of potential candidates for drug therapy from ~50% to ~65%.**
- **Assay sensitivity of ≥1% abnormal DNA surpasses other commercially-available tests and improves mutation detection in samples with low tumor burden.**
- **Specific detection and differentiation of the three mutations allows better estimate of likelihood of drug response.**

Supporting Research

Drug approval was largely due to the success of the BRIM-2 and BRIM-3 trials which showed vemurafenib to be the first single drug to improve response rates, progression-free survival, and overall survival compared to standard chemotherapy in metastatic melanoma.^{1,4} Patients in both studies tested positive for BRAF V600 mutations and approximately half responded to vemurafenib. Some were later shown to carry the V600K mutation instead of V600E. These patients showed a range of response from none to excellent,^{3,5} and in the major study, 4/10 showed partial response.¹ Data about clinical response in V600D-positive melanomas are not yet available. However, in vitro studies show BRAF pathway-specific growth inhibition in V600D cell lines and suggest clinical sensitivity.²



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www.neogenomics.com

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NeoGenomics Laboratories' BRAF V600E/K/D Mutation Test is a highly sensitive, extensively validated lab-developed test for detection of BRAF-activating mutations in melanoma.

Assay description: Allele-specific real-time PCR provides qualitative detection of the V600E (c.1799T>A) mutation by selective amplification of mutant alleles.

Sensitivity: This PCR-based assay is designed to detect 1% or more mutant DNA in a background of wildtype DNA.

Specimen requirements: Formalin-fixed paraffin embedded block. Preferred tumor size in block is 3x3 mm or more.

TAT: 7 days

Tech-only option: Clients may perform and bill for the professional component of microdissection (88381-26) by circling the area of interest on an H&E slide. Please try to enrich to at least 40% tumor and write the percent tumor on the slide. Note "Tech only" on the requisition.

Companion diagnostic policy: In the unlikely event ZELBORAF® coverage or prior authorization for coverage is denied for a V600E-positive patient because of the lab-developed nature of the test, NeoGenomics will immediately refer the positive case to a partner laboratory for re-analysis with an FDA-approved test. NeoGenomics will cover any additional costs associated with this testing. Negative cases and V600K or V600D-positive cases will be reported and not be sent for further testing.

NCCN Guidelines support either FDA-approved testing or testing in a CLIA-approved facility.⁶ NeoGenomics has full CLIA certification.

Molecular Genetics (by PCR or RT-PCR)		
<input type="checkbox"/> KRAS / BRAF	<input type="checkbox"/> B&T Cell Gene Rearrangement	<input type="checkbox"/> JAK2 V617F (Quant.)
<input checked="" type="checkbox"/> BRAF	<input type="checkbox"/> B Cell Gene Rearrangement	<input type="checkbox"/> JAK2 Exon 12 (Qual.)
<input type="checkbox"/> EGFR	<input type="checkbox"/> T Cell Gene Rearrangement	<input type="checkbox"/> MPL W515 (Qual.)
<input type="checkbox"/> KRAS	<input type="checkbox"/> PML/RARA	<input type="checkbox"/> FLT3 Mutation Analysis
<input type="checkbox"/> BCR/ABL (Quant.)	<input type="checkbox"/> MPN Reflex Panel (Qual.) (JAK2 V617F, JAK2 Exon 12, MPL W515)	<input type="checkbox"/> NPM1 Mutation Analysis
<input type="checkbox"/> BCR/ABL (Qual.)		<input type="checkbox"/> CEBPA Mutation Analysis
<input type="checkbox"/> BCL-1 (CCND1)		
<input type="checkbox"/> BCL-2		

Other: **V600E/K/D**

Sample Requisition

Other: **V600E/K/D - Tech Only**

Tech Only Sample

BRAF is a kinase member of the RAS-RAF-MAPK signaling pathway that promotes cell proliferation and survival. Mutations at position V600 lead to constitutive activation of the pathway and result in abnormal cell growth.

Vemurafenib inhibits several kinases, but its most potent effects are specific to BRAF V600-mutated cells.⁵

References:

1. Chapman PB, Hauschild A, Robert C, et al. N Engl J Med. 2011;364(26):2507-16.
2. Yang H, Higgins B, Kolinsky K, et al. Cancer Res. 2010;70:5518-5527.
3. Rubinstein JC, Sznol M, Pavlick AC, et al. J Transl Med. 2010;8:67.
4. Ribas A, Kim KB, Schuchter LM, et al. J Clin Oncol. 2011;29:Suppl:8509. Abstract.
5. Bollag G, Hirth P, Tsai J, et al. Nature. 2010;467(7315):596-599.
6. NCCN Guideline on melanoma, version 2.2012, page ME-E#1. http://www.nccn.org/professionals/physician_gls/f_guidelines.asp. Accessed October 28, 2011.

