

# KIT Mutation Analysis in Melanoma

## DETECTION OF KIT MUTATIONS TO PREDICT PATIENT RESPONSIVENESS TO GLEEVEC<sup>®</sup>

### Test Highlights

- Molecular analysis of formalin-fixed, paraffin-embedded melanoma tissue to detect activating mutations in *KIT* exons 9, 11, 13, and 17.
- Useful for predicting patient response to tyrosine kinase inhibitors (Gleevec).

### Disease Overview

- Melanoma is a malignant tumor arising from pigment-producing melanocytes in the skin, eye, or mucosal surfaces.
- Diagnosis is based primarily on histology and can be challenging.
- The pathogenesis of melanoma is not entirely elucidated but recent discoveries indicate that melanoma is quite heterogeneous.
- The genetic alterations that contribute to oncogenesis vary among melanoma subtypes and tumor location. *BRAF* mutations are most common in cutaneous melanomas derived from intermittent sun-exposed skin, while *KIT* mutations are more common in mucosal and acral melanomas.
- Molecular testing to identify these genetic alterations aids in melanoma diagnosis and therapeutic decisions.

### Epidemiology

- An estimated 68,720 new melanoma cases were reported in the United States in 2009.
- An estimated 8,650 deaths from melanoma occurred in the United States in 2009.

### Genetics

- Recent discoveries have implicated *KIT*, a receptor tyrosine kinase, in the pathogenesis of some melanomas.
- *KIT*-activating mutations, which stimulate ligand-independent cellular signaling, have been reported in mucosal melanomas (15–27 percent), acral melanomas (9–23 percent), and chronic sun-damaged melanomas (2–16 percent).
- In melanoma, 69 percent of *KIT*-activating mutations occur in exon 11 (juxtamembrane region), and are predicted to respond favorably to the tyrosine kinase inhibitor Gleevec.

### Indications for Ordering

Patients diagnosed with or suspected of having melanoma based on histology, especially those with lesions located in mucosal and acral surfaces.

### Interpretation

The presence of an activating *KIT* mutation predicts the probability of patient response to Gleevec.

### Methodology

- DNA is extracted from formalin-fixed, paraffin-embedded tumor tissue.
- Real-time PCR is used to amplify *KIT* exons 9, 11, 13, and 17.
- High-resolution amplicon melting analysis scans for mutations, which are confirmed by sequencing.

### Limitations

- Samples must contain at least 50 percent tumor and have sufficient tissue for analysis.
- Results of this test should always be interpreted within the clinical context and other relevant data, and should not be used alone for a diagnosis of malignancy.

### References

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2. Erali M, Voelkerding KV, Wittwer CT. High resolution melting applications for clinical laboratory medicine. *Exp Mol Pathol* 2008;85(1):50–58.
3. Duffaud F. and Le Cesne A. Imatinib in the treatment of solid tumors. *Target Oncol* 2009;4(1):45–56.
4. Garrido MC and Bastian BC. *KIT* as a therapeutic target in melanoma. *Invest Dermatol* 2010;130(1):20–27.
5. Blokk WAM, Van Dijk M, Ruiters DJ. Molecular cytogenetics of cutaneous melanocytic lesions—diagnostic, prognostic and therapeutic aspects. *Histopathology* 2010;56:121–32.

## Test Information

**2002695**

**KIT Mutations, Melanoma**

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For information on test selection, ordering, and interpretation, refer to ARUP Consult® at [www.arupconsult.com](http://www.arupconsult.com).