

March 29th, 2019

Re: New *KIT* D816V/F test at BC Cancer CGL

Dear all,

This letter is to update you on the Cancer Genetics and Genomics Laboratory's new test for detection of the *KIT* D816V and D816F mutations. *KIT* D816 status aids in the diagnosis of mastocytosis and is listed as one of the minor criteria according to the 2016 World Health Organization.(1) In addition it is a theranostic biomarker as it provides prognostic and predictive information for treatment with tyrosine kinase inhibitors (TKIs). *KIT* D816 status is also important in favourable or good risk acute myeloid leukemia providing prognostication to patients diagnosed with core-binding factor AML associated with either inv(16) or t(8;21) alterations.(2-3)



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How has the *KIT* D816 assay changed?

Previously, analysis of codon 816 of the *KIT* gene was performed by Sanger sequencing. This assay had a deemed limit of detection (LOD) of approximately 15%.

The new test is a quantitative PCR (qPCR) based assay that uses allele-specific primers to detect the nucleotide transition c.2447A>T in the *KIT* gene that is associated with *KIT* p.D816V (c.2447A>T) and p.D816F (c.2446_2447GA>TT) mutations. It has been validated to have a reliable LOD of 0.02%. The improvement in the LOD offered by this new test is important, especially in aiding in the diagnosis of mastocytosis, where the neoplastic mast cell burden can often be very low.

What specimens are accepted for testing?

The *KIT* D816V/F assay can be used to test DNA from the following sample types:

1. Fresh peripheral blood specimen
2. Fresh bone marrow aspirate
3. Methanol acetic acid (MAA) fixed specimen from peripheral blood or bone marrow aspirate.

What will the common results be?

Positive – A *KIT* D816V/F mutation was detected in the DNA from the specimen.

Negative – A *KIT* D816V/F mutation was NOT detected in the DNA from the specimen.

Fail – The quantity and/or quality of DNA was insufficient to obtain a result from the test.

References:

- (1) Valent, P. et al. Mastocytosis: 2016 updated WHO classification and novel emerging treatment concepts. *Blood* 2017;129(11):1420-1427.
- (2) Yui, S. et al. The Prognostic Impact of *KIT* D816 Mutations in Core Binding Factor Acute Myeloid Leukemia. *Blood* 2016;128(22):2785.
- (3) Chen, W. et al. Prognostic Significance of *KIT* Mutations in Core-Binding Factor Acute Myeloid Leukemia: A Systematic Review and Meta-Analysis. *PLOS ONE* 11(1): e0146614. <https://doi.org/10.1371/journal.pone.0146614>