BC CANCER
Provincial Health Services Authority

September 17th, 2019

Re: New *FLT3* ITD and TKD test at BC Cancer CGL

Dear all,

This letter is to update you on the Cancer Genetics and Genomics Laboratory's test for detection of Fms-related tyrosine kinase 3 gene (*FLT3*) Internal Tandem Duplications (ITD) and Tyrosine Kinase Domain (TKD) mutations in newly diagnosed Acute Myeloid Leukemia (AML) patients. *FLT3* ITD and TKD mutations have been found to occur in 25% and 7-10% of adults with newly diagnosed AML, respectively (1,2). AML patients diagnosed with *FLT3* ITD and/or TKD mutations may qualify for midostaurin during induction and consolidation therapy (2). CGL will have the results of the *FLT3* ITD and TKD test available within 6 days post specimen receipt, barring exceptional circumstances.

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How has *FLT3* testing changed?

Previously, samples were tested for *FLT3* ITD mutations by fragment analysis and only the presence or absence of an ITD was reported. The new assay continues to test for *FLT3* ITD mutations using the same method; however, for positive cases, the report will now include the allelic fraction of the ITD as well as ITD length. The performance characteristics of the *FLT3* ITD assay remain unchanged.

The *FLT3* test is now also able to detect TKD mutations using a droplet digital PCR (ddPCR) assay. The assay has been specifically designed to detect both common and rare TKD mutations in codons 835 and 836 and has a stated reliable LOD of 1%. The assay can also specifically identify the three most common *FLT3* TKD mutations being p.D835Y (c.2503G>T); p.D835V (c.2504A>T) and p.D835H (c.2503G>C). While other mutations in codons D835/I836 may be detected, these will not be identified.

What specimens are accepted for testing?

The *FLT3* ITD and TKD test can be performed on the following sample types:

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

What will the common results be?

Qualitative results (i.e. positive, negative, analysis failed, etc.) will be reported for both the *FLT3* ITD and TKD assays in a tabulated format, with corresponding quantitative values (i.e., allele fraction, ITD length and/or identity of *FLT3* TKD mutations) included for positive cases.

References:

(1) Daver, N. et al. Targeting *FLT3* mutations in AML: review of current knowledge and evidence. *Leukemia* 2019;33:299-312.

(2) Stone, R.M. et al. Midostaurin plus Chemotherapy for Acute Myeloid Leukemia with a *FLT3* Mutation. *NEJM* 2018;377:454-64.