BCR-ABL Quantitative Analysis

Versiti offers sensitive detection of *BCR-ABL* p210 and p190 translocations reported on the International Scale. The Philadelphia (Ph) chromosome translocation t(9;22) is found in >95% of patients with CML. It is also found in 10-20% of adults and 2-5% of children with ALL and more rarely in AML, lymphoma and myeloma. The BCR-ABL protein has increased tyrosine kinase activity that is implicated in the malignant transformation of hematopoietic cells. In the majority of cases the breakpoint is located in the major breakpoint cluster region resulting either the e14a2 (b3a2) or e13a2 (b2a2) variants that give rise to the p210 BCR-ABL protein. The minor breakpoint, e1a2, gives rise to the p190 BCR-ABL protein and is more common in Philadelphia positive(Ph+) ALL.[1,2,4]

Versiti *BCR-ABL* Quantitative Analysis (order#4502) provides International Scale reporting of these major and minor breakpoints. Other rare breakpoints such as b3a3, b2a3, e19a2 have been reported and can be detected with the Versiti *BCR-ABL* Breakpoint Analysis add-on (order#4504).

Indications for testing:

- Identification of Ph+ hematologic malignancy at diagnosis or relapse
- Quantitative minimal residual disease detection in Ph+ malignancy
- Monitoring tyrosine kinase inhibitor therapy
- *BCR-ABL* Breakpoint Analysis can be used to rule-out the presence of rare breakpoints at diagnosis or relapse and it is recommended to order both tests together.

The quantitative *BCR-ABL* RNA assay is used to monitor minimal residual disease in Ph+ CML or ALL patients being treated with tyrosine kinase inhibitors (TKI). Levels of *BCR-ABL* are reported on a standardized International Scale (IS). On the IS, a major molecular response (MMR) represents a 3-log reduction in *BCR-ABL* and is defined as ≤0.1%IS.[5]

Achievement of MMR is associated with durable long term cytogenetic remission and a lower rate of disease progression. High or rising *BCR-ABL* levels may indicate the possible relapse or the presence of TKI-resistant mutations.

Test method:

***BCR-ABL* Quantitative Analysis:** Reverse transcription of total RNA followed by real-time polymerase chain reaction to measure the b3a2, b2a2, and e1a2 *BCR-ABL* fusion transcripts using gene-specific hydrolysis probes. Endogenous ABL is used as a reference to report a percent relative ratio of *BCR-ABL* to ABL as well as to assess RNA quality.[3] The percent *BCR-ABL* results are converted to the International Scale (IS) using a calibrator. Alternate breakpoints are not detected by the quantitative assay.

***BCR-ABL* Breakpoint Analysis:** *BCR-ABL* breakpoint is performed using capillary electrophoresis. Breakpoints detected are: b3a2, b2a2, e1a2, b3a3, b2a3 and e19a2.

Assay sensitivity and limitations:

Sensitivity of the quantitative assay for p210 & p190 is 0.003% on the International Scale representing a 4.5 log reduction in the *BCR-ABL* translocation. *BCR-ABL* Breakpoint Analysis of rare breakpoints can be detected if above 0.1%IS.

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Reporting of results:

***BCR-ABL* Quantitative Analysis:** Order#4502

Reference Interval: Positive, Not detected, Not reportable.
If positive, percent BCR-ABL: ABL ratio will be reported based on International Scale (%IS).
Log-Fold Reduction will also be reported.
If Not reportable, commentary will be included.

***BCR-ABL* Breakpoint Analysis:** Order#4504

Reference Interval: Positive or Not detected.
If positive, the specific breakpoint transcript will be reported.
If Not reportable, commentary will be included.

Specimen requirements:

10 ml of peripheral blood drawn in EDTA (lavender top) tubes. Bone marrow is also an acceptable sample, but a minimum of 3-5 ml is required. Sample should be shipped at room temperature and must be received within 48 hours of being drawn.

SHIP

Shipping requirements:

Place the room temperature specimen and requisition in plastic bags, seal and insert in a Styrofoam container. Seal the Styrofoam container, place in a sturdy cardboard box and tape securely. Ship the package in compliance with your overnight carrier guidelines. Address package to:

Versiti Client Services
Molecular Oncology & Genetics Laboratory
638 N. 18th St.
Milwaukee, WI 53233-2121
800-245-3117, ext. 6250

ORDER

Required forms:

Versiti Molecular Oncology Requisition

CPT Codes/Billing/Turnaround time:

Test Code: 4502

CPT code: For recommended CPT codes, visit the versiti.org/test-catalog

Turnaround Time: 3-6 days

References:

1. Hughes T, Hochhaus A, Branford S, et al. Long-term prognostic significance of early molecular response to imatinib in newly diagnosed chronic myeloid leukemia: an analysis from the International Randomized Study of Interferon and STI571 (IRIS). Blood 2010; 116:3758-3765
2. Press RD, Love Z, Tronnes AA, et al. *BCR-ABL* mRNA levels at and after the time of a complete cytogenetic response (CCR) predict the duration of CCR in imatinib mesylate-treated patients with CML. Blood 2006; 107:4250-4256
3. Hessner MJ, Roth MS, et. al. Development of a sensitive, highly controlled assay for molecular detection of the Philadelphia chromosome in patients with chronic myelogenous leukemia. Genetic Analysis: Biomolecular Engineering 1994;11(4):90-4
4. Melo JV, Gordon DE, et. al. Expression of the ABL- BCR fusion gene in Philadelphia-positive acute lymphoblastic leukemia. Blood. 1993; 81: 2488-2491.
5. NCCN Guidelines; Chronic Myelogenous Leukemia http://www.nccn.org/professionals/physician_gls/pdf/cml.pdf

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