BCR-ABL1 (BCR::ABL1) Qualitative and Quantitative Testing

BCR::ABL1 (*BCR-ABL1*) quantitative testing is recommended for patients with either chronic myeloid leukemia (CML), a hematopoietic stem cell disease, or acute lymphoblastic leukemia (ALL), an aggressive type of leukemia of either B- or T-lineage immature lymphoid cells. In CML, identification of *BCR::ABL1* fusion genes is used for diagnosis and ongoing therapeutic monitoring. In ALL, *BCR::ABL1* fusion identification and quantification are used for risk stratification and treatment decisions. *BCR::ABL1* fusion quantification is used for minimal residual disease (MRD) assessment of Philadelphia chromosome positive (Ph+) ALL.

Massively parallel sequencing (MPS) is used to identify mutations that may interfere with the effectiveness of tyrosine kinase inhibitor (TKI) therapy and to further inform the management strategy in CML and a subset of ALL patients.

Tests to Consider

Diagnostic Qualitative BCR-ABL1 Assay with Reflex to p190 or p210 Quantitative Assays 3005839

Method: Reverse Transcription Polymerase Chain Reaction

- Recommended when submitting initial diagnostic specimen for CML or ALL when the *BCR::ABL1* fusion form is not known (no previous *BCR::ABL1* testing performed) or is unclear
- If the qualitative test is positive for the presence of the common fusions transcripts of p210 (major breakpoint) or p190 (minor breakpoint), then the corresponding quantitative test is performed.

Quantitative Detection of BCR-ABL1, Major Form (p210) 3005840

Method: Reverse Transcription Polymerase Chain Reaction

- Appropriate for the monitoring of individuals with CML or Ph+ ALL
- *BCR::ABL1* major (p210) fusion form is present in almost all cases of CML and in a subset of ALL cases (e13a2 or e14a2 transcripts)

BCR-ABL1, Minor (p190), Quantitative 2005016

Method: Quantitative Reverse Transcription Polymerase Chain Reaction

Appropriate for monitoring of individuals diagnosed with Ph+ ALL or CML to quantify the *BCR::ABL1* p190 fusion form

See Related Tests

Typical Testing Strategy

Chronic Myeloid Leukemia

- Bone marrow cytogenetic studies and qualitative reverse transcription polymerase chain reaction (RT-PCR) and quantitative RT-PCR (qRT-PCR) measurement of *BCR::ABL1* transcript levels are recommended before treatment initiation.
- qRT-PCR is used to monitor response to TKI therapy and detection of MRD.
- *BCR::ABL1* kinase domain variant analysis (MPS) is useful to detect variants which result in resistance to TKI therapy and is commonly seen in disease progression and refractory diseases.

Acute Lymphoblastic Leukemia

- Evaluation for the presence of recurrent genetic abnormalities at diagnosis using karyotyping and/or fluorescence in situ hybridization (FISH) assays
- MRD assessment on bone marrow using flow cytometry and qRT-PCR at the completion of therapy and at regular intervals to monitor progress

Disease Overview

Chronic Myeloid Leukemia

Incidence

- 2.6/100,000 in the United States[1]
- Represent 15% of all adult leukemias[1]
- Median age of onset is 67 years

Acute Lymphoblastic Leukemia

Incidence

- 1.8/100,000 in the U.S.[2]
- 75-80% of acute leukemias in children
- 20% of adult leukemias

Treatment Issues

The goal of TKI therapy is to achieve a complete cytogenetic response within 12 months of initiation of therapy with the goal of eventual major molecular response (*BCR::ABL1* transcripts below 0.1% IS, MR3.0). A subset of individuals will eventually achieve a deep or complete molecular response (*BCR::ABL1* transcripts below 0.0032% international scale [IS], MR4.5).

Prognostic Issues

A 3-log decrease in the level of *BCR::ABL1* fusion transcripts (major molecular response) within 18 months of beginning TKI therapy is an indicator of a favorable outcome. Monitoring for recurrence using quantitative measures is crucial for detecting MRD and early relapse.

Genetics

Gene

BCR::ABL1 (*BCR-ABL1*)

Variants

- >130 variants
- Four regions tested
  - Adenosine triphosphate binding-loop (P-loop)
  - Drug-binding sites
  - Catalytic domain
  - Activation loop

Test Interpretation

BCR-ABL1, Major (p210), Quantitative

Analytic Sensitivity

Limit of detection: 0.0032% IS

Results

Result	Variant(s) Detected	Interpretive Data
Detected	*BCR::ABL1* fusion transcripts (p210) detected	*BCR::ABL1* IS is reported
Detected above LOQ	*BCR::ABL1* fusion transcripts (p210) detected above LOQ	*BCR::ABL1* IS is above 50%
Weakly positive	*BCR::ABL1* fusion transcripts detected below the limit of quantitation	*BCR::ABL1* to *ABL1* IS result is between 0.002% to 0.0032%, cannot be quantified
Not detected	No *BCR::ABL1* fusion transcripts detected	Does not exclude *BCR::ABL1* fusion transcripts (p210) below the test limit of detection (IS below 0.002%) Does not exclude *BCR::ABL1* fusion transcripts not detected by this test (p190 or p230)

LOQ, limit of quantification

Limitation

Does not detect p190, p230, or rare variants of p210 forms

BCR-ABL1, Minor (p190), Quantitative

Analytic Sensitivity

1:125,000 normal cells (chart)

Results

Result	Variant(s) Detected	Interpretive Data
Positive	*BCR::ABL1* fusion transcripts (p190) detected	*BCR::ABL1*/*ABL1* quantitative ratio is provided by an NCN
Weakly positive	*BCR::ABL1* fusion transcripts (p190) detected below the limit of quantitation	*BCR::ABL1* to *ABL1* NCN ratio cannot be calculated
Not detected	No *BCR::ABL1* fusion (p190) transcripts detected	Does not exclude *BCR::ABL1* fusion transcripts (p190) below the test limit of detection Does not exclude *BCR::ABL1* fusion transcripts that are not detected by this test (p210 or p230)

NCN, normalized copy number

Limitation

Does not detect p230 or p210

References

1. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Chronic myeloid leukemia. Version 2.2021. [Updated: Feb 2021; Accessed: Sept 2022]
2. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Acute lymphoblastic leukemia. Version 2.2021. [Updated Feb 2021; Accessed: Sept 2022]

Related Information

Acute Lymphoblastic Leukemia - ALL
Chronic Myelogenous Leukemia - CML

Related Tests

Acute Lymphoblastic Leukemia (ALL) Panel by FISH, Adult 2002647

Method: Fluorescence in situ Hybridization (FISH)

Acute Lymphoblastic Leukemia (ALL) Panel by FISH, Pediatric 2002719

Method: Fluorescence in situ Hybridization (FISH)

BCR-ABL1 Mutation Analysis for Tyrosine Kinase Inhibitor Resistance by Next Generation Sequencing 2008420

Method: Massively Parallel Sequencing

Chromosome FISH, Interphase (Temporary Delay as of 09/21/21) 2002298

Method: Fluorescence in situ Hybridization (FISH)

Imatinib 3000539

Method: Immunoturbidimetry

Myeloid Malignancies Mutation Panel by Next Generation Sequencing 2011117

Method: Massively Parallel Sequencing

Thiopurine Metabolites by LC-MS/MS 2014484

Method: Quantitative Liquid Chromatography/Tandem Mass Spectrometry

Thiopurine Methyltransferase, RBC 0092066

Method: Enzymatic/Quantitative Liquid Chromatography-Tandem Mass Spectrometry

TPMT and NUDT15 3001535

Method: Polymerase Chain Reaction/Fluorescence Monitoring

ARUP Laboratories is a nonprofit enterprise of the University of Utah and its Department of Pathology. 500 Chipeta Way, Salt Lake City, UT 84108
(800) 522-2787 | (801) 583-2787 | aruplab.com | arupconsult.com
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