Ph-Like Acute Lymphoblastic Leukemia Panel by FISH

Indications for Ordering

- Recommended FISH panel for individuals suspected of having BCR-ABL1-like B-cell acute lymphoblastic leukemia (B-ALL) (Ph-like ALL)
- Order when other major prognostic markers (e.g., BCR-ABL1, ETV6/RUNX1) are negative
- Aid in diagnosis of BCR-ABL1-like B-ALL with chromosomal rearrangement involving CRLF2, JAK2, EPOR, CSF1R, ABL1, ABL2, PDGFRB
- Provide risk stratification and therapeutic management of patients with BCR-ABL1-like B-ALL

Test Description - Methodology

- Performed on bone marrow (BM) or peripheral blood cells on unstimulated cultures from either direct harvest or 24-hour culture
- Multiple fluorescence in situ hybridization (FISH) probes target specific genes

Tests to Consider

Primary test(s)

**Ph-Like Acute Lymphocytic Leukemia (ALL) Panel by FISH 3000455**

- Diagnosis, prognosis, and monitoring of BCR-ABL1-like B-ALL
- Probes included in this panel
  - CRLF2 rearrangement
  - JAK2 rearrangement
  - EPOR rearrangement
  - CSF1R rearrangement
  - ABL1 rearrangement
  - ABL2 rearrangement
  - PDGFRB rearrangement
- To order probes individually, see Chromosome FISH, Interphase

Related test(s)

**Leukemia/Lymphoma Phenotyping Evaluation by Flow Cytometry 3001780**

- Aid in evaluation of hematopoietic neoplasms
- Monitor therapy in patients with established diagnosis of hematopoietic neoplasms

**Chromosome Analysis, Bone Marrow 2002292**

- Diagnosis, prognosis, and monitoring of hematopoietic neoplasms

Chromosome Analysis, Bone Marrow with Reflex to Genomic Microarray 2007130

- Diagnosis, prognosis, and monitoring of hematopoietic neoplasms
- Microarray performed when karyotype results are reported as "normal" or "no growth"

Cytogenomic SNP Microarray – Oncology 2006325

- Preferred test for fresh specimens at time of diagnosis to detect prognostically important genomic abnormalities in leukemias/lymphomas and solid tumors involving
  - Loss/gain of DNA
  - Loss of heterozygosity (LOH)
- Monitor disease progression and response to therapy

Acute Lymphocytic Leukemia (ALL) panel by FISH, Pediatric 2002719

- Risk stratification and therapeutic management in children with newly diagnosed B-ALL

Acute Lymphocytic Leukemia (ALL) panel by FISH, Adult 2002647

- Risk stratification and therapeutic management in adults with newly diagnosed B-ALL

Chromosome FISH, Interphase 2002298

- Use to order individual or multiple FISH probes if standard FISH panels are not desired
- Specific FISH probes must be requested
  - CRLF2
  - JAK2
  - EPOR
  - CSF1R
  - ABL1
  - ABL2
  - PDGFRB

Disease Overview

Incidence

- B-ALL occurs in 1.6/100,000 individuals per year
- BCR-ABL1-like ALL (Ph-like ALL) occurs in
  - 10% of children with standard-risk B-ALL
  - 15% of children with NCI-defined, high-risk B-ALL
  - 21% of adolescents with B-ALL
  - 27% of young adults with B-ALL
  - 20% of adults with B-ALL
Treatment issues
● Clinical trials being developed to test hypothesis that treatment with ABL-class fusions (ABL1, ABL2, PDGFRB, CSF1R rearrangement) with tyrosine kinase inhibitors will greatly improve typically poor outcome
● Patients with JAK translocations (CRLF2, JAK2, EPOR rearrangement) may be candidates for treatment with JAK inhibitors

Prognostic issues
Overall, patients with BCR-ABL1-like ALL have a poor prognosis.

Genetics

Genes – CRLF2, JAK2, EPOR, CSF1R, ABL1, ABL2, PDGFRB

Structure/Function
● CRLF2 rearrangement
  o Results from either an interstitial deletion within Xp22.3 or Yp11.3, which juxtaposes CRLF2 to the promoter of the P2RY8 gene or a translocation; involves IGH
  o Results in CRLF2 overexpression
  o Accounts for about half of BCR-ABL1-like ALL
● JAK2 rearrangement
  o At least 10 fusion partners have been reported
  o Results in constitutive activation of JAK/STAT pathways
  o Accounts for 15% of young adults with BCR-ABL1-like ALL and 5% of children and adolescents with BCR-ABL1-like ALL
● EPOR rearrangement
  o Results from the juxtaposition of the EPOR gene to the enhancer regions of immunoglobulin heavy or κ loci
  o Results in constitutive activation of JAK/STAT pathways
  o Accounts for 4% of BCR-ABL1-like ALL
● Rearrangements of ABL-class genes
  o CSF1R rearrangement
  o ABL1 rearrangement
  o ABL2 rearrangement
  o PDGFRB rearrangement
  o Accounts for 13% of BCR-ABL1-like ALL

Test Interpretation

Results
● Normal – no evidence of rearrangement involving CRLF2, JAK2, EPOR, CSF1R, ABL1, ABL2, or PDGFRB
● Abnormal – one of the described rearrangements detected

Limitations
● Panel detects only the specific aberrations targeted by the probes
● Chromosome alterations outside the regions complementary to these FISH probes will not be detected

References