Acute Lymphoblastic Leukemia Panel by FISH, Adult

**Indications for Ordering**

Risk stratification and therapeutic management in adults with newly diagnosed B-cell acute lymphoblastic leukemia (B-ALL)

**Test Description**

Fluorescence in situ hybridization
- FISH probes detect
  - BCR-ABL1 t(9;22)
  - KMT2A (MLL) 11q23 rearrangement (partner not determined)
  - TCF3 (E2A) rearrangement (partner not determined)
  - IGH rearrangement (partner not determined)
  - MYC rearrangement (partner not determined)
- Performed on bone marrow (BM) or peripheral blood cells on unstimulated cultures from either direct harvest or 24-hour culture

**Tests to Consider**

**Typical testing strategy**

At diagnosis, minimum ALL workup includes BM aspirate for
- Morphology
- Immunophenotyping
- Cytogenetics
- ALL panel by FISH, adult
- Ph-like ALL panel by FISH

**Primary test**

Acute Lymphocytic Leukemia (ALL) Panel by FISH, Adult 2002647
- Recommended FISH panel for adults with newly diagnosed B-ALL

**Related tests**

Leukemia/Lymphoma Phenotyping by Flow Cytometry 2008003
- Aids in 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"

**Cyto genetic 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

Ph-Like Acute Lymphocytic Leukemia (ALL) Panel by FISH 3000455
- Recommended FISH panel for individuals suspected of having BCR-ABL1-like B-ALL (Ph-Like 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
  - BCR-ABL1
  - KMT2A (MLL)
  - TCF3 (E2A)
  - IGH
  - MYC

**BCR-ABL1, Qualitative with Reflex to BCR-ABL1 Quantitative 2005010**
- Recommended when submitting initial diagnostic sample for chronic myelogenous leukemia (CML) or Ph+ ALL (no previous BCR-ABL1 testing)
- If qualitative test is positive, the appropriate corresponding quantitative test is performed

**Disease Overview**

**Incidence**

B-ALL occurs in 1.6/100,000 individuals per year

**Treatment issues**

- Treatment protocols are stratified by risk factors including the presence of t(9;22) (ie, Philadelphia chromosome status) and age
- Identification of recurrent genetic alterations helps refine individual prognosis and guide management
Prognosis | Good | Poor
--- | --- | ---
Age | Younger age
• Especially <25 years when treated with a pediatric protocol | Older age
• Individuals >60 years have a particularly poor prognosis
High WBC
• >30 x 10^9/L for B-ALL

Genetic abnormalities | \(\text{BCR-ABL1} \ t(9;22)\) positive
• \(\text{KMT2A (MLL)}\) rearrangements
• Complex karyotype (>5 chromosomal abnormalities)
• Low hypodiploidy
• Near triploidy

Test Interpretation

Results
• Normal – no evidence of \(\text{BCR-ABL1} \ t(9;22), \text{KMT2A (MLL)}\) rearrangement, \(\text{TCF3 (E2A)}\) rearrangement, \(\text{IGH}\) rearrangement, or \(\text{MYC}\) rearrangement
• Abnormal – one of the above rearrangements or translocations 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

Genetics

**Genes** – \(\text{BCR-ABL1}, \text{KMT2A (MLL)}, \text{TCF3 (E2A), IGH, MYC}\)

**Structure/function**
• \(\text{BCR-ABL1} \ t(9;22)\)
  • Results in chimeric constitutively active tyrosine kinase
  • Present in 25% of adult B-ALL
• \(\text{KMT2A (MLL)} \ t(v;11q23)\)
  • Present in 10% of adult ALL
• \(\text{TCF3 (E2A)-PBX1} \ t(1;19)\)
  • Present in 3% of adult ALL
• \(\text{IGH}\) rearrangement
• \(c\)-\(\text{MYC}\) rearrangement