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 Evaluation by Flow Cytometry 3001780**
  - 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"

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

**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**

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<th>Prognosis</th>
<th>Good</th>
<th>Poor</th>
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| 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 | • BCR-ABL1 t(9;22) positive  
  • KMT2A (MLL) rearrangements  
  • Complex karyotype (>5 chromosomal abnormalities)  
  • Low hypodiploidy  
  • Near triploidy | • BCR-ABL1 t(9;22) positive  
  • KMT2A (MLL) rearrangements  
  • Complex karyotype (>5 chromosomal abnormalities)  
  • Low hypodiploidy  
  • Near triploidy |

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**Test Interpretation**

**Results**
- Normal – no evidence of BCR-ABL1 t(9;22), KMT2A (MLL) rearrangement, TCF3 (E2A) rearrangement, IGH rearrangement, or 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

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**Genetics**

**Genes** – BCR-ABL1, KMT2A (MLL), TCF3 (E2A), IGH, MYC

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