**Acute Lymphoblastic Leukemia Panel by FISH, Pediatric**

**Indications for Ordering**
Risk stratification and therapeutic management in children 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)
  - **ETV6-RUNX1** t(12;21)
  - CEP4, CEP10
- 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, pediatric
- Ph-like ALL panel by FISH

**Primary test**
*Acute Lymphocytic Leukemia (ALL) Panel by FISH, Pediatric*
2002719
*Recommended FISH panel for children with newly diagnosed B-ALL*

**Related tests**
*Leukemia/Lymphoma Pheno typing 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”*

**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
*Risk stratification and therapeutic management of patients with BCR-ABL1-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)
  - **ETV6-RUNX1** t(12;21)

**Disease Overview**

**Incidence**
- B-ALL occurs in 1.6/100,000 individuals per year
- Most common leukemia in childhood

**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
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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 10⁹/L for B-ALL |
| Genetic abnormalities | • **ETV6-RUNX1 t(12;21)** positive  
• Hyperdiploidy with gain of chromosomes 4 and 10 | • **BCR-ABL1 t(9;22)** positive  
• **KMT2A (MLL)** rearrangements  
• **RUNX1** amplification  
• Low hypodiploidy  
• Near triploidy |

### Test Interpretation

#### Results
- Normal – no evidence of **BCR-ABL1 t(9;22)**, **KMT2A (MLL)** rearrangement, **ETV6-RUNX1 t(12;21)**, **RUNX1** amplification or copy number gain with **CEP4** and/or **CEP10**
- 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
- **BCR-ABL1**, **KMT2A (MLL)**, **ETV6-RUNX1**, **CEP4**, **CEP10**

#### Structure/function
- **BCR-ABL1** t(9;22)
  - Results in chimeric constitutively active tyrosine kinase
  - Present in ~2-4% of pediatric B-ALL
- **KMT2A (MLL)** t(v;11q23)
  - Present in 60-80% of infant B-ALL; 4-5% of non-infant pediatric B-ALL
- **ETV6-RUNX1** t(12;21)(p13;q22)
  - Present in 25-30% of pediatric B-ALL
- **RUNX1** amplification
  - Present in 2% of pediatric B-ALL
- Hyperdiploidy with gain of **CEP4** and **CEP10**
  - Present in 25% of pediatric B-ALL