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 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
- 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)

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 the 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
- 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
# Prognosis

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<th>Poor</th>
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| 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 |

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<th>Genetic abnormalities</th>
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| • 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 |

## 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

## 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