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 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)

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	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	• *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