Acute Lymphocytic Leukemia (ALL) Panel by FISH, Pediatric

Indications for Ordering

Risk stratification and therapeutic management in children with newly diagnosed ALL

Test Description

Fluorescence in situ hybridization

- FISH probes detect
  - *BCR/ABL1* t(9;22)
  - *MLL* 11q23 rearrangement (partner not determined)
  - *TEL/AML* (*ETV6/RUNX1*)
  - *CEP4, CEP10*
- Each probe can be run as part of the panel or individually
- Bone marrow (BM) cells on unstimulated cultures either from 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
  - Adjunct to conventional cytogenetics (CC)
  - Option for detecting prognostically important rearrangements

Primary test

Acute Lymphocytic Leukemia (ALL) Panel by FISH, Pediatric 2002719

- Recommended FISH panel for children with newly diagnosed 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 ALL

Chromosome Analysis, Bone Marrow with Reflex to Genomic Microarray 2007130

- Diagnosis, prognosis, and monitoring of ALL
- If chromosome analysis is “normal” or “no growth,” then genomic microarray testing will be added

Cytogenomic SNP Microarray – Oncology 2006325

- Preferred test for fresh specimens at time of diagnosis for detecting 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

Chromosome FISH, Interphase 2002298

- Specific FISH probes must be requested and include
  - *BCR-ABL1*
  - *MLL*
  - *TEL/AML* (*ETV6/RUNX1*)

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 – 1.6/100,000 individuals per year

- Most common leukemia in childhood

Treatment issues

- Treatment protocols are stratified by the presence of t(9;22) (ie, Philadelphia chromosome status) and age
- Cytogenetic studies are very important for prognostication

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-cell ALL • >100 x 10^9/L for T-cell ALL
Mutations	t(12;21) positive Hyperdiploidy with gain of chromosomes 4 and 10	t(9;22) positive *MLL* rearrangements Low hypodiploidy/near triploidy

Genetics

Genes – *BCR/ABL1*, *MLL*, *TEL/AML* (*ETV6/RUNX1*), *CEP4*, *CEP10*

Structure/function

- *BCR-ABL1* t(9;22)
  - Results in chimeric constitutively active tyrosine kinase
  - Present in ~5% of pediatric ALL
- *MLL* t(v;11q23)
  - Results in disruption of regulation of Hox gene expression
  - Present in 60-80% of infant ALL; 4-5% of non-infant ALL
- *TEL/AML* t(12;21)(p13;q22)
  - Produces transcription proteins
  - Present in 25-30% of pediatric ALL

Test Interpretation

Results

- Normal – no evidence of *BCR/ABL1* t(9;22), *MLL* rearrangement*, TEL/AML* rearrangement, 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