

# Recurrent Genetic Abnormalities in Adult B-Cell Acute Lymphoblastic Leukemia/Lymphoma (B-ALL), Detected by FISH

## Test Highlights

- This test provides significant prognostic information and supplements diagnosis in adult patients with B acute lymphoblastic leukemia (B-ALL) with recurrent genetic abnormalities. It is suitable for widespread use.
- Specific recurrent genetic changes in B-ALL can be detected by using this test. These genetic abnormalities include translocation 9;22 (*ABL1/BCR*) and rearrangement of *MLL*, *TCF3(E2A)*, and *IGH*.
- Rearrangement of the *MYC* gene has been occasionally described in adults with pre-B-ALL; the probe for the *MYC* locus can detect this chromosomal abnormality.
- FISH is more sensitive than conventional cytogenetics in detecting genomic aberrations.

## Clinical Background

- B-ALL is a malignant disease of the lymphoid cell line occurring predominantly in children and to a lesser extent in adults.
- B-ALL is frequently associated with recurrent cytogenetic abnormalities. Some of these abnormalities are associated with distinctive clinical or phenotypic properties and may also have prognostic value.
- Genetic studies are required at diagnosis not only for identifying specific genetic abnormalities but also for monitoring disease progression and response to therapy.
- Identification of recurrent specific chromosome abnormalities plays an important role in the diagnostic workup of B-ALL and can also provide significant prognostic information.
- Standard chromosome analysis (karyotypic analysis) using metaphase cells requires dividing cells and remains the gold standard for the detection of cytogenetic abnormalities. Cytogenetically visible rearrangements can sometimes be missed due to suboptimal chromosome morphology or lack of dividing cells. In a diagnostic cytogenetics laboratory, FISH analysis has several advantages over chromosome studies. It has a rapid turnaround time, detects small numbers of abnormal cells, and can be performed on nondividing (interphase) cells. In addition, FISH can detect cryptic or subtle rearrangements that might be difficult to detect by routine karyotyping. The breakapart FISH probes are designed to target the critical genes with multiple translocation partners and can detect the rearrangement of the critical gene regardless of the translocation partner; however, identifying the translocation partner correlation with chromosome studies is recommended.

## Epidemiology

The incidence of B-ALL in the United States is three in 100,000.

## Genetics

- Recurrent genetic abnormalities associated with B-ALL in adults include:
  - B-ALL with t(9;22)(q34;q11.2)(*BCR/ABL-1*)
  - B-ALL with rearrangement of 11q23 (*MLL*)
  - B-ALL with t(1;19)(q23;p13.3) [*E2A/PBX1-(TCF3-PBX1)*]
  - B-ALL with t(5;14)(q31;q32)(*IL3/IGH*)

## Tests Available

FISH panel for B-ALL with recurrent genetic abnormalities in adults:

	CHROMOSOME ABNORMALITIES	PROBE NAMES (GENES INVOLVED)	PROBE TYPE
1.	t(9;22)	ABL1/BCR	Dual fusion, tri color
2.	11q23 rearrangement	MLL *	Breakapart
3.	t(1;19)	TCF3(E2A) *	Breakapart
4.	t(5;14)(q31;q32)	IGH@ **	Breakapart
5.	t(8;14), t(2;8) or t(8;18)	MYC *	Breakapart

\*The *MYC*, *MLL*, and *E2A* genes, located on 8q24, 11q23, and 19p13.3 (respectively), have multiple translocation partners. The breakapart FISH probes for these genes can detect the rearrangement but not their translocation partners.

\*\**IL3* is the target gene on chromosome 5; however, it is not commercially available. The known translocation partner for *IL3* is *IGH* on chromosome 14. Therefore, the *IGH@* probe is used instead of the *IL3* probe.

## Indications for Ordering

This FISH panel is indicated in adult patients with B-ALL at the time of diagnosis for proper classification and prognostic information. Selected probe(s) may also be also used for follow-up studies to monitor either response to therapy or progression of the disease.

### Methodology

- Bone marrow cells on unstimulated cultures either from direct harvest or 24-hour culture are analyzed by FISH using a set of commercially available FISH probes. Each probe can be run as a panel or individually.
- The FISH probes *ABL1/BCR*, *MLL*, *TCF3(E2A)*, *IGH@*, and *MYC* are set up separately for each patient.
- At least two technologists score each case.
- 200 nuclei are evaluated for each probe.
- Bone marrow samples from 20 individuals without apparent hematological diseases and with normal karyotype were used as controls to determine the cutoff value for normal variation of the probe patterns.

### Additional Ordering Notes

- A sodium-heparin (green-top) tube with 3–4 mL of bone marrow is required.
- Samples should be stored at room temperature and transported at room temperature to the laboratory within 24 hours of draw.

### Limitations

- This probe panel only detects specific imbalances (gain or loss of DNA) and rearrangements at specific loci on the chromosomes of interest.
- Chromosome alterations outside the regions complementary to these FISH probes will not be detected.
- Few other recurrent aberrations, such as hyperdiploidy and t(12;21), are rarely present in adults with B-ALL. Additional FISH test(s) and/or chromosome analysis may be warranted to detect these abnormalities.

### References

1. Chromosomal and molecular genetic aberrations of tumor cells. In *Cancer Cytogenetics*, 3rd ed. Heim S and Mitelman F, eds. 2008; Hoboken, NJ: Wiley- Blackwell, 1–736.
2. Swerdlow SH, et al. 2008. *WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues*, 4th ed. Lyon: International Agency for Research on Cancer.

## Test Information

### 2002647 Acute Lymphocytic Leukemia (ALL) Panel by FISH, Adult

For specific collection, transport, and testing information, refer to the ARUP Web site at [www.aruplab.com](http://www.aruplab.com).

For information on test selection, ordering, and interpretation, refer to ARUP Consult® at [www.arupconsult.com](http://www.arupconsult.com).