

Lymphoma (Aggressive) Panel by FISH

Indications for Ordering

- Aid in diagnosis of aggressive large B-cell lymphoma with intermediate features between Burkitt lymphoma and diffuse large B-cell lymphoma (DLBCL)
- Confirmation of suspected double hit lymphoma

Test Description

Fluorescence in situ hybridization (FISH)

- FISH probes include
 - *MYC*
 - *IGH*
 - *BCL2*
 - *BCL6*

Tests to Consider

Typical Testing Strategy

- Lymph node biopsy with morphologic and immunohistochemical evaluation
- Leukemia/lymphoma phenotyping by flow cytometry
- In aggressive B-cell lymphomas with a high proliferation index and/or with unusual morphologic, phenotypic, or clinical features
 - Tests for *MYC*, *BCL2*, and *BCL6*

Panel Tests

[Aggressive B-Cell Lymphoma Reflex Panel by FISH, Tissue 3001495](#)

- Formalin-fixed, paraffin-embedded (FFPE) tissue specimens
- If *MYC* (8q24) Gene Rearrangement by FISH is positive, then *IGH-BCL2* Fusion, t(14;18) by FISH will be added
- If *IGH-BCL2* Fusion, t(14;18) by FISH is negative, then *BCL6* (3q27) Gene Rearrangement by FISH will be added

[Lymphoma \(Aggressive\) Panel by FISH 2002650](#)

- Bone marrow (BM) or whole blood specimens; other specimens may be acceptable
- FFPE and frozen specimens unacceptable

Individual Tests

- FFPE tissue specimens

[MYC \(8q24\) Gene Rearrangement by FISH 3001300](#)

- Detects all *MYC* rearrangements, including t(8;14), t(2;8), and t(8;22)

[IGH-MYC t\(8;14\) by FISH 3001299](#)

[IGH-BCL2 Fusion, t\(14;18\) by FISH 3001298](#)

[BCL6 \(3q27\) Gene Rearrangement by FISH 3001311](#)

Related Tests

[Leukemia/Lymphoma Phenotyping Evaluation by Flow Cytometry 3001780](#)

- Aids in diagnosis of hematopoietic neoplasms

[Chromosome FISH, Interphase 2002298](#)

- Specific probes must be requested
 - *MYC* break apart, *BCL2*, *BCL6*
- Fresh tissue specimens only

[Chromosome Analysis, Bone Marrow 2002292](#)

- Diagnosis, prognosis, and monitoring of lymphoma in BM

[Chromosome Analysis, Solid Tumor 2002296](#)

- May identify additional, useful cytogenetic abnormalities in tissues that are not targeted by FISH assays

Disease Overview

Prognostic Issues

- B-cell lymphomas with two recurrent chromosomal breakpoint aberrations are referred to as double hit lymphomas and are classified as high-grade B-cell lymphomas with *MYC* and *BCL2* and/or *BCL6* (WHO 2016)
 - Usually involve *MYC* oncogene in association with *BCL2*, less often with *BCL6*
- Lymphomas with three translocations (usually *MYC/BCL2/BCL6*) are referred to as triple hit lymphomas
 - Rare
- Important to identify these lymphomas in diagnostic evaluation of morphologically aggressive lymphomas
 - They are highly resistant to standard chemotherapy
 - Poor outcome independent of regimen intensity or inclusion of rituximab
 - Individuals have shortened survival compared with those having Burkitt lymphoma or international prognostic index (IPI)-matched DLBCL

Genetics

Breakpoints Used to Identify Double Hit or Triple Hit Lymphomas			
Oncogene	Break apart <i>MYC</i>	<i>BCL2</i>	<i>BCL6</i>
Locus	8q24	18q21	3q27
Biology	Accelerator of cell proliferation	Apoptosis inhibitor	Transcription modifier
Cytogenetics	Any <i>MYC</i> translocation	<i>BCL2/IGH</i> – t(14;18)(q32;q21)	<ul style="list-style-type: none"> <i>BCL6</i> most commonly has a non-IG translocation partner – <i>BCL6</i> (3q27) Uncommon partner – <i>BCL6/IGH</i> [t(3;14)(q27;q32)]
Specific lymphomas associated with translocation	<ul style="list-style-type: none"> Burkitt lymphoma DLBCL Aggressive B-cell lymphoma not otherwise specified (NOS) 	<ul style="list-style-type: none"> Follicular lymphoma DLBCL 	<ul style="list-style-type: none"> Follicular lymphoma DLBCL High grade lymphomas (rare)

Test Interpretation

Results

- Abnormal – t(14;18)(q32;q21) (*IGH/BCL2* translocation) or other rearrangements involving *BCL6* and/or *MYC* detected
 - Presence of two or more translocations is associated with poor prognosis in mature B-cell lymphomas
 - Single rearrangements can provide diagnostic and/or prognostic information in the appropriate context
- Normal – t(14;18)(q32;q21) (*IGH/BCL2* translocation) or other rearrangements involving *BCL6* or *MYC* not detected

Limitations

- Interpretation of results requires correlation with morphology and immunophenotype
- MYC* and/or *BCL2* overexpression can be due to other mechanisms not detected by this test
- Chromosome alterations outside probe region are not detected