IGH-MYC Fusion by FISH

Indications for Ordering

Diagnosis of Burkitt lymphoma (BL) or diffuse large B-cell lymphoma (DLBCL) with features intermediate between BL and DLBCL in conjunction with clinical, morphologic, and flow cytometric data

Test Description

**IGH-MYC** (t(8;14)) by FISH
- Fluorescence in situ hybridization (FISH)
- Tricolor, dual fusion probes detect t(8;14) or *IGH-MYC* gene rearrangement

**MYC** (8q24) Gene Rearrangement by FISH
- Fluorescence in situ hybridization (FISH)

Tests to Consider

Typical testing strategy

**BL**
- Lymph node biopsy with morphological and immunohistochemical evaluation
- Leukemia/Lymphoma Phenotyping by Flow Cytometry
  - CD5-, CD10+, CD 19/20+ suggests BL
  - CD5+, CD10+, bcl6, bcl2, high Ki67 proliferation index suggests features intermediate between BL and DLBCL
- Detect cytogenetic abnormalities, if necessary
  - *IGH-MYC* (t(8;14)) by FISH
  - *MYC* (8q24) Gene Rearrangement by FISH
- Bone marrow and CSF evaluation

**B-cell lymphoma with features intermediate between BL and DLBCL**
- Above strategy plus
  - *IGH-BCL2* Fusion, t(14;18) by FISH
  - *Lymphoma (Aggressive) Panel* by FISH

Primary tests

**IGH-MYC** Fusion (t(8;14)) by FISH 2001538
- Facilitates diagnosis of BL and B-cell lymphoma with features intermediate between BL and DLBCL
- Detects all MYC rearrangements including t(8;14), t(2;8), and t(8;22) rearrangements
  - Does not identify translocation partner
  - FFPE tissue

Related tests

**MYC (8q24) Gene Rearrangement by FISH** 2002345
- Facilitates diagnosis of BL and B-cell lymphoma with features intermediate between BL and DLBCL
- Detects all MYC rearrangements including t(8;14), t(2;8), and t(8;22) rearrangements
  - Does not identify translocation partner
  - FFPE tissue

**Leukemia/Lymphoma Phenotyping by Flow Cytometry** 2008003
- Aids in diagnosis of hematopoietic neoplasms

**IGH-BCL2 Fusion, t(14;18) by FISH** 2001536
- Most sensitive method to detect *IGH-BCL2* fusion in FFPE tissue

**Chromosome FISH, Interphase** 2002298
- Specific FISH probe t(8;14) must be requested
- Fresh tissue specimens only

**Chromosome Analysis, Bone Marrow** 2002292
- Diagnosis, prognosis, and monitoring of hematopoietic neoplasms
- Fresh tissue specimens only

**Chromosome Analysis, Solid Tumor** 2002296
- May identify additional, useful cytogenetic abnormalities in tissues that are not targeted by FISH assays

**Lymphoma (Aggressive) Panel by FISH** 2002650
- Aid in diagnosis/prognostication for aggressive morphology and unclear features between BL and DLBCL
- Probes detect MYC, BCL2, IGH, BCL6
- Fresh tissue specimens only
Disease Overview

Diagnostic issues
- BL is often diagnosed using the combination of morphology, immunohistochemistry, immunophenotyping, and clinical presentation
  - Cytogenetic testing may be necessary if morphology has aggressive features and the BL categorization cannot be made
  - IGH-MYC t(8;14) and MYC t(8q24) gene rearrangement by FISH may be useful when the above combination does not yield a diagnosis
- B-cell lymphomas with features intermediate between BL and DLBCL
  - These lymphomas have recurrent chromosomal breakpoint aberrations
    - B-cell lymphomas with 2 recurrent chromosomal breakpoint aberrations are referred to 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 3 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
    - Highly resistant to standard chemotherapy
    - Poor outcome independent of regimen intensity or inclusion of rituximab
  - Individuals have shortened survival compared with those having BL or international prognostic index (IPI)-matched DLBCL

Genetics

Gene – MYC

Translocations
  - IGH-MYC t(8;14), IGK-MYC t(2;8), IGL-MYC t(8;22)
    - Translocations involving MYC are characteristic but not specific for BL
    - IGH-MYC t(8;14) most common translocation
    - Other nonimmunoglobulin transcription partners have been identified

Test Interpretation

IGH-MYC t(8;14) by FISH

Results
- Positive – presence of the IGH-MYC t(8;14) translocation supports a diagnosis of BL or B-cell lymphomas with features intermediate between BL and DLBCL, depending on clinical presentation, morphology, and immunophenotyping
- Negative – absence of the IGH-MYC t(8;14) translocation

Limitations
- Negative result does not rule out BL or B-cell lymphomas with features intermediate between BL and DLBCL involving MYC with other translocation partners, such as t(2;8) or t(8;22)
- IGH-MYC t(8;14) by FISH has not been validated for tissue fixed in alcohol-based or nonformalin fixatives
- MYC is not specific for BL or B-cell lymphomas with features intermediate between BL and DLBCL

MYC (8q24) Gene Rearrangement by FISH

Results
- Positive – presence of the IGH-MYC translocation supports a diagnosis of BL or B-cell lymphomas with features intermediate between BL and DLBCL
- Negative – absence of any MYC rearrangements

Limitations
- Negative result does not rule out BL or B-cell lymphomas with features intermediate between BL and DLBCL
- MYC (8q24) gene rearrangement by FISH has not been validated for tissue fixed in alcohol-based or nonformalin fixatives
- MYC is not specific for BL or B-cell lymphomas with features intermediate between BL and DLBCL