IGH-MYC Fusion t(8;14) 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 Fusion 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
- 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 3001299
- Facilitates diagnosis of BL and B-cell lymphoma with features intermediate between BL and DLBCL
- Formalin-fixed, paraffin-embedded (FFPE) tissue

MYC (8q24) Gene Rearrangement by FISH 3001300
- 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

Leukemia/Lymphoma Phenotyping Evaluation by Flow Cytometry 3001780
- Aids in diagnosis of hematopoietic neoplasms

IGH-BCL2 Fusion, t(14;18) by FISH 3001298
- 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 two 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 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
    - 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 non-formalin 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 non-formalin fixatives
- *MYC* is not specific for BL or B-cell lymphomas with features intermediate between BL and DLBCL