

IGH-CCND1 Fusion, t(11;14) in Mantle Cell Lymphoma

Indications for Ordering

Diagnosis of mantle cell lymphoma (MCL) particularly when individual presents with

- Atypical morphology
- Aberrant immunophenotype
- Unusual clinical presentation
- Equivocal cyclin D1 staining

Test Description

Cyclin D1

- Immunohistochemistry

IGH-CCND1 Fusion, t(11;14) by FISH

- Fluorescence in-situ hybridization (FISH)
- Dual color, dual fusion probes detect t(11;14)

Tests to Consider

Typical testing strategy

Lymph node biopsy with morphologic and immunohistochemical evaluation

- Cyclin D1
 - Surrogate marker for t(11;14)
 - Present in 97% of MCL cases

Leukemia/lymphoma phenotyping by flow cytometry

- CD5+, CD10- in combination with bright CD20, CD23-, and high light-chain intensity suggests MCL

Detect cytogenetic abnormalities, if necessary

- IGH-CCND1 fusion, t(11;14) by FISH

Bone marrow (BM) evaluation for staging

Chromosome analysis – sometimes necessary

Primary tests

[Cyclin D1, SP4 by Immunohistochemistry 2003842](#)

- Diagnosis of MCL in conjunction with morphology and immunohistochemical studies
- Formalin-fixed, paraffin-embedded (FFPE) tissue specimens only

[IGH-CCND1 Fusion, t\(11;14\) by FISH 2007226](#)

- Aid in diagnosis of MCL if cyclin testing is noninformative
- FFPE tissue specimens

Related tests

[Leukemia/Lymphoma Phenotyping by Flow Cytometry 2008003](#)

- Aid in evaluation of hematopoietic neoplasms
- Monitor therapy in patients with established diagnosis of hematopoietic neoplasms

[Chromosome FISH, Interphase 2002298](#)

- Specific FISH probe for t(11;14)(q13;q32) must be requested
- Fresh tissue specimens only

[Chromosome Analysis, Bone Marrow 2002292](#)

- Diagnosis, prognosis, and monitoring of hematopoietic neoplasms (eg, 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

Incidence – 3-10% of all non-Hodgkin B-cell lymphomas

Symptoms

- Majority present at advanced stage
- Lymphadenopathy – usually widespread
- Extranodal sites most commonly include
 - Gastrointestinal tract
 - Waldeyer's ring

Diagnostic criteria

- Morphology
 - Small- to medium-sized lymphoid cells with irregular nuclear contours (centrocyte-like) with dispersed chromatin and inconspicuous nuclei
 - Nodular, diffuse, mantle zone pattern has been described
 - Associated hyalinized small vessels are common
- Flow cytometry immunoprofile
 - Bright CD20, monoclonal light chains, CD5+, CD10-, CD23-
- Immunohistochemistry
 - Cyclin D1 expression is present in the majority of cases

Diagnostic issues

MCL is often diagnosed using combination of morphology, immunohistochemistry (cyclin D1), immunophenotyping, and clinical presentation

- Variants of MCL (small cell, marginal-zone-like) that phenotypically resemble other non-Hodgkin lymphomas, such as CLL/SLL may present problems for diagnosis in atypical cases
 - *IGH-CCND1* fusion, t(11;14) FISH testing most useful in this setting

Genetics

Gene – *IGH-CCND1*

Structure/function

- The translocation juxtaposes the *CCND1* gene located on the long arm of chromosome 11 (q13) with the *IGH* gene located on the long arm of chromosome 14 (q32)
- *IGH-CCND1* fusion causes overexpression of cyclin D1
 - Overexpression is oncogenic and defines disease
 - Cyclin D1 promotes cell division and growth

Test Interpretation

IGH-CCND1 Fusion, t(11;14) by FISH

Sensitivity

- Analytical sensitivity – 20%

Results

- Positive – presence of the t(11;14) translocation supports a diagnosis of MCL
- Negative – absence of the t(11;14) translocation

Limitations

- *IGH-CCND1* Fusion, t(11;14) by FISH has not been validated for
 - Tissue fixed in alcohol-based or nonformalin fixatives
 - Decalcified tissue
- Negative result does not exclude the possibility of translocations involving other partners
- Variant is not specific for MCL
 - Results need to be analyzed in conjunction with morphology, immunohistochemistry, and immunophenotyping results