Ewing Sarcoma Family of Tumors

Indications for Ordering

Individuals diagnosed with or suspected of having Ewing sarcoma based on morphology or immunophenotypic studies

Test Description

- Fluorescence in situ hybridization (FISH) analysis on formalin-fixed, paraffin-embedded (FFPE) tissue
- Break-apart DNA probes flank the 22q12 locus
- 100 cells evaluated from regions of tumor identified on histopathologic review of a matching hematoxylin and eosin stained section

Tests to Consider

Primary Test

**EWSR1 (22q12) Gene Rearrangement by FISH**

- Diagnose members of Ewing sarcoma family of tumors (ESFT)
- Does not identify the translocation partner

Related Test

**Chromosome FISH, Interphase**

- Specific probe for 22q12.2 must be specified
- Fresh tissue or touch-prep

Disease Overview

**Prevalence and/or incidence** – ~4/million children/year

- ESFT—most common malignant bone and soft-tissue tumors in childhood and young adulthood

**Age of onset** – peak incidence in adolescence

Diagnostic issues

- ESFT types
  - Ewing sarcoma, peripheral neuroectodermal tumors (PNET), and Askin sarcoma
  - Differentiating tumors in Ewing family from each other or from other small, round cell tumors may be difficult
  - Accurate diagnosis of the tumor type is essential for prognosis and determining therapy
    - **EWSR1** translocations are the hallmark of Ewing family tumors

Genetics

**Gene – EWSR1**

**Variants**

- **EWSR1-FLI1** fusion \( [t(11;22)(q24;q12)] \) – ~85%
- **EWSR1-ERG** fusion \( [t(21;22)(q22;q12)] \) – ~10%
- Other chimeric translocations – rare
  - **EWSR1-ETV1** \( [t(7;22)] \)
  - **EWSR1-TVA** \( [t(17;22)] \)
  - **EWSR1-FEV** \( [t(2;22)] \)

Test Interpretation

**Results**

- Positive – **EWSR1** gene rearrangement detected in ≥25% of nuclei
  - Strongly supportive of a diagnosis of Ewing sarcoma
- Negative – **EWSR1** gene rearrangement not detected
  - Does not exclude the diagnosis of Ewing sarcoma

**Limitations**

- Results may be compromised if the recommended fixation procedures have not been followed
- Does not identify specific translocation partner