Pediatric Ewing’s Family of Tumors

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Note: Consider Clinical Trials as treatment options for eligible patients. Referral to a center with both pediatric oncology and orthopedic surgery is essential.

CLINICAL EVALUATION

- History and physical
- CBC with differential, total protein, albumin, calcium, total bilirubin, alkaline phosphatase, LDH, AST, sodium, potassium, chloride, carbon dioxide, and PT/INR
- Plain films of primary tumor
- MRI of primary tumor
- Bone scan
- Chest x-ray
- CT chest
- Whole body PET/CT (optional)
- Biopsy (open vs. core needle)
- Histology review by bone tumor pathologist
- Screening MRI of spine or bone marrow biopsy and aspirate
- EKG and cardiac scan (ECHO)
- Central venous access device (CVAD) placement
- Pregnancy test if clinically indicated
- Discuss fertility
- Cytogenetics and/or molecular studies (may require re-biopsy)

1 Greater than 95% of Ewing sarcoma will have one of four fusion variants. For patients with Ewing-like sarcoma (e.g., CIC-DUX4) an alternate treatment paradigm can be considered. For those who are negative, additional molecular testing is recommended.

2 Vincristine, doxorubicin (with dexrazoxane for cardioprotection) and cyclophosphamide alternating with ifosfamide plus etoposide for 4-6 weeks

3 Temozolomide plus irinotecan (5 days every 3 weeks), or clinical trial if available

PRIMARY TREATMENT

- Metastasis?
  - Yes
  - Neoadjuvant chemotherapy for a total of 6 cycles depending on tumor response
  - Assess treatment response at 6 weeks:
    - Clinical exam of primary tumor
    - Reimage if concerned with progression
  - Tumor response?
    - Yes
    - See Page 2 for treatment of metastatic disease
    - No
    - Metastasis?
      - Yes
      - Restage
      - No
      - Tumor resectable?
        - Yes
        - Primary tumor resectable?
          - Yes
          - Surgery
          - No
          - Are there positive or close margins?
            - Yes
            - Chemotherapy with radiation to tumor bed for 6 weeks followed by chemotherapy for a total of 14 cycles
            - No
            - Continue chemotherapy to complete at least 14 cycles
          - No
          - Are there positive or close margins?
            - Yes
            - Chemotherapy with radiation to tumor bed for 6 weeks followed by chemotherapy for a total of 17 cycles
            - No
            - Initiate different chemotherapy to complete a total of 14 cycles
        - No
        - Surgery
        - Are there positive or close margins?
          - Yes
          - Chemotherapy with radiation to tumor bed for 6 weeks followed by different chemotherapy for a total of 17 cycles
          - No
          - Initiate different chemotherapy to complete a total of 14 cycles
  - No
  - Metastasis?
    - Yes
    - See Page 2 for treatment of metastatic disease
    - No
    - Tumor resectable?
      - Yes
      - Primary tumor resectable?
        - Yes
        - Surgery
        - No
        - Are there positive or close margins?
          - Yes
          - Chemotherapy with radiation to tumor bed for 6 weeks followed by chemotherapy for a total of 14 cycles
          - No
          - Continue chemotherapy to complete at least 14 cycles
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        - Chemotherapy with radiation to tumor bed for 6 weeks followed by chemotherapy for a total of 17 cycles
        - No
        - Initiate different chemotherapy to complete a total of 14 cycles
    - No
    - Surgery
    - Are there positive or close margins?
      - Yes
      - Chemotherapy with radiation to tumor bed for 6 weeks followed by different chemotherapy for a total of 17 cycles
      - No
      - Initiate different chemotherapy to complete a total of 14 cycles

ADJUVANT TREATMENT

- Chemotherapy with radiation to tumor bed for 6 weeks followed by chemotherapy for a total of 14 cycles
- Continue chemotherapy to complete at least 14 cycles
- Chemotherapy with radiation to tumor bed for 6 weeks followed by chemotherapy for a total of 17 cycles
- Initiate different chemotherapy to complete a total of 14 cycles

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Department of Clinical Effectiveness V6

Approved by The Executive Committee of the Medical Staff 12/21/2021
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**PRIMARY TREATMENT**

- **Metastatic Disease**
  - Neoadjuvant chemotherapy
  - Assess treatment response after 2 months of chemotherapy
    - Is tumor(s) responsive to treatment?
      - Yes
        - Give additional chemotherapy for a total of 3 months
        - Is tumor(s) responsive to treatment?
          - Yes
            - Continue same chemotherapy
          - No
            - Give additional chemotherapy for a total of 3 months
  - Local control of primary
  - Assess treatment response after 2 months of chemotherapy

**ADJUVANT TREATMENT**

- Is there progression of metastatic disease?
  - Yes
    - Consider surgical resection and/or radiation for pulmonary and other metastatic sites as consolidative therapy to untreated sites
    - Give chemotherapy for approximately one year from initial diagnosis
  - No
    - Palliative treatment options:
      - Consider radiation and/or surgery to metastatic sites
      - Second line chemotherapy
        - Vincristine, irinotecan, and temozolomide
        - Topotecan and cyclophosphamide
      - Clinical trial
      - Supportive care

**SURVEILLANCE**

- Individual surveillance based on treatment provided

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1 Vincristine, doxorubicin (with dexrazoxane for cardioprotection) and cyclophosphamide alternating with ifosfamide plus etoposide for 4-6 weeks
2 Local control: axial lesions undergo radiation, extremity lesions undergo surgery and/or radiation, and head and neck lesions are treated individually based on clinical indications
3 Monitor for progression after 2-3 months of chemotherapy for approximately 1 year of treatment. If no progression of disease following completion of chemotherapy regimen then move patient to surveillance (see Page 3).
# Pediatric Ewing’s Family of Tumors Surveillance

## Total years for Surveillance

<table>
<thead>
<tr>
<th>Frequency of Surveillance by month</th>
<th>Year 1</th>
<th>Year 2</th>
<th>Year 3</th>
<th>Year 4</th>
<th>Year 5</th>
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<td>9</td>
<td>12</td>
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<td>CBC with differential</td>
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<td>without history of bone metastases</td>
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</table>

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SUGGESTED READINGS


Children’s Oncology Group Protocol: COG AEWS 0031


DEVELOPMENT CREDITS

This practice algorithm is based on majority expert opinion of the Pediatric Center Faculty at the University of Texas MD Anderson Cancer Center. It was developed using a multidisciplinary approach that included input from the following:

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