# Pediatric Ewing's Family of Tumors





**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

## PRIMARY TREATMENT

## ADJUVANT TREATMENT

Metastasis?

Yes → See Page 2 for treatment of metastatic disease

No → Neoadjuvant chemotherapy[1]

Assess treatment response at 6 weeks:
- Clinical exam of primary tumor
- Reimage if concerned with progression

Tumor response?

Yes → Resume neoadjuvant chemotherapy for a total of 6 cycles depending on tumor response

No → Restage

Metastasis?

Yes → See Page 2 for treatment of metastic disease

No → Tumor resectable?

Primary tumor resectable?

Yes → Surgery

No → Chemotherapy with radiation to tumor bed for 6 weeks followed by chemotherapy for a total of 17 cycles

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

Surgery

Yes → Chemotherapy with radiation to tumor bed for 6 weeks followed by different chemotherapy[2] for a total of 17 cycles

No → Initiate different chemotherapy[2] to complete a total of 14 cycles

Are there positive or close margins?

Yes → Chemotherapy with radiation to tumor bed for 6 weeks followed by different chemotherapy[2] for a total of 14 cycles

No → Chemotherapy with radiation to tumor bed for 6 weeks followed by different chemotherapy[2] for a total of 14 cycles

See Page 3 for surveillance

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

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



Department of Clinical Effectiveness V5
Approved by The Executive Committee of the Medical Staff 03/26/2019

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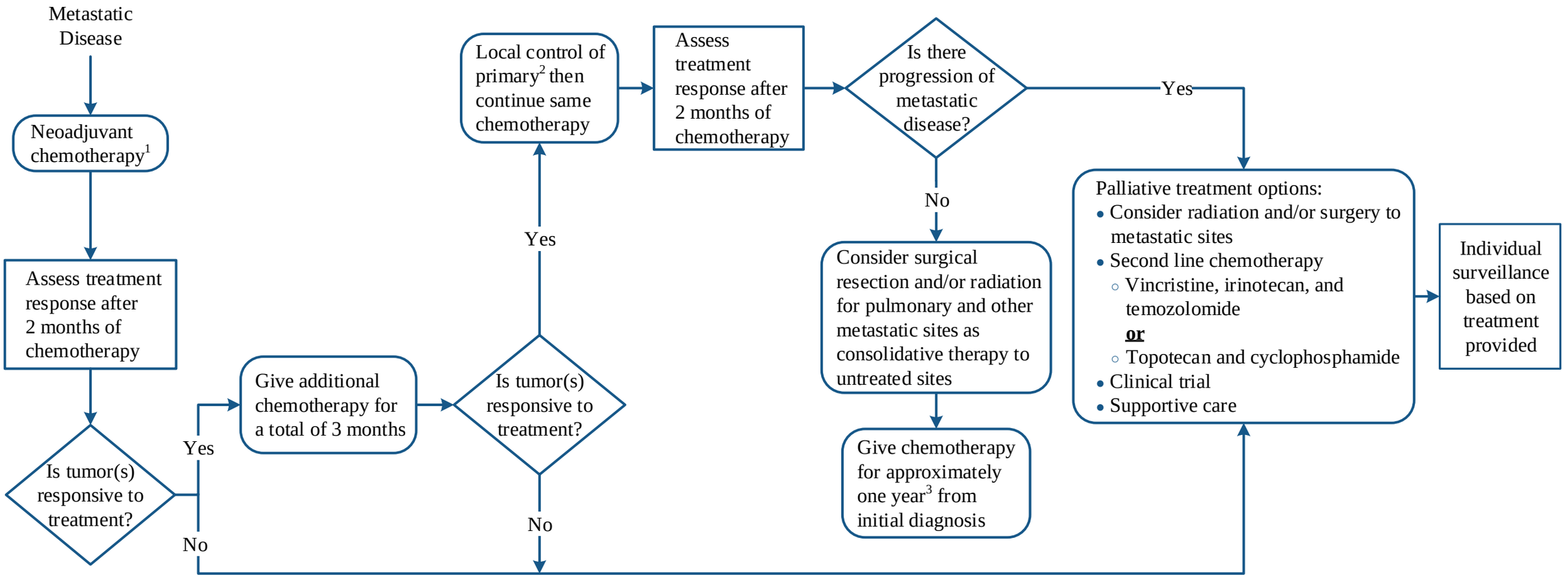
**PRIMARY TREATMENT** **ADJUVANT TREATMENT** **SURVEILLANCE**




[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).



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## Pediatric Ewing's Family of Tumors Surveillance

| **Total years for Surveillance** | | | | **Year 1** | | | | **Year 2** | | | **Year 3** | | | **Year 4** | | **Year 5** |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Frequency of Surveillance by month** | **3** | **6** | **9** | **12** | **15** | **18** | **21** | **24** | **28** | **32** | **36** | **40** | **44** | **48** | **54** | **60** |
| History and physical | x | x | x | x | x | x | x | x | x | x | x | x | x | x | | x |
| Monitor and discuss with patient late effects of primary treatment | x | x | x | x | x | x | x | x | x | x | x | x | x | x | x | x |
| CBC with differential | | x | | x | | x | | x | | x | | x | | x | | x |
| Total protein, albumin, calcium, phosphate, magnesium, glucose, creatinine, total bilirubin, alkaline phosphatase, LDH | | x | | x | | x | | x | | x | | | | x | | x |
| Plain films of primary | x | x | x | x | x | x | x | x | x | x | x | x | x | x | x | x |
| Pelvic primaries: MRI | x | x | x | x | x | x | x | x | x | x | x | x | x | x | x | x |
| Bone scan and/or PET scan for symptomatic patients with and/or without history of bone metastases | x | x | x | x | | x | | x | | | x | | | | | |
| Chest x-ray | x | x | x | x | x | x | x | x | x | x | x | | x | x | x | x |
| CT chest (higher risk patients) | x | x | x | x | | | | x | | | x | | | x | | x |

## SUGGESTED READINGS

Anderson, P., Kopp, L., Anderson, N., Cornelius, K., Herzog, C., Hughes, D., & Htth, W. (2008). Novel bone cancer drugs: Investigational agents and control paradigms for primary bone sarcomas (ewing's sarcoma and osteosareoma). *Expert Opinion on Investigational Drugs, 17*(11), 1703-1715. https://doi:10.1517/13543780802434436

Children's Oncology Group Protocol: COG AEWS 0031

De Angulo, G., Hernandez, M., Morales-Arias, J., Herzog, C. E., Anderson, P., Wolff, J., & Kleinerman, E. S. (2007). Early lymphocyte recovery as a prognostic indicator for high-risk ewing sarcoma. *Journal of Pediatric Hematology/Oncology, 29*(1), 48-52. https://doi:10.1097/MPH.0b013e31802d3e3e

Huh, W. W., Daw, N. C., Herzog, C. E., Munsell, M. F., McAleer, M. F., & Lewis, V. O. (2017). Ewing sarcoma family of tumors in children younger than 10 years of age. *Pediatric Blood & Cancer, 64*(4), e26275. https://doi:10.1002/pbc.26275

Imran, H., Enders, F., Sim, F., Okuno, S., Arndt, C. A. S., Krailo, M., . . . Mascarenhas, L. (2009). Effect of time to resumption of chemotherapy after definitive surgery on prognosis for non-metastatic osteosarcoma. *Journal of Bone and Joint Surgery, 91*(3), 604-612. https://doi:10.1016/S0021-9355(09)72084-3

Letourneau, P. A., Shackett, B., Xiao, L., Trent, J., Tsao, K. J., Lally, K., & Hayes-Jordan, A. (2011). Resection of pulmonary metastases in pediatric patients with ewing sarcoma improves survival. *Journal of Pediatric Surgery, 46*(2), 332-335. https://doi:10.1016/j.jpedsurg.2010.11.013

National Comprehensive Cancer Network. (2018). *Bone Cancer* (NCCN Guideline Version 1.2019). Retrieved from https://www.nccn.org/professionals/physician_gls/pdf/bone.pdf.

Pishas, K. I., & Lessnick, S. L. (2016). Recent advances in targeted therapy for ewing sarcoma. *F1000research,* 5. https://doi.org/10.12688/f1000research.8631.1

## DEVELOPMENT CREDITS

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