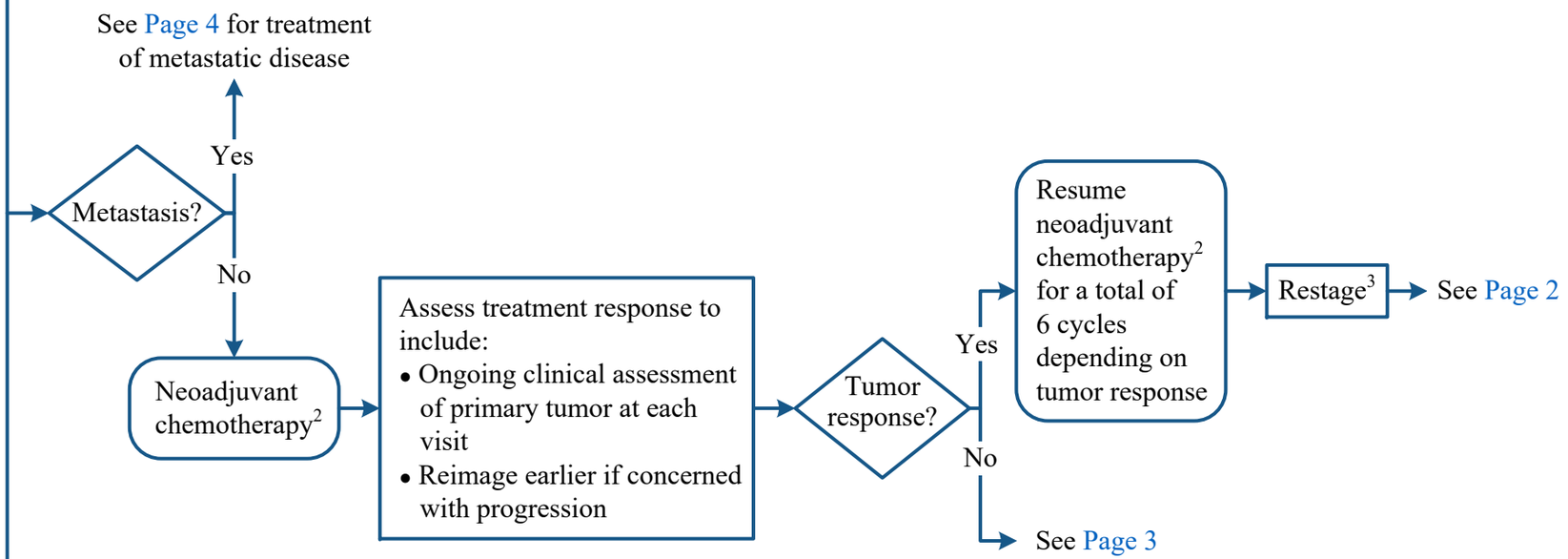
Pediatric Ewing's Family of Tumors

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 with and without contrast
- Bone scan
- CT chest with contrast
- Whole body PET/CT with or without contrast (optional)
- Biopsy (open vs. core needle)
- Histology review by appropriate sub-specialty pathologist
- Screening MRI of spine with and without contrast or bone marrow biopsy and aspirate
- EKG and echocardiogram (ECHO)
- Central venous access device (CVAD) placement
- Urine pregnancy test, if clinically indicated
- Discuss fertility
- Cytogenetics and/or molecular studies (may require re-biopsy)[1]
- Consult Physical Therapy/Occupational Therapy and Child Life

PRIMARY TREATMENT



ADJUVANT TREATMENT

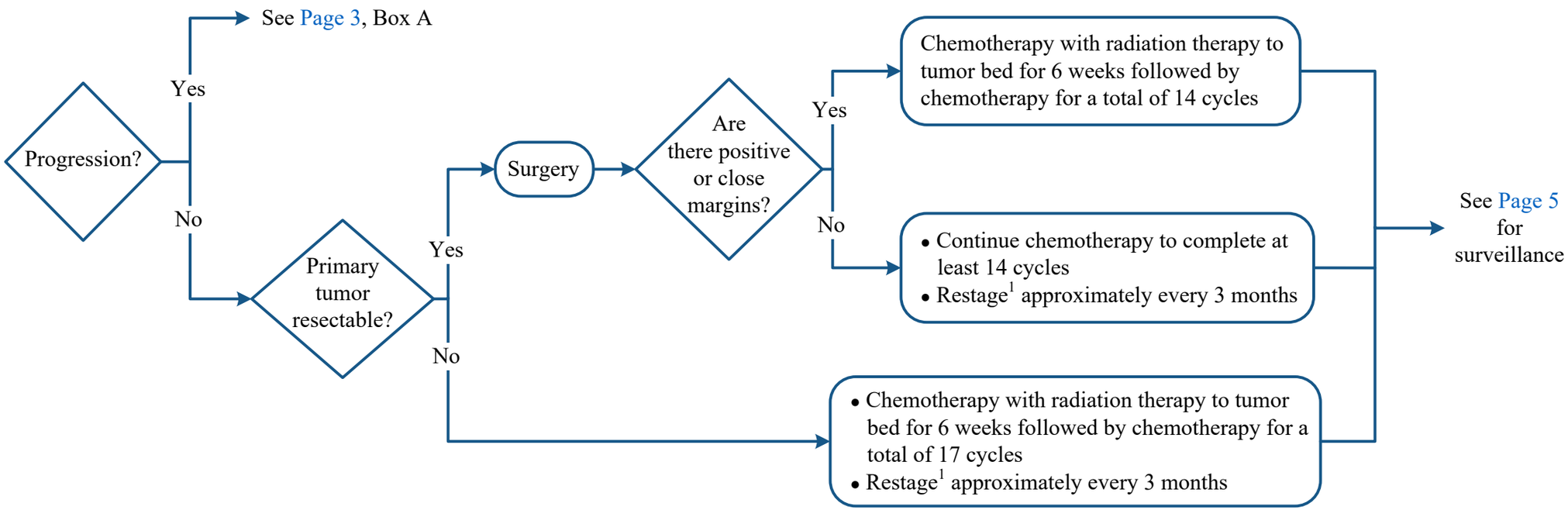
[1] Greater than 95% of Ewing sarcoma will have one of four fusion variants. For patients with Ewing-like sarcoma (*e.g.,* CIC-DUX4) an alternate treatment paradigm can be considered. For those who are negative, additional molecular testing is recommended.
[2] Vincristine, doxorubicin (with dexrazoxane for cardioprotection) and cyclophosphamide alternating with ifosfamide plus etoposide for 4-6 cycles or clinical trials
[3] CT chest, x-ray and MRI of primary site

Department of Clinical Effectiveness V7
Approved by The Executive Committee of the Medical Staff 10/15/2024

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.

ADJUVANT TREATMENT



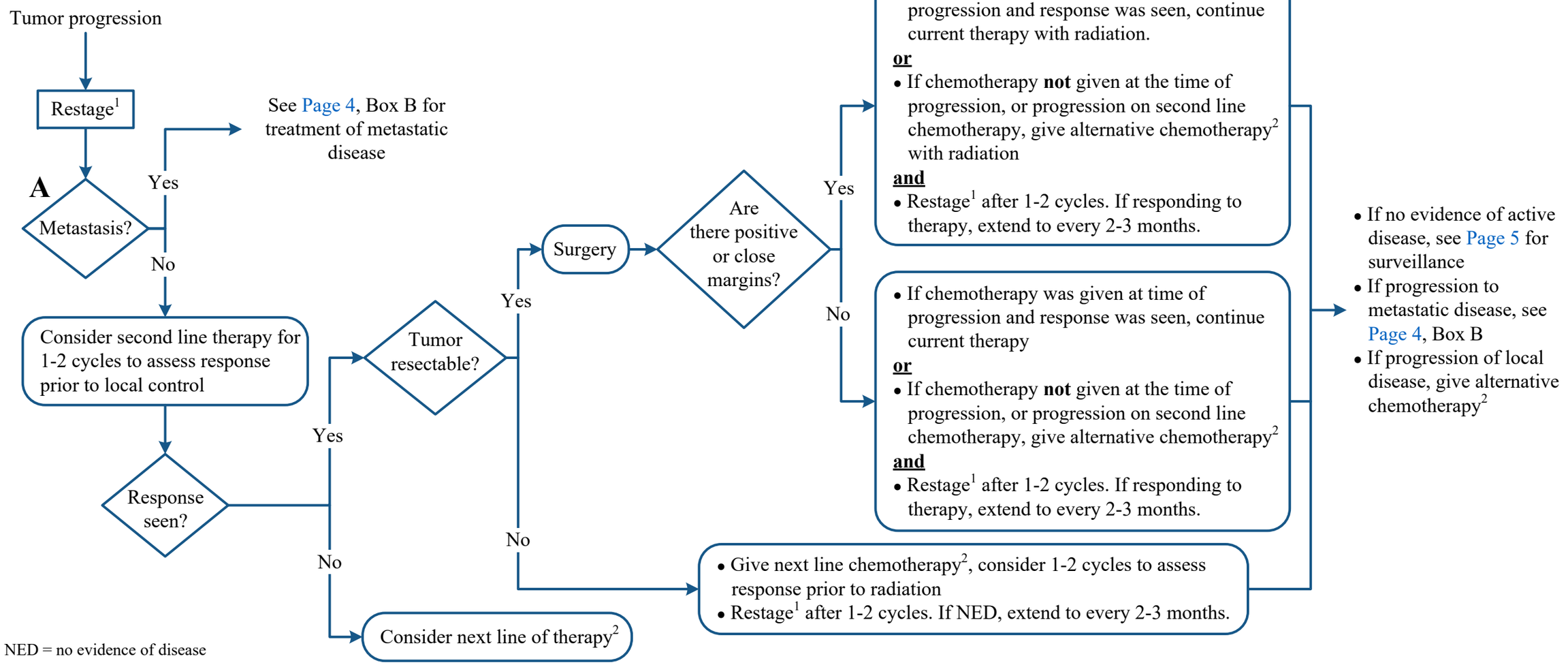
[1] CT chest, x-ray and MRI of primary site

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.

PRIMARY TREATMENT

ADJUVANT TREATMENT



NED = no evidence of disease

[1] PET/CT, x-ray and MRI of primary site

[2] Options include temozolomide plus irinotecan (5 days every 3 weeks) with or without vincristine; cyclophosphamide plus topotecan; high-dose ifosfamide; or clinical trial if available

Department of Clinical Effectiveness V7
Approved by The Executive Committee of the Medical Staff 10/15/2024

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.

PRIMARY TREATMENT

Initial presentation: Metastatic Disease

- Neoadjuvant chemotherapy[1]
- Consider discussion Goal Concordant Care (GCC) with the Patient Representative and if indicated, with patient[2]

Assess treatment response to include:
- Ongoing clinical assessment of primary tumor at each visit
- Reimage approximately every 3 months or if concerned with progression

Tumor(s) responsive to treatment?

Yes → Local control of primary[3] then continue same chemotherapy

Assess treatment response approximately every 3 months or if concerned with progression

No

ADJUVANT TREATMENT

Is there progression of metastatic disease?

Yes → **B**

Palliative treatment options:
- Discuss GCC with the Patient Representative and if indicated, with patient[2]
- Consider radiation therapy and/or surgery to metastatic sites. Consider radiation therapy and/or surgery to primary site if not already addressed
- Second line chemotherapy
  - Temozolomide, irinotecan, and vincristine **or**
  - Cyclophosphamide and topotecan **or**
  - High-dose ifosfamide
- Clinical trial
- Supportive care

→ Individual surveillance based on treatment provided (see Page 5)

No

Consider surgical resection and/or radiation therapy for pulmonary and other metastatic sites as consolidative therapy

Give chemotherapy for approximately one year from initial diagnosis

- Monitor for progression[4] approximately every 3 months for 1 year of treatment
- If no progression of disease following completion of chemotherapy regimen, move patient to surveillance (see Page 5)

[1] Vincristine, doxorubicin (with dexrazoxane for cardioprotection) and cyclophosphamide alternating with ifosfamide plus etoposide for 2-3 cycles

[2] GCC should be initiated by the Primary Oncologist. If Primary Oncologist is unavailable, Primary Team/Attending Physician to initiate GCC discussion and notify Primary Oncologist. The Patient Representative and if indicated, the patient, should be informed of therapeutic and/or palliative options. GCC discussion should be consistent, timely, and re-evaluated as clinically indicated. The Advance Care Planning (ACP) note should be used to document GCC discussion. Refer to GCC home page (for internal use only).

[3] 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

[4] CT chest, x-ray and MRI of primary site

Department of Clinical Effectiveness V7
Approved by The Executive Committee of the Medical Staff 10/15/2024

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.

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
X-rays of osseous sites of disease at discretion of oncologist	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
Pelvic primaries: MRI with and without contrast, pelvic x-ray	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
PET/CT scan for symptomatic patients with and/or without history of bone metastases. Nuclear medicine bone scan as needed and when PET/CT is not available or feasible.	x	x	x	x		x		x			x					
Chest x-ray (when CT chest or PET/CT not done)					x	x	x		x	x		x	x		x	
CT chest (higher risk patients)[1]	x	x	x	x				x			x			x		x

[1] If PET/CT is being done for clinical reasons, it can replace CT chest for one or two follow ups within the first year of surveillance

Department of Clinical Effectiveness V7
Approved by The Executive Committee of the Medical Staff 10/15/2024

SUGGESTED READINGS

Anderson, P., Kopp, L., Anderson, N., Cornelius, K., Herzog, C., Hughes, D., & Huh, 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.org/10.1517/13543784.17.11.1703

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.org/10.1097/MPH.0b013e31802d3e3e

Huang, T., Li, F., Yan, Z., Ma, Y., Xiong, F., Cai, X., . . . Dong, J. (2018). Effectiveness of ^{18}F-FDG PET/CT in the diagnosis, staging and recurrence monitoring of Ewing sarcoma family of tumors: A meta-analysis of 23 studies. *Medicine, 97*(48), e13457. https://doi.org/10.1097/MD.0000000000013457

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.org/10.1002/pbc.26275

Imran, H., Enders, F., Krailo, M., Sim, F., Okuno, S., Hawkins, D., . . . Arndt, C. A. S. (2009). Effect of time to resumption of chemotherapy after definitive surgery on prognosis for non-metastatic osteosarcoma. *The Journal of Bone and Joint Surgery, 91*(3), 604-612. https://doi.org/10.2106/JBJS.H.00449

Johnsen, B., Fasmer, K. E., Boye, K., Rosendahl, K., Trovik, C., Biermann, M., & Aukland, S. M. (2018). Added value of ^{18}F-FDG PET-CT in staging of Ewing sarcoma in children and young adults. *European Journal of Hybrid Imaging, 2*(13), 1-11. https://doi.org/10.1186/s41824-018-0031-5

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.org/10.1016/j.jpedsurg.2010.11.013

MD Anderson Institutional Policy #CLN1202 – Advance Care Planning Policy
Advance Care Planning (ACP) Conversation Workflow (ATT1925)

National Comprehensive Cancer Network. (2023). *Bone Cancer* (NCCN Guideline Version 1.2024). 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

Shankar, K., Shamim, S. A., Rastogi, S., Dhamija, E., Barwad, A., Khan, S., & Bal, C. (2022). Prospective comparison of 18F-FDG PET/CT and conventional modalities for staging Ewing sarcoma family of tumours. *The Journal of Nuclear Medicine, 63*(Suppl 2), 3152. Retrieved from https://jnm.snmjournals.org/content/63/supplement_2/3152

DEVELOPMENT CREDITS

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

Core Development Team Leads

Cynthia Herzog, MD (Pediatrics)
Valerae Lewis, MD (Orthopaedic Oncology)

Workgroup Members

Wendy Garcia, BS♦
Tamara Haygood, MD, PhD (Diagnostic Imaging)
Eugenie Kleinerman, MD (Pediatrics)
Patrick Lin, MD (Orthopaedic Oncology)
Joseph Ludwig, MD (Sarcoma Medical Oncology)
Mary Frances McAleer, MD, PhD (Radiation Oncology)
Maria Estela Mireles, PharmD (Pharmacy Clinical Programs)
Bryan Moon, MD (Orthopaedic Oncology)
Amy Pai, PharmD♦
Shreyaskumar Patel, MD (Sarcoma Medical Oncology)
Ravin Ratan, MD (Sarcoma Medical Oncology)
Janie Rutledge, RN, MSN, ANP, OCN (Orthopaedic Oncology)
Wei-Lien Wang, MD (Anatomical Pathology)
Hannah Warr, MSN, RN, CPHON♦
Sireesha Yedururi, MBBS (Diagnostic Imaging)

♦Clinical Effectiveness Development Team