COG-AOST2031: A Phase 3 Randomized Controlled Trial Comparing Open vs Thoracoscopic Management of Pulmonary Metastases in Patients with Osteosarcoma

FAST FACTS
Eligibility Reviewed and Verified By
_____ MD/DO/RN/LPN/CRA Date _____
_____ MD/DO/RN/LPN/CRA Date _____
Consent Version Dated_____

PATIENT ELIGIBILITY:
Important note: The eligibility criteria listed below are interpreted literally and cannot be waived (per COG policy posted 5/11/01). All clinical and laboratory data required for determining eligibility of a patient enrolled on this trial must be available in the patient's medical research record which will serve as the source document for verification at the time of audit.

___1. Timing
Patients must be enrolled before treatment (i.e., surgery) begins. On this study, the term treatment and surgery will be used interchangeably. Chest CT scans must be obtained within 14 days prior to enrollment and within 28 days prior to surgery (or 28 days prior to the first side if undergoing staged bilateral procedures). The date surgery is projected to start must be no later than 28 calendar days after the date in which scans are obtained. Newly diagnosed patients should not be enrolled at time of initial diagnosis. Patients will be enrolled on this study at the time thoracic surgery is being planned.

___2. Determining Patient Suitability for Enrollment
A multidisciplinary approach to treatment involving the oncologist and the surgeon is indispensable, and planning should begin immediately upon diagnosis. It is essential that the pediatric or thoracic surgeon who will be performing the pulmonary metastasectomy be involved in determining patient suitability and enrollment (see Section 13.1.1).

___3. Rapid Central Imaging Review
Chest CT scans must be submitted for rapid central imaging review within 5 days after study enrollment. Please see Sections 16.2 and 16.5 for details.

___4. PRO/HRQoL Timing
Immediately upon study entry, age- and language-eligible participants must complete the Quality of Life Contact Information Form found in Appendix V. We strongly encourage sites to scan and upload this form to Medidata Rave within 24 hours of enrollment to ensure timely completion of the baseline instruments. The information collected in the contact form is required for administration of assessments by the PRO/HRQoL team via planned electronic data capture. See Section 15.1 for complete PRO/HRQoL eligibility, administration and timing details.

___5. **Clinical Studies**
Clinical studies (eg, cardiac imaging, pulmonary function tests), if applicable, must be obtained within 21 days prior to *enrollment* and *start of protocol therapy* (repeat if necessary).

___6. **Disease/Staging Imaging**
Disease/staging imaging studies, if applicable, must be obtained within 14 days prior to *enrollment* and within 28 days prior to *the projected surgery date*. Timing and approach to staging beyond the required chest CT can be performed according to local standard of care. Re-staging is not required between staged bilateral chest procedures.

___7. Age
Patients must be < 50 years at the time of enrollment.

___8. Diagnosis
- Patients must have ≤ 4 nodules per lung consistent with or suspicious for metastases, with at least one of which being ≥ 3 mm and all of which must be ≤ 3 cm size (see Section 16.4.2).
  Note: Patient must have **eligibility confirmed by rapid central imaging review (see Section 16.2)**
- Lung nodules must be considered resectable by either open thoracotomy or thoracoscopic surgery. Determination of resectability is made by the institutional surgeon.
- Patients must have a histological diagnosis of osteosarcoma.
- Patients must have evidence of metastatic lung disease at the time of initial diagnosis, or at time of 1st recurrence following completion of therapy for initially localized disease.
- Patients with newly diagnosed disease must have completed successful gross tumor resection for their primary tumor or surgical local control of primary tumor must be planned to be performed simultaneously with thoracic surgery.

A series of clinical scenario examples are provided in Appendix III to assist investigators in their consideration of patient eligibility.

___9. Prior Therapy

- Newly diagnosed patients must be receiving or recently completed (within 60 days) systemic therapy considered by the treating physician to be standard treatment for newly diagnosed osteosarcoma (eg, cisplatin-doxorubicin or ifosfamide-based drug regimens) at the time of enrollment on this study. Dose and drug modifications for toxicity do not exclude patients from participation.
- Patients at time of 1st recurrence must have completed systemic therapy for their initial primary tumor, considered by the treating physician to be standard treatment for newly diagnosed osteosarcoma (eg, cisplatin-doxorubicin or ifosfamide-based drug regimens) at the time of enrollment on this study. Dose and drug modifications for toxicity do not exclude patients from participation.

Please see Section 4.1 for the concomitant therapy restrictions for patients during treatment.

Assent of children age 14 and older is a necessary condition for proceeding with the research.

EXCLUSION CRITERIA

___1. Patients with unresectable primary tumor.
___2. Patients with pulmonary metastatic lesions that would require anatomic resection (lobectomy or pneumonectomy) or lesions that are defined as "central" (i.e., central lesion involves or is proximal to segmental bronchi and peripheral is lesion distal to segmental bronchi).
___3. Patients with chest wall or mediastinal based metastatic lesions, or with pleural effusion.
___4. Patients with disease progression at either the primary or pulmonary metastatic site while on initial therapy. Note: Once the patient has been enrolled on the study, additional CT scans are not anticipated prior to thoracic surgery. Note: Some variation in nodule size measurements over the course of pre-operative therapy is anticipated and does not qualify for exclusion unless deemed true disease progression by the primary treatment team.
___5. Patients with evidence of extrapulmonary metastatic disease.
___6. Patients who received therapeutic pulmonary surgery for lung metastasis prior to enrollment.
___7. Regulatory Requirements

- All patients and/or their parents or legal guardians must sign a written informed consent.
- All institutional, FDA, and NCI requirements for human studies must be met.

TREATMENT PLAN:

This is a prospective randomized controlled trial evaluating surgical management of oligometastatic pulmonary osteosarcoma. Patients enrolled on study and who consent to surgical randomization will have resection of pulmonary metastatic disease either by thoracotomy or thoracoscopic procedure.

REQUIRED OBSERVATIONS:

All pre-op studies must be performed prior to starting protocol therapy unless otherwise indicated below.

Observation	Pre-op	Date of surgical procedure	24-72 hours post-op (prior to discharge)	Day of hospital discharge	7-14 days post-op	4-6 weeks post-op	3 months post-op
Chest CT scan	X[1]						X[8]
Operating surgeon's report [2]		X					
Collection of Tumor Tissue and Adjacent Normal Tissue [3]		X					
Post-operative hospitalization [4]				X			
Peripheral blood for banking [5]	X		X				X[8]
PRO studies [6]	X[7]		X		X	X	

[1] Scan must be done within 28 days prior to surgical procedure (28 days prior to first side if undergoing staged bilateral procedures).
[2] See Section 4.1.4.
[3] See Sections 15.2 for fresh tissue for models and Section 15.3.2 for tissue requested for banking.
[4] Pain medications received, date of insertion and removal of chest tube and date of hospital discharge.
[5] See Section 15.3.3.
[6] See Section 15.1.
[7] Complete within 4 weeks prior to surgery.
[8] Complete 3-month post-op (+/- 14 days)

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Rapid Central Imaging Review for Eligibility (Pre-op) – scans must be submitted for review within 5 calendar days after study enrollment

- Chest CT
- PET-CT or PET-MR (if available at your site)
- Other chest CT scans (such as before initiation of neoadjuvant therapy) should be submitted if available.
- Central review results will be available in RAVE in approximately 72 hours after receipt of complete and evaluable central review materials.
- Also see Section 16

BIOLOGY REQUIREMENTS:

Optional Tissue and Blood

Tissue: See 14.1.2.3. Also see Appendix IV

Blood: Streck Tubes Pre Tx, Post Op and as indicated in 15.3.3