

AEWS1031: A Phase III Randomized Trial of Adding Vincristine-Topotecan-Cyclophosphamide to Standard Chemotherapy in Initial Treatment of Non-Metastatic Ewing Sarcoma

Type	Status	Age Range	Sponsors	Protocol ID
Interventional	Open	Up to 50 years	CCHMC	AEWS1031

Rationale

Drugs used in chemotherapy work in different ways to stop the growth of tumor cells, either by killing the cells or by stopping them from dividing. Giving more than one drug (combination chemotherapy) may kill more tumor cells.

Purpose

This randomized phase III trial is studying combination chemotherapy in treating patients with non-metastatic extracranial Ewing sarcoma.

Objectives

Primary

- Event-free survival (EFS) [Designated as safety issue: No]
- Overall survival [Designated as safety issue: No]

Secondary

- Histologic response [Designated as safety issue: No]
- Initial volumetric tumor size as a prognostic factor for EFS [Designated as safety issue: No]
- Prognostic significance of imaging response by FDG-positron emission tomography (PET) and EFS [Designated as safety issue: No]
- Effect of local surgical margins in conjunction with histologic response on EFS [Designated as safety issue: No]
- Effect of local therapy modality (surgery, radiotherapy or a combination) as well as the type of surgical reconstruction on musculoskeletal complications [Designated as safety issue: No]

Eligibility

Ages available for study: Up to 50 years

Disease Characteristics

- Newly diagnosed extracranial, non-metastatic Ewing sarcoma or primitive neuroectodermal tumors of bone or soft tissue
 - For the purpose of this study, any of the following are considered localized disease:
 - Chest wall tumors with ipsilateral pleural effusions
 - Ipsilateral positive pleural fluid cytology

- Ipsilateral pleural-based secondary tumor nodules
- Regional node involvement, based on clinical suspicion confirmed by pathologic documentation, are considered to be non-metastatic disease
- Tumors arising in the bony skull (extra-dural) are considered to be extracranial
- No evidence of metastatic disease, including the following:
 - Lesions that are discontinuous from the primary tumor, are not regional lymph nodes, and do not share a body cavity with the primary tumor
 - Contralateral pleural effusion and contralateral pleural nodules
 - Distant lymph node involvement
 - Pulmonary nodules that meet the following criteria:
 - Solitary nodule > 0.5 cm or multiple nodules of > 0.3 cm unless biopsied and negative for Ewing sarcoma
 - Biopsies of solitary nodule < 0.5 cm or multiple nodules < 3.0 cm (are not required but if performed positive for metastatic disease)
- No tumors arising in the intra-dural soft tissue

Patient Characteristics

- Creatinine clearance or radioisotope GFR ≥ 70 mL/min OR serum creatinine based on age and/or gender as follows:
 - 0.4 mg/dL (1 month to < 6 months of age)
 - 0.5 mg/dL (6 months to < 1 year of age)
 - 0.6 mg/dL (1 year to < 2 years of age)
 - 0.8 mg/dL (2 years to < 6 years of age)
 - 1.0 mg/dL (6 years to < 10 years of age)
 - 1.2 mg/dL (10 years to < 13 years of age)
 - 1.5 mg/dL (male) or 1.4 mg/dL (female) (13 years to < 16 years of age)
 - 1.7 mg/dL (male) or 1.4 mg/dL (female) (≥ 16 years of age)
- Total bilirubin < 1.5 times upper limit of normal (ULN)
- AST or ALT < 2.5 times ULN
- Shortening fraction of $\geq 27\%$ by echocardiogram OR ejection fraction $\geq 50\%$ by radionuclide angiogram
- Not pregnant or nursing
- Negative pregnancy test
- Fertile patients must use effective contraception for the duration of study treatment

Prior Concurrent Therapy

- No prior chemotherapy or radiotherapy
- Prior biopsy of the primary tumor without an attempt at complete or partial resection allowed
 - Patients are still allowed if unplanned excision was attempted or accomplished as long as adequate imaging was obtained prior to surgery
- No other concurrent chemotherapy or immunomodulating agents (including steroids unless used as an antiemetic)
- No concurrent sargramostim (GM-CSF)

For more information contact:

Cincinnati Children's Hospital Medical Center
Division of Hematology/Oncology
3333 Burnet Ave., Cincinnati, OH 45229-3039
Phone: 513-636-2799
cancer@cchmc.org