

COG-AEWS0331: European Ewing Tumor Working Initiative of National Groups Ewing Tumor Studies 1999 (EURO-E.W.I.N.G.99)

FAST FACTS

PATIENT ELIGIBILITY:

Important note: The eligibility criteria listed below are interpreted literally and cannot be waived (per COG policy posted 5/11/01).

1. Treatment must begin within 30 days of definitive diagnostic biopsy. Diagnostic studies excluding metastatic disease outside of the lungs must be completed at most 2 weeks prior to the initiation of therapy. Baseline physiologic tests (biochemistry, echocardiogram, etc.) must be completed at most 10 days prior to the initiation of therapy.
2. Patients must be less than 50 years old at time of study enrollment. For patients < 3 years of age call the COG Study Chair; infants and small children are eligible for this study, however, the treating physicians and family must be prepared to deliver adequate local control as required in this study. This will often involve surgery or radiation therapy resulting in disability or disfigurement. **If there is doubt about whether adequate primary tumor treatment can be delivered without unacceptable morbidity, do not enter the patient on study.**
3. Patients with isolated pulmonary or pleural metastases at the initial diagnosis of Ewing sarcoma (these are the only patients from COG who are eligible for this study). As a rule, one pulmonary/pleural nodule of > 1 cm, or more than one nodule of > 0.5 cm are considered evidence of pulmonary/pleural metastases, as long as there is no other clear medical explanation for these lesions. In case of doubt, biopsies should be considered. Solitary nodules of 0.5 – 1.0 cm or multiple nodules of 0.3 – 0.5 cm are questionable evidence of metastatic disease, and biopsy proof is recommended. One solitary nodule of < 0.5 cm or several nodules of < 0.3 cm are not regarded as clear evidence of lung disease. In such cases, individual decisions regarding biopsy have to be considered.
4. Pleural effusions in patients with chest wall tumors are not regarded as proof for lung/pleural metastases, but are considered to represent loco-regional disease. The site(s), size, and number of involved sites should be documented.
5. The use of a venous access device is strongly suggested.
6. No previous chemotherapy.
7. Adequate renal function defined as:
 - Radioisotope GFR \geq 60ml/min/1.73m² **OR**
 - confirmation of normal renal function for age by institutional preferred method
8. Adequate cardiac function defined as:
 - Shortening fraction of \geq 29% by echocardiogram, **or**
 - Ejection fraction of \geq 40% by radionuclide angiogram.
9. Any medical, psychiatric, or social reason incompatible with the protocol treatment.

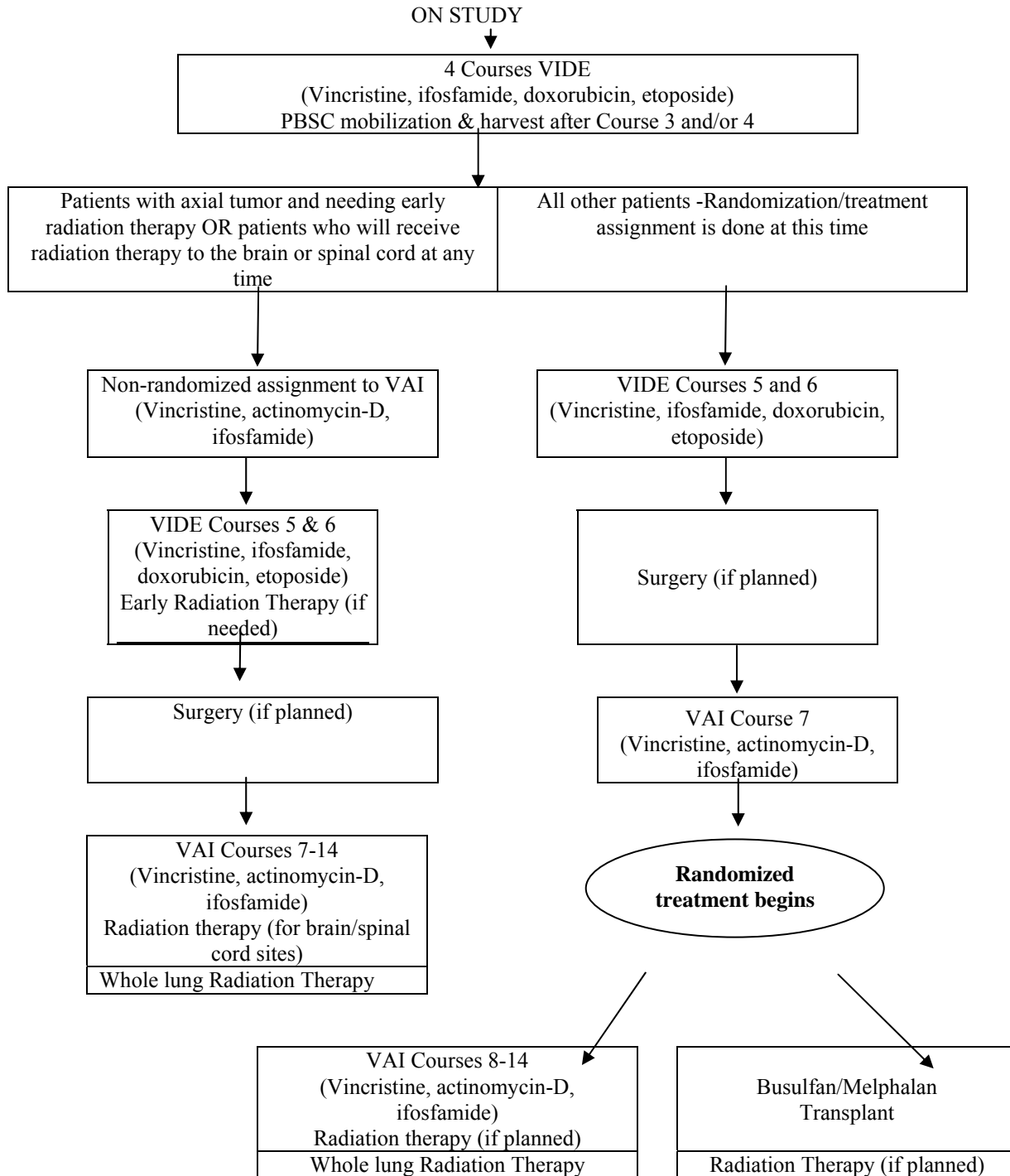
REQUIRED OBSERVATIONS:

- Biopsy
- MRI or CT of primary
- Plain Xray of primary site
- Total body bone scan (MRI of suspicious sites)
- Bilateral bone marrow aspirates and biopsies (with surgery)
- CXR
- CT chest
- Height, weight, BSA
- CBC/ANC, BUN, Cr, electrolytes, calcium, magnesium, phosphate
- SGPT, bilirubin, Alk Phos, LDH
- Urine phosphate and urine Cr (calculate T_p/C_{crea} , see Section XII.3.2 for formula)
- ECHO or MUGA (#and as clinically indicated)
- EKG (#and as clinically indicated)
- PFTs
- HSV/CMV/VZV serologies
- Specimens for diagnostic confirmation – see Table I
- Specimens for optional biology tests (if patient is also enrolled on AEWS02B1) see Table I

Representative histological material should be sent for central pathology review.

TREATMENT PLAN:

Treatment Schema



Randomization will occur after Course 4 (see Treatment Schema) although the randomized treatment will not begin until after VAI Course 7. The COG Statistics and Data Center (SDC) will act as the contact point for COG institutions for the treatment assignments.

TOXICITIES AND DOSAGE MODIFICATIONS:

See Section IX 5, IX 8 (of EURO-E.W.I.N.G.99)

SPECIMEN REQUIREMENTS:

Central review (required) and optional biology studies (if patient is enrolled on **AEWS02B1**):

COG Biopathology Center

Children's Hospital

700 Children's DR

Columbus OH 43205

Phone: 614 722-2894

Fax: 614 722-2897

E-mail: smithw@pediatrics.ohio-state.edu

Histologic confirmation of diagnosis is required for enrollment on AEWS0331 (see page 130 of the protocol document, Appendix A). Send these things to the BPC:

- Paraffin-embedded block or alternatively, 20 unstained slides from the initial biopsy and, if applicable, definitive surgical procedure.
- Specimen x-ray and photograph (if available) from biopsy and if applicable, definitive surgical procedure.
- Peripheral blood: 5-10 cc's in purple top (EDTA) tube and 5-10 cc's in red top tube obtained from patient prior to starting chemotherapy.
- EM photographs, or copies (if available) from biopsy and, if applicable, definitive surgical procedure.
- Institutional surgical pathology report, Operative report, Pathology Checklist, and Specimen Transmittal Form from biopsy and if applicable, definitive surgical procedure.
- Reports of all molecular biologic studies and cytogenetics studies done, if applicable.

BIOLOGY REQUIREMENTS:

Consider enrollment to AEWS02B1

For more information on this protocol, contact GRCOP at 616.391.1230