

COG-ARST0331: Vincristine, Dactinomycin, and Lower Doses of Cyclophosphamide With or Without Radiation Therapy for Patients with Newly Diagnosed Low-Risk Embryonal/Botryoid/Spindle Cell Rhabdomyosarcoma

FAST FACTS

Eligibility Reviewed and Verified By

_____ MD/DO Date _____

_____ RN 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. Patients must be enrolled on ARST0331 BEFORE treatment begins. All patients must enroll on D9902 prior to enrollment on ARST0331. Refer to D9902 for requirements for tissue submission and time limitations for submission. The results of rapid central review as part of D9902 must be received prior to Week 4 of protocol therapy. The date protocol therapy is projected to start must be no later than **five (5)** calendar days after the date of study enrollment
- ___2. Patients must start protocol therapy within 42 days of the date of the pathology report that establishes the diagnosis of rhabdomyosarcoma.
- ___3. Patients must be < 50 years of age at the time of enrollment. The patient may be 50 years old if that birthday occurs during the period of rapid central review of the diagnostic material.
- ___4. Diagnosis
 - Patients with newly diagnosed embryonal rhabdomyosarcoma (RMS), botryoid or spindle cell variants of embryonal RMS, or embryonal ectomesenchymoma are eligible for this study.
 - Enrollment on D9902 to confirm local histologic diagnosis with central pathology review is required for all patients.
 - Patients may be enrolled on ARST0331 and start protocol treatment prior to receipt of central pathology review results.
- ___5. All patients will be evaluated for Stage and a Clinical Group (See Appendices II [Staging classification], III [Grouping classification], IV [Anatomic definitions of parameningeal, orbit and other head and neck sites for use in pre-treatment staging] and V [Designation of the primary site for use in pre-treatment staging]). Note that Clinical Group designation assigned at the time of enrollment on study remains unchanged regardless of any second-look operation that may be performed.
 - Patients will be eligible for **Subset 1** if they meet one of these criteria:
 - The tumor is Stage 1 (favorable primary site [i.e. orbit, head and neck (excluding parameningeal), GU (non-bladder/prostate), or biliary tract/liver]), Clinical Group I (completely resected) or II (microscopic residual disease and/or regional lymph node involvement)
 - The tumor is Stage 1, Clinical Group III (gross residual disease) and arises in the orbit
 - The tumor is Stage 2 (unfavorable primary site [i.e. bladder/prostate, extremity, cranial parameningeal], or other [includes trunk, retroperitoneum, pelvis, perineal/perianal, intrathoracic, gastrointestinal], ≤ 5cm and no regional node involvement), Clinical Group I or II
 - Patients will be eligible for **Subset 2** if they meet one of these criteria:
 - The tumor is Stage 1 (favorable primary site [i.e. orbit, head and neck (excluding parameningeal), GU (non-bladder/prostate), or biliary tract/liver]), Clinical Group III (gross residual disease) arising in non-orbit sites
 - The tumor is Stage 3 (unfavorable primary site [i.e. bladder/prostate, extremity, cranial parameningeal], or other [includes trunk, retroperitoneum, pelvis, perineal/perianal, intrathoracic, gastrointestinal], > 5cm and/or regional node involvement), Clinical Group I or II
- ___6. A patient previously registered on another STS study based on their institutional pathology review and found to have embryonal histology on Rapid Central Review of pathology may fit the above criteria for Subset 1 or 2. Such a patient must switch to ARST0331 by week 4 of therapy. If the results of the Rapid Review are not available prior to the scheduled start of week 4 therapy, institutions should contact the STS Pathology Center (Phone: 614 722-2810 or FAX: 614 722-2897) to confirm histologic type.

- ___7. Paratesticular tumors - Staging ipsilateral retroperitoneal lymph node dissection (SIRLND) is required for all patients ≥ 10 years of age with paratesticular tumors and patients < 10 years with clinically or radiographically involved lymph nodes (except when extensive lymph node involvement is identified by imaging studies). If there is extensive gross node involvement only confirmatory node biopsy is recommended and the patient is classified as Clinical Group III.
- ___8. Extremity tumors - Regional lymph node sampling is **required** for histologic evaluation in patients with extremity tumors (See Sections 14.4.2 and 14.5.4).
- ___9. Clinically or radiographically enlarged nodes - Clinically or radiographically enlarged nodes should be sampled for histologic evaluation (See Section 14.4.2).
- ___10. Patients must have a performance status of 0, 1, or 2. The Lansky performance score should be used for patients < 16 years and the Karnofsky performance score for patients ≥ 16 years.
- ___11. Patients who have received prior chemotherapy, excluding steroids, or radiation therapy, except for patients transferring from the intermediate risk study, are not eligible.
- ___12. Concomitant Medications Restrictions
 - Please see Section 4.1.1 for the concomitant therapy restrictions for patients during treatment.
- ___13. Organ Function Requirements

- Adequate renal function defined as
 - Creatinine clearance or radioisotope GFR $\geq 70\text{mL}/\text{min}/1.73\text{m}^2$ or
 - A serum creatinine based on age/gender as follows:

Age	Maximum Serum Creatinine (mg/dl)	
	Male	Female
1 month to < 6 months	0.4	0.4
6 months to < 1 year	0.5	0.5
1 to < 2 years	0.6	0.6
2 to < 6 years	0.8	0.8
6 to < 10 years	1	1
10 to < 13 years	1.2	1.2
13 to < 16 years	1.5	1.4
≥ 16 years	1.7	1.4

The threshold creatinine values in this Table were derived from the Schwartz formula for estimating GFR utilizing child length and stature data published by the CDC.

Patients with urinary tract obstruction by tumor must meet the renal function criteria listed above AND must have unimpeded urinary flow established via decompression of the obstructed portion of the urinary tract. (See Section 5.5).

- Adequate liver function defined as:
 - Total bilirubin ≤ 1.5 x upper limit of normal for age, and
 - Patients with biliary or hepatic primaries with bilirubin values greater than 1.5 x the upper limit of normal for age, may be enrolled on study if all other eligibility criteria are met (see Section 5.7 for dose modifications in this situation).
- Adequate bone marrow function defined as:
 - Peripheral absolute neutrophil count (ANC) $\geq 750/\mu\text{L}$
 - Platelet count $\geq 75,000/\mu\text{L}$ (transfusion independent)
- No evidence of uncontrolled infection
- ___14. Other criteria
 - Patients must be able to undergo Radiation Therapy, if necessary, as specified in the protocol.
 - Female patients of childbearing age must have a negative pregnancy test.
 - Female patients who are breast feeding must agree to stop breast feeding.
 - Sexually active patients of childbearing potential must be willing to use effective contraception.

REQUIRED OBSERVATIONS:

All entry/eligibility studies must be performed within 21 days prior to entry onto the trial.

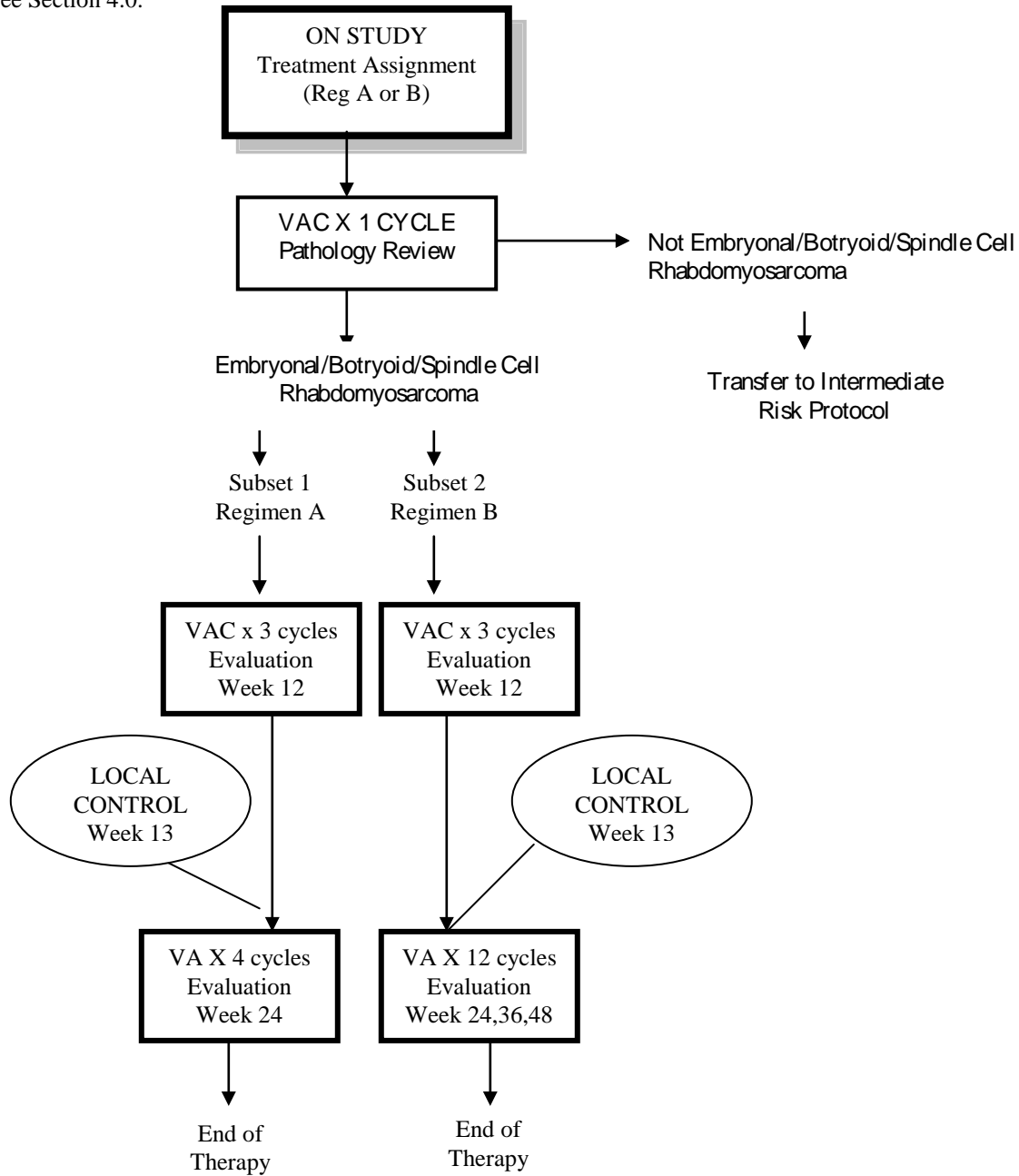
Pre-Study and On Therapy Evaluations

- History
- Physical (Ht, Wt, BSA, VS)
- Performance status⁶
- CBC/Diff/Plt
- Urinalysis
- Lytes
- Cr, SGPT, SGOT, bili
- Ca/Phos
- Bilateral BM Asp/Bx¹
- Chest X-ray (PA & lat.)
- MRI or CT 1° site
- CT chest¹
- CT retroperitoneum and liver³
- MRI or CT Head²
- Bone scan¹
- Lymph node biopsy⁴
- CSF cytology^{1,7}
- Pregnancy test⁵

1. If marrow, lung, or bone metastases are found, or if CSF cytology is positive, enter patient on protocol for Stage 4 disease
2. For possible cranial parameningeal tumors, including orbital primary tumors and paraspinal tumors
3. For GU tumors and tumors below the diaphragm. If omental implants are present or if malignant cells are present in pleural or peritoneal fluid, the patient has Stage 4 disease.
4. For paratesticular (≥ 10 years of age), extremity, or if enlarged nodes on clinical exam or imaging
5. For females of childbearing age
6. The Lansky performance score should be used for patients < 16 year and the Karnofsky performance scale for patients ≥ 16 years.
7. CSF cytology is required for possible cranial parameningeal tumors, including orbital primary tumors and paraspinal tumors. CSF cytology is not necessary for other primary sites.

TREATMENT PLAN:

Also See Section 4.0.



VAC = vincristine, dactinomycin, cyclophosphamide

VA = vincristine, dactinomycin

Local control = radiation therapy and/or surgery

Progressive or recurrent disease at any evaluation – patient is off protocol therapy

TOXICITIES AND DOSAGE MODIFICATIONS:

See Section 5.0

SPECIMEN REQUIREMENTS:

Prior enrollment on D9902 is required. See D9902 for instructions for specimen preparation and shipment.

PATHOLOGY REVIEW:

Rapid Central Review on D9902 at diagnosis

All patients enrolling on this protocol will have *Rapid Central Review* as part of prior enrollment on D9902 because eligibility is based on histology. **Refer to D9902 for specimen submission requirements. Patients who do not enroll on D9902 prior to starting therapy are not eligible for this protocol.**

If there is clinical urgency to start therapy, treatment assignment will occur at study entry based on institutional pathology prior to completion of Rapid Central Review. The diagnosis will be confirmed/corrected within 14 days after D9902 study enrollment. If patient therapy needs to be changed because of a change of the histologic diagnosis based on rapid central review, the patient should be switched to an appropriate treatment regimen before Week 4 therapy is started.

The STS Pathology Center will notify the institution with the rapid review results via fax or overnight mail with a copy of the report being submitted to the STS Data Management Center for tracking.

If Pathology Center and institutional diagnosis agree, treatment should continue based on the institutional histologic subtype.

If the results of the rapid review make a patient previously enrolled on another STS protocol eligible for ARST0331, the patient must be switched to, enrolled on, and begin therapy according to ARST0331 by Week 4. Consent for ARST0331 Therapy must be signed prior to start of therapy.

Materials to send:

Send within **48 hours** after enrollment on study:

Representative formalin-fixed paraffin blocks of tumor material (paraffin blocks will be returned after sectioning). If blocks absolutely cannot be sent, then send 1 H&E section of all available blocks **and** 10 plus-charged (polarized) unstained sections for immunoperoxidase studies from 1-2 representative blocks and 1-2 H&E slides from the same blocks.

Documentation including:

- Institutional Pathology Report *
- ARST0331 Pathology Checklist
- Institutional Operative Report
- COG Specimen Transmittal form

Material must be sent by **OVERNIGHT** carrier for next day delivery.

Label all materials with the patient's COG patient identification number.

Please call the STS Pathology Center at 614-722-2898 to notify them of the shipment.

Label the parcel "**STS Rapid Review**".

Please use the phone number listed below, which is for the central receiving area, on all packages shipped to the STS Pathology Center.

Send all pathology central rapid review materials to:

COG Soft Tissue Sarcoma
Columbus Children's Hospital
700 Children's Drive WA1340
Columbus, OH 43205
Phone: (614) 722-2810
FAX: (614) 722-2897

**a preliminary report may be sent with the review material, but please fax the final report when available*