

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

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Synopsis:

The Soft Tissue Sarcoma Committee of the Children's Oncology Group (COG), formerly known as the Intergroup Rhabdomyosarcoma Study Group (IRSG), has completed a series of studies over the last thirty years that have improved the outcome for patients with rhabdomyosarcoma using chemotherapy consisting of VAC (vincristine, actinomycin-D, and cyclophosphamide) plus radiation therapy and/or surgery; these treatments are now considered the standard of care for rhabdomyosarcoma patients. Children with rhabdomyosarcoma are classified by the Soft Tissue Sarcoma Committee into one of three risk-groups (low, intermediate, or high) based on the likelihood that their tumor will come back, either during treatment or after finishing treatment. Patients in the low-risk category have the lowest risk of the tumor coming back and therefore the highest chance of cure. Risk is determined by:

- looking at the cancer cells under a microscope (some types of rhabdomyosarcoma cells are more difficult to treat than others)
- using X-rays and scans to find out where in the body the tumor is located and whether the tumor is contained in the place where it first developed or has spread to other areas of the body (including to lymph nodes)
- using the X-ray and scan information to decide whether the tumor can be taken out completely with surgery

ARST0331 is only for patients who are classified as low-risk. With information gathered in the past studies, it has been found that "low risk patients" should also be subdivided into two groups (called Subsets 1 and 2). Patients in Subset 2 require stronger therapy than patients in Subset 1 because their tumors are larger, or tumor cells have spread to the nearby lymph nodes, or the tumor cannot be taken out completely by surgery; in past studies patients in Subset 2 have generally been treated with VAC chemotherapy while patients in Subset 1 have been treated with only vincristine and actinomycin-D (VAC minus cyclophosphamide).

ARST0331 is being done to see:

- if lower doses of the chemotherapy drug cyclophosphamide (with standard doses of vincristine and actinomycin-D) with or without radiation therapy for patients in Subset 1 will make the outcome even better than it has been with the standard treatment
- if lower doses of the chemotherapy drug cyclophosphamide (with standard doses of vincristine and actinomycin-D) with or without radiation therapy for patients in Subset 2 will maintain the outcome as good as standard treatment but lower the possibility of late effects caused by using standard treatment methods (late

effects are health problems that happen to patients later in life because of the drugs used to treat their cancers). Possible late effects include problems with growth, inability to have children, or developing a second type of cancer.

Patients assigned to Subset 1 will receive treatment according to Regimen A; these patients will have four cycles of VAC chemotherapy. At this point, the treatment team at the hospital where the patient is receiving care will do evaluation tests and scans and decide whether to do surgery and/or radiation therapy. Chemotherapy on Regimen A will continue with four cycles of VA (VAC minus the cyclophosphamide). This will be the end of protocol therapy, at about 24 weeks. This is a shorter length of therapy (24 weeks versus 48 weeks) than has been used for rhabdomyosarcoma in other COG studies. We think the shorter length of therapy will be safe and effective based on research conducted in Europe on patients with low-risk rhabdomyosarcoma.

Patients assigned to Subset 2 will receive treatment according Regimen B; these patients will have four cycles of VAC chemotherapy. At this point, the treatment team at the hospital where the patient is receiving care will do evaluation tests and scans and decide whether to do surgery and/or radiation therapy. However, Regimen B patients will continue with VA chemotherapy (with periodic evaluations) for up to 48 weeks.

The chemotherapy drugs in the study are given I.V. (I.V. means intravenously, into a vein, preferably by injection into a central line). Along with the study drugs, patients may receive a drug to help the blood counts recover during chemotherapy (Filgrastim) and will receive a drug (MESNA) to help protect the bladder during chemotherapy with cyclophosphamide. Other drugs may be used to counteract nausea and vomiting that can occur during chemotherapy with these study drugs.

The combination of drugs used in these protocols carries a slight risk of serious health effects such as liver problems or another cancer later in life, but not more risk than that of patients who are not on this study and receive the standard drug therapy. If you decide to participate in this study you will discuss all the risks in greater detail, including the risks of surgery and radiation therapy, with the doctors who will be giving the treatment.

Once therapy on the protocol is finished, the researchers will continue to provide periodic standard medical tests (such as chest X-rays and CT or MRI scans, physical exams, and blood tests) to watch for any recurrences of the tumor.