A Study Comparing Higher Dose Chemotherapy Over a Shorter Amount of Time to Lower Dose Chemotherapy Plus Maintenance Over a Longer Amount of Time in Patients With Newly Diagnosed Intermediate-Risk Rhabdomyosarcoma (IR RMS)

Status: RECRUITING

Eligibility Criteria

Age: Up to 50 years old

This study is NOT accepting healthy

Healthy Volunteers: volunteers

Inclusion Criteria:

* Patient must be ≤ 50 years of age at the time of enrollment * Patients with newly diagnosed soft tissue RMS of any subtype, except adult-type pleomorphic, based upon institutional histopathologic classification, are eligible to enroll on the study based upon FOXO1 fusion status, Stage, Intergroup Rhabdomyosarcoma Study (IRS) group, and age, as below. FOXO1 fusion status must be determined prior to enrollment. RMS types included under embryonal rhabdomyosarcoma (ERMS) include those which are reclassified in the 2020 World Health Organization (WHO) classification as ERMS (typical, dense and botryoid variants) and spindle cell/sclerosing RMS (encompassing the historical spindle cell ERMS variant and the newly recognized sclerosing RMS variant). Classification of alveolar Rhabdomyosarcoma (ARMS) in the 2020 WHO Classification is the same as in the International Classification of Rhabdomyosarcoma (ICR) and includes classic and solid variants. * FOXO1 fusion negative (FN) * Stage 2/3, Group III * Stage 4, Group IV, \< 10 years old * FOXO1 fusion positive (FP) * Stages 1-3, Groups I-III * Disease/staging imaging studies, if applicable, must be obtained within 21 days prior to enrollment and start of protocol therapy (repeat if necessary) * FOXO1 status results must be available to enroll. All patients will undergo institutional pathology review and institutional FOXO1 fusion determination regardless of histology prior to enrollment. FOXO1 status may confirmed by cytogenetic, fluorescence in situ hybridization (FISH), or next generation sequencing techniques. FOXO1 fusion results should be SUBMITTED as an upload to RAVE at study enrollment because this information is required for randomization. Please note the following: * Institutional PAX3 versus (vs.) PAX7 determination is not required but should be submitted if available. Institutional FOXO1 testing may be performed at a contract or commercial lab as long as reports can be submitted and uploaded to RAVE. Additional molecular pathology reports, including the MCI report, are not required but should be submitted if available. * Patients who are \< 10 years old with distant metastatic disease (Stage 4) who have institutional molecular testing indicating fusion negative (FN) RMS but are later found to have fusion positive (FP) RMS by MCI or other testing will be considered to have metastatic FP disease and will go off study * Appropriate lymph node sampling based on primary site of disease is required * Patients must have a performance status of Lansky performance status score ≥ 50 for patients ≤ 16 years of age or Karnofsky performance status score ≥ 50 for patients \> 16 years of age * Peripheral absolute neutrophil count (ANC) ≥ 750/µL (All laboratory studies to determine eligibility must be performed within 7 days prior to enrollment unless otherwise indicated. Laboratory studies must be repeated prior to the start of protocol therapy if \> 7 days have elapsed from their most recent prior assessment. Laboratory tests need not be repeated if therapy starts within seven (7) days of their most recent prior assessment. If the result of a laboratory study that is repeated at any time post-enrollment and prior to the start of protocol therapy is outside the limits for eligibility, then the evaluation must be rechecked within 48 hours prior to initiating protocol therapy. The results of the recheck must be within the limits for eligibility to proceed. If the result of the recheck is outside the limits of eligibility, the patient may not receive protocol therapy and will be considered off protocol therapy.) * Platelet count ≥ 75,000/µL (All laboratory studies to determine eligibility must be performed within 7 days prior to enrollment unless otherwise indicated. 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If the result of the recheck is outside the limits of eligibility, the patient may not receive protocol therapy and will be considered off protocol therapy.) * For pediatric patients \< 18 years of age: * A serum creatinine based on age/sex as follows: * 1 month to \< 6 months: Maximum serum creatinine 0.4 mg/dL (male), 0.4 mg/dL (female) * 6 months to \< 1 year: Maximum serum creatinine 0.5 mg/dL (male), 0.5 mg/dL (female) * 1 to \< 2 years: Maximum serum creatinine 0.6 mg/dL (male), 0.6 mg/dL (female) * 2 to \< 6 years: Maximum serum creatinine 0.8 mg/dL (male), 0.8 mg/dL (female) * 6 to \< 10 years: Maximum serum creatinine 1 mg/dL (male), 1 mg/dL (female) * 10 to \< 13 years: Maximum serum creatinine 1.2 mg/dL (male), 1.2 mg/dL (female) * 13 to \< 16 years: Maximum serum creatinine 1.5 mg/dL (male), 1.4 mg/dL (female) * ≥ 16 years: Maximum serum creatinine 1.7 mg/dL (male),1.4 mg/dL (female) * OR a 24-hour urine Creatinine clearance ≥ 50 mL/min/1.73 m\^2 * OR a glomerular filtration rate (GFR) ≥ 70 mL/min/1.73 m\^2. GFR must be performed using direct measurement with a nuclear blood sampling method OR direct small molecule clearance method (iothalamate or other molecule per institutional standard). * Note: Estimated GFR (eGFR) from serum creatinine, cystatin C or other estimates are not acceptable for determining eligibility. * Patients with an elevated serum creatinine due to obstructive hydronephrosis secondary to tumor are still eligible. However, patients with urinary tract obstruction by tumor must have unimpeded urinary flow established via diversion (ie, percutaneous nephrostomies or ureteric stents) of the urinary tract. For adult patients (aged 18 years or older): * Creatinine clearance ≥ 50 mL/min, as estimated by the Cockcroft and Gault formula or as a 24-hour urine collection. Estimated creatinine clearance is based on actual body weight. (All laboratory studies to determine eligibility must be performed within 7 days prior to enrollment unless otherwise indicated. Laboratory studies must be repeated prior to the start of protocol therapy if \> 7 days have elapsed from their most recent prior assessment. Laboratory tests need not be repeated if therapy starts within seven (7) days of their most recent prior assessment. If the result of a laboratory study that is repeated at any time post-enrollment and prior to the start of protocol therapy is outside the limits for eligibility, then the evaluation must be rechecked within 48 hours prior to initiating protocol therapy. The results of the recheck must be within the limits for eligibility to proceed. If the result of the recheck is outside the limits of eligibility, the patient may not receive protocol therapy and will be considered off protocol therapy.) * Total bilirubin ≤ 1.5 x upper limit of normal (ULN) for age (All laboratory studies to determine eligibility must be performed within 7 days prior to enrollment unless otherwise indicated. Laboratory studies must be repeated prior to the start of protocol therapy if \> 7 days have elapsed from their most recent prior assessment. Laboratory tests need not be repeated if therapy starts within seven (7) days of their most recent prior assessment. If the result of a laboratory study that is repeated at any time post-enrollment and prior to the start of protocol therapy is outside the limits for eligibility, then the evaluation must be rechecked within 48 hours prior to initiating protocol therapy. The results of the recheck must be within the limits for eligibility to proceed. If the result of the recheck is outside the limits of eligibility, the patient may not receive protocol therapy and will be considered off protocol therapy.) * If there is evidence of biliary obstruction by tumor, then total bilirubin must be \< 3 x ULN for age * Serum glutamic pyruvic transaminase (SGPT) (alanine aminotransferase \[ALT\]) ≤ 135 U/L (All laboratory studies to determine eligibility must be performed within 7 days prior to enrollment unless otherwise indicated. Laboratory studies must be repeated prior to the start of protocol therapy if \> 7 days have elapsed from their most recent prior assessment. Laboratory tests need not be repeated if therapy starts within seven (7) days of their most recent prior assessment. If the result of a laboratory study that is repeated at any time post-enrollment and prior to the start of protocol therapy is outside the limits for eligibility, then the evaluation must be rechecked within 48 hours prior to initiating protocol therapy. The results of the recheck must be within the limits for eligibility to proceed. If the result of the recheck is outside the limits of eligibility, the patient may not receive protocol therapy and will be considered off protocol therapy.) * Note: For the purpose of this study, the ULN for SGPT (ALT) has been set to the value of 45 U/L. * Known HIV-infected patients on effective anti-retroviral therapy with undetectable viral load within 6 months are eligible for this trial

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Exclusion Criteria:

* Patients with evidence of uncontrolled infection are not eligible * Previous or concurrent cancer(s) that is/was being treated with chemotherapy and/or radiation. * Note:

Surgical resection alone of previous or concurrent cancer(s) is allowed * Patients with central nervous system involvement of RMS as defined below: * Malignant cells detected in cerebrospinal fluid * Intra-parenchymal brain metastases separate and distinct from primary tumor (i.e., direct extension from parameningeal primary tumors is allowed) * Diffuse leptomeningeal disease * Patients with known Charcot-Marie-Tooth disease * Patients who have received any chemotherapy (excluding steroids) and/or radiation therapy for RMS prior to enrollment. Note: the following exception: * Patients requiring emergency radiation therapy for life-threatening complications of tumor burden due to RMS. These patients are eligible, provided they are consented to ARST2531 prior to administration of radiation. * Note: Patients who have received or are receiving chemotherapy or radiation for non-malignant conditions (eg, autoimmune diseases) are eligible. Patients must discontinue chemotherapy for non-malignant conditions prior to starting protocol therapy * Female patients who are pregnant since fetal toxicities and teratogenic effects have been noted for several of the study drugs. A pregnancy test is required for female patients of childbearing potential * Lactating females who plan to breastfeed their infants * Sexually active patients of reproductive potential who have not agreed to use an effective contraceptive method for the duration of their study participation

Conditions & Interventions

Interventions:
PROCEDURE: Biospecimen Collection, PROCEDURE: Bone Marrow Aspiration, PROCEDURE: Bone Marrow Biopsy, PROCEDURE: Bone Scan, PROCEDURE: Computed Tomography, DRUG: Cyclophosphamide, BIOLOGICAL: Dactinomycin, DRUG: Irinotecan Hydrochloride, PROCEDURE: Lumbar Puncture, PROCEDURE: Lymph Node Biopsy, PROCEDURE: Magnetic Resonance Imaging, PROCEDURE: Positron Emission Tomography, RADIATION: Radiation Therapy, PROCEDURE: Resection, OTHER: Survey Administration, DRUG: Vincristine Sulfate, DRUG: Vinorelbine Tartrate
Conditions:
Rhabdomyosarcoma

More Information

Contact(s): ctrrecruit@vcu.edu
Principal Investigator:
IRB
Number:
System ID: NCT07466316

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