Trastuzumab Deruxtecan (DS-8201a) for the Treatment of Recurrent or Refractory Osteosarcoma, Wilms Tumor, and Desmoplastic Small Round Cell Tumor

Status: RECRUITING

Eligibility Criteria

Sex: ALL
Age: 12 years to 39 years old
Healthy Volunteers: This study is NOT accepting healthy volunteers
Inclusion Criteria:

- Phase 1 (Part A): Patients must be at least 2 years and less than 12 years of age at the time of study enrollment
- Phase 2: Wilms tumor patients (Part B1): All Wilms tumor patients enrolled must be less than 18 years of age at enrollment
    - Until the completion of the Phase 1 dose confirmation, patients must be at least 12 years of age and less than 18 years of age at the time of study enrollment
    - Following dose confirmation of DS-8201a in children at least 2 to less than 12 years old in the Phase 1 component, Wilms tumor patients at least 2 to less than 18 years of age will be allowed on the Phase 2 component
- Phase 2: DSRCT patients (Part B2): Until the completion of the Phase 1 component, patients enrolling on the Phase 2 component of the study must be from at least 12 to 39 years of age at the time of study enrollment
    - Following dose confirmation of DS-8201a in children at least 2 to less than 12 years old in the Phase 1 component, DSRCT patients at least 2 to 39 years of age will be allowed on the Phase 2 component
- Patients must have had histologic verification of Wilms tumor or desmoplastic small round cell tumor at original diagnosis or relapse
- Solid tumors: Patients must have measurable disease according to Response Evaluation Criteria in Solid Tumors (RECIST) 1.1. Patients with clinically inactive brain metastases may be included in the study. Patients with treated brain metastases that are no longer symptomatic and who require no treatment with corticosteroids or anticonvulsants may be included in the study if they have recovered from the acute toxic effect of radiotherapy. Lastly, patient must have unresectable lesions or lesions with no intention to surgically remove the lesions in the 6 months following enrollment
- Wilms tumor: WT patients must have either refractory disease or a very high risk relapse, defined as ANY of the following:
    - Relapse after initial treatment with 4 or more chemotherapy agents (e.g. Regimens vincristine, dactinomycin, doxorubicin, cyclophosphamide, etoposide and radiation [M], vincristine, dactinomycin and doxorubicin, vincristine, and irinotecan [MVI], doxorubicin, vincristine, cyclophosphamide, carboplatin, etoposide and radiation [UH-1], doxorubicin, vincristine, cyclophosphamide, carboplatin, etoposide, vincristine, and irinotecan [UH-2], vincristine, irinotecan, cyclophosphamide, carboplatin, etoposide and doxorubicin [UH-3], and etoposide, carboplatin, cyclophosphamide, and doxorubicin [HR-1])
    - Relapse with high risk histology (anaplasia, blastemal predominant)
    - Multiple relapses
- Desmoplastic small round cell tumor: DSRCT patients with relapsed or refractory disease are eligible
- Patient's current disease state must be one for which they have received at least standard initial therapy, defined as systemic therapy combined with either radiation or surgery for local control of the primary tumor at diagnosis. Prior therapy after relapse is not required
- Patients must have a performance status corresponding to Eastern Cooperative Oncology Group (ECOG) scores of 0 or 1. Use Karnofsky for patients older than 16 years of age and Lansky for patients 16 years of age and younger
- Patients must have recovered from the acute toxic effects of all prior anti-cancer therapy and must meet the following minimum duration from prior anti-cancer directed therapy prior to enrollment. If after the required timeframe, the numerical eligibility criteria are met, e.g., blood count criteria, the patient is considered to have recovered adequately
    - Cytotoxic chemotherapy or other anti-cancer agents known to be myelosuppressive: For agents not listed, the duration of this interval must be discussed with the study chair and the study-assigned Research Coordinator prior to enrollment
    - >= 21 days after the last dose of myelosuppressive chemotherapy (42 days if prior nitrosourea)
    - Anti-cancer agents not known to be myelosuppressive (e.g., not associated with reduced platelet or absolute neutrophil count [ANC] counts): >= 7 days after the last dose of agent
    - Antibodies: >= 4 weeks (28 days) must have elapsed from infusion of last dose of antibody, and toxicity related to prior antibody therapy must be recovered to grade =< 1
    - Corticosteroids
    - Hematopoietic growth factors: >= 14 days after the last dose of a long-acting growth factor (e.g. pegfilgrastim) or 7 days for short-acting growth factor. For agents that have known adverse events occurring beyond 7 days after administration, this period must be extended beyond the time during which adverse events are known to occur
    - Interleukins, interferons and cytokines (other than hematopoietic growth factors): >= 21 days after the completion of interleukins, interferon or cytokines (other than hematopoietic growth factors)
    - Stem cell Infusions (with or without total body irradiation [TBI]):
    - Allogeneic (non-autologous) bone marrow or stem cell transplant, or any stem cell infusion including donor lymphocyte infusion (DLI) or boost infusion: >= 84 days after infusion and no evidence of graft versus host disease (GVHD)
    - Autologous stem cell infusion including boost infusion: >= 20 days

    - Autologous stem cell infusion including boost infusion: >= 30 days
    - Cellular therapy: >= 30 days after the completion the infusion of any type of cellular therapy (e.g., modified T cells, natural killer [NK] cells, dendritic cells, etc.)
    - Radiation therapy (XRT)/external beam irradiation including protons: >= 4 weeks (28 days) including palliative radiation therapy to the chest. >= 14 days after palliative local XRT to areas other than the chest or for whole brain radiotherapy
    - Radiopharmaceutical therapy (e.g., radiolabeled antibody, samarium): >= 42 days after systemically administered radiopharmaceutical therapy
    - Patients must not have received prior HER2 therapies including antibody drug conjugates (e.g. TDM-1 or DS-8201a), HER2 directed cellular therapies, HER2 receptor therapy (e.g. trastuzumab, pertuzumab, margetuximab, zanidatamab, zenocutuzumab) or small molecule antagonists of HER2 (e.g lapatinib, tucatinib, or neratinib). Prior exposure to antibody drug conjugates which do not target HER2 as well as prior treatment with topoisomerase 1 inhibitors (e.g. irinotecan, topotecan) are permitted
- Patients must be at least 14 days from the date of last surgery
- Peripheral absolute neutrophil count (ANC) >= 1000/uL, (for patients with solid tumors without known bone marrow involvement)
- Platelet count >= 100,000/uL (transfusion independent, defined as not receiving platelet transfusions for at least 7 days prior to enrollment) (for patients with solid tumors without known bone marrow involvement)
- Hemoglobin >= 8.0 g/dL at baseline (Red Blood Cell transfusion is not allowed within 1 week prior to enrollment) (for patients with solid tumors without known bone marrow involvement)
- For patients less than or equal to 17 years old, "Bedside" Schwartz formula (2009)
- Estimated glomerular filtration rate (GFR) (eGFR) ≥ 70 mL/min/1.73 m^2 (> 70mL/min/1.73 m^2 for patients > 17 years old)
    - For patients older than 17 years of age the Cockroft-Gault equation should be utilized to calculate creatinine clearance ≥ 70 ml/min:
    - OR for any age group:
    - A 24 hour urine creatinine clearance ≥ 70 mL/min/1.73 m^2 (> 70mL/min for patients ≥ 17 years old) OR
    - A directly measured 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)
- Bilirubin (sum of conjugated + unconjugated or total) =< 1.5 x upper limit of normal (ULN) for age. For patients with documented Gilbert's syndrome (unconjugated hyperbilirubinemia) bilirubin must be < 3 x ULN for age (patients with solid tumors)
- Aspartate aminotransferase (AST) =< 3 x ULN
- Serum albumin >= 2.5 g/dL (patients with solid tumors)
- International normalized ratio (INR)/prothrombin time (PT) =< 1.5 x ULN. Exception for patients receiving coumarin-derivative anticoagulants or other similar anticoagulant therapy, who must have INR/PT within the therapeutic range as deemed appropriate by the investigator
- Shortening fraction of >= 27% by echocardiogram, or ejection fraction of >= 50% by either an echocardiogram (ECHO) or multigated acquisition (MUGA) scan within 28 days before Step 1 enrollment
- Corrected QT interval (QTc) prolongation to < 480 ms based on average triplicate 12-lead electrocardiogram (ECG)
- Pulse oximetry > 93% on room air
- Patients with seizure disorder may be enrolled if on anticonvulsants and well controlled as evidenced by no increase in seizure frequency in the prior 7 days
- Nervous system disorders (Common Terminology Criteria for Adverse Events [CTCAE] version [v]5) resulting from prior chemotherapy, surgery, and/or radiation must be =< grade 2, with the exception of decreased tendon reflex (DTR). Any grade of DTR is eligible
- HIV-infected patients on effective anti-retroviral therapy with undetectable viral load within 6 months of enrollment are eligible
- All patients and/or their parents or legally authorized representatives must sign a written informed consent. Assent, when appropriate, will be obtained according to institutional guidelines

Exclusion Criteria:

- Pregnant, planning to become pregnant, or breast-feeding women will not be entered on this study. Pregnancy tests must be obtained in girls who are post-menarchal. Males or females of reproductive potential may not participate unless they have agreed to use two effective methods of birth control, including a medically accepted barrier or contraceptive method (e.g., male or female condom) for the duration of the study and upon completion of the study and for at least 7 months for females and 4 months for males after the last dose of study drug. Abstinence is an acceptable method of birth control
    - Methods considered as highly effective methods of contraception include:
    - Combined (estrogen and progestogen containing) hormonal contraception associated with inhibition of ovulation:
        - Oral
        - Intravaginal
        - Transdermal
    - Progestogen-only hormonal contraception associated with inhibition of ovulation:
        - Oral
        - Injectable
        - Implantable
    - Intrauterine device (IUD)
    - Intrauterine hormone-releasing system (IUS)
    - Bilateral tubal occlusion
    - Vasectomized partner
    - Complete sexual abstinence defined as refraining from heterosexual intercourse. Periodic abstinence (calendar, symptothermal, post

    - Complete sexual abstinence defined as refraining from heterosexual intercourse. Periodic abstinence (calendar, symptothermal, post-ovulation methods) is not an acceptable method of contraception
- Non-child-bearing potential defined as pre-menopausal females with a documented tubal ligation or hysterectomy; or postmenopausal defined as 12 months of spontaneous amenorrhea (in questionable cases, a blood sample with simultaneous follicle-stimulating hormone [FSH] > 40 mIU/mL and estradiol < 40 pg/mL [< 147 pmol/L] is confirmatory). Females on hormone replacement therapy (HRT) and whose menopausal status is in doubt will be required to use one of the contraception methods outlined for women of child-bearing potential if they wish to continue their HRT during the study. Otherwise, they must discontinue HRT to allow confirmation of post-menopausal status prior to study enrollment. For most forms of HRT, at least 2-4 weeks will elapse between the cessation of therapy and the blood draw; this interval depends on the type and dosage of HRT. Following confirmation of their post-menopausal status, they can resume use of HRT during the study without use of a contraceptive method
- Male patients must not freeze or donate sperm starting at enrollment and throughout the study period, and at least 4 months after the final study drug administration. Preservation of sperm should be considered prior to enrolment in this study
- Female patients must not donate, or retrieve for their own use, ova from the time of enrollment and throughout the study treatment period, and for at least 7 months after the final study drug administration
- Patients receiving corticosteroids who have not been on a stable or decreasing dose of corticosteroid for at least 7 days prior to enrollment are not eligible. If used to modify immune adverse events related to prior therapy, >= 14 days must have elapsed since last dose of corticosteroid
- Patients who are currently receiving another investigational drug are not eligible
- Patients who are currently receiving other anti-cancer agents are not eligible
- Patients who are receiving cyclosporine, tacrolimus or other agents to prevent graft-versus-host disease post bone marrow transplant are not eligible for this trial
- Patients who are receiving chloroquine or hydroxychloroquine within 14 days are not eligible for this trial
- Patients who received a live, attenuated vaccine (messenger ribonucleic acid [mRNA] and replication deficient adenoviral vaccines are not considered attenuated live vaccines) within 30 days prior to enrollment are not eligible for this trial
    - Note: Participants, if enrolled, should not receive live vaccines during the study and up to 90 days after the last dose of study intervention. It is recommended that patients receive a yearly influenza killed vaccination and additional killed vaccinations based on local or national recommendations. Consider vaccination against viral pathogens that cause pneumonias according to local or national guidelines
- Patients who have received a prior solid organ transplantation are not eligible
- Patients with a medical history of myocardial infarction within 180 days before enrollment, symptomatic congestive heart failure (CHF) (New York Heart Association Class II to IV) or troponin levels consistent with myocardial infarction as defined according to the manufacturer 28 days prior to enrollment are not eligible
- Additionally, patients with a history of any of the following congenital heart disease are not eligible:
    - Single ventricle heart defects (hypoplastic left heart syndrome, unbalanced atrioventricular septal defects, double inlet left ventricle, tricuspid atresia, the presence of superior cavopulmonary anastomosis or Fontan palliation);
    - Unpalliated defects with significant hemodynamic alterations or palliated lesions with residual hemodynamic alterations (ductal-dependent or shunt-dependent physiology, large unrestrictive ventricular septal defect, transposition of the great arteries, greater than moderate atrioventricular valve insufficiency, moderate or greater aortic valve stenosis, moderate or greater aortic valve insufficiency, large atrial septal defects with significant right ventricular volume overload, large patent ductus arteriosus)
- Patients who have a pleural effusion, ascites or pericardial effusion that requires drainage, peritoneal shunt, or cell-free and concentrated ascites reinfusion therapy (CART) are not eligible. (Drainage and concentrated ascites reinfusion therapy are not allowed within 2 weeks prior to enrollment)
- Patients who have spinal cord compression or clinically active central nervous system metastases, defined as untreated and symptomatic, or requiring therapy with corticosteroids or anticonvulsants to control associated symptoms are not eligible
- Patients with a known history of severe hypersensitivity to DS-8201a, any excipient contained in the DS-8201a drug formulation, or HER2-targeted monoclonal antibodies (trastuzumab, pertuzumab, margetuximab) are not eligible
- Patients who have an uncontrolled infection or non-healing surgical site are not eligible
- Patients with a known history of substance abuse or any other clinically significant medical conditions (i.e. psychological conditions) that may, in the opinion of the investigator, interfere with the patient's participation in the clinical study or evaluation of the clinical study results are not eligible
- Patients who have pulmonary compromise, ex hypoxia, resulting from intercurrent pulmonary illnesses including, but not limited to, any underlying pulmonary disorder (i.e. pulmonary emboli within three months of the study enrollment, severe asthma, severe chronic obstructive pulmonary disease (COPD), restrictive lung disease, pleural effusion etc.), or prior pneumonectomy are not eligible
- Patients who have a history of (non-infectious) ILD (interstitial lung disease)/pneumonitis that required steroids, has current ILD/pneumonitis, or for whom suspected ILD/pneumonitis cannot be ruled out by imaging at screening are not eligible. Patients who have history of genetic disorders of the lung (i.e. cystic fibrosis are not eligible)
- Patients who, in the opinion of the investigator, may not be able to comply with the safety monitoring requirements of the study are not eligible
- Patients with known hepatitis B or C with detectable viral load are not eligible

- Patients with any autoimmune, connective tissue or inflammatory disorders (e.g., rheumatoid arthritis, Sjogren's, sarcoidosis etc.) where there is documented, or a suspicion of pulmonary involvement at the time of enrollment or genetic diseases involving the lung are not eligible
- Patients with an active primary immunodeficiency are not eligible

Conditions & Interventions

Interventions:
PROCEDURE: Biospecimen Collection, PROCEDURE: Computed Tomography, PROCEDURE: Echocardiography Test, PROCEDURE: Magnetic Resonance Imaging, PROCEDURE: Multigated Acquisition Scan, BIOLOGICAL: Trastuzumab Deruxtecan
Conditions:
Desmoplastic Small Round Cell Tumor, Osteosarcoma, Recurrent Desmoplastic Small Round Cell Tumor, Recurrent Kidney Wilms Tumor, Recurrent Osteosarcoma, Refractory Desmoplastic Small Round Cell Tumor, Refractory Wilms Tumor, Wilms Tumor

More Information

Description:
This phase I/II trial studies the effects of trastuzumab deruxtecan (DS-8201a) in treating patients with osteosarcoma, Wilms tumor (WT) or desmoplastic small round cell tumor (DSRCT) that is newly diagnosed or has come back after a period of improvement (recurrent) or that has not responded to previous treatment (refractory). Trastuzumab deruxtecan is in a class of medications called antibody-drug conjugates. It is composed of a monoclonal antibody, called trastuzumab, linked to a chemotherapy drug, called deruxtecan. Trastuzumab attaches to HER2 positive tumor cells in a targeted way and delivers deruxtecan to kill them.

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