Silmitasertib (CX-4945) in Combination With Chemotherapy for Relapsed Refractory Solid Tumors

Status: RECRUITING

Eligibility Criteria

Age: Up to 30 years old

This study is NOT accepting healthy

Healthy Volunteers: volunteers

Inclusion Criteria:

1. Age: Less than 30 years old at initial diagnosis 2. Pathology All subjects must have a confirmed diagnosis of tumor type. Phase I: Relapsed/refractory solid tumors: Neuroblastoma, Ewing Sarcoma, Osteosarcoma, Rhabdomyosarcoma, Liposarcoma Phase II: * Relapsed/refractory Neuroblastoma * Relapsed/refractory Ewing sarcoma 3. Tumor assessment: Disease assessment is required for eligibility and must be done after last dose of previous therapy and prior to first dose of study drug. 4. Disease Status: Relapsed/Refractory Neuroblastoma Relapsed disease defined as neuroblastoma that was previously in remission after standard therapy (at least 4 cycles of aggressive multi-drug induction chemotherapy, with or without radiation and surgery, followed by immunotherapy, or according to a standard high-risk treatment/neuroblastoma protocol) and has now relapsed and is in any number of relapses. Refractory disease defined as High-risk neuroblastoma (as defined by INRG) that failed to achieve CR after at least 4 cycles of aggressive multi-drug induction chemotherapy, progression during upfront therapy or with disease remaining after standard immunotherapy. International Neuroblastoma Risk Group Staging System (INRG) High Risk NB defined as one of the following: 1. Any age with International Neuroblastoma Risk Group (INRG) Stage L2, MS, or M with MYCN amplification 2. Age ≥ 547 days and INRG Stage M regardless of biologic features 3. Any age initially diagnosed with INRG Stage L1 MYCN amplified NBL who have progressed to Stage M without systemic chemotherapy 4. Age ≥ 547 days of age initially diagnosed with INRG Stage L1, L2, or MS who have progressed to Stage M without systemic chemotherapy Relapsed/refractory Sarcoma Subjects that have relapsed following standard of care therapy or having progressed during standard of care therapy. Standard of care therapy for sarcoma includes multi-agent chemotherapy with local control consisting of either surgery or radiation therapy. 5. Measurable or evaluable disease, including at least one of the following: * Measurable tumor by CT or MRI * MIBG or PET that is positive for disease * Bone Marrow biopsy/aspirate that is positive for disease 6. Timing from prior therapy: Subjects must have fully recovered from the acute toxic effects of all prior anti- cancer therapy and be within the following timelines: 1. Myelosuppressive chemotherapy: Must not have received within 2 weeks of enrollment onto this study. 2. Small Molecule Inhibitors (anti-neoplastic agent): At least 2 weeks from the completion of therapy with a small molecule inhibitor. 3. Immunotherapy: At least 4 weeks since the completion of any type of immunotherapy, e.g. tumor vaccines, CAR-T cells, anti-GD2 Monoclonal antibodies (ex. naxitamab, dinutuximab, etc.). 4. Radiotherapy: At least 30 days since the last treatment except for radiation delivered with palliative intent to a non-target site. 5. Stem Cell Transplant: * Allogeneic: No evidence of active graft vs. host disease * Allogeneic/Autologous: ≥ 2 months must have elapsed since transplant. 6. MIBG Therapy: At least 6 weeks since treatment with MIBG therapy. 7. Subjects must have a Lansky or Karnofsky Performance Scale score of \>/= 50. 8. Subjects must have adequate organ function at the time of enrollment: * Cardiac: Subjects must have a QTcF ≤ 480 msc. * Hematological: Hematological recovery as defined by ANC ≥750/µL * Liver: Adequate liver function as defined by AST and ALT \<5x upper limit of normal * Renal: Subjects must have adequate renal function defined as an estimated Glomerular Filtration rate (eGFR) as calculated from the Bedside Schwartz equation (in units of mL/min/1.73 m2) or via radioisotope GFR ≥ 70. The Bedside Schwartz equation is: \[(0.413) X (Height in cm)\] / SCr 9. Subjects of childbearing potential must have a negative serum pregnancy test. Subjects of childbearing potential must agree to use effective measures to avoid pregnancy. 10. Written informed consent in accordance with institutional and FDA guidelines must be obtained from all subjects (or subjects' legal representative).

Exclusion Criteria:

1. Investigational Drugs: Subjects who are currently receiving another investigational drug are excluded from participation. 2. Anti-cancer Agents: Subjects who are currently receiving other anticancer agents are not eligible. Subjects must have fully recovered from the hematological and bone marrow suppression effects of prior therapy. 3. Subjects who are currently receiving Vitamin K antagonists (warfarin). 4. Subjects who are currently receiving the class of lipid-lowering medications HMG-CoA reductase inhibitors (statins). 5. Infection: Subjects who have an uncontrolled infection are not eligible until the infection is judged to be well controlled in the opinion of the investigator. 6. Subjects who, in the opinion of the investigator, may not be able to comply with the safety monitoring requirements of the study, or in whom compliance is likely to be suboptimal, should be excluded. 7. Subjects with any clinically significant unrelated systemic illness (serious infections or significant cardiac, pulmonary, hepatic or other organ dysfunction), that in the opinion of the investigator would compromise the subject's ability to tolerate protocol therapy, put them at additional risk for toxicity or would interfere with the study procedures or results. 8. Subjects with any of the following gastrointestinal disorders: 1. Active malabsorption (e.g. short gut) syndrome. 2. Uncontrolled diarrhea (excess of 4 stools/day) 3. Gastritis, ulcerative colitis, Chron's disease or hemorrhagic coloproctitis 4. History of gastric or small bowel surgery involving any extent of gastric or small bowel resection 9. Lactating subjects are not eligible unless they have agreed to not breastfeed their infants. There is an unknown but potential risk for adverse events in nursing infants secondary to treatment of the nursing subject with silmitasertib. (NOTE: breast milk cannot be stored for future use while the nursing subject is being treated on study.) 10. Subjects with a history of any other malignancy.

Conditions & Interventions

Interventions:
DRUG: Silmitasertib, DRUG: Irinotecan, DRUG: Temozolomide, DRUG: Vincristine
Conditions:
Neuroblastoma, Ewing Sarcoma, Osteosarcoma, Rhabdomyosarcoma, Liposarcoma

More Information

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