Study of Lurbinectedin Monotherapy in Pediatric and Young Adult Participants With Relapsed/Refractory Ewing Sarcoma

Status: RECRUITING

Eligibility Criteria

Sex: ALL
Age: 2 years to 30 years old
Healthy Volunteers: This study is NOT accepting healthy volunteers
Key Inclusion Criteria:

Age

- Participant must meet the following age requirements at the time the informed consent form (ICF) (and assent form, if applicable) is signed:
    - Phase 1 Part 1: participants must be ≥ 2 to < 18 years of age.
    - Phase 1 Part 2: participants must be ≥ 2 to ≤ 30 years of age.
    - Phase 2: participants must be ≥ 2 to ≤ 30 years of age.

Type of Participant and Disease Characteristics

- Participant has a confirmed solid tumor
- The participant has a Lansky/Karnofsky performance status score of ≥ 50%.
- The participant has adequate liver function, evidenced by the following laboratory values:
    - Aspartate aminotransferase (AST), alanine aminotransferase (ALT) ≤ 2.5 × upper limit of normal (ULN).
    - Total bilirubin ≤ 1.5 × institutional ULN (with the exception of participants with Gilbert's syndrome who must have bilirubin < 3 × institutional ULN).
- The participant has adequate bone marrow function, evidenced by the following:
    - Absolute neutrophil count (ANC) ≥ 1.0 × 10^9/L (independent of growth factor support within 1 week of screening laboratories).
- Platelets ≥ 100 × 10^9/L (without platelet transfusion within previous 7 days of screening laboratories).
    - Hemoglobin ≥ 8 g/dL (note: may have been transfused).
- The participant has an adequate renal function:
    - Calculated creatinine clearance (use Cockcroft-Gault formula for participants ≥ 18 years; Schwartz equation for participants < 18 years) ≥ 60 mL/min.
- The participant has an adequate cardiac function:
    - Left ventricular ejection fraction or shortening fraction per institutional norm ≥ institutional lower level of normal.
- The participant has creatine phosphokinase ≤ 2.5 × institutional ULN.

Weight

- The participant has body weight ≥ 15 kg.

Sex and Contraceptive/Barrier Requirements

Male participants:

Male participants are eligible to participate if they agree to the following during the study intervention period and for at least 4 months after the last dose of study intervention:

- Refrain from donating sperm.

PLUS, either:

- Be abstinent from heterosexual intercourse as their preferred and usual lifestyle (abstinent on a long-term and persistent basis) and agree to remain abstinent.

OR

- Must agree to use contraception/barrier as detailed below:
    - Agree to use a male condom with female partner and use of an additional highly effective contraceptive method with a failure rate of < 1% per year when having sexual intercourse with a Woman of childbearing potential (WOCBP) who is not currently pregnant.
    - Note: male participants who are azoospermic (vasectomized or due to a medical cause) are still required to follow the protocol-specified contraception/barrier criteria.

Female participants:

A female participant is eligible to participate if she is not pregnant or breastfeeding, and one of the following conditions applies:

- Is a Woman of nonchildbearing potential (WONCBP). OR
- Is a WOCBP and using an acceptable contraceptive method during the study intervention period (at least 7 months after the last dose of study intervention). The investigator should evaluate the potential for contraceptive method failure (eg, noncompliance, recently initiated) in relationship to the first dose of study intervention.
- A WOCBP must have a negative highly sensitive pregnancy test (urine or serum as required by local regulations) within 7 days before the first dose of study intervention.
    - If a urine test cannot be confirmed as negative (eg, an ambiguous result), a serum pregnancy test is required. In such cases, the participant must be excluded from participation if the serum pregnancy result is positive.
- Additional requirements for pregnancy testing during and after study intervention.
- The investigator is responsible for review of medical history, menstrual history, and recent sexual activity to decrease the risk for inclusion of a woman with an early undetected pregnancy.

Informed Consent

- Capable of giving signed informed consent, which includes compliance with the requirements and restrictions listed in the ICF and in this protocol.

Key Exclusion Criteria:

Medical Conditions

- corrected QT interval (QTc) prolongation defined as a QTc ≥ 460 ms using the Bazett formula in age < 18 years and QTc ≥ 470 ms using the Bazett formula in age ≥ 18 years.
- Known symptomatic Central nervous system (CNS) metastases requiring steroids. Participants with previously diagnosed CNS metastases are eligible if they have completed their treatment and have recovered from the acute effects of radiation therapy or surgery prior to enrollment, have discontinued high dose steroid treatment for these metastases for at least 2 weeks, and are neurologically stable (physiologic doses of steroids and short courses of steroids for other indications are acceptable).
- Persisting toxicity related to prior therapy; however, alopecia, sensory neuropathy, hypothyroidism, and rash Grade ≤ 2 are acceptable, and other Grade ≤ 2 adverse events (AEs) not constituting a safety risk based on the investigator's judgement are acceptable.
- An uncontrolled intercurrent illness including but not limited to ongoing or active infection requiring antibiotic, antifungal, or antiviral therapy, symptomatic heart failure, cardiac arrhythmia, or psychiatric illness/social situations that would limit compliance with study requirements.
- Any other major illness that, in the investigator's judgment, could substantially increase the risk associated with participation in this study.
- Any other diseases, metabolic dysfunction, physical examination finding, or clinical laboratory finding giving reasonable suspicion of a disease or condition that contraindicates the use of an investigational drug or that may affect the interpretation of the results or render the participant at high-risk for treatment complications.

Prior/Concomitant Therapy

- Received prior treatment with lurbinectedin or trabectedin.
- Received prior treatment with any investigational product within 4 weeks of first infusion of study intervention. Observational studies are permitted.
- Received live or live attenuated vaccines within 4 weeks of the first dose of study treatment or plans to receive live vaccines during study participation. Administration of inactive vaccines or messenger ribonucleic acid (mRNA) vaccines (for example, inactivated influenza vaccines or COVID-19 vaccines) are allowed.
- Had major surgery ≤ 4 weeks or radiation therapy ≤ 2 weeks prior to enrollment unless fully recovered. Prior palliative radiotherapy is permitted, provided it was completed at least 2 weeks prior to participant enrollment.
- Received prior allogeneic bone marrow transplantation or solid organ transplant.
- Received chemotherapy ≤ 3 weeks prior to start of study intervention.

Diagnostic Assessments

- Hepatitis B virus (HBV) or Hepatitis C virus (HCV) infection at screening (positive HBV surface antigen or Polymerase chain reaction (PCR) test for HCV RNA if HCV antibody test is positive).
- Human immunodeficiency infection at screening (positive anti-HIV antibody).

Other Exclusions

- Has a known or suspected hypersensitivity to any of the components of the study intervention.
- The participant or parent(s)/guardian(s) is/are unable to comply with the study visit schedule and other protocol requirements, in the opinion of the investigator

Conditions & Interventions

Interventions:
DRUG: Lurbinectedin
Conditions:
Refractory Ewing Sarcoma, Relapsed Ewing Sarcoma, Ewing Sarcoma
Keywords:
Solid Tumors, lurbinectedin, ewing's sarcoma, soft tissue sarcoma, sarcomas

More Information

Description:
This study is conducted in two phases. The phase 1 portion of the study evaluates the safety, tolerability, pharmacokinetics (PK), recommended phase 2 dose (RP2D), and effectiveness of lurbinectedin monotherapy in pediatric participants with previously treated solid tumors. This is followed by the phase 2 portion, to further assess the effectiveness and safety in pediatric and young adult participants with recurrent/refractory Ewing

by the phase 2 portion, to further assess the effectiveness and safety in pediatric and young adult participants with recurrent/refractory Ewing sarcoma.

Contact(s): cancer@cchmc.org
Principal Investigator:
Principal Investigator ID:
Phase: PHASE1
IRB Number:
System ID: NCT05734066
