Testing a Standardized Approach to Surgery and Chemotherapy for Type I Pleuropulmonary Blastoma or the Addition of an Anti-cancer Drug, Topotecan, to the Usual Treatment for Types II and III Pleuropulmonary Blastoma

Status: RECRUITING

Eligibility Criteria

Sex: ALL
Age: Up to 21 years old
Healthy Volunteers: This study is NOT accepting healthy volunteers
Inclusion Criteria:

- 21 years of age or younger
- Newly diagnosed PPB. Note that patients with known germline DICER1 variant or mosaicism with a large, solid unresectable thoracic mass with imaging features characteristic for Type II or III PPB are eligible without histologic confirmation of the diagnosis if a biopsy of the mass is not considered safe or feasible
    - Individuals are eligible based on institutional diagnosis of Type I, Ir, II or III PPB diagnosed within 60 days prior to enrollment. Children with Type II or III PPB at risk for clinical decompensation may receive protocol therapy while awaiting rapid central pathology review. Children with Type I or Ir PPB will be assigned to chemotherapy vs. observation based on imaging and central pathology review diagnosis. Type I and Ir patients should not begin chemotherapy prior to return of central pathology results
- For patients with Type II or III PPB (within 7 days prior to enrollment): A serum creatinine based on age/sex as follows:
    - Age: 1 month to < 6 months - Maximum Serum Creatinine (mg/dL): 0.4 (Male), 0.4 (Female)
    - Age: 6 months to < 1 year - Maximum Serum Creatinine (mg/dL): 0.5 (Male), 0.5 (Female)
    - Age: 1 to < 2 years - Maximum Serum Creatinine (mg/dL): 0.6 (Male), 0.6 (Female)
    - Age: 2 to < 6 years - Maximum Serum Creatinine (mg/dL): 0.8 (Male), 0.8 (Female)
    - Age: 6 to < 10 years - Maximum Serum Creatinine (mg/dL): 1 (Male), 1 (Female)
    - Age: 10 to < 13 years - Maximum Serum Creatinine (mg/dL): 1.2 (Male), 1.2 (Female)
    - Age: 13 to < 16 years - Maximum Serum Creatinine (mg/dL): 1.5 (Male), 1.4 (Female)
    - Age: ≥ 16 years - Maximum Serum Creatinine (mg/dL): 1.7 (Male), 1.4 (Female) OR - A 24 hour urine creatinine clearance ≥ 60 mL/min/1.73 m^2 OR - A glomerular filtration rate (GFR) ≥ 60 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
- For patients with Type II or III PPB (within 7 days prior to enrollment): Total bilirubin ≤ 1.5 x upper limit of normal (ULN) for age
- For patients with Type II or III PPB (within 7 days prior to enrollment): Serum glutamate pyruvate transaminase (SGPT) (alanine aminotransferase [ALT]) ≤ 135 U/L
    - Note: For the purpose of this study, the ULN for SGPT (ALT) has been set to the value of 45 U/L
- Shortening fraction of ≥ 27% by echocardiogram, or ejection fraction of ≥ 50% by radionuclide angiogram (within 21 days prior to start of protocol therapy)
- HIV-infected patients on effective anti-retroviral therapy with undetectable viral load within 6 months are eligible as long as they are NOT receiving anti-retroviral agents that are strong inhibitors or inducers of CYP3A4

Exclusion Criteria:

- Administration of prior PPB-directed chemotherapy is an exclusion criterion. Prior treatment for another malignancy is not an exclusion criterion
- Patients with known Charcot-Marie-Tooth disease
- 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
- All patients and/or their parents or legal guardians must sign a written informed consent
- All institutional, Food and Drug Administration (FDA), and National Cancer Institute (NCI) requirements for human studies must be met

Conditions & Interventions

Interventions:
PROCEDURE: Biospecimen Collection, PROCEDURE: Biospecimen Collection, PROCEDURE: Bone Scan, PROCEDURE: Computed Tomography, DRUG: Cyclophosphamide, BIOLOGICAL: Dactinomycin, DRUG: Dexrazoxane, DRUG: Doxorubicin, PROCEDURE: Echocardiography Test, DRUG: Ifosfamide, PROCEDURE: Magnetic Resonance Imaging, PROCEDURE: Multigated Acquisition Scan, OTHER: Patient Observation, PROCEDURE: Positron Emission Tomography, DRUG: Topotecan, PROCEDURE: Ultrasound Imaging, DRUG: Vincristine
Conditions:
Pleuropulmonary Blastoma

Pleuropulmonary Blastoma

More Information

Description:
This phase III trial tests how well surgery plus chemotherapy compared to surgery alone works in treating patients with type I pleuropulmonary blastoma (PPB), and tests how well surgery plus standard chemotherapy with the addition of topotecan works compared to surgery plus standard chemotherapy alone in treating patients with type II and III PPB. Historically, most children with type I PPB had surgery and approximately 40% of children with type I PPB received chemotherapy following their surgery, usually for 22-42 weeks. There has not been a consistent standard for which children with type I PPB receive chemotherapy after surgery. For patients whose tumor has been removed completely with surgery, observation without chemotherapy may work as well as giving chemotherapy after surgery in preventing a return of the PPB tumor. The standard chemotherapy for patients with types II or III PPB in the United States is four cycles of IVADo (ifosfamide, vincristine, dactinomycin, and doxorubicin) followed by 8 cycles of IVA (ifosfamide, vincristine and dactinomycin). Ifosfamide is in a class of medications called alkylating agents. It works by slowing or stopping the growth of tumor cells in the body. Vincristine is in a class of medications called vinca alkaloids. It works by stopping tumor cells from growing and dividing and may kill them. Dactinomycin is a type of antibiotic that is only used in cancer chemotherapy (antineoplastic antibiotic). It works by damaging the cell's deoxyribonucleic acid (DNA) and may kill tumor cells. Doxorubicin is in a class of medications called anthracyclines. Doxorubicin damages the cell's DNA and may kill tumor cells. It also blocks a certain enzyme needed for cell division and DNA repair. Topotecan is in a class of medications called topoisomerase I inhibitors. It works by interfering with tumor cell DNA which kills them. Giving topotecan in addition to standard IVADo and IVA chemotherapy regimens may shrink the cancer as well as or better than the standard therapy or could decrease the chance the tumor spreads while causing fewer side effects.

Contact(s): - cancer@cchmc.org
Principal Investigator:
Principal Investigator ID:
Phase: PHASE3
IRB Number:
System ID: NCT06647953
