CBL0137 for the Treatment of Relapsed or Refractory Solid Tumors, Including CNS Tumors and Lymphoma

Status: RECRUITING

Eligibility Criteria

Sex: ALL
Age: 12 months to 21 years old
Healthy Volunteers: This study is NOT accepting healthy volunteers
Inclusion Criteria:

- Parts A and B: Patients must be >= 12 months and =< 21 years of age at the time of study enrollment
- Patients must have had histologic verification of malignancy at original diagnosis or relapse, except in patients with diffuse intrinsic brain stem tumors, or patients with pineal tumors and elevations of cerebrospinal fluid (CSF) or serum tumor markers, including alpha-fetoprotein or beta-human chorionic gonadotropin (HCG)
    - Part A: Patients with relapsed or refractory solid tumors or lymphoma, including patients with CNS tumors or known CNS metastases (including untreated or progressive) are eligible
    - Part B: Patients with progressive or recurrent DIPG (diagnosed by biopsy or imaging characteristics) and other H3 K27-altered DMG previously treated with radiation therapy
- Part A: Patients must have either measurable or evaluable disease
- Part B: Patients must have measurable disease
- Patient's current disease state must be one for which there is no known curative therapy or therapy proven to prolong survival with an acceptable quality of life
- Patients must have a performance status corresponding to Easter Cooperative Oncology Group (ECOG) scores of 0, 1 or 2. Use Karnofsky for patients > 16 years of age and Lansky for patients =< 16 years of age. Patients must have a Karnofsky or Lansky score >= 50%
- Patients must have fully 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
    - Solid tumor patients: >= 21 days after the last dose of myelosuppressive chemotherapy (42 days if prior nitrosourea)
    - Anti-cancer agents not known to be myelosuppressive (eg, not associated with reduced platelet or absolute neutrophil count [ANC] counts): >= 7 days after the last dose of agent
    - Antibodies: >= 21 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: If used to modify immune adverse events related to prior therapy, >= 14 days must have elapsed since last dose of corticosteroid. Patients with CNS tumors receiving corticosteroids must have been on a stable or decreasing dose of corticosteroid for at least 7 days prior to enrollment
    - 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: >= 30 days
    - Cellular therapy: >= 42 days after the completion 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: >= 14 days after local XRT; >= 150 days after TBI, craniospinal XRT or if radiation to >= 50% of the pelvis; >= 42 days if other substantial bone marrow (BM) radiation
    - Radiopharmaceutical therapy (e.g., radiolabeled antibody, I-131 metaiodobenzylguanidine [131I MIBG]): >= 42 days after systemically administered radiopharmaceutical therapy
    - Patients must not have received prior exposure to CBL0137
- For patients with solid tumors without known bone marrow involvement:
    - Peripheral absolute neutrophil count (ANC) >= 1000/uL (performed within 7 days prior to enrollment unless otherwise indicated)
    - Patients with known bone marrow metastatic disease will be eligible for study provided they meet the blood counts (may receive transfusions provided they are not known to be refractory to red cell or platelet transfusions). These patients will not be evaluable for hematologic toxicity. At least 5 of every cohort of 6 patients must be evaluable for hematologic toxicity for the dose-escalation part of the study. If dose-limiting hematologic toxicity is observed, all subsequent patients enrolled must be evaluable for hematologic toxicity
- 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) (performed within 7 days prior to enrollment unless otherwise indicated)
    - Patients with known bone marrow metastatic disease will be eligible for study provided they meet the blood counts (may receive transfusions provided they are not known to be refractory to red cell or platelet transfusions). These patients will not be evaluable for hematologic toxicity. At least 5 of every cohort of 6 patients must be evaluable for hematologic toxicity for the dose-escalation part of the study. If dose-limiting hematologic toxicity is observed, all subsequent patients enrolled must be evaluable for hematologic toxicity
- Creatinine clearance or radioisotope glomerular filtration rate (GFR) >= 70 mL/min/1.73 m^2 or a creatinine based on age/sex as follows (performed within 7 days prior to enrollment unless otherwise indicated):

    - Age: Maximum serum creatinine (mg/dL)
    - 1 to < 2 years: 0.6 (male); 0.6 (female)
    - 2 to < 6 years: 0.8 (male); 0.8 (female)
    - 6 to < 10 years: 1 (male); 1 (female)
    - 10 to < 13 years: 1.2 (male); 1.2 (female)
    - 13 to < 16 years: 1.5 (male); 1.4 (female)
    - >= 16 years: 1.7 (male); 1.4 (female)
- Patients with solid tumors:

    - Bilirubin (sum of conjugated + unconjugated or total) =< 1.5 x upper limit of normal (ULN) for age (performed within 7 days prior to enrollment unless otherwise indicated)
- Patients with solid tumors:

    - Serum glutamate pyruvate transaminase (SGPT) (alanine aminotransferase [ALT]) =< 135 U/L. For the purpose of this study, the ULN for SGPT is 45 U/L (performed within 7 days prior to enrollment unless otherwise indicated)
- Shortening fraction of >= 27% by echocardiogram (performed within 7 days prior to enrollment unless otherwise indicated) or
- Ejection fraction of >= 50% by gated radionuclide study (performed within 7 days prior to enrollment unless otherwise indicated)
- Corrected QT (QTC) < 480 msec (performed within 7 days prior to enrollment unless otherwise indicated)
- Patients with seizure disorder may be enrolled if seizures well controlled without the use of enzyme-inducing anti-convulsant agents. Well controlled is defined 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 therapy must be =< grade 2, with the exception of decreased tendon reflex (DTR). Any grade of DTR is eligible
- Patients have consented to receive a central venous catheter prior to the administration of CBL0137. A central line is required for CBL0137 administration

Exclusion Criteria:

- Pregnant or breast-feeding women will not be entered on this study due to risks of fetal and teratogenic adverse events as seen in animal/human studies, OR because there is yet no available information regarding human fetal or teratogenic toxicities. 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. Abstinence is an acceptable method of birth control
- 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 (except leukemia patients receiving hydroxyurea, which may be continued until 24 hours prior to start of protocol therapy)
- 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 drugs that are strong inducers or inhibitors of CYP3A4, CYP2B6 (e.g., carbamazepine) and CYP1A2 (e.g., ciprofloxacin, enoxacin, fluvoxamine, smoking) are not eligible. These agents are to be avoided for 7 days prior to the start of CBL0137 and for the duration of the protocol therapy. Sensitive substrates of CYP2D6 (e.g., atomoxetine, desipramine, dextromethorphan, eliglustat, nebivolol, nortriptyline, perphenazine, tolterodine, R-venlafaxine) should also be avoided for the duration protocol therapy
- Patients who are receiving drugs associated with a known risk of Torsades de Pointes (TdP) are not eligible. Drugs associated with known risk of Torsades de Pointes (TdP) are to be avoided for 7 days prior to the start of CBL0137 and for duration of the protocol therapy
- Patients with known peripheral vascular disease are excluded
- Patients with a history of pro-thrombotic disorder are not eligible
- Patients who have an uncontrolled infection are not eligible
- Patients who have received a prior solid organ transplantation 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

Conditions & Interventions

Interventions:
PROCEDURE: Biospecimen Collection, PROCEDURE: Bone Marrow Aspirate, PROCEDURE: Bone Marrow Biopsy, PROCEDURE: Echocardiography Test, DRUG: FACT Complex-targeting Curaxin CBL0137
Conditions:
Diffuse Midline Glioma, H3 K27-Altered, Metastatic Malignant Neoplasm in the Central Nervous System, Recurrent Diffuse Intrinsic Pontine Glioma, Recurrent Diffuse Midline Glioma, H3 K27-Altered, Recurrent Lymphoma, Recurrent Malignant Solid Neoplasm, Recurrent Primary Malignant Central Nervous System Neoplasm, Refractory Lymphoma, Refractory Malignant Solid Neoplasm, Refractory Primary Malignant Central Nervous System Neoplasm

More Information

Description:
This phase I/II trial evaluates the best dose, side effects and possible benefit of CBL0137 in treating patients with solid tumors, including central nervous system (CNS) tumors or lymphoma that has come back (relapsed) or does not respond to treatment (refractory). Drugs, such as CBL0137, block signals passed from one molecule to another inside a cell. Blocking these signals can affect many functions of the cell, including cell division and cell death, and may kill cancer cells.

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