Tegavivint for the Treatment of Recurrent or Refractory Solid Tumors, Including Lymphomas and Desmoid Tumors

Status: RECRUITING

Eligibility Criteria

Sex: ALL
Age: 12 months to 30 years old
Healthy Volunteers: This study is NOT accepting healthy volunteers
Inclusion Criteria:

- PART A: Patients must be >= 12 months and =< 21 years of age at the time of study enrollment
- PART B: Patients must be >= 12 months and =< 30 years of age at the time of study enrollment
- Patients with recurrent or refractory solid tumors including non-Hodgkin lymphoma and desmoid tumors are eligible. Patients must have had histologic verification of malignancy at original diagnosis or relapse
- PART A: Patients with relapsed or refractory solid tumors, including patients with non-Hodgkin lymphoma and desmoid tumors
- PART B: Patients with recurrent or refractory Ewing sarcoma, desmoid tumors, osteosarcoma, liver tumors (HCC and hepatoblastoma), Wilms tumor, and tumors with Wnt pathway aberrations. For the Wnt pathway aberrations cohort we will include the most common CTNNB1 mutations (S37F, S45F, T41A, S45P, S33C, S37C, D32Y, S33F, T41I, G34R, G34V, D32N, S33P, G34E, D32G) as well as any loss of function mutations in the APC, Axin2FBXW7, TCF7L2, and RNF43 genes or any gain-of-function mutations in the GSK3B, LRP6, and LGR5 genes. For patients without prior sequencing, immunohistochemistry (IHC), is required. IHC showing strong nuclear beta-catenin staining will be accepted for the following tumor types: colorectal carcinoma, melanoma, endometrial cancer, ovarian cancer, neuroblastoma, non-Hodgkin lymphoma, pancreatic ductal adenocarcinoma, and solid pseudopapillary tumor of the pancreas
- PART A: Patients must have either measurable or evaluable disease. For desmoid tumors, the patient must have disease that the investigator deems unresectable or sufficiently morbid or potentially life-threatening that there is favorable risk/benefit to the patient to participate in the trial
- PART B: Patients must have measurable disease. For desmoid tumors, the patient must have measurable disease that the investigator deems unresectable or sufficiently morbid or potentially life-threatening that there is favorable risk/benefit to the patient to participate in the trial
- Patients must have a performance status corresponding to Eastern 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 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)
    - Non-Hodgkin lymphoma patients
        - A waiting period prior to enrollment is not required for patients receiving standard maintenance chemotherapy (i.e., corticosteroid, vincristine, thioguanine [6MP], and/or methotrexate)
        - >= 14 days must have elapsed after the completion of other cytotoxic therapy, with the exception of hydroxyurea, for patients not receiving standard maintenance therapy
        - NOTE: Cytoreduction with hydroxyurea must be discontinued >= 24 hours prior to the start of protocol therapy
    - Anti-cancer agents not known to be myelosuppressive (e.g., not associated with reduced platelet or absolute neutrophil counts [ANC]): >= 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
    - 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: >= 42 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.).
    - External beam 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, iobenguane I-131 [131I MIBG]): >= 42 days after systemically administered radiopharmaceutical therapy
    - Patients must not have received prior exposure to tegavivint
- PATIENTS WITH SOLID TUMORS WITHOUT KNOWN BONE MARROW INVOLVEMENT: Peripheral absolute neutrophil count (ANC) >= 1000/uL (within 7 days prior to enrollment)

- 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) (within 7 days prior to enrollment)
- PATIENTS WITH SOLID TUMORS WITHOUT KNOWN BONE MARROW INVOLVEMENT: Hemoglobin >= 8.0 g/dL at baseline (may receive red blood cell [RBC] transfusions) (within 7 days prior to enrollment)
- Patients with known bone marrow metastatic disease will be eligible for study provided they meet 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 on Part A 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/gender as follows (within 7 days prior to enrollment):
    - Age; maximum serum creatinine
    - Age 1 to < 2 years; 0.6 mg/dL (male); 0.6 mg/dL (female)
    - Age 2 to < 6 years; 0.8 mg/dL (male); 0.8 mg/dL (female)
    - Age 6 to < 10 years; 1 mg/dL (male); 1 mg/dL (female)
    - Age 10 to < 13 years; 1.2 mg/dL (male); 1.2 mg/dL (female)
    - Age 13 to < 16 years; 1.5 mg/dL (male); 1.4 mg/dL (female)
    - Age >= 16 years; 1.7 mg/dL (male); 1.4 mg/dL (female)
- PATIENTS WITH SOLID TUMORS: Bilirubin (sum of conjugated + unconjugated or total) =< 1.5 x upper limit of normal (ULN) for age (within 7 days prior to enrollment)
- PATIENTS WITH SOLID TUMORS: Serum glutamic pyruvic transaminase (SGPT) (alanine aminotransferase [ALT]) =< 135 U/L. For the purpose of this study, the ULN for SGPT is 45 U/L (within 7 days prior to enrollment)
- PATIENTS WITH SOLID TUMORS: Albumin >= 2 g/dL (within 7 days prior to enrollment)

Exclusion Criteria:

- Pregnant or breast-feeding women will not be entered on this study 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
- 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 currently receiving drugs that are strong inducers or inhibitors of CYP3A4 are not eligible. Strong inducers or inhibitors of CYP3A4 should be avoided from 14 days prior to the 1st dose of tegavivint to the end of the study
- Patients who have received bisphosphonates within 4 weeks prior to study enrollment will be excluded
- Patients who have received denosumab within 180 days prior to study enrollment will be excluded
- Patients with primary brain tumors are ineligible
- Patients with known central nervous system (CNS) metastasis, except for craniopharyngeal tumors, will be excluded
- Patients with a known metabolic bone disease (ex: hyperparathyroidism, Paget's disease, osteomalacia) are not eligible
- Patients with a disorder associated with abnormal bone metabolism will be excluded
- Patients with grade >= 2 hypocalcemia that is not corrected with oral calcium supplementation will be excluded
- Patients with vitamin D < 20 ng/mL will require supplementation, or will otherwise be excluded. Patients must agree to take vitamin D +/- calcium supplements (if necessary) according to institutional or published guidelines. Additional calcium supplementation is not required if adequate dietary intake can be ascertained
- Patients with pre-existing grade 3 osteoporosis are excluded
- 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: Dual X-ray Absorptiometry, DRUG: Tegavivint, PROCEDURE: X-Ray Imaging
Conditions:
Colorectal Carcinoma, Endometrial Carcinoma, Melanoma, Neuroblastoma, Ovarian Carcinoma, Pancreatic Ductal Adenocarcinoma, Recurrent Desmoid Fibromatosis, Recurrent Ewing Sarcoma, Recurrent Hepatoblastoma, Recurrent Hepatocellular Carcinoma, Recurrent Malignant Solid Neoplasm, Recurrent Non-Hodgkin Lymphoma, Recurrent Osteosarcoma, Refractory Desmoid Fibromatosis, Refractory Ewing Sarcoma, Refractory Hepatoblastoma, Refractory Hepatocellular Carcinoma, Refractory Malignant Solid Neoplasm, Refractory Non-Hodgkin Lymphoma, Refractory Osteosarcoma, Solid Pseudopapillary Neoplasm of the Pancreas, Wilms Tumor

More Information

Description:
This phase I/II trial evaluates the highest safe dose, side effects, and possible benefits of tegavivint in treating patients with solid tumors that has come back (recurrent) or does not respond to treatment (refractory). Tegavivint interferes with the binding of beta-catenin to TBL1, which may help stop the growth of tumor cells by blocking the signals passed from one molecule to another inside a cell that tell a cell to grow.

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Phase: PHASE1
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