A Phase II, Open Label, Two Arm Study of Therapeutic Iobenguane (131I) as Single Agent or in Combination with Vorinostat for Recurrent or Progressive High-Risk Neuroblastoma Subjects (OPTIMUM Trial) Protocol Number: MIBG 2014-01

Status: Recruiting

Eligibility Criteria

Sex: All
Age Group: 1 year and over

Inclusion Criteria:

Subjects with a diagnosis of iobenguane avid, high-risk neuroblastoma based on Revised INRC criteria at the time of study enrollment with recurrent or progressive disease at any time prior to enrollment, regardless of overall response to frontline therapy, where frontline therapy includes a minimum of 4 cycles of induction therapy at any time prior to enrollment. May have had prior 131I-MIBG therapy, provided: It has been at least 6 months from the date of last 131I-MIBG ; Response was other than progressive disease on first restaging after 131I-MIBG ; Prior 131I-MIBG was given as monotherapy and not in combination with systemic anticancer agents; Cumulative lifetime dose of 131I-MIBG at enrollment does not exceed 18 mCi/kg. All soft tissue lesions identified on CT/MRI scans must be iobenguane avid lesions on an (123I)-iobenguane scan, or any progressive non-iobenguane avid lesion is proven by biopsy to be a non-neuroblastoma lesion. any other non-avid lesion is comprised of a fibrotic or scarred mass as shown by routine imaging and confirmed by the investigator. Adequate cryopreserved autologous peripheral blood stem cells or bone marrow (at least 2 aliquots of 2.0 × 10exp6 CD34/kg at the time of study enrollment). If a male, must agree to use an adequate contraception method as deemed appropriate by the Investigator (e.g., vasectomy, condoms) or partner using effective contraception and to not donate sperm during the study and for 90 days after receiving the last dose of study drug. If a female of childbearing potential, have a negative serum pregnancy test result prior to each dosing and, if sexually active, be practicing an effective method of birth control [e.g., intrauterine device, double-barrier method (i.e., diaphragm, or a cervical cap) with intravaginal spermicidal foam, cream or gel], or male partner sterilization throughout the study. Age at study entry ≥1 year. Previous platelet transfusions are permitted, as long as the subject has a platelet count ≥50,000/µL without transfusion support for at least 1 week. Subjects must have a minimum pulse oximetry measurement of at least 94% at baseline. An absolute neutrophil count ≥750/µL without growth factor for 5 days. Liver function parameter results: total bilirubin ≤2 × upper limit of normal for age, and Serum alanine aminotransferase (glutamic-pyruvic transaminase) and serum aspartate aminotransferase (glutamic-oxaloacetic transaminase) ≤ 10 times the upper limit of normal (for all sites, the upper limit of normal for alanine aminotransferase is defined as 45 U/L). Normal thyroid function as measured by T4 or TSH or have abnormal results that are not considered clinically important by the Investigator or may be receiving levothyroxine. Cardiac Function: shortening fraction of ≥ 27% by echocardiogram or ejection fraction ≥ 50% documented by echocardiogram or radionuclide angiogram within 1 month prior to Visit 1 (Baseline). Karnofsky Performance Status (for subjects >16 years of age) or the Lansky Performance Status Performance Status (for subjects 1 to 16 years of age) ≥50%. Full recovery from the toxic effects of any prior therapy. Coagulation Function: International Normalized Ratio (INR) < 1.5 Partial thromboplastin time (PTT) < 1.5 times upper limit of normal.

Exclusion Criteria:

Subjects within 5 half-lives after any antibody-based immunotherapy, or have not recovered from effects of any biologic therapy. Subjects <12 weeks after myeloablative therapy with autologous stem cell transplant. Subjects who have had an allogeneic stem cell treatment less than 4 months from Visit 1 are excluded. Those who have received allogeneic stem cell treatment more than 4 months from Visit 1 must have recovered and have no active graft versus host disease (GVHD) to be eligible. Subjects must not have received radiation for a minimum of 2 weeks prior to study enrollment. Subjects whose only site(s) of disease have been radiated are eligible as long as the subject has MIBG avidity 2 weeks after completion of radiation. A minimum of 12 weeks prior to study enrollment is required following prior large field radiatior therapy (ie, craniospinal, whole abdominal, total lung, > 50% marrow space) History of total body irradiation. Subjects do not have adequate renal function defined as GFR ≥ 70 mL/min/1.73 m2 either by creatinine clearance or radioisotope direct measurement or by calculation with the Schwartz formula Subjects who are on hemodialysis. Pregnancy or breastfeeding. Significant active infections including active hepatitis B, or hepatitis C infection, or known infection with human immunodeficiency virus (HIV) (testing for HIV is not required prior to study entry). Clinically important cardiac, pulmonary, and hepatic impairment. Vorinostat treatment exclusion criteria (subjects, who meet any one of these criteria and otherwise meet eligibility criteria, are still eligible for 131I-MIBG monotherapy) Since valproic acid has HDAC inhibitory activity, patients must not have received valproic acid within 30 days of study entry. Since vorinostat may prolong the QT interval, patients must not be receiving other medications known to prolong the QT interval at the time of study entry . Pentamidine must not have been received within 1 week of study enrollment. Patients with a history of deep venous thrombosis that was not associated with the presence of a central venous catheter. Patients who are receiving Coumadin.

Conditions & Interventions

More Information

Description: This will be a Phase II, two-arm, nonrandomized, non-comparative, open-label study in participants ≥ 1 year of age with iobenguane avid, recurrent or progressive high-risk neuroblastoma. Participants not eligible for vorinostat treatment may receive 131I-MIBG as monotherapy.
Study Contact: Allison Fullenkamp - fulle631@umn.edu
Principal Investigator: Emily Greengard
Phase: Phase 2
IRB Number: STUDY00005792