131-I-MIBG Expanded Access: An Open Label, Expanded Access Protocol Using I-Metaiodobenzylguanidine (131I-MIBG) Therapy in Patients With Refractory Neuroblastoma

Basic Study Information

Type	Status	Age Range (yrs.)	Sponsor
Therapeutic	Active	>1 year	Draximage

Outline

- This research study will continue to evaluate the side effects of 131I-MIBG when treating children and adults with neuroblastoma.
- The 131I-MIBG compound is intended to work by selectively delivering the radioactive iodine to the cancer cells, which is then intended to result in their destruction.
- One treatment cycle of 131I-MIBG therapy is 7 to 9 weeks long. The patient will be evaluated to receive additional 131I-MIBG therapy at the end of each cycle. If they qualify and their blood counts are good, it is possible that they could receive a total of three treatment cycles, for a total of 21 to 27 weeks. Hospitalization is required for approximately 3-5 days after each dose.

Objectives

Primary:

- Provide palliative therapy with MIBG for patients with advanced neuroblastoma
- Gain more information about acute and late toxicity of 131I-MIBG therapy for patients with refractory neuroblastoma

Projected Accrual:

- About 5-20 people each year

Mechanism of Action:

- Metaiodobenzylguanidine (MIBG) is a substance that is taken up by neuroblastoma tumor cells. MIBG is combined with radioactive iodine (131I) in the laboratory to form the radioactive compound 131I-MIBG. The 131I-MIBG compound is designed to deliver radiation specifically to the neuroblastoma cancer cells with the objective of causing them to die. 131I-MIBG is experimental, meaning that it is not approved by the United States Food and Drug Administration (FDA).

Entry Criteria

Disease Characteristics:

- Refractory or relapsed neuroblastoma with original diagnosis based on tumor histopathology or elevated urine catecholamines with typical tumor cells in the bone marrow

- Failure to respond to standard therapy (usually combination chemotherapy with or without radiation and surgery) or development of progressive disease at any time (any new lesion or an increase in size of >25% of a pre-existing lesion). Disease evaluable by MIBG scan must be present within 8 weeks of study entry and subsequent to any intervening therapy. If patient has received prior treatment with MIBG, they must have a response or stable disease after the most recent MIBG infusion.

Patient Characteristics:

Age:

- *> 1 year*

> 1 year

Performance Status:

- Not specified

Life Expectancy:

- Not specified

Stem Cells:

- Patients must have a hematopoietic stem cell product available for re-infusion after 131I-MIBG treatment at doses of ≥12 mCi/kg
- The only acceptable allogeneic product is CD34-selected PBSC (which will minimize the risk of GVHD)
- If no stem cells are available, then the dose of 131I-MIBG should be <12 mCi/kg

Hematopoieteic:

- ANC ≥ 750/μL; Platelets ≥ 50,000/μL without transfusion if stem cells are not available
- ANC ≥ 500 and any platelet count allowed if stem cells available
- If the patient has received prior treatment with MIBG, they may be thrombocytopenic, but requiring no more than 2 platelet transfusions per week to maintain counts above 20,000

Hepatic:

- Bilirubin ≤ 2x upper limit of normal
- AST/ALT ≤ 10x upper limit of normal

Renal:

- One of the following must be met:
  Serum Creatinine ≤ 2x upper limit of normal OR
  24-hr creatinine clearance OR GFR ≥ 60 ml/min/1.73m2
  (For example, a patient would meet this criteria if GFR<60 ml/min/1.73m2
  but serum creatinine ≤ 3x upper limit of normal)

Pulmonary:

- Normal lung function as manifested by no dyspnea at rest or exercise intolerance, no oxygen requirement

Other:

- Patients of childbearing potential must practice an effective method of birth control while participating on this study
- Patient must not be pregnant or lactating
- Patients who meet the following criteria will be excluded from this study:
- Patients with disease of any major organ system that would compromise their ability to withstand therapy
- Patients who are on hemodialysis
- Patients with active infections that meet grade 3-4 according to the NCI CTCAE v3.0

Prior/Concurrent Therapy:

Biologic Therapy:

- Cytokine therapy (e.g. G-CSF, GM-CSF, IL-6, erythropoietin) must be discontinued a minimum of 24 hours prior to 131I-MIBG therapy

Radiotherapy:

- 3 months should have elapsed in the case of completing radiation to any of the following fields: craniospinal, total abdominal, whole lung, total body irradiation)

Other:

- At least 2 weeks should have elapsed since any anti-tumor therapy and the patient must meet hematologic criteria
- Minimum of six weeks from previous 131I-MIBG therapy
- For patients previously treated with MIBG and with remaining stored stem cells that meet protocol criteria, treatment must not exceed a lifetime cumulative injected activity of 50 mCi/kg

- For patients previously treated with MIBG and without remaining stored stem cells that meet protocol criteria, retreatment must not exceed a lifetime cumulative injected activity of 36 mCi/kg
- Other criteria as outlined in the detailed protocol

For more information contact:

Cincinnati Children's Hospital Medical Center
Division of Hematology/Oncology
3333 Burnet Ave., Cincinnati, OH 45229-3039
Phone: 513-636-2799
cancer@cchmc.org