ANBL09P1: A COG Pilot Study of Intensive Induction Therapy and 131I-MIBG With Myeloablative Carboplatin, Etoposide and Melphalan (CEM) for Newly Diagnosed High-Risk Neuroblastoma

Basic Study Information

Study Type: Interventional
Study Design: Open Label, Treatment

Rationale

Radioisotope therapy, such as iobenguane I 131, releases radiation that kills tumor cells. Drugs used in chemotherapy, such as carboplatin, etoposide, busulfan, and melphalan, work in different ways to stop the growth of tumor cells, either by killing the cells or by stopping them from dividing. A peripheral stem cell transplant may be able to replace blood-forming cells that are destroyed by iobenguane I 131 and chemotherapy.

Purpose

This clinical trial is studying induction therapy followed by iobenguane I 131 and high-dose chemotherapy in treating patients with newly diagnosed high-risk neuroblastoma undergoing stem cell transplant, radiation therapy, and maintenance therapy with isotretinoin.

Objectives

Primary

- Proportion of patients treated with iodine I 131 meta-iodobenzylguanidine (131 I-MIBG), carboplatin, etoposide phosphate, and melphalan
- 1-year event-free survival rate

Secondary

- Response rate
- Tumor burden
- Toxicity
- Relationship of sinusoidal obstruction syndrome to dosages of myeloablative consolidation therapy and autologous stem cell rescue, and whole-body radiation dose or delay of radiation clearance due to 131 I-MIBG

Ages Eligible for Study: 1 Year to 30 Years

Entry Criteria

Disease Characteristics:

- Diagnosis of neuroblastoma (ICD-O morphology 9500/3) or ganglioneuroblastoma by histology or demonstration of clumps of tumor cells in bone marrow with elevated urinary catecholamine metabolites meeting 1 of the following staging criteria:
    - Newly diagnosed International Neuroblastoma Staging System (INSS) stage 4 disease meeting 1 of the following criteria:

        - MYCN amplification (> 4-fold increase in MYCN signals as compared to reference signals) and age ≥ 365 days regardless of additional biologic features
        - Age > 18 months (> 547 days) regardless of biologic features
        - Age 12-18 months (365-547 days) with any of the following 3 unfavorable biologic features: MYCN amplification, unfavorable pathology, and/or DNA index = 1, or any biologic feature that is indeterminant, unsatisfactory, or unknown
    - Newly diagnosed INSS stage 3 disease meeting 1 of the following criteria:
        - MYCN amplification (> 4-fold increase in MYCN signals as compared to reference signals) and age ≥ 365 days, regardless of additional biologic features
        - Age > 18 months (> 547 days) with unfavorable pathology, regardless of MYCN status
    - Newly diagnosed INSS stage 2a/2b with MYCN amplification (> 4-fold increase in MYCN signals as compared to reference signals) and age ≥ 365 days, regardless of additional biologic features
    - Age ≥ 365 days initially diagnosed with INSS stage 1, 2, or 4S who progressed (within the past 4 weeks) to a stage 4 without interval chemotherapy
    - No patients aged 12-18 months with INSS stage 4 and all 3 favorable biologic features (i.e., non-amplified MYCN, favorable pathology, and DNA index > 1)
- Must be enrolled onto ANBL00B1 biologic study
- Must have ≥ 1 "MIBG-avid target lesion" present on MIBG scan in the past 4 weeks

Patient Characteristics:

- Total bilirubin ≤1.5 times upper limit of normal (ULN)
- AST or ALT ≤ 10 times ULN
- Creatinine clearance or radioisotope GFR ≥ 70 mL/min OR serum creatinine based on age and/or gender as follows:
    - ≤ 0.6 mg/dL (1 to < 2 years of age)
    - ≤ 0.8 mg/dL (2 to < 6 years of age)
    - ≤ 1.0 mg/dL (6 to < 10 years of age)
    - ≤ 1.2 mg/dL (10 to < 13 years of age)
    - ≤ 1.5 mg/dL (male) or 1.4 mg/dL (female) (13 to < 16 years of age)
    - ≤ 1.7 mg/dL (male) or 1.4 mg/dL (female) (≥ 16 years of age)
- Not pregnant or nursing
- Negative pregnancy test
- Fertile patients must use effective contraception
- Shortening fraction ≥ 27% by ECHO OR ejection fraction ≥ 50% by radionuclide evaluation
- Able to tolerate peripheral blood stem cell (PBSC) collection
    - No contraindications to PBSC collection including weight, size, or physical condition that would preclude apheresis

Prior/Concurrent Therapy

- No prior systemic therapy
    - Localized emergency radiotherapy to sites of life-threatening or function-threatening disease and ≥ 1 measurable lesion is not irradiated

  - No more than 1 course of chemotherapy per low- or intermediate-risk neuroblastoma therapy before determination of MYCN amplification and histology
- No local radiotherapy that includes any of the following:
  - 1,200 cGy to more than 33% of both kidneys
    - Patient must have ≥ 1 kidney that has not exceeded the dose/volume of radiation listed
  - 1,800 cGy to more than 30% of liver and/or 900 cGy to more than 50% of liver
- No other concurrent cancer chemotherapy or immunomodulating agents (including steroids)

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