Dinutuximab With Chemotherapy, Surgery and Stem Cell Transplantation for the Treatment of Children With Newly Diagnosed High Risk Neuroblastoma

Status: RECRUITING

Eligibility Criteria

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

- Patients must be enrolled on APEC14B1 and have consented to testing through the Molecular Characterization Initiative (MCI), prior to enrollment on ANBL2131
- ≤ 30 years at the time of initial diagnosis with high-risk disease
- * Must have a diagnosis of neuroblastoma (NBL) or ganglioneuroblastoma (nodular) verified by tumor pathology analysis or demonstration of clumps of tumor cells in bone marrow with elevated urinary catecholamines
    - Newly diagnosed, high risk neuroblastoma (HRNBL) defined as one of the following:
    - Any age with International Neuroblastoma Risk Group (INRG) Stage L2, MS, or M and MYCN amplification
    - Age ≥ 547 days and INRG stage M regardless of biologic features (clinical MYCN testing not required prior to enrollment)
    - Any age initially diagnosed with INRG Stage L1 MYCN amplified NBL who have progressed to stage M without systemic chemotherapy
    - Age ≥ 547 days of age initially diagnosed with INRG Stage L1, L2, or MS who have progressed to stage M without systemic chemotherapy (clinical MYCN testing not required prior to enrollment)
- Patients must have a body surface area (BSA) ≥ 0.25 m^2
- No prior anti-cancer therapy except as outlined below:
    - Patients initially recognized to have high-risk disease treated with topotecan/cyclophosphamide initiated on an emergent basis and within allowed timing, and with consent
    - Patients observed or treated with a single cycle of chemotherapy per a low or intermediate risk neuroblastoma regimen (e.g., as per ANBL0531, ANBL1232 or similar) for what initially appeared to be non-high-risk disease but subsequently found to meet the criteria
    - Patients who received localized emergency radiation to sites of life threatening or function-threatening disease prior to or immediately after establishment of the definitive diagnosis
- Human immunodeficiency virus (HIV) -infected patients on effective anti-retroviral therapy with undetectable viral load within 6 months are eligible for this trial
- A serum creatinine based on age/sex as follows:
    - 1 month to < 6 months: Male 0.4 mg/dL and female 0.4mg/dL
    - 6 months to < 1 year: Male 0.5 mg/dL and female 0.5 mg/dL
    - 1 to < 2 years: Male 0.6 mg/dL and female 0.6 mg/dL
    - 2 to < 6 years: Male 0.8 mg/dL and female 0.8 mg/dL
    - 6 to < 10 years: Male 1 mg/dL and female 1 mg/dL
    - 10 to < 13 years: Male 1.2 mg/dL and female 1.2 mg/dL
    - 13 to < 16 years: Male 1.5 mg/dL and female 1.4 mg/dL
    - ≥ 16 years: Male 1.7 mg/dL and female 1.4 mg/dL
    - The threshold creatinine values were derived from the Schwartz formula for estimating glomerular filtration rate (GFR) utilizing child length and stature data published by the Centers for Disease Control (CDC)
    - or a 24-hour urine creatinine clearance ≥ 70 mL/min/1.73 m^2 or
    - or a GFR ≥ 70 mL/min/1.73 m^2. GFR must be performed using direct measurement with a nuclear blood sampling method or direct small molecule clearance method (iothalamate or other molecule per institutional standard)
    - Note: Estimated GFR (eGFR) from serum creatinine, cystatin C or other estimates are not acceptable for determining eligibility
- Total bilirubin ≤ 1.5 x upper limit of normal (ULN) for age
- Serum glutamic pyruvic transaminase (SGPT) (Alanine aminotransferase [ALT]) ≤ 10 x ULN*
    - Note: For the purpose of this study, the ULN for SGPT (ALT) has been set to the value of 45 U/L
- * Shortening fraction of ≥ 27% by echocardiogram, or
    - Ejection fraction of ≥ 50% by echocardiogram or radionuclide angiogram
- Ability to tolerate Peripheral Blood Stem Cell (PBSC) collection:

No known contraindication to PBSC collection. Examples of contraindications might be a weight or size less than the collecting institution finds feasible, or a physical condition that would limit the ability of the child to undergo apheresis catheter placement (if necessary) and/or the apheresis procedure

Exclusion Criteria:

- Patients who are 365-546 days of age with INRG Stage M and MYCN non-amplified NBL, irrespective of additional biologic features

- Patients ≥ 547 days of age with INRG Stage L2, MYCN non-amplified NBL, regardless of additional biologic features
- Patients with known bone marrow failure syndromes
- Patients on chronic immunosuppressive medications (e.g., tacrolimus, cyclosporine, corticosteroids) for reasons other than prevention/treatment of allergic reactions and adrenal replacement therapy are not eligible. Topical and inhaled corticosteroids are acceptable
- Patients with a primary immunodeficiency syndrome who require ongoing immune globulin replacement therapy
- Female patients who are pregnant since fetal toxicities and teratogenic effects have been noted for several of the study drugs. A pregnancy test is required prior to enrollment for female patients of childbearing potential
- Lactating females who plan to breastfeed their infants
- Sexually active patients of reproductive potential who have not agreed to use an effective contraceptive method for the duration of their study participation
- All patients and/or their parents or legal guardians must sign a written informed consent
- All institutional, food and drug administration (FDA), and National Cancer Institute (NCI) requirements for human studies must be met

Conditions & Interventions

Interventions:
PROCEDURE: Biospecimen Collection, PROCEDURE: Bone Marrow Aspiration, PROCEDURE: Bone Marrow Biopsy, DRUG: Carboplatin, DRUG: Cisplatin, PROCEDURE: Computed Tomography, DRUG: Cyclophosphamide, BIOLOGICAL: Dinutuximab, DRUG: Doxorubicin, PROCEDURE: Echocardiography Test, DRUG: Etoposide, PROCEDURE: FDG-Positron Emission Tomography and Computed Tomography Scan, PROCEDURE: Hematopoietic Cell Transplantation, DRUG: Irinotecan, DRUG: Isotretinoin, PROCEDURE: Leukapheresis, PROCEDURE: Magnetic Resonance Imaging, DRUG: Melphalan, PROCEDURE: Multigated Acquisition Scan, RADIATION: Radiation Therapy, PROCEDURE: Radionuclide Imaging, OTHER: Survey Administration, DRUG: Temozolomide, DRUG: Thiotepa, DRUG: Topotecan, PROCEDURE: Tumor Resection, DRUG: Vincristine
Conditions:
Ganglioneuroblastoma, Nodular, Neuroblastoma

More Information

Description:
This phase III trial tests how well the addition of dinutuximab to Induction chemotherapy along with standard of care surgical resection of the primary tumor, radiation, stem cell transplantation, and immunotherapy works for treating children with newly diagnosed high-risk neuroblastoma. Dinutuximab is a monoclonal antibody that binds to a molecule called GD2, which is found on the surface of neuroblastoma cells, but is not present on many healthy or normal cells in the body. When dinutuximab binds to the neuroblastoma cells, it helps signal the immune system to kill the tumor cells. This helps the cells of the immune system kill the cancer cells, this is a type of immunotherapy. When chemotherapy and immunotherapy are given together, during the same treatment cycle, it is called chemoimmunotherapy. This clinical trial randomly assigns patients to receive either standard chemotherapy and surgery or chemoimmunotherapy (chemotherapy plus dinutuximab) and surgery during Induction therapy. Chemotherapy drugs administered during Induction include, cyclophosphamide, topotecan, cisplatin, etoposide, vincristine, and doxorubicin. These drugs work in different ways to stop the growth of cancer cells, either by killing the cells, by stopping them from dividing or by stopping them from spreading. Upon completion of 5 cycles of Induction therapy, a disease evaluation is completed to determine how well the treatment worked. If the tumor responds to therapy, patients receive a tandem transplantation with stem cell rescue. If the tumor has little improvement or worsens, patients receive chemoimmunotherapy on Extended Induction. During Extended Induction, dinutuximab is given with irinotecan, temozolomide. Patients with a good response to therapy move on to Consolidation therapy, when very high doses of chemotherapy are given at two separate points to kill any remaining cancer cells. Following, transplant, radiation therapy is given to the site where the cancer originated (primary site) and to any other areas that are still active at the end of Induction. The final stage of therapy is Post-Consolidation. During Post-Consolidation, dinutuximab is given with isotretinoin, with the goal of maintaining the response achieved with the previous therapy. Adding dinutuximab to Induction chemotherapy along with standard of care surgical resection of the primary tumor, radiation, stem cell transplantation, and immunotherapy may be better at treating children with newly diagnosed high-risk neuroblastoma.

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