A prospective open label, multicenter study to evaluate the feasibility of using molecularly guided therapy in combination with standard therapy followed by maintenance therapy with DFMO in subjects with newly diagnosed high risk neuroblastoma.

This study outlines an approach by which we can use our expanding knowledge of the individual genetics of tumors to understand the mechanisms which cause tumors to grow. This knowledge is used to identify specific targeted therapies for each patient.

**Objectives:**

**Primary**

To determine the feasibility of identifying a targeted agent by molecular methods and incorporating that agent into standard upfront high risk neuroblastoma treatment in cycles 3-6 of induction. Following standard consolidation therapy with ASCT, XRT (if indicated), the feasibility and safety of adding DFMO to standard maintenance therapy with Ch14:18 antibody and cis-retinoic acid, the feasibility of adding further maintenance therapy with DFMO will be assessed.

**Secondary**

- Monitor for acute toxicity
- To determine the activity of treatments chosen based on:
  - Overall response rate (ORR)
  - Progression free survival (PFS)
  - During Maintenance: Event Free Survival

**Methodology:**

- Guided therapy will allow the use of one targeted agent to be added to standard treatment during Cycles 3-6 of induction chemotherapy.
- After induction, subjects will then complete standard consolidation.
- All subjects will receive DFMO along with standard immunotherapy and continue to receive maintenance DFMO for an additional 2 years after immunotherapy ends.
- All patients will be followed for survival, disease response, and safety.

The following will be monitored:

- Physical examinations
- Vital signs, including temperature, pulse rate, and blood pressure
- Blood tests and Urine VMA/HVA
- Adverse Events
- CT/MRI, Bone Marrow, and MIBG or PET scan
- Response to therapy

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**Eligibility**

**Inclusion**: *

- Age: >12 months and ≤21 years of age at initial diagnosis
- Diagnosis: Subjects must have a new diagnosis of high risk neuroblastoma or ganglioneuroblastoma.
- Must not have had prior systemic therapy except for localized emergency radiation to sites of life-threatening or function-threatening disease and/or no more than 1 cycle of chemotherapy per a low or intermediate risk neuroblastoma regimen
- Adequate liver, renal, and cardiac function
- Ability to tolerate PBSC collection
- A negative urine pregnancy test is required for female subjects of child bearing potential (onset of menses or ≥13 years of age)

**Exclusion**: *

- Subjects who are 12-18 months of age with INSS Stage 4 and all stage 3 subjects with favorable biologic features (ie, non-amplified MYCN, favorable pathology, and DNA index > 1) are not eligible.
- Lactating females are not eligible unless they have agreed not to breastfeed their infants.
- Concurrent anti-cancer and/or investigational agents

*Additional criteria apply

**Enrolling Sites (subject to change)**

- Helen DeVos Children’s Hospital in Grand Rapids, MI
- Cardinal Glennon Children’s Medical Center in St. Louis, MO
- Rady Children’s Hospital in San Diego, CA
- Arnold Palmer Hospital for Children, Orlando, FL
- Medical University of South Carolina, Charleston, SC
- Levine Children’s Hospital, Charlotte, NC
- Connecticut Children’s Medical Center, Hartford, CT
- Dell Children’s Blood and Cancer Center – Austin, TX
- Children's Hospitals and Clinics of Minnesota, Minneapolis, MN
- Kapi‘olani Medical Center, Honolulu, HI
- Penn State Milton S. Hershey Medical Center and Children’s Hospital, Hershey, PA
- Arkansas Children’s Hospital, Little Rock, AR

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**To Participate, Contact:**

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