NANT 2021-01 Phase II STING (Sequential Temozolomide, Irinotecan, NK Cells and GD2 mAb) Trial

Status: RECRUITING

Eligibility Criteria

Sex: ALL
Age: 1 year to 31 years old
Healthy Volunteers: This study is NOT accepting healthy volunteers
Inclusion Criteria:

- Patients must be ≥ 1 year and ≤31 years of age at the time of enrollment on the study.
- Patients must have a diagnosis of neuroblastoma either by histologic verification of neuroblastoma and/or demonstration of tumor cells in the bone marrow with increased urinary catecholamines.
- Patients must have high-risk neuroblastoma according to COG risk classification at the time of study registration. Patients whose disease was initially considered low or intermediate risk but then reclassified as high-risk neuroblastoma prior to enrollment also meet this criteria.
- Patients must have at least ONE of the following:

1) Recurrent/progressive disease after the diagnosis of high risk neuroblastoma at any time prior to enrollment - regardless of response to frontline therapy. (Note that this excludes patients initially considered low or intermediate risk that progressed to high risk disease but have not progressed after the diagnosis of high risk neuroblastoma).

2) If no prior history of recurrent/progressive disease since the diagnosis of high-risk neuroblastoma,

2a) Refractory disease: A best overall response of no response/stable disease since diagnosis of high-risk neuroblastoma AND after at least 4 courses of induction therapy.

2b) Persistent disease: A best overall response of partial response since diagnosis of high-risk neuroblastoma AND after at least 4 courses of induction therapy
* Patients must have at least ONE of the following (lesions may have received prior radiation therapy as long as they meet the other criteria listed below) based on institutional assessment:

1) Bone Sites
1. a) MIBG avid tumors: patients must meet one of the following criteria:

a. Patients with recurrent/progressive or refractory disease: i. Must have at least one MIBG avid bone site on planar imaging OR ii. Must have \> 2 avid bone lesions on SPECT. iii. A biopsy is not required unless the above imaging criteria are not met. b. Patients with persistent disease: i. If a patient has 3 or more MIBG avid sites by planar or SPECT imaging (including soft tissue and/or bone), then no biopsy is required.

ii. If a patient has only 1 or 2 MIBG avid sites by planar or SPECT imaging (including soft tissue and/or bone) then biopsy confirmation of neuroblastoma and/or ganglioneuroblastoma in at least one MIBG avid site present at the time of enrollment is required. Bone lesions may be biopsied at any time point prior to enrollment.

1b) For MIBG non-avid tumors, patients must have biopsy confirmation of neuroblastoma and/or ganglioneuroblastoma from a lesion at any time prior to enrollment of at least one site (with or without FDG-PET uptake).

2) Bone Marrow Any amount of tumor cells in the bone marrow (including neuroblasts, mature and maturing ganglion cells) done at the time of study enrollment based on routine morphology and/or immunohistochemistry in at least one sample from bilateral aspirates and biopsies.

3) Soft Tissue Sites

3a) At least one soft tissue lesion that meets criteria for a TARGET lesion as defined by:
1. SIZE: Lesion can be accurately measured in at least one dimension with a longest diameter ≥ 10 mm, or for discrete lymph nodes ≥ 15mm on short axis. Lesions meeting size criteria will be considered measurable.
2. In addition to size, a lesion needs to meet ONE of the following criteria except for patients with parenchymal CNS lesions which will only need to meet size criteria:

1. For MIBG avid tumors: lesion must be MIBG avid and meet one of the following criteria:

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1. For patients with recurrent/progressive or refractory disease:

   i. No biopsy is required

2. For patients with persistent disease:

   i. If a patient has 3 or more MIBG avid sites by planar or SPECT imaging (including soft tissue and/or bone), then no biopsy is required.

   ii. If a patient has only 1 or 2 MIBG avid sites by planar or SPECT imaging (including soft tissue and/or bone), then biopsy confirmation of neuroblastoma and/or ganglioneuroblastoma in at least one MIBG avid site present at the time of enrollment is required. Soft tissue lesions may be biopsied at any time point prior to enrollment.

   b. For MIBG non-avid tumors, patient must have biopsy confirmation of neuroblastoma and/or ganglioneuroblastoma at any time prior to

b. For MIBG non-avid tumors, patient must have biopsy confirmation of neuroblastoma and/or ganglioneuroblastoma at any time prior to enrollment from soft tissue lesion (with or without FDG uptake) present at time of enrollment.

3b) At least one non-target soft tissue lesion that is not measurable, but had a biopsy positive for neuroblastoma and/or ganglioneuroblastoma at any time prior to enrollment OR is MIBG avid on planar imaging.
* Patients must have a Lansky (≤ 16 years) or Karnofsky (> 16 years) score of ≥ 50 (Appendix I).

Note: Patients who are unable to walk because of paralysis, but who are up in a wheelchair, will be considered ambulatory for the purpose of assessing the performance score.

- Patients must have fully recovered from the acute toxic effects of all prior chemotherapy, immunotherapy, or radiotherapy prior to study registration.
- Patients must not have received the therapies indicated below after disease evaluation or within the specified time period prior to registration on this study as follows:

1. Myelosuppressive chemotherapy: must not have received within 2 weeks prior to registration.
2. Biologic anti-neoplastics- agents not known to be associated with reduced platelet or ANC counts (including retinoids): must not have received within 7 days prior to registration.
3. Monoclonal antibodies: must not have received last dose within 14 days of registration and resolution of all toxicities.
4. Cellular Therapy (e.g. modified T cells, NK cells, dentritic cells etc.): must not have received within 3 weeks and resolution of all toxicities.
5. Radiation: must not have received small port radiation within 7 days prior to registration, large field radiation within 12 weeks, and 131I-MIBG therapy or other radiopharmaceutical within 6 weeks.
6. Hematopoietic Stem Cell Transplant- none following myeloblative therapy within 6 weeks
7. Any other investigational agents (covered under another IND within 14 days
8. Strong inducers or inhibitors of CYP3A4
    - Hematologic Function:

NOTE: No short acting hematopoietic growth factors within 7 days of blood draw documenting eligibility and no long-acting hematopoietic growth factors within 14 days of blood draw documenting eligibility

1. Absolute Neutrophil count ≥750/µL
2. Platelet count ≥ 75,000/µL, transfusion independent (no platelet transfusions within 7 days of blood draw documenting eligibility)

Patients with known bone marrow metastatic disease will be eligible for study as long as they meet hematologic function criteria above.

- Renal Function Patients must have adequate renal function defined as age-adjusted serum creatinine ≤1.5 ULN for age
- Liver Function

1. Total bilirubin ≤ 1.5 x ULN for age; and,
2. SGPT (ALT) ≤ 135 U/L (≤ 3x ULN). Note that for ALT, the upper limit of normal for all sites is defined as 45 U/L.

    - Cardiac Function
3. Normal ejection fraction (≥ 55%) documented by either echocardiogram OR

4. Normal fractional shortening (≥ 27%) documented by echocardiogram

    - Pulmonary Function No evidence of dyspnea at rest
    - Reproductive Function All females ≥ Tanner stage 2 and post-menarchal of childbearing potential must have a negative beta-HCG within 7 days prior to study registration. Males and females of reproductive age and childbearing potential must commit to using effective contraception for the duration of their participation.
    - Central Nervous System (CNS) Patients with a history of intraparenchymal or leptomeningeal based CNS disease must have no clinical or radiological evidence of active CNS disease at the time of study enrollment.

Patients with skull-based tumors with direct intracranial extension are eligible as long as there are no neurologic signs or symptoms related to the lesion.

Exclusion Criteria:

- Patients who are pregnant, breast feeding, or unwilling to use effective contraception during the study
- Patients who, in the opinion of the investigator, may not be able to comply with the safety monitoring requirements of the study.
- Patients with disease of any major organ system that would compromise their ability to withstand therapy.
- Patients with > Grade 2 diarrhea.
- Patients who have undergone a prior allogeneic stem cell or solid organ transplant.
- Patients who are on hemodialysis.
- Patients with an active or uncontrolled infection. Patients on prolonged antifungal therapy are still eligible if they are culture negative, afebrile, and meet other organ function criteria.
- Patients with known history of human immunodeficiency virus (HIV) infection, hepatitis B, or hepatitis C. Testing is not required in the absence of clinical findings or suspicion.
- Patients must not have been diagnosed with any other malignancy.
- Patients with history of Grade 4 Allergic reactions to anti-GD2 antibody therapy or reactions that caused permanent discontinuation of therapy.
- Patients with history of progressive disease while receiving therapy per ANBL1221.
- Patient declines participation in the NANT biology study and the site has not been granted a waiver from participation.
- Systemic Steroids and Immunosuppressive Medications
- Patients who have received pharmacologic doses of systemic steroids 7 days prior to study registration or likely to require them after study registration.

Note: Exceptions are the following:

1. Patients known to require 2 mg/kg or less of hydrocortisone (or an equivalent dose of an alternative corticosteroid) as premedication for blood product administration.
2. The use of conventional doses of inhaled steroids for the treatment of asthma
3. The use of physiologic doses of steroids for patients with known adrenal insufficiency.

- Patients on any other immunosuppressive medications (e.g., cyclosporine, tacrolimus) at the time of study registration.

Conditions & Interventions

Interventions:
DRUG: Universal Donor (UD) TGFβi NK Cells, DRUG: Temozolomide, DRUG: Irinotecan, DRUG: Dinutuximab, DRUG: GM-CSF
Conditions:
Neuroblastoma
Keywords:
Relapsed Neuroblastoma, Refractory Neuroblastoma, Cellular Therapy, Immunotherapy, Chemoimmunotherapy

More Information

Description:
This is a phase II study looking at patient response to treatment with the combination dinutuximab, temozolomide, irinotecan, and GM-CSF.

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Phase: PHASE2
IRB Number:
System ID: NCT06450041
