Study: NANT 2013-02

Sorafenib with Cyclophosphamide and Topotecan for patients with Relapsed or Refractory Neuroblastoma

Protocol Title:
Phase I Study of Sorafenib and Cyclophosphamide/Topotecan in Patients with Relapsed or Refractory Neuroblastoma

Study Chair: Hung C. Tran, MD Children's Hospital Los Angeles

What is this study about:

This study will combine an oral drug called sorafenib with two chemotherapy medicines called cyclophosphamide and topotecan.

Sorafenib blocks the function of a protein that is important in the growth of cancer cells. This drug has been tested by itself (as a single-agent) in children with relapsed solid tumors, including patients with neuroblastoma. In the laboratory, sorafenib appears to make neuroblastoma tumors smaller, and can help immune cells to be more active in attacking tumors and blocks other harmful immune cells from promoting tumor growth and function. Sorafenib also helps to block tumor cells from developing blood vessels used to "feed" to tumor. Sorafenib is an FDA-approved drug currently widely used for adults with specific types of liver and kidney cancer. Its use in the treatment of neuroblastoma in children is experimental.

Cyclophosphamide and topotecan are both FDA-approved chemotherapy drugs. These drugs are approved for the treatment of certain adult cancers, but have also been used to treat children with cancer. These drugs have been used in combination in many people with neuroblastoma. In some patients with neuroblastoma, this combination reduces the amount of neuroblastoma.

Adding sorafenib to cyclophosphamide and topotecan may increase the effectiveness of this combination. We first need to find out the highest dose of sorafenib that can be given safely together with cyclophosphamide and topotecan. This is the first study to test giving these three drugs together and will help determine the highest dose of sorafenib that can safely be given together with cyclophosphamide and topotecan to patients with resistant/relapsed neuroblastoma.

Why is this study being done:

- To find the highest dose of sorafenib that can be given with cyclophosphamide and topotecan without causing severe side effects.
- To find out the side effects seen by giving sorafenib at different dose levels together with cyclophosphamide and topotecan.
- To measure the levels of sorafenib in the blood at different dose levels.
- To determine if your tumor gets smaller after treatment with sorafenib, cyclophosphamide and topotecan.
- To learn how sorafenib changes immune cells in tumor cells.
- To describe the amount of neuroblastoma tumor found in the blood and bone marrow by testing samples with a new test (called TLDA) that has been found to be more sensitive.

Criteria that need to be met to participate in this study:

- Patients must be ≤ 30 years of age and have reached a minimum size for dosing sorafenib when registered on study.

- Patients must have high risk neuroblastoma and have a response to prior therapy that fits into at least one of the following categories:
    - Relapsed or progressive disease at any time before study enrollment.
    - Refractory disease: patients had "no response" and still have persistent sites of disease after receiving a minimum of 4 cycles of induction treatment and have never had a disease relapse or progression.
    - Persistent disease: patients had a "partial response" and still have persistent sites of disease after receiving a minimum of 4 cycles of induction treatment and have never had a disease relapse or progression.

        - Some patients will need a surgical biopsy done of the tumor to confirm it is neuroblastoma before they will be able to enroll on study. Please check with your doctor as they will be able to tell you if your child will need a biopsy to meet the requirements to enroll on this study.

- Patients must have adequate heart, kidney, liver, pancreas, clotting and bone marrow function. Patients who have bone marrow disease must still have adequate bone marrow function to enter the study.

- Patients with other ongoing serious medical issues must be approved by the study chair prior to registration.

Patients cannot participate in the study if:

Females of childbearing potential must have a negative pregnancy test.

Pregnancy, breast feeding, or unwillingness to use effective contraception during the study

Patients status post allogeneic stem cell transplant are not eligible.

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 a past history of bleeding in the head are not eligible. Patients with a history of strokes or mini-strokes (known as TIA) within 6 months before study enrollment are not eligible.

Patients with a history of clots in veins or arteries (except for central lines) or this same history of clots in immediate family members before they reached 40 years of age are not eligible.

Patients with particular heart problems are not eligible.

Patients who are smaller than a certain physical size based on current height and weight will not be eligible.

Patients with an active or uncontrolled infection. Patients on prolonged antifungal therapy are still eligible if they are culture and biopsy negative in suspected radiographic lesions and meet other organ function criteria.

Study procedures:

This study will test up to 3 sorafenib doses with fixed doses of cyclophosphamide and topotecan in groups of 3-6 patients, which will be assigned upon enrollment. The starting sorafenib dose for the first group of patients is approximately 63% of the tolerated dose determined in a previous clinical study in pediatric solid tumor patients.

Each treatment course is 28 days with the exception of the first cycle which will have a lead in of 7 days when patients will only receive sorafenib.
This diagram outlines one course of therapy on this study:

Drug Administration

7 day lead-in Cycle 1

CYCLE ONE (1):		
Day -6 to 0	**Day 1-5**	**Day 6-28**
Sorafenib	Sorafenib	Sorafenib
	Cyclophosphamide/Topotecan	

CYCLES 2 – 12:	
Day 1-5	**Day 6-28**
Sorafenib	Sorafenib
Cyclophosphamide/Topotecan	

Growth factor support using either Filgrastim or Pegfilgrastim is required beginning on day 6.

Patients will have their neuroblastoma evaluated by bone marrow tests and scans after finishing two cycles of this treatment and then again after the 4th cycle, and then every fourth cycle. Each cycle is 28 days, with the exception of cycle 1 which is 35 days.

Patients may receive up to 12 cycles of therapy (~1 year) on study in the absence of progressive disease. Decisions regarding additional therapy on this study will be made by the study chair and treating physician in collaboration with the NANT Medical Director.

If you would like to download or print a sample consent form for this clinical trial, please click here: N13-02 consent form

If you would like to download this page in Microsoft Word format, please click here: N2013-02

If you are interested in getting more information about this clinical trial, please click here to send us an email.