

Protocol Title: NANT 2004-05: NEUROBLASTOMA BIOLOGY STUDY

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What is this study about?

This is a biology research study where research is done on normal cells and/or tumor cells in the samples collected from you. This biology study includes only subjects who choose to take part. Please take your time to make your decision about participating. You may discuss your decision with your friends, family, and health care team. If you have questions, you may ask your doctor.

You are being asked to take part in this study because your doctors have determined that you have neuroblastoma, a type of solid cancer that usually affects children. Learning more about patients with neuroblastoma, by studying their tumor and normal cells in the laboratory may help doctors to develop better therapies for neuroblastoma. This protocol will create a storage place or "bank" where samples of blood, bone marrow, and tumor will be kept to provide a number of samples large enough to allow researchers to do studies on neuroblastoma tumor cells and other normal cells that interact with the tumor. This study will also use a highly accurate new test to identify and measure tumor cells that may be in your bone marrow or blood to see if this new method improves evaluating the effect of treatment. All research studies done using the banked samples will first be reviewed by a committee of NANT scientists for approval.

The purposes of this study are:

- To establish a storage place or "bank" of samples of blood, bone marrow, and/or tumor, and molecular components isolated from these samples from children with neuroblastoma. The stored specimens will be shared with laboratory researchers studying high risk neuroblastoma.
- To evaluate a new test of blood and bone marrow specimens to find tumor cells. The results of this new test, called 5-gene TaqMan® Low Density Array or TLDA, will be compared between blood and bone marrow and imaging (radiology) studies. Radiology studies (CT scans, MRI scans, and MIBG scans) and the TLDA test will be compared for their ability to measure the amount of tumor present and how this changes with therapy.
- To collect clinical data (such as treatments received, date of diagnosis, tumor stage, etc) and radiology scans to provide this information as needed for the laboratory studies to be done on the specimens.
- To obtain neuroblastoma tumor cells from tumor tissue, bone marrow, and/or blood to use to start "cell lines", or tumor cells that will keep growing in the laboratory. These cell lines will be shared with laboratory researchers studying high risk neuroblastoma.

This research is being done because:

Medical scientists want to find better ways to treat neuroblastoma and to find ways to prevent the tumor from growing back. To do this, they need more information about the characteristics of neuroblastoma cells. Therefore, they want to study samples of neuroblastoma tissues and neuroblastoma and normal cells in the blood and bone marrow that may be related to the growth of neuroblastoma cells. Doctors and other medical scientists also want to find better ways to detect and measure neuroblastoma to improve the ability to follow the response of tumor cells to therapy.

Some research looks at diseases that are passed on in families (called genetic research). Research done with your tumor tissue, blood, and/or bone marrow may look for genetic causes and signs of disease. If your tissue is used for this kind of research, the results will not be put in your health record. The results of these studies will not directly affect decisions made regarding therapy for you, but

may lead to a better understanding of the genes that control neuroblastoma growth.

Study Procedures

Extra bone marrow tests are not done just for this biology study, but we ask patients to provide 1-2 teaspoons of bone marrow when a bone marrow evaluation is being done as part of the requirements of their therapy or medical status. We ask for bone marrow specimens from a minimum of two serial timepoints. Ideally these timepoints would be prior to the start of the treatment they are currently receiving, and then at the next timepoint when their tumor response is checked. However, any two serial timepoints are acceptable. Patients will also be asked to give two teaspoonfuls of blood for special research studies at the same timepoints that bone marrow is obtained, as explained above, for at least two different serial timepoints. Characteristics in the samples of blood may be compared with those in the bone marrow.

Radiologic scans (CT, MRI and MIBG scans) are also done to evaluate the patients' tumor status and its response. Scans are done at timepoints required by the therapy they are receiving and will be submitted and stored in an electronic storage system. Results of the scans will be compared with results from the bone marrow and blood samples taken at the same timepoints. No extra scans are required to be done just for this study.

If patients have tumor tissue removed for medical reasons, then the extra tissue not needed for routine medical purposes can also be submitted to be stored in the storage bank for future research. No surgical procedures to remove tumor tissue will be done just for this biology study.

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

- Patients must be ≥ 31 days of age.
- Patients must have had a diagnosis of high risk neuroblastoma either by histological verification of neuroblastoma and/or demonstration of tumor cells in the bone marrow with increased urinary catecholamines.
- All patients with refractory or recurrent high risk neuroblastoma at NANT institutions are eligible regardless of disease status (including no measurable or evaluable tumor) as long as they undergo a disease evaluation and appropriate samples are submitted.
- Additionally, all patients with high risk neuroblastoma without relapse treated at a NANT institution are eligible if undergoing a disease evaluation, as long as Children's Oncology Group specimens are prioritized.

Patients cannot participate in this study if:

There are no exclusion criteria on this study.