SAMPLE INFORMED CONSENTS

^{131}I-METAIODOBENZYLGUANIDINE (MIBG) WITH INTENSIVE CHEMOTHERAPY AND AUTOLOGOUS STEM CELL RESCUE FOR HIGH-RISK NEUROBLASTOMA

New Approaches to Neuroblastoma Therapy Consortium (NANT) Protocol

This is a clinical trial, a type of research study. Your study doctor will explain the clinical trial to you. Clinical trials include only people who choose to take part. Please take your time to make your decision about taking part. You may discuss your decision with your friends and family. You can also discuss it with your health care team. If you have any questions, you can ask your study doctor for more explanation.

You are being asked to take part in this study because you have high-risk neuroblastoma. Neuroblastoma is a type of solid tumor seen in children. Your cancer has relapsed or is at high risk of relapsing after having standard treatment. Standard treatment may have included chemotherapy, surgery and/or radiation therapy.

WHY IS THIS STUDY BEING DONE?

The purposes of this study are:

- To determine how many tumors get smaller after treatment with ^{131}I-MIBG + high dose chemotherapy (CEM) followed by infusion of autologous blood forming stem cells and local radiation in patients with high-risk neuroblastoma that has either relapsed or is at high risk for relapsing after standard treatment.

- To continue to look at both the good and bad effects of ^{131}I-MIBG + CEM + autologous stem cell infusion and local radiation on patients who are treated with this regimen.

- To determine the amount of ^{131}I-MIBG which is taken up by the tumor and if this can be related to how small the tumor gets after ^{131}I-MIBG treatment.

This research is being done because:

This study will combine three chemotherapy drugs that have been used together in many patients with neuroblastoma (carboplatin, etoposide and melphalan [CEM]) with the chemical agent called Metaiodobenzylguanidine (MIBG). MIBG is taken up by neuroblastoma tumor cells. MIBG can be combined together with radioactive iodine (^{131}I) in the laboratory to form the radioactive compound ^{131}I-MIBG. The ^{131}I-MIBG compound delivers radiation to the neuroblastoma cancer cells and causes them to die. The ^{131}I-MIBG would be given to you followed two weeks later by giving high doses of CEM chemotherapy. This would be followed by an infusion of your own bone marrow cells (called autologous bone marrow or stem cell transplant) to allow your blood cells and bone marrow to grow back. Approximately six weeks following the ^{131}I-MIBG therapy, further radiation therapy, called external beam radiation may be given to specific tumor sites that still remain after this intensive treatment.

Preliminary results using this regimen in both the University of Michigan pilot study of 14 patients, and the larger multi-center NANT 9901 phase I trial in which 24 patients with high risk neuroblastoma were treated with increasing doses of ^{131} I-MIBG + CEM followed by stem cell transplant indicate that this combination of ^{131}I-MIBG with chemotherapy and stem cell transplant may be an effective therapy for patients with “high risk disease.”

This current research study will build upon the results from the phase I trial, NANT 9901. The ^{131}I-

MIBG and chemotherapy dosing used in this study are based upon results from NANT 9901. The current study will determine if ^{131}I-MIBG, in combination with high dose chemotherapy, stem cell transplant and post transplant radiation is an effective method to treat patients with “high risk” neuroblastoma. The primary aim of this phase II trial is to assess your response to this combination therapy.

HOW MANY PEOPLE WILL TAKE PART IN THE STUDY?

About 40 patients will be treated on this study.

WHAT WILL HAPPEN IF I TAKE PART IN THIS RESEARCH STUDY?

Before you begin the study, you will need to have the following exams, tests, or procedures to find out if you can be in the study. These exams, tests or procedures are part of regular cancer care and may be done even if you do not join the study. If you have had some of them recently, they may not need to be repeated. This will be up to your study doctor.

- Stem cell collection.

Before you can get treatment on this study, stem cells must be available. If you have stem cells already stored they must meet the study requirements for you to be able to participate in this clinical study.

- Central line

This study requires that a central line be in place to be used for giving chemotherapy, other medicines or blood and fluids and to remove blood samples during the study treatment.

- Physical Exam
- Blood tests, Urine tests, Pregnancy test
- Bone marrow tests
- Various scans (including MIBG scan), Chest X-Ray, CT (or MRI scan).
- Tests of heart function
- Tests of kidney function
- Hearing test

During the study:
If the exams, tests and procedures show that you can be in the study, and you choose to take part, then you will need to the following tests and procedures. They are part of regular cancer care.

Exams, tests and procedures during the study are broken down in to those that are done during and after treatment with MIBG, and before admission and during transplant.

During ^{131}I-MIBG Treatment

- Readings to measure whole body radiation are done each day to determine when you can leave the special room.
- No medical tests will be done while the patient is in the special room for ^{131}I-MIBG treatment unless the doctor feels it is necessary.

- **After ^{131}I-MIBG Treatment**
- MIBG scan performed when discharged from radiation isolation after ^{131} I-MIBG treatment. For patients with disease in soft tissue (such as within lymph nodes or other organs), an additional MIBG scan may also be obtained 5 – 7 days after ^{131} I-MIBG treatment.

Before being admitted for Transplant

- Physical exams
- Blood tests

During Transplant

- Physical Exam
- Blood tests
- Urine tests
- X-rays other tests or procedures that your study doctor feels are necessary for your care.

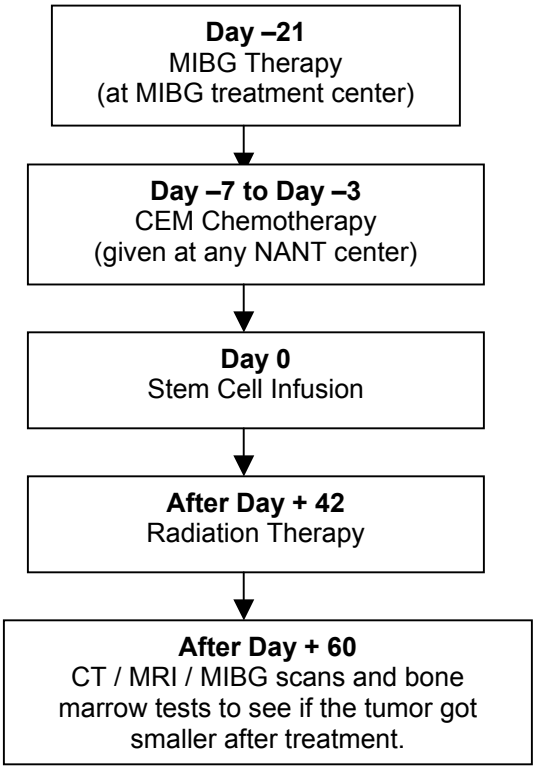
Because you are in this study, blood and urine tests and x-rays may be done more often during

transplant.

When you are finished with your transplant you will have the following tests done:

- Physical Exam
- Blood tests, Urine tests
- Bone marrow tests
- Various scans (including MIBG scan), Chest X-Ray, CT (or MRI scan).
- Tests of heart function
- Tests of kidney function
- Hearing test

Treatment Plan:
You will be referred to an MIBG treatment center for the MIBG portion of therapy. Patients require 3-5 days of admission for this part of the treatment. The following CEM chemotherapy, stem cell transplant and radiation therapy may be given at any NANT member hospital. An overview of the treatment is shown below:



a. MIBG therapy:
Treatment with ^{131}I-MIBG will be done at a hospital that is set up to take care of patients that are treated with radioactive substances. This means that you may need to travel some distance to another hospital to get this treatment. Your doctor, will talk with you about where the different hospitals are that can give the ^{131}I-MIBG treatment. Your nurse and other members of the team that take care of you can help you plan to the trip to get this treatment.

Patients will be admitted to a MIBG treatment center on day -22 of therapy. ^{131}I-MIBG is a type of radiation treatment that is given by vein. On the following day (Day –21), ^{131}I-MIBG is given as a 2 hour infusion through a peripheral IV catheter usually placed in a vein in the hand or arm. This IV catheter is separate from your central venous catheter and will be removed after the ^{131}I-MIBG infusion has finished. IV fluids for hydration and other medicines will be given through the central venous catheter.

Patients who get ^{131}I-MIBG are considered to be “hot” or radioactive and special precautions are

taken to care for you during this time until the radiation level has gone down to a level where these precautions are no longer needed (Usually 4 –5 days). Special care precautions include:

- A single room in a bed surrounded by a lead shield to keep family and the staff who take care of you from being exposed to radiation from the ^{131}I-MIBG treatment. This usually is about 5 days.

- The length of time family can visit inside the room in front of the protective lead shield that is around your bed will depend on how much radiation is measured in the room each day by the radiation specialist. Usually family can visit 30-45 minutes on the first day and longer on days 2 through 5 because there will be less radiation measured in the room each day.

- Family may visit anytime outside of the room behind a lead shield. You will be able to see who is visiting over this shield.

- No one will be able to spend the night in this special room with you during this time.

Your urine will be radioactive after treatment with ^{131}I-MIBG. A urinary catheter will be inserted through your urethra into the bladder to drain the radioactive urine from your body. This catheter will be removed 3 –5 days following the treatment.

You will also take 2 medicines by mouth, (potassium iodide and postassium perchlorate) to prevent thyroid damage from the radioactive iodine contained in the ^{131}I-MIBG compound. The two medicines will be taken together by mouth beginning the night before treatment for a total of 5 days then the potassium iodide alone will be continued for a total of 6 weeks.

b. Chemotherapy and Stem Cell Transplant + Local Radiation:
Following the MIBG therapy, you will be discharged home. You will be re-admitted to the hospital on Day -8 to begin the CEM chemotherapy / transplant portion of treatment. In most cases, you may be hospitalized for three to six weeks following the stem cell transplant. However, in some cases, hospitalization may last longer.

Day -15	Travel home from MIBG treatment center; Get ready to be admitted to the hospital for transplant
Day -8	Admitted to hospital for transplant
Day -7	Start Chemotherapy: Carboplatin/Etoposide Melphalan
Day -6	Carboplatin/Etoposide Melphalan
Day -5	Carboplatin/Etoposide Melphalan
Day -4	Carboplatin/Etoposide
Day -3	REST
Day -2	REST
Day -1	REST
Day 0	Stem Cell Transplant
Following Day +42	Radiation therapy to local sites of tumor if needed

Three chemotherapy drugs will be given over four days. Carboplatin and VP-16 (etoposide) will be given by continuous infusion into your central venous catheter, over all four days (Days –7, -6, -5, -4). Melphalan will be given by injection over 15 to 30 minutes into the central venous line on days –7, -6, -5.

It may take longer for a few patients to be discharged from the radiation isolation room used with MIBG treatment. If this happens, these patients may be given less CEM chemotherapy if the doctors determine this is needed. Your doctor will discuss this with you.

Your stem cells will be infused into the central line, 72 hours (3 days) after all the chemotherapy has finished on Day 0. Four hours after the stem cell infusion, you will get granulocyte colony stimulating factor (G-CSF, a medicine to help the growth of white blood cells) given by IV over 1 hour every day until enough white blood cells are present to fight infection.

Patients whose kidney function is less than normal will get lower doses of carboplatin/etoposide and melphalan than children who have normal kidney function because they will not be able handle higher doses of these drugs without having serious side effects.

Approximately 6 – 8 weeks after the stem cell transplant (Day +42), you may receive additional local radiation therapy to sites that have not previously received radiation treatment. Such radiation therapy will be determined by your treating physicians, and may include masses in the chest or belly, or areas of bone that have tumor present. The radiation therapy would be given by a radiation therapy doctor (Radiation Oncologist) who will explain to you the exact treatment plan and possible side effects. Radiation is given in the clinic once each day for 12 days.

c. Consideration to change chemotherapy dosing: This protocol combines both radiation therapy (^{131}I-MIBG) with chemotherapy (Carboplatin-Etoposide-Melphalan) and stem cell transplant. While patients are receiving MIBG therapy, measurements are normally taken to assess how quickly the radio-active MIBG is being cleared from your body. In some cases, your physicians may determine that the radio-active MIBG isn't being cleared quickly enough from your body. If this were to occur, your body may be exposed to a higher level of radiation than patients who clear the MIBG normally. In the event this happens, your chemotherapy dosage will have to be decreased. If the radiation level exceeds a certain limit, the chemotherapy may be held altogether. You would still receive a stem cell transplant if this were to occur, though no chemotherapy would be given with the transplant. Your physician will discuss with you if the chemotherapy dose needs to be decreased after the MIBG therapy. We do not know how a change in your chemotherapy dosing will affect the success of your treatment.

HOW LONG WILL I BE IN THE STUDY?

You will be treated on this study until 8 – 12 weeks after the stem cell infusion (2 - 3 months) or for as long as it takes for your stem cells to produce enough normal blood cells and for you to recover after the transplant therapy. You will only be treated once with ^{131} I-MIBG and chemotherapy followed by stem cell infusion. You will continue to have tests and scans done to assess the status of your tumor. Blood tests to monitor thyroid and liver function will be done at 6 months, 1 year, and 2 years post transplant, and then as often as your doctor feels they are necessary for your care. Researchers will continue to collect information about you for a lifetime. Information will be collected about whether you are is still alive, whether your tumor has grown back and at what sites in the body; whether you have developed any side effects from the treatment or any additional cancer. This information may be gotten from your oncologist or family doctor at regular intervals.

CAN I STOP BEING IN THE STUDY?

Yes. If you are thinking about stopping the study, you should talk to your doctor before making a final decision so he/she can tell you how to do this safely. There are certain time points in the study where it would be strongly recommended that you complete the medical supportive care required to avoid very bad and/or fatal side effects.

- Once you have gotten MIBG treatment, it is better that you stay in the special room until you are no longer radioactive (usually 5 days), since you could expose others to radiation.

- The combination of MIBG treatment and CEM chemotherapy is strong enough to kill all normal blood cells. So it could be potentially life threatening to stop the study treatment after you have gotten both MIBG and CEM but <u>before</u> the stem cells have been infused.

The study doctor may stop you from taking part in this study at any time if he/she believes it is in your best interest; if you do not follow study rules; or if the study is stopped.

WHAT SIDE EFFECTS OR RISKS CAN I EXPECT FROM BEING IN THIS STUDY?

You may have side effects while on the study. Everyone taking part in the study will be watched carefully for any side effects. However, doctors don't know all the side effects that may happen. Side effects may be mild or very serious. Your health care team may give you medicines to help lessen the side effects. Many side effects go away soon after you stop treatment. In some cases, side effects can be serious, long lasting, or may never go away. There is also a risk of death on this study. In similar studies, fatal side effects have been seen in 5-10% of patients. One patient died in a previous study using MIBG + CEM + ASCT. You should talk to your study doctor about any side effects that you have while taking part in the study.

Possible side effects of ^{131} I-MIBG

Likely Side Effects (21-100%)

- MIBG therapy is commonly (> 50%) associated with the development of low blood counts (requiring red cell or platelet transfusions) and the requirement for stem cell infusions. This drop in blood counts typically begins 2 - 4 weeks after therapy. In the current study, you will receive a dose of MIBG that is anticipated to lower your blood counts.
- Decrease or increase of blood pressure during the ^{131} I-MIBG infusion
- Nausea
- Dry mouth

Less likely Side Effects (5-20%)

- Decreased function of the thyroid gland. A decrease in the function of the thyroid gland can lead to a feeling of being tired (fatigued), weight gain, constipation, and lower blood pressure. Life long supplementation with a medication to supplement the thyroid gland (i.e. Synthroid or related thyroid supplement) may be required.
- Sterility; you may not be able to become pregnant or father a child.

Rare Side Effects (< 5%)

- Pain in the salivary glands
- Urinary tract infection from having a urinary catheter placed
- Decreased function of the adrenal gland. A decrease in the function of the adrenal gland may affect your activity level and growth. This can lead to a feeling of being tired (fatigued), weight changes, and increase or decreased in your blood pressure. An oral medication may be required for months to years to supplement the adrenal gland.
- Decreased function of the heart.
- Irritation of the liver. Because some of the radioactive MIBG is taken up by the liver, there is a possible risk of future liver damage from the MIBG alone.
- Secondary leukemia: you may develop a second cancer [leukemia] that is different from neuroblastoma.

Possible side effects of Potassium Perchlorate: This medication is given for 5 days after the MIBG infusion, to protect your thyroid gland.

Less Likely Side Effects (5-20%)

- Nausea and stomach irritation. Taking this medicine with food or meals may prevent these side effects.

Rare Side Effects (< 5%)

- Unable to make red and white blood cells, platelets
- Hives
- Skin rashes

Possible side effects of Potassium Iodide: This medication is given for 42 days after the MIBG infusion, to protect your thyroid gland.

Less Likely Side Effects (5-20%)

- Nausea and stomach irritation**.** Taking this medicine with food or meals may prevent these side effects.

Rare Side Effects (< 5%)

- Tingling, pain or weakness in arms and legs
- Flare up of adolescent acne
- Irregular heart beat
- Confusion
- Feeling tired
- Fever, hives
- Burning in mouth / throat
- Metallic taste in mouth
- Rashes
- Decreased function of the thyroid gland with over use. (See MIBG for explanation of low thyroid function)

Possible side effects of Carboplatin

Likely side effects (21-100%)

- Blood tests show decreased body salts and minerals

Less Likely side effects (5-20%)

- Hypersensitivity reactions (allergic reaction with rash, difficulty breathing, low blood pressure) This is more common when carboplatin is given weekly. It is rare when carboplatin is given continuously over many hours as in this study
- Decreased kidney function
- Decreased hearing (ringing in ears and loss of hearing)

Rare side effects (less than 5%)

- Altered taste
- Rash
- Decreased sensation with changes in ability to feel vibrations, light touch, pinpricks or position of joints
- Temporary loss of vision to light and colors

Possible side effects of Etoposide (VP-16)

Likely side effects (21-100%)

- Alopecia

Less Likely side effects (5-20%)

- Weakness and not feeling quite right
- Itchiness and rashes

Rare Side Effects (< 5%)

- Low blood pressure during infusion This is more common when Etoposide is given over a short period of time (ie: 30 minutes to 1 hour). It is rare when Etoposide is given continuously over many hours as in this study.
- Anaphylaxis (difficulty breathing, rapid heart beat and low blood pressure)

- Effects on the peripheral nerves (abdominal pain, constipation, clumsiness, or poor coordination)
- Irritation or inflammation of veins
- Chest pain
- Lowered heart function (congestive heart failure)
- Redness and irritation of the skin and sometimes eyes, lips and mouth. There can also be peeling of skin
- Muscle weakness

Possible side effects of Melphalan

Likely side effects (21-100%)

- Low blood salt (happens only with high doses of the drug)

Rare Side Effects (<5%)

- Allergic reaction (may cause hives, and /or difficulty breathing, and / or lowered blood pressure. Symptoms of an allergic reaction can be treated with anti-allergy medicines.)
- Sweating or itching
- Fast irregular heartbeat (happens only with high doses of the drug)
- Damage to skin and surrounding tissues if drug leaks out of the vein. (Rare when drug is given through a central line as in this study)
- Imbalance in body salts
- Seizures
- Yellowing of skin and whites of eyes (called jaundice), hepatitis
- Bone marrow failure
- Anemia caused by the breakdown of red blood cells
- Lung scarring known as stiff lungs or pulmonary fibrosis
- Lung irritation called interstitial pneumonitis

Possible side effects of the combination of ^{131}I-MIBG and chemotherapy

- Lowering of the number of blood cells (Likely 21-100%)

  The blood cells will be destroyed in all patients who get this treatment. This might be fatal if you were not "rescued" by the stem cell infusion. Stem cells make white blood cells, red blood cells and platelets which are needed for you to live. Until the new stem cells begin making enough of the new blood cells, you will have side effects from having low blood cells.

  White blood cells prevent and fight infection. Your will be at high risk for an infection when the white blood cells are low. Almost all patients develop a fever at some time in the first two weeks after transplant. You will be in an isolation room during the transplant to help decrease the chance for infection

  Low red blood cells causes anemia. You will need blood transfusions for the anemia. You may still need blood transfusions after going home from the hospital after the transplant. With transfusion, there is a risk of allergic reaction, hepatitis, and other viral infections (including the virus that causes AIDS).

Platelets prevent bleeding. With low platelets you will be at a higher risk for bruising and bleeding. Bleeding can happen anywhere but is most common from the nose, stomach, and intestines. Bleeding is treated with both red blood cell and platelet transfusions. You may still need platelet transfusions after going home from the hospital after the transplant.

There is a risk that you may never fully recover normal red blood cell, or platelet counts after this treatment and that long term (months – years) transfusions may be required.

- Irritation of the liver
  ^{131}I-MIBG has rarely (< 10%) been associated with irritation to the liver when used alone, commonly associated with changes in blood tests and minimal symptoms in the patient being seen. However, when ^{131}I-MIBG has used together with high doses of chemotherapy, significant liver irritation has been seen in
  20 – 30 % of patients, either as jaundice (a yellowing of skin), enlargement of the belly with fluid, pain in the liver area (called hepatic veno-occlusive disease), or as just an abnormal liver blood test.

- Increased risk of a second cancer or leukemia, different from the kind of cancer you have now. (Rare < 5%)

Possible side effects of the combination of chemotherapy (Carboplatin, Etoposide, Melphalan):

Likely Side Effects (21-100%)

- Mouth sores, mouth swelling that affect the Gastrointestinal (GI) system (mouth, esophagus, stomach, intestines) are common. Such effects on the GI system may include nausea and vomiting, constipation or diarrhea which can be mild, moderate or severe. Mouth sores and mouth swelling can be painful. Mouth sores and mouth swelling can also make it difficult to breathe.
- Hair loss

Less Likely side effects (5-20%)

- Skin damage. Red skin is common. Blistering or peeling skin is not as common.
- Veno-occlusive disease of the liver.
  Veno-occlusive (VOD) is a scarring of the small blood vessels in the liver. When this happens, fluid collects in the abdomen or lungs, weight increases, yellow jaundice may occur, and an increased tendency for bleeding may happen. In many cases, the VOD is mild (with improvement noted following recovery of blood counts. In other cases, the VOD may be severe and even life threatening.

Rare side effects (< 5%)

- Multiple organ system failure. Intensive therapy may have severe effects on many body organs such as blood vessels, lungs, heart, kidneys, liver and brain.

Possible side effects of local radiation to tumor sites:

The types of side effects each patient may have will be different based on the part of the body that is radiated, since radiation only affects organs and structures within the treatment area. Common side-effects which can be seen are listed below. The doctor who specializes in radiation therapy will discuss in more depth side-effects related to your specific radiation sites.

- Skin; Red skin in the radiation area is common. Blistering or peeling skin is not as common.

- Hair loss; Radiation to the skull may cause local hair loss that is permanent.

- Bone growth and appearance
  Radiation affects bone growth and appearance and these changes if they occur are permanent (example: unequal leg length or arm length, unequal development of the bones of the skull, or shorter height than would be expected because of radiation to the spine).

- Alteration in organ function
  Radiation to the chest area can result in altered heart and/or lung function. Radiation to the abdomen can cause altered kidney, liver, bladder and/or intestinal function. Radiation to the skull near the ear may affect the nerve for hearing and cause hearing loss. Some effects may be short term and resolve once the radiation is completed. Other effects may be long lasting.

- Occurrence of second cancer
  Radiation is a cause of cancer and may lead to the development of another type of cancer (different than neuroblastoma) years afterwards within the area that was treated with radiation. These second cancers usually occur in the bone and/or rarely in the kidney

Possible Side Effects of Granulocyte Colony Stimulating Factor (G-CSF):

G-CSF is not an anti-cancer medicine. It helps the growth of white blood cells that fight infection.

Likely side effects (21-100%)

- Bone pain

Less Likely side effects (5-20%)

- Pain or irritation at injection site
- Headache
- Increased blood tests for alkaline phosphatase, LDH and uric acid
- Low platelet count

Rare side effects (<5%)

- Allergic reactions (more common with giving the drug IV than as an injection under the skin)
- Skin rash, itching, puffiness in the face
- Shortness of breath or wheezing
- Low blood pressure, fast heart rate
- Low grade fever
- Enlargement of the spleen.
- Rupture of the spleen

- Worsening of existing skin rashes
- Sickle cell crises in patients with sickle cell disease
- High white blood cell count in the blood
- Irritation / inflammation of veins in the skin
- Adult respiratory distress syndrome
- Bone marrow dysfunction (MDS) or secondary leukemia in patients with very bad ongoing neutropenia (not as seen in cancer patients) and long term administration.

Possible side effects associated with stem cells:

- ANY TIME BEFORE STEM CELL INFUSION: The freezer where the stem cells are stored could malfunction, the container holding them could break and the stem cells could be damaged so they could not be used. This is expected to be an extremely rare event, however, if it occurs, another stem cell collection may be attempted or the back-up stem cells (if available) may be used if they were not damaged.

- If stem cells needed to be shipped from one location to another, they could be lost or damaged during shipping such that they could not be used. This is expected to be an extremely rare event. If this occurs, another stem cell collection may be attempted or the back-up stem cells, if available, may be used.

- PURGED STEM CELLS ONLY: Purging may injure the normal stem cells so they will not grow to make a normal working bone marrow after they are infused. This is expected to be an extremely rare event, but could be fatal if it happened. There would be the option to give medicine(s) to stimulate bone marrow growth, or infuse additional back-up stem cells, if they are available.

Possible side effects of stem cell infusion

Less Likely side effects (5-20%)

- Fever and chills

Rare Side Effects <5%

- Allergic reaction
- Allergic reactions cause difficulty breathing and / or a decreased blood pressure. You are given anti-allergy medicines before the stem cell infusion to help prevent an allergic reaction from occurring
- Increased blood pressure
- Infection
- Infusion of tumor cells

  Tumor cells may still be present in the harvested stem cells and they could regrow in the patient receiving them.

Possible risks to unborn child:

Patients who agree to participate in this study should not become pregnant while on this study and receiving ^{131}I-MIBG + CEM + Local Radiation. This study and the medicines used in this study may be hazardous to an unborn child. Patients and their sexual partners should use

abstinence and /or an effective method of contraception that is medically appropriate based on your personal doctor's recommendation at that time.

Possible risks to the caregiver(s) of the patient getting MIBG treatment:

Caregivers (example: parent, other family member, guardian, friend, sexual partner) will be exposed to radiation while you are being treated with MIBG. Caregivers who could possibly become pregnant during this time need to avoid contact with the patient because the radiation exposure may increase the unborn baby's risk of developing cancer or other health problems.

If your caregiver is pregnant, then special precautions should be used to avoid contact with you during and for 4 weeks after getting MIBG treatment. Should your caregiver or your caregiver's sexual partner be found to have been pregnant while you were getting MIBG treatment and did not know it at the time, please contact your doctor immediately.

Possible long term side effects of this treatment

- Recurrence of the tumor
- Infection
- Sterility and / or delayed onset of sexual maturity
- Increased risk of a second cancer, different from the kind of cancer (such as leukemia) you have now

ARE THERE BENEFITS TO TAKING PART IN THE STUDY?

Based on other experience with ^{131}I-MIBG with or without CEM + stem cells in adults and children, researchers believe that this treatment may offer some benefit to patients with poorly responding or recurrent neuroblastoma by stopping the growth and spread of the disease for a time. However, because each person responds differently to treatment; you may not respond to this treatment. We do know that the information from this study will help doctors learn more about ^{131}I-MIBG + CEM + stem cells as a treatment for cancer. This information could help future cancer patients.

WHAT OTHER CHOICES DO I HAVE IF I DO NOT TAKE PART IN THIS STUDY?

If you chose not to participate in this study you may be eligible for treatment with other high dose chemotherapy, radiation therapy, other standard dose chemotherapy, or other investigational drugs. You cannot receive treatment with MIBG and high dose chemotherapy outside of this study, since it is investigational. Getting comfort care, also called palliative care. This type of care helps reduce pain, tiredness, appetite problems and other problems caused by cancer. It does not treat the cancer directly, but instead tries to improve how you feel. Comfort care tries to keep you as active and comfortable as possible.

Talk to your doctor about your choices before you decide if you will take part in this study.

WILL MY MEDICAL INFORMATION BE KEPT PRIVATE?

We will do our best to make sure that the personal information in your medical record will be kept private. However, we cannot guarantee total privacy. Your personal information may be given

out if required by law. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used.

Organizations that may look at and/or copy your medical records for research, quality assurance and data analysis include:

- NANT Consortium
- Independent auditor evaluating quality assurance for the NANT Consortium.
- The National Cancer Institute (NCI) and other governmental agencies, like the Food and Drug Administration (FDA), involved in keeping research safe for people.
- Draximage (supplier of ^{131}I-MIBG) a division of Draxis Specialty Pharmaceuticals, Inc.

WHAT ARE THE COSTS OF TAKING PART IN THIS STUDY?

Taking part in this study may lead to added costs to your insurance company. Your health insurance company will be billed for many expenses associated with the costs of this study. These expenses include medications, treatments, hospital charges, and doctor fees related to your/your child's participation in this study that are considered standard of care. You or your primary insurer may be charged for expenses associated with the manufacture or infusion of the MIBG.

Carboplatin, Etoposide and Melphalan are commercially available agents. Your primary insurer will be charged for these drugs and for other drugs you need to complete this study. Normally, this cost is covered by your insurance company. In addition, your insurance company will be charged for continuing medical care, evaluation and / or hospitalization.

You may have to pay for other things during this study, such as but not limited to, your time, the cost of food you buy while you are being treated at the hospital, car fare, travel to and from the hospital for ^{131} I-MIBG treatment, parking and baby sitter fees.

You will not paid for taking part in this study.

For more information on clinical trials and insurance coverage, you can visit the National Cancer Institute's Web site at http://cancer.gov/clinicaltrials/understanding/insurance-coverage . You can print a copy of the "Clinical Trials and Insurance Coverage" information from this Web site.

Another way to get the information is to call 1-800-4-CANCER (1-800-422-6237) and ask them to send you a free copy.

WHAT HAPPENS IF I AM INJURED BECAUSE I TOOK PART IN THIS STUDY?
It is important that you tell your study doctor, _____ *[investigator's name(s)],* if you feel that you have been injured because of taking part in this study. You can tell the doctor in person or call him/her at _____ *[telephone number].*

You will get medical treatment if you are injured as a result of taking part in this study. You and/or your health plan will be charged for this treatment. The study will not pay for medical treatment.

WHAT ARE MY RIGHTS IF I TAKE PART IN THIS STUDY?
Taking part in this study is your choice. You may choose either to take part or not to take part in the study. If you decide to take part in this study, you may leave the study at any time. No matter what decision you make, there will be no penalty to you and you will not lose any of your regular benefits. Leaving the study will not affect your medical care. You can still get your medical care from our institution.

We will tell you about new information or changes in the study that may affect your health or your willingness to continue in the study.

In the case of injury resulting from this study, you do not lose any of your legal rights to seek payment by signing this form.

WHO CAN ANSWER MY QUESTIONS ABOUT THE STUDY?
You can talk to your study doctor about any questions or concerns you have about this study. Contact your study doctor _____ *[name(s)]* at _____ *[telephone number].*

For questions about your rights while taking part in this study, call the _____ *[name of center]* Institutional Review Board (a group of people who review the research to protect your rights) at _____ *(telephone number).*

WHERE CAN I GET MORE INFORMATION?

You may call the NCI's **Cancer Information Service** at

1–800–4–CANCER (1–800–422–6237) or **TTY: 1–800–332–8615**

You may visit the NCI Web sites at http://cancer.gov/

1. For NCI's clinical trials information, go to **http://cancer.gov/clinicaltrials/**
2. For NCI's general information about cancer, go to **http://cancer.gov/cancerinfo/**

You will get a copy of this consent form. If you want more information about this study, ask your study doctor.

STATEMENT OF CONSENT

I have been given a copy of all _____ [*insert total number of pages*] page of this form. I have read it or it has been read to me. I understand the information and have had my questions answered. I agree to take part in this study.

_____
Patient Name

_____ _____/_____/_____
Signature of Parent or Guardian **Date**

_____ _____/_____/_____
Signature of Parent or Guardian **Date**

_____ _____/_____/_____
Signature of Patient (If > 7 years old) **Date**

_____ _____/_____/_____
Signature of Physician or Date
Responsible Investigator

_____ ____/_____/_____
Signature of Witness Date

_____ ____/_____/_____
Signature of Translator Date
(If applicable)