15.0 SAMPLE INFORMED CONSENT

NANT 2011-01: STUDY OF SINGLE-AGENT ^{131}I-MIBG, ^{131}I-MIBG WITH VINCRISTINE AND IRINOTECAN, OR ^{131}I-MIBG WITH VORINOSTAT FOR RESITANT/RELAPSED NEUROBLASTOMA

A New Approaches to Neuroblastoma Therapy (NANT) treatment protocol.

The word "you" used throughout this document refers to you or your child.

WHAT IS THIS STUDY ABOUT?

This study is a clinical trial, a type of research study. Clinical trials include only patients 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 any questions, you may ask your study doctor.

You are being asked to participate in this study because you have been diagnosed with neuroblastoma, a type of solid cancer that usually affects children. Your cancer has either grown back (relapsed) or has never gone away (persistent tumor) after standard treatment. Standard treatment may have included chemotherapy, surgery, radiation therapy and/or high-dose chemotherapy with a stem cell transplant.

The purpose of this study is to compare three different treatments aimed at maintaining or improving your response to previous treatments. This study involves the use of an investigational medicine called Metaiodobenzylguanidine (MIBG) alone and in combination with either Irinotecan and Vincristine or Vorinostat. These combinations are also investigational, though the dose and side effects of these combinations have been tested in previous clinical trials.

Once you are registered on this study, you will be randomly assigned to one of three treatments. You will either receive ^{131}I-MIBG by itself or, ^{131}I-MIBG with Vincristine and Irinotecan, OR ^{131}I-MIBG WITH Vorinostat. Patients on all treatment arms will receive the same dose of ^{131}I-MIBG. Patients on all treatment arms will receive blood stem cells as part of this therapy.

Random assignment means that the treatment to which a patient is assigned is based on chance. It is like a flip of a coin, except assignment is done by a computer. Neither you or your doctor will choose which treatment you will receive. All patients will have an equal chance of being placed in either treatment group. During the study, if fewer patients are responding to one treatment arm, then that treatment arm will close early and only the two best treatment arms will continue.

The three treatment arms are the following:

^{131}I-MIBG Alone:
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 treatment to the neuroblastoma cancer cells throughout the body.

^{131}I-MIBG with irinotecan and Vincristine:
This study will combine the two chemotherapy drugs, irinotecan and vincristine, that have been used together in some patients with neuroblastoma with the medicine called Metaiodobenzylguanidine (MIBG). The irinotecan / vincristine will be given during the same hospital stay as the ^{131}I-MIBG. Giving the chemotherapy together with the ^{131}I-MIBG may increase the number of patients who respond to ^{131}I-MIBG.

^{131}I-MIBG with Vorinostat:
Vorinostat is a drug that is FDA-approved to treat a certain type of cancer mainly seen in adults. Vorinostat affects the way the DNA that carries our genes is folded in cells. In the laboratory, vorinostat causes neuroblastoma cells to stop growing. This effect is even greater when vorinostat is combined with radiation. Giving vorinostat together with the ^{131}I-MIBG may increase the number of patients who respond to ^{131}I-MIBG.

WHY IS THIS STUDY BEING DONE?

The purposes of this study are:

- To find out which of the three ^{131}I-MIBG therapies have a better tumor response rate after one treatment course.
- To compare the side effects seen by giving ^{131}I-MIBG alone, and ^{131}I-MIBG in combination with Vincristine and Irinotecan and ^{131}I-MIBG with Vorinostat
- To describe the describe which of the three ^{131}I-MIBG treatment regimens has the best tumor effect after two courses, including response in the bone marrow, MIBG lesions, soft tissue lesions and overall survival.
- To describe how many patients who agree to send blood and bone marrow specimens for a special testing are found to have tumor cells by this new more sensitive test (called TLDA) after the each of the three ^{131}I-MIBG treatment regimens
- To compare the exposure of whole body radiation from ^{131}I-MIBG received on the three regimens using radiation measurements and blood markers of radiation.
- To learn about a new computerized way of reading MIBG scans.
- To learn whether the amount of a certain protein on neuroblastoma cells impacts whether a patient responds to ^{131}I-MIBG therapy or not.

The research is being done because:

Currently there is no known effective treatment for your type of cancer.

This study will compare three ^{131}I-MIBG treatment regimens that have already been used for treatment of neuroblastoma and compare their effects on tumor response and associated side effects. We are trying to see if one therapy is better for people with neuroblastoma.

HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?

A total of 105 patients are expected to enroll on this study. There will be 35 patients on each arm. All patients will be assigned randomly.

WHAT WILL HAPPEN TO ME IF I TAKE PART IN THIS STUDY?

Medical Tests 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. These tests will also be done at various times throughout the study and at the end of the study. The purpose of these tests is to see how well the treatment works and to measure the status of your neuroblastoma. If you have had some of them recently, they may not need to be repeated. This will be up to your study doctor.

Physical exam	Bone marrow tests[#]
Blood tests	Various scans*
Pregnancy test	Echocardiogram and EKG to check the heart function
Urine tests	Test of kidney function (laboratory testing)

[#] Bone marrow tests are done by inserting a needle into the hip bone to remove the marrow which is inside the bone.

* Various scans that are done for diagnosis and checking the response of the tumor to treatment. These may include CT and /or MRI scans and MIBG scans. We will recommend scans specific for your case and we will answer your questions about these scans**.**

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 the following tests and procedures during the study. They are part of regular cancer care.

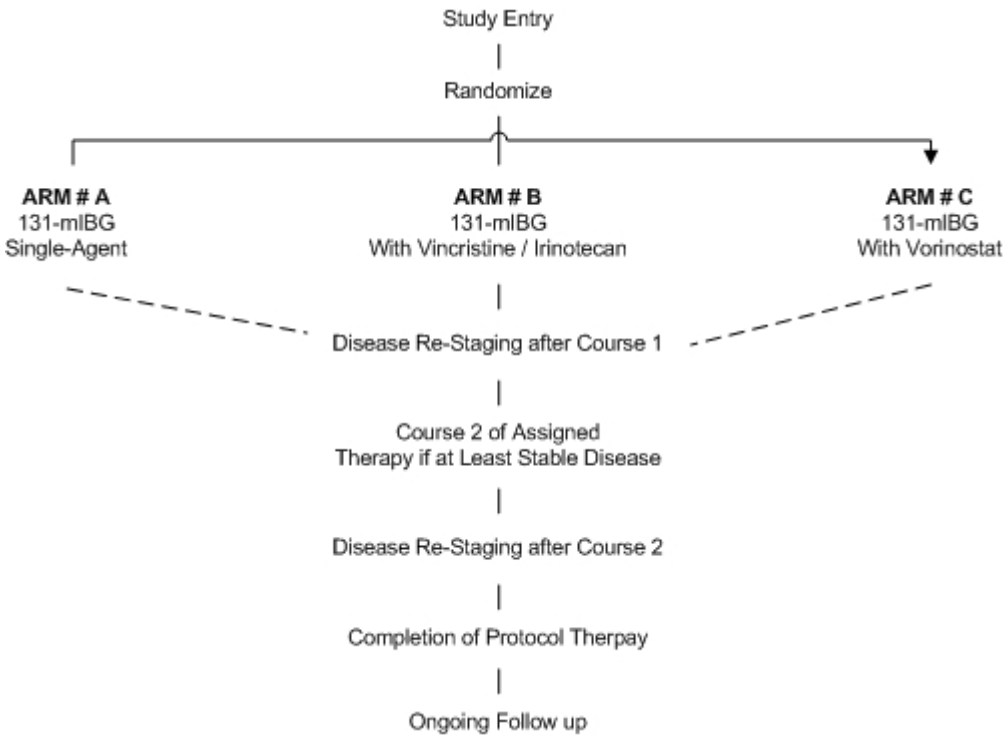
Physical exam	Bone marrow tests
Blood tests and scans	Various tests
Pregnancy test	Echocardiogram and EKG to check the heart function
Urine tests	Test of kidney function (laboratory testing)

You will also be expected to join a companion study to collect blood, bone marrow, and tumor tissue (if available) from patients with neuroblastoma. Your study doctor will talk with you about this study.

Treatment Plan

Before you can get treatment on this study, blood stem cells must be available that meet the study requirements. We will check your child's previously stored stem cells to make sure that they could be used for your child's stem cell infusion.

Patients will then be randomized at study entry to one of three treatment arms.



A map of one treatment course on each treatment arm is shown here:

TREATMENT ARM A: ^{131}I-MIBG ALONE:

Days	1	15	43-50
Therapy	M	HSC	Eval

^{131}I-MIBG	M	Day 1
Stem Cell Infusion	HSC	Day 15
Evaluation	Eval	Day 43-50

TREATMENT ARM B: ^{131}I-MIBG + VINCRISTINE/IRINOTECAN:

Days	-1	0	1	2	3	4	5	6	15	43-50
Therapy	C	C VCR I	C I M	C I	C I	C I	C	C	HSC	Eval

Cefixime	C	Days -1 through Day 6
^{131}I-MIBG	M	Day 1
Irinotecan	I	Days 0 through 4
Vincristine	VCR	Day 0
Stem Cell Infusion	HSC	Day 15
Evaluation	Eval	Day 43-50

TREATMENT ARM C: ^{131}I-MIBG + Vorinostat

Days	-1	0	1	2	3	4	5-12	15	43-50
Therapy	V	V	V M	V	V	V	V	HSC	EVAL

Vorinostat	V	Days -1 through +12 (14 total days)
^{131}I-MIBG	M	Day 1
Stem Cells	HSC	Day 15
Evaluation	Eval	Day 43-50

Treatment with ^{131}I-MIBG

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 for the trip to get this treatment.

Patients will be admitted to an ^{131}I-MIBG treatment center one day before starting MIBG therapy. On the following day (Day 1), ^{131}I-MIBG is given into a temporary IV or in your central venous catheter over 90-120 minutes. IV fluids for hydration and other medicines will be given through your 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 takes 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 for a total of 30-45 minutes on the first day and longer on the days after that because there will be less radiation measured in the room each day.

- Family may visit anytime outside of the room or 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 a medicine by mouth (potassium iodide) to prevent thyroid damage from the radioactive iodine contained in the ^{131}I-MIBG compound. The medicine will be taken together by mouth beginning before treatment and continuing for a total of 6 weeks.

Treatment with Vincristine and Irinotecan (Treatment Arm B only)

If you are randomized to **treatment arm B**, you will receive vincristine and irinotecan in addition to the ^{131}I-MIBG. All patients will get the same irinotecan and vincristine dose.

Before chemotherapy starts on this arm, you will be given the antibiotic Cefixime (on Day -1) and will continue taking the Cefixime for a total of 8 days (until Day +6). Cefixime can be taken in tablet or liquid form. The purpose of the Cefixime is to reduce your chance of having bad diarrhea while getting the irinotecan. If there is trouble getting Cefixime, another antibiotic called cefpodixime can be used instead. After one day of Cefixime, you will start taking irinotecan and vincristine.

Irinotecan is given daily for 5 days in a row (Day 0 through Day 4). Irinotecan is given each day by IV over 60-90 minutes. Vincristine is given by IV over 5-15 minutes only on the first day irinotecan is given (Day 0). Because the most common side effect of irinotecan is diarrhea, you will be instructed to take Loperamide (Imodium) after the first loose stool. You will be given written instructions on how much and how often this medicine should be taken. Additional medicines will be used if the diarrhea is severe.

The day after vincristine and the first dose of irinotecan are given, you will be treated with ^{131}I-MIBG (Day 1).

Treatment with Vorinostat (Treatment Arm C only)

If you are randomized to **treatment arm C**, you will receive vorinostat in addition to the ^{131}I-MIBG. All patients enrolled will get the same Vorinostat dose. You will receive vorinostat orally once daily for 14 days (Days -1 to +12). Two days after starting Vorinostat, ^{131}I-MIBG will be given (Day 1).

All Treatment Arms:
All patients on this study will receive the same dose of ^{131}I-MIBG on Day 1 and autologous blood stem cell infusion on Day 15. You will receive your stored stem cells back by vein two weeks after the ^{131}I-MIBG infusion. This may be done as a day visit to the hospital or may require a brief (one night) stay in the hospital. The stem cells must be given at a NANT hospital, but do not necessarily need to be given at the same NANT hospital that treated you with ^{131}I-MIBG.

If you develop a low white blood count, your may receive G-CSF (Neupogen) or pegfilgrastim in order to help your white blood cells recover faster after treatment. G-CSF (or pegfilgrastim) will be given either as an under the skin (subcutaneous) shot or through your IV (intravenous) once a day Pegfilgrastim, if given, is usually given as a one-time under the skin (subcutaneous) shot. You may also get a dose (or doses) of one of these medicines after you have received your stem cells, even if your blood counts are not low yet. Your doctor will let you know if you will receive GSCF or pegfilgrastim, if needed.

You can receive this therapy (each time on the same treatment arm) two times as part of this study, as long as:

--your tumor is not getting worse;
--you have not had any other anti-cancer treatments since the first course;
--you have enough stem cells to get a second course; and
--you have not had any bad side effects from the first course.

The second course cannot start earlier 6 weeks from the date of the first ^{131}I-MIBG infusion.

When you have finished treatment on this study:

After you stop treatment on your assigned treatment arm, you will continue to have tests and scans done (listed below) to measure how much tumor is left. If test results show you have abnormal organ functions,

tests will be repeated monthly until test results are stable or normal. You doctor will tell you how often these tests and evaluations will be done.

Medical Tests after the Study:

Physical exam	Bone marrow tests[#]
Blood tests	Various scans*
Urine tests	Pregnancy Testing
	Echocardiogram and EKG to check the heart function

A table detailing the tests and procedures required before, during and after the study has been attached to the end of this consent.

Optional Tests in this Study

You will be asked if you want to participate in the following tests that are being done to learn more about ^{131}I-MIBG therapy. **This part of the study is voluntary.** The results of these tests would not be told to you or your doctor or become part of your medical record. These results would also not be used to make decisions about your care while enrolled on this study. You can decide not to let the doctors do these tests and will still be able to be treated as part of this clinical study. There are checkboxes on the next to last page of this consent form to mark whether you are willing to participate in these voluntary studies.

- **Evaluation of Blood Markers of Radiation Exposure**

  Part of the research goal for this study is to look at changes in certain proteins and genes in the blood before and after you have been treated with on each arm of this study**.** For this test, 12.5 mL of blood (2 and a half teaspoons) will be taken 3-4 times during each course of therapy to measure certain proteins and genes in the blood cells. You will not need separate clinic visits to participate in this part of the study. The total amount of blood drawn for testing will be about 50 mL (about 10 teaspoons) over 5-6 days. The blood can be drawn or taken from your central line (or port). This amount of blood drawn over this time period is considered safe to donate. Samples will be sent to the University of California in San Francisco for research testing.

- **Evaluation of Transport Protein on Neuroblastoma Cells**

  Part of the research goal for this study is to look to see if the amount of a specific transport protein on neuroblastoma cells corresponds to response to ^{131}I-MIBG therapy. If you give permission, 5 pathology slides from previous tumor biopsies or tumor surgeries will be sent to the University of California in San Francisco for research testing. Only tumor material already collected will be used and no new biopsies will be performed to help with this research testing.

- **Evaluation of Automated MIBG Scoring System**

  On this study, a new scoring system for MIBG scans will be evaluated using MIBG scans from patients who are willing to participate. You will not need to get extra MIBG scans to participate in this portion of the study. If you agree, your scans will be forwarded to the University of Chicago for this automated MIBG scoring. The researchers in Chicago will not have access to the reports from your treating institution.

HOW LONG WILL I BE ON THIS STUDY?

You will receive up to two courses of treatment on this study.

After you stop treatment, you will continue to have tests and scans done to measure how much tumor is left. Your doctor will tell you how often these tests will be done. Researchers will continue to collect information about you for a lifetime. Information will be collected about whether you are 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 whether you have developed any additional cancer. Your oncologist or family doctor will give the researchers this information 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 ^{131}I-MIBG treatment, you will stay in the special room until you are no longer radioactive (usually 5 days), since you could expose others to radiation.

- Once you have gotten ^{131}I-MIBG treatment, it would be strongly recommended that you complete the medical supportive care needed to avoid very bad and/or fatal side effects. This includes the stem cell infusion and the potassium iodide for thyroid protection.

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 ARE THE RISKS OF THE STUDY?

This study looks at how common and serious side effects can be for each patient at a specific dose of a drug. In this type of study, some patients may have very serious side effects and could die as a result of these side effects. For example, in rare instances, patients treated with ^{131}I-MIBG for neuroblastoma or other diseases have died due to liver or lung damage. You may be one of those patients who has serious side effects as a result of participating in this study.

In this study, researchers will be looking at side effects and tumor responses seen in patients all taking ^{131}I-MIBG with different treatment combinations. Since subjects will be assigned to different treatment arms, consisting of either ^{131}I-MIBG alone or in combination with irinotecan/vincristine or vorinostat subjects will have differing tumor responses and side effects. The goal of this study is to see which treatment arm has the best response for your neuroblastoma while comparing the side effects of the different treatments.

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. Other drugs may be given to make side effects less serious and more comfortable (such as for nausea, headache or itching). Many side effects go away soon after you stop taking the therapies, but it is always possible that side effects can be serious, long lasting or may never go away. There is also a risk of death, including death from bleeding or infection due to low blood counts. Patients are watched carefully and treatment will be stopped if bad side effects develop. There may also be risks we do not know about. You should talk to your doctor about any side effects that you have while taking part in this study.

While on the study, you are at risk for the side effects listed on the following pages.

Possible side effects of ^{131}I-MIBG

Likely (happens to 21-100 children out every 100 children)	**Less Likely** (happens to 5-20 children out every 100 children)	**Rare** (happens to < 5 children out every 100 children)
• Decrease in the number of red and white blood cells and platelets made in the bone marrow. You may need blood and platelet transfusions and sometimes stem cell infusions are necessary. (Stem cells are required on this trial) The dose of ^{131}I-MIBG used in this study will lower your blood counts. • Nausea • Dry mouth • Increase in blood marker of salivary gland irritation (your serum amylase will increase)	• Decreased function of the thyroid gland. This causes tiredness (fatigue), weight gain, constipation, and lower blood pressure. Treatment for life with a medicine to supplement the thyroid gland (i.e. Synthroid or related thyroid supplement) may be needed. • Not being able to get pregnant or father a child • High or low blood pressure during or after the ^{131}I-MIBG infusion • Thinning of the hair • Vomiting • Infection due to low white blood cells • Fatigue due to low red blood cells • Bleeding/bruising due to low platelets • Loss of appetite	• Pain in salivary glands or mouth • Decreased function of adrenal gland. This affects your activity level and growth. It causes tiredness (fatigue), weight changes and blood pressure changes. You may need to take medicine to supplement the adrenal gland. • Decreased heart function • Irritation of the liver. Because some of the radioactive ^{131}I-MIBG is taken up by the liver, there is a possible risk of future liver damage from the ^{131}I-MIBG alone. • Second cancer (such as leukemia) that is different from the kind of cancer you have now • Trouble breathing due to infection or damage to the lung • Overactive thyroid gland

Possible risks from having a bladder catheter placed
In order to safely receive MIBG therapy, you will need to a have a tube or catheter called a Foley catheter temporarily placed in your bladder. The catheter may cause you some discomfort and may increase your risk for getting a bladder infection.

Possible side effects of Potassium Iodide

Likely (happens to 21-100 children out every 100 children)	**Less Likely** (happens to 5-20 children out every 100 children)	**Rare** (happens to < 5 children out every 100 children)
	• Gastrointestinal distress (nausea / vomiting / diarrhea / stomach pain)	• Tingling, pain or weakness in arms and legs • Flare up of acne in teenagers • Irregular heartbeat • Confusion • Tiredness • Fever • Allergic reaction (hives) • Burning of mouth / throat • Metallic taste • Rash • Decreased function of the thyroid gland with overuse

		• Swelling of lymph glands

This medication is given for 45 days after the ^{131}I-MIBG infusion to protect your thyroid gland.

Possible side effects of Vorinostat

Likely (happens to 21-100 children out of every 100 children)	Less Likely (happens to 5-20 children out every 100 children)	Rare (happens to < 5 children out every 100 children)
• Low blood counts, including low red blood cells (which can cause fatigue or pale appearance) and platelets (which can cause bruising or bleeding). • Fatigue • Poor appetite • Diarrhea • Nausea • Vomiting	• Decrease in specific types of blood cells–(white blood cells which can cause increased risk of infection • Weight loss • Effects on blood coagulation lab tests • Decreased kidney function • High blood sugar • Fever, with or without low blood counts • Chills • Hair loss • Constipation • Dehydration • Dry mouth • Heartburn • Taste changes • Infection • Low protein in the blood (albumin) • Changes in liver blood tests • Changes in blood salts • Muscle spasm or weakness • Dizziness • Abdominal pain • Cough • Shortness of breath • Blood clot	• Skin breakdown • Changes in a specific part of the heart tracing known as an EKG. (Mild changes in a specific part of the heart tracing known as an EKG has been rarely reported in patients treated with vorinostat, though it is not clear whether vorinostat caused these changes or not.)

Other side effects have been reported in patients receiving vorinostat, but it is unknown whether the vorinostat caused the side effect. These side effects include: irregular heart rhythm; heart attack; blurry vision; trouble swallowing; gassiness; mouth sores; gum pain; swelling of arms/legs; trouble walking; chest pain; low blood sugar; aches and pains; tumor pain; trouble talking; changes in a blood test that measures blood clotting factors; headache; increased pressure in the brain; bleeding into the brain; stroke; confusion and memory changes; decreased skin sensation; fainting; tremor; anxiety; blood and/or protein in the urine; difficulties with urination; bleeding into the lungs; nose bleeds; trouble sleeping; stuffy nose; throat pain; increased sweating; nail changes; itchiness; other rashes; flushing; bruising; changes in blood pressure; and inflammation of blood vessels.

Possible side effects of Irinotecan

Likely (happens to 21-100 children out of 100)	**Less Likely** (happens to 5 -20 children out of 100)	**Rare** (happens to less than 5 children out of 100)
• Diarrhea (can be immediate) and may be associated with abdominal cramping, a runny nose, tearing, salivation, sweating, flushing (feeling of warmth and red cheeks), and difficulty adjusting your eyes to light. • Inflammation and/or sores in the mouth • Nausea and vomiting • Stomach pain • Loss of appetite • Fever • Loss of body water • Loss of strength and energy • An increase in the blood of a type of white blood cell called an eosinophil. These are sometimes associated with allergic reactions. • Elevation of the liver and bone enzymes in the blood and of bilirubin (yellow pigment formed in the liver) • Decrease in the number of red and white blood cells and platelets made in the bone marrow • Hair loss	• Increased blood tests for liver and kidney function • Constipation • Diarrhea that may occur later from 1 day to 2 weeks after irinotecan which could cause excessive loss of water and salts from the body • Inflammation and/or sores in the mouth, throat and/or esophagus • Headache • An upset stomach • Fewer red blood cells and platelets in the blood • Rash • Blood-clots**. This is seen when Irinotecan is given with other drugs not used in this treatment plan.	• Skin irritation and/or inflammation • Headache • Dehydration • Trembling • Blood in the urine • Mildly increased level of protein and glucose in the urine • Low amount of protein in the blood • Mouth sores • Allergic reaction, that may be life threatening. • Dizziness and low blood pressure • Sensation of warmth on face • Confusion and/or disorientation • Pain at the infusion site • Slow heart beat • Inflammation of the large intestine • Intestinal blockage • Inflammation of the lungs with cough and congestion • Risk to the unborn child in pregnant patients *

* Birth defects and other serious abnormalities in the unborn baby have been noted with irinotecan in animal studies at doses similar to or less than those used in humans. The timing and frequency of these effects is as yet unknown. These may include multiple birth defects and abnormalities of bone formation,
** This toxicity is seen more commonly when irinotecan is given in combination with fluorouracil and leucovorin. It may rarely be a life threatening event.
small size of baby at birth and increased risk of death of the unborn baby. Irinotecan is excreted in rat milk but this is unknown for humans

Possible side effects of Vincristine (Oncovin):

Likely (happens to 21-100 children out of 100)	**Less Likely** (happens to 5 -20 children out of 100)	**Rare** (happens to less than 5 children out of 100)
• Hair loss • Constipation • Reversible nerve problem that may affect the way you walk or the feelings in your fingers and toes	• Jaw pain • Headache • Feeling weak (in muscles) • Belly pain and bloating • Low blood counts that is mild and doesn't last very long • Changes in feeling and sensation in the hands and feet including numbness, tingling and pain, clumsiness, wrist drop, foot drop, abnormal walking with foot slapping	• Local damage to nearby tissue if vincristine leaks out of the vein and into the skin • Difficulty breathing • Your intestine stops working properly which can lead to a blocked intestine. • Drooping eyelids, double vision, and trouble seeing at night • Hoarse voice • Vocal cord paralysis • Low levels of body salts • Seizures • Defective sweating • Trouble walking or not being able to walk • Liver damage when used together with other chemotherapy drugs • Damage to the nerves to the eye leading to decreased vision and possible blindness • Trouble urinating, pain with urination, or having to urinate more often • Low blood pressure when going from sitting down to standing up which can make you dizzy. • Nerve damage with dizziness & a spinning sensation, uncontrolled eye movements and hearing loss

Possible side effects of Cefixime:

Likely (happens to 21-100 children out of 100)	**Less Likely** (happens to 5 -20 children out of 100)	**Rare** (happens to less than 5 children out of 100)

	• Diarrhea
	• Belly pain
	• Nausea and vomiting
	• Indigestion
		• Headache
		• Dizziness
		• Seizures
		• Allergic reaction
		• Hypersensitivity reactions
		  ◦ Low white blood cell, neutrophil and platelet counts,
		  ◦ High eosinophil count (one type of white blood cell),
		• Irritation of the colon
		• Increased blood tests of kidney and liver function
		• Hepatitis, yellowing of skin and whites of eyes
		• Redness and irritation of the skin and sometimes the eyes, lips and mouth. There can also be skin peeling.

Possible side effects of Cefpodoxime (Vantin-R)

Likely (happens to 21-100 children out of 100)	**Less Likely** (happens to 5 -20 children out of 100)	**Rare** (happens to less than 5 children out of 100)
	• Diarrhea • Diaper rash	• Belly pain • Nausea and vomiting • Headache • Seizures • Anaphylaxis • Chest pain • Hypersensitivity reactions • Low white blood cell, neutrophil and platelet counts, • High eosinophil count (one type of white blood cell), • Pseudomembranous colitis: causing abdominal cramping watery diarrhea with bloody stools, fever and a feeling of needing to go to the bathroom • High blood tests for liver and kidney function • Change in blood tests for blood clotting factors (prolonged) • Chest pain • Vaginal infection • Bone marrow failure: bone marrow does not produce enough new cells to replenish blood cells • Redness and irritation of the skin, eyes, lips and mouth. There can also be peeling of skin (a little to a lot)

Possible side effects loperamide (Imodium):
Sleepiness, trouble thinking, constipation, and nausea,

Possible side effects of G-CSF (Neupogen)
G-CSF is not an anti-cancer medicine. It helps the growth of white blood cells that fight infection.

Likely (happens to 21-100 children out every 100 children)	**Less Likely** (happens to 5-20 children out every 100 children)	**Rare** (happens to < 5 children out every 100 children)
• Bone pain	• Pain or irritation at injection site • Increased blood tests for alkaline phosphatase, LDH and uric acid • Low platelet count • Fever	• 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 of veins in the skin • Adult respiratory distress syndrome (life-threatening lung condition that prevents enough oxygen from getting to the lungs

		and into the blood) • 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 of Pegfilgrastim:
Pegfilgrastim is not an anti-cancer medicine. It helps the growth of white blood cells that fight infection

Likely (happens to 21-100 children out every 100 children)	**Less Likely** (happens to 5-20 children out every 100 children)	**Rare** (happens to < 5 children out every 100 children)
• Bone pain	• Pain or irritation at injection site • Headache • Increased blood tests for alkaline phosphaste, lactate dehydrogenase and uric acid • Low platelet count	• Low grade fever • Allergic reactions • Generalized redness and flushing • Enlarged spleen or rupture of the spleen splenic rupture • Pain or other crises in patients with sickle cell disease (SCD) • High white blood cell count in the blood • Adult respiratory distress syndrome (life-threatening lung condition that prevents enough oxygen from getting to the lungs and into the blood.) • Sweet's Syndrome

<u>Possible side effects associated with stem cells</u>

- ANY TIME BEFORE STEM CELL INFUSION: The freezer where PBSC 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 this 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.

- Some patients may need extra fluids given into the vein after getting their stem cells. This is to protect the kidneys from the red blood cells mixed in with the stem cells.

Possible side effects of stem cell infusion

Likely (happens to 21-100 children out every 100 children)	**Less Likely** (happens to 5-20 children out every 100 children)	**Rare** (happens to < 5 children out every 100 children)
	• Fever and chills	• Allergic reaction. Can cause difficulty breathing and low blood pressure. • High blood pressure • Infection • Infusion of tumor cells. Tumor cells may still be present in the harvested stem cells and they could regrow after stem cells are infused. • Cough • Chest Tightness • Flushing • Nausea and/or vomiting • Rash • Irregular Heart Beat

Possible risks to unborn child

Patients who agree to participate in this study should not become pregnant while on this study. This study and the medicines used in this study may be hazardous to an unborn child. Patients and their sexual partners should avoid sex 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, 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 tumor
- Infection
- Sterility and/or delayed onset of puberty
- Increased risk of a second cancer (such as leukemia) different from the kind of cancer you have now.
- Patients who have more than one ^{131}I-MIBG treatment will have greater doses of radiation to the normal organs than those patients having one treatment. It is possible that there may be later damage to the normal function of the liver or other organs.

Possible risks from having blood drawn

The risks from having your blood taken are minimal, but can include an infection or a blood clot. Experienced doctors or nurses will perform these blood draws to minimize this risk. . You will be asked to sign a separate consent for any procedure that needs sedation.

Unknown risks
The treatment combinations may have side effects that no one knows about yet. The researchers will let you and your child know if they learn anything that might make you change your mind about participating in the study.

ARE THERE BENEFITS TO TAKING PART IN THE STUDY?

There may or may not be direct medical benefit to you. The information learned from this study may or may not benefit other children or young people with solid cancers in the future.

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

Yes there are other options for treatment. Instead of being in this study, you have these options:

- Treatment with chemotherapy medicines without MIBG.
- Treatment with other experimental agents that may be available.
- No neuroblastoma therapy at this time, with care to help you feel more comfortable.

Please talk about these options with your doctor.

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
- Nuclear Diagnostic Products (NDP; alternate supplier of ^{131}I-MIBG)
- Merck (supplier of vorinostat)

NANT has received a Certificate of Confidentiality from the federal government, which will help us protect the privacy of our research subjects. Information about the certificate is included at the end of this consent.

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 doctors' fees related to your participation in this study.

Irinotecan, vincristine, cefixime/cefpodoxime, loperamide, and G-CSF/Pegfilgrastim are commercially available agents. The cost of these drugs will be billed to your child and/or your child's insurance company. The cost is normally covered by your child's insurance company.

Vorinostat will be provided by Merck, the company that makes this drug. However they do not cover the cost of getting Vorinostat ready and giving it to you, so you or your insurance company may have to pay for this.

^{131}I-MIBG will be supplied by Draximage or NDP, two companies that makes this drug, and will be paid for by the NANT consortium. Your insurance company will be charged for the cost of the administration of the drug.

The optional studies will be done at no cost to if you agree to participate in this voluntary study. However, you or your health plan may need to pay for the costs of the supplies and personnel who draw the blood from you for these tests.

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 MIBG treatment, parking, and baby sitter fees.

Taking part in this study may lead to added costs that may be covered by your insurance company. Please ask about any expected added costs or insurance problems.

You will not be 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 AS A STUDY PARTICIPANT?

Taking part in this study is your choice. You may choose not to take part or not take part in the study. If you decide to take part in this study, you may remove yourself from 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. If you remove yourself from the study, we will still take care of you. We will explain what stopping the treatment may do and we will offer other treatments if they are available.

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

A Data Safety and Monitoring Board, an independent group of experts, will be reviewing data from this research throughout the study. We will tell you about new information from this Board or other studies that may affect your health or willingness to stay in the study.

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

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at anytime.

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

CONSENTS FOR EXTRA STUDIES FOR RESEARCH

The following tests are optional. You may still participate in the study even if you do not agree to these tests.

Evaluation of Blood Markers of Radiation Exposure

Circle YES, if you agree to let researchers take blood to evaluate blood markers of radiation exposure. These are extra blood draws. The results of these tests will be confidential and not made available to you or your treating physician.

Circle NO, if you do not want researchers to take extra blood samples to evaluate blood markers of radiation exposure.

YES NO

Signature

Participant: _____ Date: _____

Evaluation of Transport Protein on Neuroblastoma Cells

Circle YES, if you agree to allow pathology slides from previous neuroblastoma biopsies or surgeries to be sent to the University of California in San Francisco for research testing.

Circle NO, if you do not want to allow your pathology slides to be sent for research testing.

YES NO

Signature

Participant: _____ Date: _____

Evaluation of Automated MIBG Scoring System

Circle YES, if you agree to allow your MIBG scans to be forwarded to the University of Chicago for automated MIBG scoring.

Circle NO, if you do not want to allow your MIBG scans to be forwarded to the University of Chicago for automated MIBG scoring.

YES NO

Signature

Participant: _____ Date: _____

SIGNATURE OF RESEARCH SUBJECT

Your signature below indicates

- You have read this document and understand its meaning;
- You have had a chance to ask questions and have had these questions answered to your satisfaction;
- You consent/assent to your participation in this research study; and

_____

Name of Subject

_____ _____

Signature of Subject Date

SIGNATURE OF PARENT(S)/LEGAL GUARDIAN(S) (If the subject is a minor)

Your signature(s) below indicates

- You have read this document and understand its meaning;
- You have had a chance to ask questions and have had these questions answered to your satisfaction;
- You agree to your child's participation in this research study; and

_____ _____

Name(s) of Parent(s)/Legal Guardian(s)

_____ _____

Signature of Parent/Legal Guardian Date

_____ _____

Signature of Parent/Legal Guardian Date

SIGNATURE OF INVESTIGATOR/PERSON OBTAINING CONSENT

I have explained the research to the subject and/or the subject's parent(s)/legal guardian(s) and have answered all of their questions. I believe that they understand all of the information described in this document and freely give assent/consent/permission to participate.

_____

Name of Investigator/Person obtaining consent

_____ _____
Signature of Investigator/Person obtaining consent Date

SIGNATURE OF WITNESS (if applicable)

My signature as Witness indicates that the subject and/or the subject's parent(s)/legal guardian(s) voluntarily signed this assent/consent/permission form in my presence.

_____
Name of Witness

_____ _____
Signature of Witness Date

SIGNATURE OF INTERPRETER (if applicable)

_____
Name of Interpreter

_____ _____
Signature of Interpreter Date

Complete if applicable:

Please check appropriate box and sign below.

☐Investigator/person obtaining consent's statement of certification for subjects less than seven years of age (assent):

The undersigned, _____, hereby certifies that he/she has discussed all the information contained in the study consent to the subject, and has explained all the information in the study consent to the participant/patient, including any risks that may reasonably be expected to occur. The undersigned further certifies that the subject was encouraged to ask questions, that all questions were answered, and that assent was obtained.

☐ Assent was not obtained for a subject under 18 years of age. *(Please state the reason. Examples include: child is an infant; child is comatose; child lacks cognitive abilities to understand the information.)*

_____

_____

Date:_____

Time:_____

Signature_____

Consent Addendum I: Tests that will be done on this study.

Observation	Before Entry	Days -1 to Day +7 of Each Course	Days 8 to 43 of each course	Day 43-50 of each course
Physical Exam	X	Day 4	Every other week	X
Blood Tests	X	Day 1* and Day 4	Up to two times a week	X
Urine tests (including Urine Catecholamines)	X			X
Pregnancy test	X			X
Heart tests (echocardiogram and EKG)	X	Day 4 EKG*		X
Bone Marrow Aspirate/biopsy	X			X
CT, MRI and/or MIBG scans	X			X
MIBG scan after MIBG treatment; no extra MIBG is given to you for this scan.		After you get out of your radiation isolation room		
Blood samples for blood markers of radiation exposure (optional)		Three or four blood draws over 5-6 days		
Tumor slides sent for research (optional)		X		

***only for patients on Treatment Arm C (^{131}I-MIBG + Vorinostat)**

Consent Addendum 2

Certificate of Confidentiality Information

NANT has received a Certificate of Confidentiality from the federal government, which will help us protect the privacy of our research subjects. The Certificate protects against the involuntary release of information about subjects collected during the course of our covered studies. The researchers involved in the studies cannot be forced to disclose the identity or any information collected in the study in any legal proceedings at the federal, state, or local level, regardless of whether they are criminal, administrative, or legislative proceedings. However, the subject or the researcher may choose to voluntarily disclose the protected information under certain circumstances. For example, if the subject or his/her guardian requests the release of information in writing, the Certificate does not protect against that voluntary disclosure. Furthermore, federal agencies may review our records under limited circumstances, such as a DHHS request for information for an audit or program evaluation or an FDA request under the Food, Drug and Cosmetics Act. The Certificate of Confidentiality will not protect against the required reporting by hospital staff of information on suspected child abuse, reportable communicable diseases, and/or possible threat of harm to self or others.

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16.0 SAMPLE ASSENT FORM

STUDY OF SINGLE-AGENT ^{131}I-MIBG, ^{131}I-MIBG WITH VINCRISTINE AND IRINOTECAN, OR ^{131}I-MIBG WITH VORINOSTAT FOR RESITANT/RELAPSED NEUROBLASTOMA

A New Approaches to Neuroblastoma Therapy (NANT) treatment protocol

1. Dr. _____ is doing a research study.

2. You have a kind of cancer called **Neuroblastoma.** We are asking you to take part in a research study because doctors want to learn more about treating neuroblastoma using three different types of treatment choices. You will only receive one of the treatments and which treatment you get will be decided by a computer. You will get one medicine called **MIBG** for sure and then the other choices include 3 other medicines.

Here are the three options:

- **MIBG all by itself**
- **MIBG with two other medicines: VINCRISTINE AND IRINOTECAN**
- **MIBG with one other medicine: VORINOSTAT**

Doctors are trying to see and to see what effects (both good and bad) these medicines have on patients and their cancer, and which medicines given together (or by themselves) are better in treating your neuroblastoma. MIBG is a radioactive medicine that is given into the bloodstream (either through your central line or through a small tube placed in a vein in your hand or arm) Vincristine and Irinotecan are also medicines given into your blood stream. Vorinostat is a medicine that is given by mouth as a liquid or pill. The MIBG goes mostly to where the cancer is in your body to give it radiation. The doctors think that giving MIBG may kill neuroblastoma cancer cells and are trying to see if it works better by itself or when its given together with either Vincristine and Irinotecan or Vorinostat.

3. If you agree to be in this study this is what will happen:

You will get this therapy up to two times. Each time you will get the same medicines.

MIBG (Given on all Treatment Arms):

You will get MIBG, which is a radioactive medicine given into an IV over 1 hour. Because of this radiation treatment you will need to stay in your room until you go home. This is usually about 5 days. Your parents cannot sleep in your room but they will be able to stay just outside your room and you will be able to see and talk to them anytime you want. They can visit inside your room for a short time each day.

Because not all hospitals can give the MIBG, you might have to go with your parents to another hospital to get the MIBG part. Your doctor will talk with you and your parents about the different hospitals that can give the MIBG, and which one will be the best for you.

You will need to have a **Urinary Catheter** placed to help drain your urine while you are getting the MIBG treatment. A soft tube will be put inside your urethra (the hole where urine comes out of our bodies), and up into your bladder (the place where urine waits inside our bodies until we go to the bathroom). Because the MIBG will be in your urine, and can cause damage to your bladder, the catheter is necessary to prevent this from happening by keeping your bladder completely empty all the time.

Vincristine and Irinotecan (Treatment Arm B only):
You will get vincristine in your IV once on Day 0. You will get Irinotecan in your IV once a day for 5 days (Day 0 through Day 4**)**

Vorinostat (Treatment Arm C only):
You will take vorinostat liquid by mouth once a day for 14 days.

Stem Cells:
MIBG is a medicine that can lower the numbers of your normal blood cells. Stem cells make all the normal blood cells your body needs to be healthy. This includes white blood cells that fight infection, platelets that stop you from bleeding, and red blood cells that carry oxygen to your body. When MIBG is given at higher doses it can damage stem cells so they don't make enough of the normal blood cells we need to live. Your stem cells will be given back to you like a blood transfusion after the MIBG and other treatment is finished. This is called Stem Cell Infusion or Stem Cell Rescue. We give the stem cells back through your central line either in the hospital or in the clinic. It is a lot like getting a platelet transfusion – the stem cells look like watery blood.

Filgrastim/G-CSF:
The G-CSF helps the blood cells grow back faster after treatment. You will get G-CSF if your blood cells are low after getting MIBG. G-CSF is given through your IV or as an injection (shot) from a very small needle into your leg that your parents will learn how to give you. It is given one time a day until your blood cells have started to grow back. We will know when the blood counts are high enough to stop the G-CSF by doing a blood test.

Coming to See the Doctors:

During and after you have finished the treatment, you will have appointments with the doctors who are taking care of you. This is called "**Follow-Up**". This is to see how well the treatment has worked so far. The doctors will want to do some special tests to find this information out. They will include;

- Blood tests (we will do this twice each week to start with, and then less often)
- MRI, CT, and MIBG Scans (special pictures of your tumor)
- Bone marrow test (to look for tumor in your bone marrow)
- Tests for your heart, and your kidneys
- Check your pee
- Feel your belly, look into your eyes and ears, and listen to your heart and lungs.
- Ask you and your parents a lot of questions about how you are feeling, how you are doing in school, and any problems you might be having.
- You may have to come to the clinic to have blood and platelet transfusions when the blood counts are low or stay in the hospital if you have a fever with low blood counts.

You will come to visit your doctor every week or so to start with, then less often if everything is going well.

4. Sometimes things happen to kids in research studies that may make them feel bad. These are called "risks'. Some of the risks of this study are:
    - You may feel sick to your stomach and you may throw up.
    - You may feel tired.
    - You may have a bad appetite.
    - You might have a fever and maybe an infection where you will need to be in the hospital to get medicines to treat the infection. You may feel tired and weak and need a blood transfusion or you may get bruises or have bleeding (most often a nosebleed) and need a platelet transfusion.
    - During MIBG**,** the urinary catheter may be uncomfortable, and some people feel embarrassed having it – but you will only need it for a few days. It may also be hard to be in a room for a long time by yourself until the radiation levels are low enough that it is safe for your parents and everyone else to be around you all the time.
    - The treatments may not work, and your tumor may grow, or it might come back again after the treatment has finished. If this happens we will try other ways to stop the tumor from growing.
    - You could get a different kind of cancer, this doesn't happen often, but can happen years later.
    - It is possible that you could die from the treatment or cancer.

Not all of these things may happen to you. Or things may happen that the doctors don't know about yet.

5. People also have good things that happen to them when they are in research studies. These are called "benefits". The benefits to you of being in this research study are that this treatment might

make your neuroblastoma tumor stay the same size or get smaller for some time. We hope to learn more about this new treatment which could help other children with neuroblastoma.

6. Please talk this over with your parents before you decide whether or not to be in this study. We will also ask your parents to give their permission for you to take part in this study. But even if your parents say "yes" you can still decide not to do this.

7. Being in this study is up to you. You do not have to be in this study if you don't want to. You may stop being in this study at any time but there are two times where you would be at more risk for being sick or having side effects or being dangerous to other people if you stopped being in the study. 1. If you got MIBG and left the special room before the doctors said it was ok to leave, then you would still be radioactive and this would be dangerous to everyone who was around you since you would give them radiation from your body. 2. If you decided to stop treatment after getting MIBG but before you were given your stem cells back, the high dose of MIBG could kill your blood cells so they would not grow back on their own without getting back your stem cells. In this case you would not be able to make your own blood cells and could have bad infections or bleeding, and you could die from not having enough normal blood cells.

8. You can ask any questions that you have about the study. If you have a question later that you didn't think of now, you can call me or ask me next time. Study doctor's phone number: _____.

9. Optional Blood Samples

   Please check to show if you do or do not agree to allow us to take the 3 or 4 extra blood samples to learn more about the effect of MIBG on the body. These blood samples are usually drawn from your central line.

   _____Yes, it is okay to take the extra blood samples.

   _____ No, it is not okay to take the extra blood samples.

10. Optional Tissue Samples

    Please check to show if you do or do not agree to allow us to use some of your neuroblastoma tumor tissue already removed during previous surgeries or biopsies. You will not have extra surgeries or biopsies just because you say "Yes" to this part of the study.

    _____Yes, it is okay to take the extra blood samples.

    _____ No, it is not okay to take the extra blood samples.

11. Optional MIBG Scan Study

    Please check to show if you do or do not agree to allow us to send copies of your MIBG scans to a hospital that is testing a new way to read MIBG scans. You will not have extra MIBG scans just because you say "Yes" to this part of the study.

_____Yes, it is okay to send copies of my MIBG scans.

_____ No, it is not okay to send copies of my MIBG scans.

Signing your name at the bottom means that you agree to be in this study. You and your parents will be given a copy of this form after you have signed it.

Name of Subject: _____

_____ _____
Signature of Subject: **Date**

_____ _____
Signature of Investigator **Date**

_____ _____
Signature of Person Conducting Discussion **Date**