

## **SAMPLE INFORMED CONSENTS**

### **IRINOTECAN AND VINCRIStINE FOR RADIOSENSITIZATION OF <sup>131</sup>I-MIBG THERAPY IN RESISTANT/RELAPSED HIGH-RISK 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 having gotten standard treatment. Standard treatment may have included chemotherapy, surgery, radiation therapy and/or high-dose chemotherapy with a stem cell transplant.

#### **WHY IS THIS STUDY BEING DONE?**

**The purposes of this study are:**

- To find the highest dose of <sup>131</sup>I-MIBG that can be given intravenously with irinotecan and vincristine without causing severe side effects.
- To find out the side effects seen by giving <sup>131</sup>I-MIBG on this schedule at different dose levels.
- To measure blood levels of irinotecan during treatment
- To find out if specific genes affect blood levels of irinotecan
- To find out if specific genes affect side effects caused by irinotecan
- To determine if your tumor gets smaller after treatment with <sup>131</sup>I-MIBG and irinotecan/vincristine.

**The research is being done because:**

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

This study will combine the two chemotherapy drugs, irinotecan and vincristine, that have been used together in some patients with neuroblastoma with the chemical agent called Metaiodobenzylguanidine (MIBG). MIBG is taken up by neuroblastoma tumor cells. MIBG can be combined together with radioactive iodine (<sup>131</sup>I) in the laboratory to form the radioactive compound <sup>131</sup>I-MIBG. The <sup>131</sup>I-MIBG compound delivers radiation to the neuroblastoma cancer cells and causes them to die. The irinotecan / vincristine will be given at the same time as the <sup>131</sup>I-MIBG. Giving the chemotherapy together with the <sup>131</sup>I-MIBG may help the <sup>131</sup>I-MIBG to kill more

neuroblastoma cells. <sup>131</sup>I-MIBG lowers the number of blood forming cells (called stem cells) in the bone marrow when it is given at higher doses. All patients will get back their own stem cells since it is expected that as the dose of <sup>131</sup>I-MIBG is increased, the blood cells will not recover to normal without this support. This study will be the first study to test giving irinotecan / vincristine together with <sup>131</sup>I-MIBG and will help determine the highest <sup>131</sup>I-MIBG dose that can safely be given together with irinotecan/vincristine to patients with resistant/relapsed neuroblastoma.

## HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?

Between 15 and 30 people will take part in this study.

## 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 main part of 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. However, you may need to have these exams and tests more often if you participate in this 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 <sup>#</sup>
Blood tests	Various scans*
Pregnancy test	Echocardiogram to check the heart function
Urine tests	Test of kidney function

<sup>#</sup> 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	Various scans
Pregnancy test	Test of kidney function
Urine tests	

Because you are in this study, physical exams, blood and urine tests, bone marrow tests and various scans that are part of your regular cancer care will be done more often.

You will be asked if you want to participate in tests that are being done to see how the study drugs are affecting your body. **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 still be able to be treated with irinotecan / vincristine and <sup>131</sup>I-MIBG 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.

- **Determining Blood Levels of irinotecan (called Pharmacokinetics)**

Part of the research goal for this study is to look at the level of irinotecan in the blood. For this test, 3 ml of blood (about ½ teaspoon) will be taken 7 times to check drug levels in the blood. This testing will be done when irinotecan is given during the second week of treatment. A separate IV will be placed to take the blood for these tests since your central line cannot be used to do this. The total amount of blood drawn for drug level testing will be 21ml ( about 5 teaspoons). Samples will be sent to St. Jude Children's Research Hospital in Memphis, TN for analysis.

- **Biology Studies of Blood**

Another part of the research goal is to look for genetic changes in normal blood cells of patients to see if these are related to how the liver handles irinotecan, or whether you will have diarrhea after getting irinotecan. These tests are done on one sample of blood (one teaspoon, 5 ml) taken from your central line (or port) on the first day of treatment.

### **Treatment Plan**

Before you can get treatment on this study, stem cells must be available that meet the study requirements.

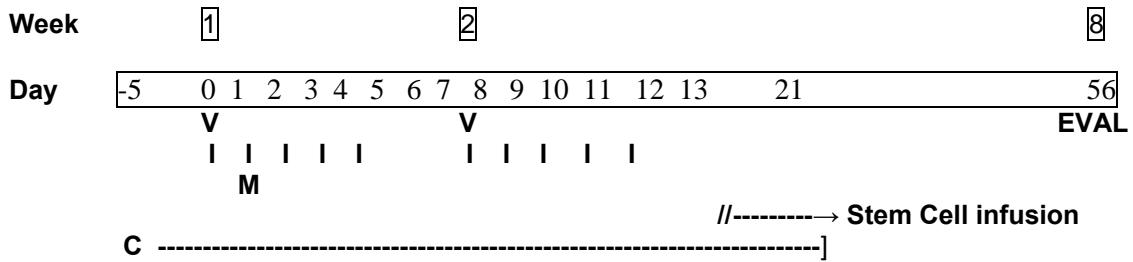
Before chemotherapy starts, you will be given the antibiotic cefixime up to twice a day by mouth for five days. Cefixime can be taken in tablet or liquid form. The purpose of the cefixime is to reduce your chance of having bad diarrhea while you are getting irinotecan. Cefixime will be given every day for a total of 27 days. If there is trouble getting Cefixime, another antibiotic called cefpodoxime (Vantin-R) can be used instead.

After 5 days of cefixime you will start taking irinotecan, vincristine and <sup>131</sup>I-MIBG. Irinotecan is given daily for 5 days in a row then 2 days of rest followed by another 5 days for a total of 10 doses over 2 weeks. Irinotecan is given by IV over 1 hour each day. Vincristine is given by IV over 5 minutes on the first day irinotecan is given of each week for a total of 2 doses.

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.

In the first week of treatment on day 1 you will be treated once with <sup>131</sup>I-MIBG. (See below: Treatment with MIBG).

If you develop a low white blood count, you may receive G-CSF (Neupogen) in order to help your white blood cells recover faster after treatment. G-CSF will be given either intravenously or as an under the skin (subcutaneous) shot once a day after the last dose of irinotecan until the blood counts recover with giving stem cells.



<b>MIBG:</b>	<b>M</b>	<b>Day 1</b>
<b>Vincristine:</b>	<b>V</b>	<b>Day 0 and Day 7</b>
<b>Irinotecan:</b>	<b>I</b>	<b>Days 0 to 4 and Days 7 to 11</b>
<b>Cefixime:</b>	<b>C</b>	<b>Days -5 to Day 21</b>
<b>G-CSF</b>	<b>G-CSF</b>	<b>Given any time after day 11 if blood counts are low.</b>
<b>Stem Cells:</b>	<b>SC</b>	<b>Day 13. You will receive your stem cells.</b>
<b>Evaluation:</b>	<b>Eval</b>	<b>Day 56. Evaluations are done after finishing treatment. Treatment may be repeated every 6-8 weeks as long as your neuroblastoma is responding to treatment and you do not have bad side effects.</b>

All patients will get the same irinotecan and vincristine dose. You will be assigned a certain <sup>131</sup>I-MIBG dose, which will be one of up to 5 doses studied in groups of 3-6 patients. The starting dose for the first group of patients is about 30-50% lower than what is currently being given to patients receiving <sup>131</sup>I-MIBG alone without the irinotecan and vincristine without bad side effects. The <sup>131</sup>I-MIBG dose will then be increased (“dose escalation”) in groups of 3-6 patients until serious side effects are seen. At that point, investigators will have found the highest dose of <sup>131</sup>I-MIBG that can be given along with irinotecan and vincristine without bad side effects. It will be possible for certain patients, who show a response to treatment, to receive another treatment course, but if this is the case, the dose of <sup>131</sup>I-MIBG will not be increased the second time. Your doctor will tell you what dose you will receive and answer your questions about dose escalation.

### Treatment with <sup>131</sup>I-MIBG

Treatment with <sup>131</sup>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 <sup>131</sup>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 <sup>131</sup>I-MIBG treatment center on the day 0 of therapy. On the following day (Day 1), <sup>131</sup>I-MIBG is given as a 1½ hour to 2 hour IV infusion through a temporary IV usually placed in a vein in the hand or arm that is taken out once the MIBG infusion has finished. IV fluids for hydration and other medicines will be given through the central venous catheter.

Patients who get <sup>131</sup>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 <sup>131</sup>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 the days after that 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  $^{131}\text{I}$ -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 potassium perchlorate) to prevent thyroid damage from the radioactive iodine contained in the  $^{131}\text{I}$ -MIBG compound. The two medicines will be taken together by mouth beginning the night before treatment for a total of 6-8 days then the potassium iodide alone will be continued for a total of 6 weeks.

**When you have finished treatment with irinotecan/vincristine and  $^{131}\text{I}$ -MIBG**

After you stop treatment with  $^{131}\text{I}$ -MIBG and vincristine/irinotecan, 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 <sup>#</sup>
Blood tests	Various scans*
Urine tests	

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

**HOW LONG WILL I BE ON THIS STUDY?**

You can continue to get treatment every 8 weeks for as long as your neuroblastoma responds to the treatment or you do not have bad side effects. 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 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, 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 <sup>131</sup>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.

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 is a Phase I study. A Phase I study looks at how common and serious side effects can be for each patient at a specific dose of a drug. In a Phase I study, some patients may have very serious side effects and could die as a result of these side effects. You may be one of those patients who have serious side effects as a result of participating in this Phase I study.

In this study, researchers will be looking at side effects seen in patients taking different doses of <sup>131</sup>I-MIBG together with fixed doses of irinotecan/vincristine. Since subjects will be assigned to different doses of <sup>131</sup>I-MIBG, some subjects may receive a dose of <sup>131</sup>I-MIBG that is too small to be effective while others may receive a higher dose that may cause increased side effects.

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 irinotecan, vincristine and <sup>131</sup>I-MIBG, 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. Patients are watched carefully and treatment will be stopped if bad side effects develop. Because this combination has never been given to children before, there may 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 Irinotecan (CPT-11):**

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)
<ul style="list-style-type: none"> <li>• Diarrhea (can be immediate)</li> <li>• Nausea and vomiting</li> <li>• Stomach pain</li> <li>• Loss of appetite</li> <li>• Fever</li> <li>• Loss of body water</li> <li>• Loss of strength and energy</li> </ul>	<ul style="list-style-type: none"> <li>• Increased blood tests for liver and kidney function</li> <li>• Constipation</li> <li>• Pain at injection site</li> <li>• Blood-clots. This is seen when Irinotecan is given with other drugs not used in this treatment plan.</li> </ul>	<ul style="list-style-type: none"> <li>• Skin inflammation</li> <li>• Trembling</li> <li>• Blood in the urine</li> <li>• Mildly increased level of protein and glucose in the urine</li> <li>• Low amount of protein in the blood</li> <li>• Mouth sores</li> <li>• Headache</li> <li>• Dizziness</li> </ul>

<ul style="list-style-type: none"> <li>• Decrease in the number of red and white blood cells and platelets made in the bone marrow</li> <li>• Hair loss</li> </ul>		<ul style="list-style-type: none"> <li>• Sensation of warmth on face</li> <li>• Confusion</li> <li>• Inflammation of the large intestine</li> <li>• Inflammation of the lungs with cough and congestion</li> </ul>
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**Possible side effects of Vincristine (Oncovin):**

<b>Likely</b> (happens to 21-100 children out of 100)	<b>Less Likely</b> (happens to 5 -20 children out of 100)	<b>Rare</b> (happens to less than 5 children out of 100)
<ul style="list-style-type: none"> <li>• Hair loss</li> <li>• Constipation</li> <li>• Reversible nerve problem that may affect the way you walk or the feelings in your fingers and toes</li> </ul>	<ul style="list-style-type: none"> <li>• Jaw pain</li> <li>• Headache</li> <li>• Feeling weak</li> <li>• Belly pain</li> <li>• Bone marrow suppression that is mild and doesn't last very long</li> <li>• 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</li> </ul>	<ul style="list-style-type: none"> <li>• Local damage to nearby tissue if vincristine leaks out of the vein and into the skin</li> <li>• Difficulty breathing</li> <li>• Your intestine stops working properly which can lead to a blocked intestine.</li> <li>• Drooping eyelids, double vision, and trouble seeing at night</li> <li>• Hoarse voice</li> <li>• Vocal cord paralysis</li> <li>• Low levels of body salts</li> <li>• Seizures</li> <li>• Defective sweating</li> <li>• Trouble walking or not being able to walk</li> <li>• Liver damage when used together with other chemotherapy drugs</li> <li>• Damage to the nerves to the eye leading to decreased vision and possible blindness</li> <li>• Trouble urinating, pain with urination, or having to urinate more often</li> <li>• Low blood pressure when going from sitting down to standing up which can make you dizzy.</li> <li>• Nerve damage with dizziness &amp; a spinning sensation, uncontrolled eye movements and hearing loss</li> </ul>

**Possible side effects of Cefixime:**

<b>Likely</b> (happens to 21-100 children out of 100)	<b>Less Likely</b> (happens to 5 -20 children out of 100)	<b>Rare</b> (happens to less than 5 children out of 100)
<ul style="list-style-type: none"> <li>•</li> </ul>	<ul style="list-style-type: none"> <li>• Diarrhea</li> <li>• Belly pain</li> <li>• Nausea and vomiting,</li> <li>• Indigestion</li> </ul>	<ul style="list-style-type: none"> <li>• Headache</li> <li>• Dizziness</li> <li>• Seizures</li> <li>• Anaphylaxis</li> <li>• Hypersensitivity reactions</li> <li>• Decrease in the number of white blood cells and platelets in the blood</li> <li>• Pseudomembranous colitis,</li> <li>• Increased blood tests of kidney and liver function</li> <li>• Hepatitis, yellowing of skin and whites of eyes</li> <li>• Redness and irritation of the skin and sometimes the eyes, lips and mouth. There can also be skin peeling.</li> </ul>

**Possible side effects of Cefpodoxime (Vantin-R)**

<b>Likely</b> (happens to 21-100 children out of 100)	<b>Less Likely</b> (happens to 5 -20 children out of 100)	<b>Rare</b> (happens to less than 5 children out of 100)
	<ul style="list-style-type: none"> <li>• Diarrhea</li> <li>• Diaper rash</li> </ul>	<ul style="list-style-type: none"> <li>• Belly pain</li> <li>• Nausea and vomiting,</li> <li>• Headache</li> <li>• Seizures</li> <li>• Anaphylaxis</li> <li>• Chest pain</li> <li>• Hypersensitivity reactions</li> <li>• Low white blood cell, neutrophil and platelet counts,</li> <li>• High eosinophil count (one type of white blood cell),</li> <li>• Pseudomembranous colitis: causing abdominal cramping watery diarrhea with bloody stools, fever and a feeling of needing to go to the bathroom.</li> <li>• High blood tests for liver and kidney function</li> <li>• Change in blood tests for blood clotting factors (prolonged)</li> <li>• Chest pain</li> <li>• Vaginal infection</li> <li>• Bone marrow failure:</li> </ul>

		<ul style="list-style-type: none"> <li>• Redness and irritation of the skin, eyes, lips and mouth. There can also be peeling of skin (a little to a lot)</li> </ul>
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**Possible side effects loperamide (Imodium):**

Sleepiness, depression of the functions of the central nervous system, constipation, and nausea.

**Possible side effects of <sup>131</sup>I-MIBG**

<b>Likely</b> (happens to 21-100 children out every 100 children)	<b>Less Likely</b> (happens to 5-20 children out every 100 children)	<b>Rare</b> (happens to < 5 children out every 100 children)
<ul style="list-style-type: none"> <li>• Decrease in the number of red and white blood cells and platelets made in the bone marrow . You will need blood and platelet transfusions and sometimes stem cell infusions are necessary. The dose of <sup>131</sup>I-MIBG used in this study will lower your blood counts.</li> <li>• High or low blood pressure during <sup>131</sup>I-MIBG infusion</li> <li>• Nausea</li> <li>• Dry mouth</li> </ul>	<ul style="list-style-type: none"> <li>• 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.</li> <li>• Not being able to get pregnant or father a child</li> </ul>	<ul style="list-style-type: none"> <li>• Pain in salivary glands</li> <li>• Urinary tract infection from having a urinary catheter placed. (This is a risk from having a urinary catheter placed for the MIBG treatment not from the MIBG drug itself.)</li> <li>• 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.</li> <li>• Decreased heart function</li> <li>• Irritation of the liver. Because some of the radioactive <sup>131</sup>I-MIBG is taken up by the liver, there is a possible risk of future liver damage from the <sup>131</sup>I-MIBG alone.</li> <li>• Second cancer, different from the kind of cancer you have now (leukemia).</li> </ul>

**Possible side effects of Potassium Iodide:**

This medication is given for 45 days after the <sup>131</sup>I MIBG infusion, to protect your thyroid gland.

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)
	<ul style="list-style-type: none"> <li>• Gastrointestinal distress (nausea / vomiting / diarrhea / stomach pain)</li> </ul>	<ul style="list-style-type: none"> <li>• Tingling, pain or weakness in arms and legs</li> <li>• Flare up of adolescent acne</li> <li>• Irregular heartbeat</li> <li>• Confusion</li> <li>• Tiredness</li> <li>• Fever</li> <li>• Hypersensitivity (hives)</li> <li>• Burning of mouth / throat</li> <li>• Metallic taste</li> <li>• Rash</li> <li>• Decreased function of the thyroid gland with overuse</li> <li>• Swelling of lymph glands</li> </ul>

**Possible side effects of Potassium Perchlorate:**

This medication is given for 5 days after the MIBG infusion, to protect your thyroid gland.

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)
	<ul style="list-style-type: none"> <li>▪ Nausea and stomach irritation. Taking this medicine with food or meals may prevent these side effects.</li> </ul>	<ul style="list-style-type: none"> <li>▪ Unable to make red and white blood cells, platelets</li> <li>▪ Hives</li> <li>▪ Skin rashes</li> </ul>

**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)
<ul style="list-style-type: none"> <li>• Bone pain</li> </ul>	<ul style="list-style-type: none"> <li>• Pain or irritation at injection site</li> <li>• Increased blood tests for alkaline phosphatase, LDH and uric acid</li> <li>• Low platelet count</li> <li>• Fever</li> </ul>	<ul style="list-style-type: none"> <li>• Allergic reactions (more common with giving the drug IV than as an injection under the skin)</li> <li>• Skin rash, itching, puffiness in the face</li> <li>• Shortness of breath or wheezing</li> <li>• Low blood pressure, fast heart rate</li> <li>• Low grade fever</li> </ul>

		<ul style="list-style-type: none"> <li>• Enlargement of the spleen.</li> <li>• Rupture of the spleen</li> <li>• Worsening of existing skin rashes</li> <li>• Sickle cell crises in patients with sickle cell disease</li> <li>• High white blood cell count in the blood</li> <li>• Irritation / inflammation of veins in the skin</li> <li>• Adult respiratory distress syndrome</li> <li>• Bone marrow dysfunction (MDS) or secondary leukemia in patients with very bad ongoing neutropenia (not as seen in cancer patients) and long term administration.</li> </ul>
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**Possible side effects associated with stem cells**

- 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 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: Purged stem cells are treated (purged) to take out neuroblastoma cancer cells and leave the normal cells. 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**

<b>Likely</b> (happens to 21-100 children out every 100 children)	<b>Less Likely</b> (happens to 5-20 children out every 100 children)	<b>Rare</b> (happens to < 5 children out every 100 children)
	<ul style="list-style-type: none"> <li>• Fever and chills</li> </ul>	<ul style="list-style-type: none"> <li>• Allergic reaction. Can cause difficulty breathing and low blood pressure.</li> <li>• High blood pressure</li> <li>• Infection</li> <li>• Infusion of tumor cells. Tumor cells may still be present in the harvested stem cells and they could regrow after stem cells are infused.</li> </ul>

### **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 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 tumor
- Infection
- Sterility and/or delayed onset of sexual maturity
- Increased risk of a second cancer (such as leukemia) different from the kind of cancer you have now.
- Patients who have more than one <sup>131</sup>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. These have risks that will be discussed with you. You will be asked to sign a separate consent for any procedure that needs sedation.

### **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 MIBG alone.
- Treatment with other experimental agents that may be available.
- No 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 <sup>131</sup>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 doctors' fees related to your participation in this study.

Irinotecan, vincristine, cefixime/cefpodoxime, loperamide, and G-CSF are commercially available agents. You will pay for the amount of drugs needed to complete this study. This cost is normally covered by your insurance company.

The cost of <sup>131</sup>I-MIBG will be billed to the patient. Although this drug is still considered investigational, the Food and Drug Administration has approved charging for the cost of <sup>131</sup>I-MIBG production and infusion. This cost will be billed to your insurance company.

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 your 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/>

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 already read the information in this informed consent document. I have read all the attachments that were included with this informed consent document. I have asked all of my questions and I have gotten answers. I agree to enroll myself (my child) 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  
Responsible Investigator

\_\_\_\_/\_\_\_\_/\_\_\_\_  
Date

\_\_\_\_\_  
Signature of Witness

\_\_\_\_/\_\_\_\_/\_\_\_\_  
Date

\_\_\_\_\_  
Signature of Translator  
**(If applicable)**

\_\_\_\_/\_\_\_\_/\_\_\_\_  
Date