IRB NUMBER: 10-00822
IRB APPROVAL DATE: 07/13/2010
IRB EXPIRATION DATE: 06/09/2011

Patient Name:_____

DOB: ___ / ___ / ___

UCSF MR#: _____

UNIVERSITY OF CALIFORNIA SAN FRANCISCO

CONSENT TO BE A RESEARCH SUBJECT (adolescent/adult)

^{131}I-Metaiodobenzylguanidine (^{131}I-MIBG) Therapy for Patients with Malignant Pheochromocytoma and Related Tumors: A Best Available Therapy / Compassionate Use Protocol (IND 32,147)

WHAT IS THIS STUDY ABOUT?

This is a clinical trial, a type of research study. Your study doctor, Dr. Paul Fitzgerald, and his associates from the University of California Medical Center at San Francisco will explain the clinical trial to you.

Clinical trials include only people who choose to take part. Please take your time to make your decision about participating. You may discuss your decision with your family and friends and with your health care team. If you have any questions, you may ask your study doctor.

You are being asked to take part in this study because you have advanced (metastatic) pheochromocytoma or a related tumor. Your cancer has either grown back (relapsed) or has never gone away (persistent tumor) after having received standard treatment.

The above physicians are investigating a method of treating metastatic pheochromocytoma with a radioactive compound called ^{131}I-metaiodobenzylguanidine (^{131}I-MIBG) which is taken up by the pheochromocytoma (and related tumor) cells. This compound delivers the radioactive iodine to the cancer cells selectively, resulting in their destruction. Previous research studies testing ^{131}I-MIBG in patients with pheochromocytoma have shown that ^{131}I-MIBG made tumors smaller in some patients.

WHY IS THIS STUDY BEING DONE?

The purpose of this research study is to gain further evidence of the effectiveness of this treatment and to further assess the side effects of ^{131}I-MIBG therapy.

HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?

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About 50 people are expected to be treated on this study at UCSF.

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

You will need to have the following exams, tests or procedures to find out if you can be in this study. These exams, tests or procedures are part of routine care for your cancer and may be done even if you do not join the study. These tests will be performed approximately 2-6 weeks prior to and 8-12 weeks after the MIBG treatment.

1. Physical examination, blood and urine tests: Includes a medical history, blood and urine tests, and a pregnancy test if appropriate.

2. MIBG Scan: An MIBG scan is used to identify pheochromocytoma (and related tumor) cells that are present in the body. When performing an MIBG scan, the MIBG must first be combined with a small amount of radioactivity. The level of radioactivity is only large enough to identify pheochromocytoma (and related tumor) cells and so it is not large enough to damage normal cells and most organs of the body. However, an organ located in the neck called the thyroid is sensitive to this small amount of radioactivity. Because of this, you will need to take a medicine by mouth before, and for several days after, the MIBG scan to protect your thyroid from the radiation effects. You will receive MIBG by vein and will return one day later for the scan. During the scan, you will need to lie on a scanning bed while two special cameras above and below you take pictures of your entire body. You will need to stay very still during the scan, which will take about one hour. Your doctor and the doctor who does the MIBG scan will further explain this procedure to you and answer all of your questions.

3. CT Scan: A CT Scan is a form of x-ray imaging that requires you to have a dye injected. The dye makes tissues and organs more visible in the pictures. Although the CT Scan does not cause any pain, you will need to lie still for 30–60 minutes inside a large doughnut-shaped machine. The table will move and the machine will make clicking and whirring noises as the pictures are taken. You may have a CT scan and/or an MRI of your disease site.

4. MRI: Based on the location of your disease and other clinical factors, your doctor may decide to do a magnetic resonance imaging (MRI) scan of your primary disease location. An MRI uses magnets, instead of x-rays, to produce detailed images of the body. For the MRI test, you will lie down on a narrow bed, which will then be placed in a tunnel that is 6 feet long by 22 inches wide and open at each end. You will lie there quietly for about one hour, during which time you will hear a loud banging noise. You may feel warm and "closed in" during this procedure.

5. Bone marrow aspirate and biopsy: A bone marrow aspirate and biopsy involves the removal of cells from the central portion of the bone, through the insertion of a needle, usually in both hip bones. The cells are removed only after a numbing medicine has been injected under the skin or after a general anesthetic has been given. These procedures are needed to measure your clinical condition (signs and symptoms of side effects and/or cancer) and progress. This

procedure takes only 5-10 minutes; however, if a general anesthetic is given, a recovery period of ½ - 2 hours is needed afterwards.

Some of the procedures described above may require that you be given a general anesthetic or be consciously sedated (put in a sleep-like state) before your doctor can start the procedure. If this is determined to be necessary, you will receive a separate consent form discussing the procedures and risks to read and sign by the anesthesiologist before the procedure is to take place. The doctor will be able to answer all of your questions. The procedures will be completed at UCSF in the appropriate departments for each specific scan and test or at your referring medical facility.

Specific Procedures to this Study:

If you agree to participate as a research subject in this study, the following procedures will happen:

Pre-Treatment:

1. If you do not already have a central line, you will need to have a peripheral intravenous catheter (tube) placed in a vein before you can begin treatment on this study.

2. Because your urine will be radioactive, a urinary catheter will be inserted through your urethra into the bladder to ensure drainage of the urine. The catheter will be removed 3-5 days following the treatment. You may be sedated for this procedure, if necessary.

3. Stem Cell Harvest: If you do not already have stored blood stem cells, then before admission for ^{131}I-MIBG treatment, you may have your blood stem cells collected for later use, if necessary. The blood stem cells will be used in case your blood cells do not recover from the ^{131}I-MIBG treatment. If it is necessary to harvest stem cells, a separate consent form discussing the procedures and risks will be provided. If you are unable to have blood stem cells collected, you may receive ^{131}I-MIBG at a lower dose that does not require stem cells.

Treatment:

1. You will be treated at UCSF. Upon admission, the nursing staff will instruct your caretaker on the care s/he will give you during and following the MIBG infusion. Because of the frequent exposure of the nursing staff to radiation and the high level of radiation surrounding you during therapy, the nurses' contact will be limited to complex medical care so that they are available for you in the event of an emergency. Adult family members or friends will be expected to be present at all times during the hospitalization to:

    - Assist with hygiene
    - Give oral medications
    - Offer and empty bedpans
    - Assist with meals

- Change clothing and bed linens if soiled

Attached to this consent form is an Appendix that describes in detail the duties that will be expected of your caretaker while you are being treated with ^{131}I-MIBG. After your caretaker has read all of the information, and her/his questions have been answered, s/he will be asked to sign the form.

2. Isolation: You will be placed in a single room with a bed surrounded by lead shielding to prevent exposure of visitors and hospital personnel to radioactivity for 3-5 days. Family members may visit in the room for approximately 15-20 minutes on the first day. On the other days family members may visit, but the amount of time a family member will be allowed to visit will be based on how much radiation has been measured by the radiation specialist. Usually the time allowed to visit on days 2 through 5 is more than 30-45 minutes, because less radiation will be measured in your room each day. You will be kept informed by your doctor or the radiation specialist about how much time is allowed for visits. Family members may visit with you anytime from outside of the room.

3. You will receive fluids through a central or peripheral venous catheter. The fluids will begin at least four hours before and continue at least 72 hours after the ^{131}I-MIBG treatment.

4. You will take 2 medications by mouth, potassium iodide and potassium perchlorate, to prevent thyroid damage from the radioactive iodine contained in the ^{131}I-MIBG. These two medications will be taken starting the night before the treatment and for 5 days after. After five days, you will continue to take the potassium iodide for a total of 6 weeks.

5. If you already have a central line in place, the ^{131}I-MIBG will be given through your central catheter. If you do not have a central catheter, ^{131}I-MIBG will be given through a peripheral intravenous catheter (usually placed in a vein in your hand or arm) over a 2-hour period. The peripheral intravenous catheter will be removed after the ^{131}I-MIBG has been given.

6. During the administration of the drug, your blood pressure and heart rate will be checked frequently.

7. For the first 3 days, you may receive an injection of an anti-clotting medication (such as enoxaparin) to reduce the likelihood of blood clots developing in your veins.

8. Before and at regular intervals after treatment, you will have routine blood tests to check your blood counts, hormone, liver, and kidney functions. Blood will be checked at least twice weekly for 4 - 6 weeks, then weekly for 4 weeks, then monthly until normal. Blood tests for endocrine studies will be required at 1, 3, 6 and 12 months post-treatment, and at least every 6 months thereafter. A 24-hour urine will be collected about every 3 months for 12 months and at least every six months thereafter.

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9. A single nuclear medicine scan will be performed to see where the drug is concentrating in the body between the 3rd and 7th day following treatment. No injection of a radioactive marker will be required for this scan.

10. The radioactive iodine in the MIBG will likely have a damaging effect on your normal blood forming cells in your bone marrow. This will cause you to have low blood counts. Between your discharge from the hospital and your scan evaluations 8-12 weeks after treatment, you may need:

    - A red blood cell transfusion (cells from a blood donor given to you by vein) if your red blood cell count drops too low
    - A platelet transfusion to prevent or treat bleeding
    - Antibiotics to treat infections in the blood, lungs or bladder that can occur when the number of white blood cells is too low.

    If your white blood cell and/or platelet count has not recovered by 8-12 weeks after treatment, you will need to have your stem cells returned to you by vein, if available, to speed the recovery of the bone marrow in making blood cells.

11. If your heart has significant uptake of ^{131}I-MIBG, a cardiac ultrasound will be repeated after treatment. If your lungs are involved with tumor, pulmonary (breathing) function tests will be done after treatment as necessary.

12. Eight to twelve weeks after treatment, x-rays, bone marrow tests, and other scans will be done to evaluate the response of the tumor to the treatment.

HOW LONG WILL I BE ON THIS STUDY?

Physicians (home town or UCSF) visits will be necessary every 1-2 weeks for the first 2 months, then monthly for the first year after treatment, every 2 months during the second year and every 3 months thereafter. Lab tests (including CBC with differential and platelet count, ALT, AST, bilirubin, T_4, TSH) and MIBG scan are required every 3 months until 1 year post treatment, then every 6 months until progression, death or other therapy. Other disease evaluation as recommended by your physician may also be required. You will require regular follow-up for your entire life. After one year following ^{131}I-MIBG treatment, you will see a physician at least every 3 months. If having follow-up with a hometown physician, written follow-up with U.C.S.F. physicians will be required after each visit. Copies of laboratory and radiologic tests will need to be sent to UCSF so that your progress can be monitored.

If your tumor is responding or stable 8-12 weeks after each treatment, you may be eligible for further courses of treatment, as long as your white blood counts have fully recovered from the treatment without requiring use of the stem cells. You may be treated on this study anywhere from 6 weeks to 6 months. The total lifetime dose of ^{131}I-MIBG that patients can receive is based on weight.

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After the completion of all treatment, the researchers will continue to collect information about you for an indefinite period of time. This information will include whether you are still alive and whether you have developed any side effects from the treatment or any additional cancer. This information will be obtained from your oncologist and/or family doctor at regular intervals.

Your doctor may decide to take you off this treatment if your disease becomes worse, side effects become severe, new scientific developments suggest that the treatment is no longer in your best interest, or if your doctor feels that this is no longer the best available treatment for you.

CAN I STOP BEING IN THE STUDY?

Yes. You can decide to stop at any time. Tell the study doctor if you are thinking about stopping or decide to stop. He or she will tell you how to stop your participation safely.
It is important to tell the study doctor if you are thinking about stopping so any risks from the treatment can be evaluated by your doctor. Another reason to tell your doctor that you are thinking about stopping is to discuss what follow-up care and testing could be most helpful for you.

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

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

Any treatment has potential side effects. The drug used in this treatment plan may cause some or none of the side effects listed below. There is always the risk that very uncommon or previously unknown side effects may occur. Many side effects go away shortly after treatment has stopped, but in some cases, side effects can be serious, long-lasting, or may never go away, and on rare occasions may even be fatal. The risk of death associated with MIBG therapy is less than 5%.

You should talk to your study doctor about any side effects you experience while taking part in the study.

^{131}I-METAIODOBENZYLGUANIDINE (^{131}I-MIBG)

Likely (happens to 21-100 patients out every 100 patients)	**Less Likely** (happens to 5-20 patients out every 100 patients)	**Rare** (happens to < 5 patients out every 100 patients)
• 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 usually stem cell infusions are	• Fever or infection as a result of the low white blood cells. The infection may become serious. • Fatigue from low red blood cells	• Pain and swelling in salivary glands • Urinary tract infection from having a urinary catheter placed. (This is a risk from having a urinary catheter placed for the ^{131}I-MIBG treatment not from the ^{131}I-MIBG itself.)

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necessary. The dose of ^{131}I-MIBG infusion used in this study may lower your blood counts. • Lowering the number of red blood cells, which may make you tired or pale • Nausea • Dry mouth • Alopecia (hair loss) • High or low blood pressure during ^{131}I-MIBG infusion • Loss of appetite	• Not being able to get pregnant or have a child • 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 (you.e. Synthroid or related thyroid supplement) may be needed.	• Bruising or bleeding from the low platelet count. Bleeding can rarely become serious. • 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 and/or kidneys. Because some of the radioactive ^{131}I-MIBG is taken up by the liver and kidneys, there is a possible risk of future liver and/or kidney damage from the ^{131}I-MIBG alone. • Second cancer, different from the kind of cancer you have now (leukemia). • Complications related to taking ^{131}I-MIBG may result in death • Dehydration • Respiratory or breathing problems • Pain at tumor site • Autonomic Neuropathy • Blood Clots

POTASSIUM IODIDE (KI, SSKI)

Likely (happens to 21-100 patients out of every 100 patients)	**Less Likely (happens to 5-20 patients out of every 100 patients)**	**Rare (happens to <5 patients out of every 100 patients)**
	• Gastrointestinal distress (nausea / vomiting / diarrhea / stomach pain) • Hyperthyroidism	• Pain, tingling or weakness in arms and legs • Vasculitis • Flare-up of adolescent acne • Irregular heartbeat • Confusion • Tiredness • Fever • Hypersensitivity (rash, hives) • Burning of mouth / throat • Metallic taste

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		• Rash • Hypothyroidism • Swelling of lymph glands

POTASSIUM PERCHLORATE (KCLO4)

Likely (happens to 21-100 patients out of every 100 patients)	**Less Likely (happens to 5-20 patients out of every 100 patients)**	**Rare (happens to <5 patients out of every 100 patients)**
• Gastrointestinal distress (nausea / vomiting / diarrhea / stomach pain)		• Unable to make red and white blood cells, platelets • Hypersensitivity (rash, hives)

Risk of Bone Marrow Supression and Low Blood Counts: This treatment will likely (greater than 50% of the time) cause a lowering of the white blood cell count and a decrease in red blood cell count and/or platelet count, thus increasing the risk of bleeding or infection.. Such infections may include: yeast infections in your mouth or on your skin or genitalia, bladder infections, pneumonia, and sepsis. Sepsis is a very serious infection with bacteria in the blood that can cause serious illness and death. The lowered blood counts are usually transient, lasting about 2 - 3 weeks. Low blood counts may necessitate blood (20% chance) and/or platelet (75% chance) transfusions; you may require G-CSF (20% chance) to stimulate your white blood cells. Bone marrow function usually returns with time. If bone marrow function does not return after this possible side effect, a peripheral blood stem cell (PBSC) infusion will be necessary. This procedure would return your PBSCs that may have been removed prior to treatment with ^{131}I-MIBG. There is an additional risk that the returned cells may contain residual cancer cells or will not adequately replace the damaged bone marrow, leaving you open to increased infections, bleeding and possible death. The infusion of peripheral blood stem cells can occasionally be associated with nausea, a metallic taste, shortness of breath, flushing, a slowing of the heart rate, and temporary high blood pressure. It can also occasionally cause headache, flushing and red urine for one day. Occasionally (1-10% of the time), without stem cells, reduced blood counts may never return to normal.

Autonomic Neuropathy: This treatment may rarely cause damage to the autonomic (sympathetic) nervous system that controls heart rate, blood pressure, sweating, and digestive organs. Such damage is called "autonomic neuropathy" with symptoms such as fast heart rate, fatigue, light-headedness when standing, and unusual sweating. Other symptoms include nausea after eating, abdominal bloating, constipation, diarrhea, difficulty beginning to urinate, urinary incontinence, bladder infections, and male impotence.

Risk of Blood Clots: Prolonged bed rest may rarely cause blood clots to form in the veins of the legs that can travel to the lungs; such clots can cause death.

Risks of Anti-coagulants: Anti-clotting medication, such as heparin or enoxaparin, may be given by injection to reduce the risk of blood clots developing in the veins while at bed rest. Such anti-coagulants can rarely cause major hemorrhage (Such as intestinal bleeding), spinal bleeding with paralysis, heart failure, pneumonia, fluid in the lungs, fever, severe allergic reactions such as rash or shock, bruising, injection site bleeding, and injection site pain.

Risk of Breathing Problems: Rarely, patients with pheochromocytomas can spontaneously develop serious shortness of breath, due to the release of substances from the tumor that causes the lungs to suddenly fill with fluid that interferes with breathing. This condition is known as "acute respiratory distress syndrome" (ARDS) and is frequently (10 – 50% of the time) fatal. Therapy with ^{131}I-MIBG can occasionally trigger an attack of ARDS.

Rarely, this therapy may also cause a lung problem called bronchiolitis obliterans organizing pneumonia (BOOP). This is a rare condition that can cause significant shortness of breath and coughing due to a pneumonia-like process. You should contact your physician if you experience these symptoms. Patients with this condition usually recover when treated with prednisone (a steroid). However, patients with BOOP may have to be hospitalized to receive additional treatment for their condition. BOOP can occasionally be fatal or leave the patients with permanent breathing problems.

Risk of Cancer: In the general population, the lifetime risk of developing cancer is about 35%. This treatment will slightly increase the lifetime risk of developing a second cancer, such as leukemia or thyroid cancer. Following the ^{131}I-MIBG therapy in adults, the lifetime malignancy risk is estimated to be increased by 0.5 - 1%. Following one ^{131}I-MIBG therapy in children or adolescents, the lifetime risk of malignancy is estimated to be increased by 1-2%. Multiple treatments with ^{131}I- MIBG will further increase lifetime risk of developing a second cancer.

Risk of Myelofibrosis and Leukemia: A serious condition known as "myelofibrosis" or "myelodysplastic syndrome" (MDS) can occur occasionally (5-20% risk) months to years after treatment with ^{131}I-MIBG. The risk for this side effect increases with the cumulative dose of ^{131}I-MIBG, such that each treatment increases this risk. After multiple treatments with ^{131}I-MIBG, this side effect becomes likely (21-100% risk). Myelofibrosis may occur alone or in association with leukemia and causes permanent bone marrow failure that can be treated but is likely fatal.

Risk of Other Organ Failure: Decreased function of the thyroid gland may occur (10-20% risk); this could cause fatigue and weight gain, but is correctable with thyroid medication. Decreased function of the adrenal glands might rarely occur; this could cause low blood pressure that might progress to shock and death. The decreased function is correctable with adrenal hormones. Decreased heart function might occur rarely; this could rarely cause a change in heart rate or rhythm or permanent heart failure symptoms such as fatigue, shortness of breath, swelling of your body or even death; heart medications may help, but not permanently cure heart failure. Decreased lung function may occur occasionally after multiple treatments if the tumor has spread through the lungs; this could cause permanent shortness of breath or death. Decreased liver function might rarely occur; this could cause jaundice, swelling, bleeding, and death.

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Risk of Infertility: The ^{131}I-MIBG treatment may make you infertile (unable to produce eggs or sperm needed for pregnancy).

> ***Women:*** The risk of female infertility in the general population is about 10%. It is estimated that the risk of female infertility (and premature menopause) after ^{131}I-MIBG treatment may be increased to about 30% after one therapy, 50% after two therapies, and 70% after three therapies.
>
> ***Men:*** The risk of male infertility in the general population is about 10%. It is estimated that the risk of male infertility after ^{131}I-MIBG treatment may be increased to about 20% after one therapy, 30% after two therapies, and 40% after three therapies.

Risks of MIBG Scan: The possible side effects of this scan include damage to the thyroid gland if potassium iodide drops are not taken as directed, pain or infection from the IV injection and allergic reaction to the radioactive iodine injection.

Risks of G-CSF/Neulasta: (Likely: > 20%): The possible side effects of this treatment include pain at the injection site; **(Occasional: 5-20%):** bone (deep) pain; **(Rare: < 5%):** flu-like symptoms (fever, chills, nausea, headache and malaise), low blood pressure, shortness of breath or enlargement of the spleen.

Risks of Stem Cell Infusion: As thawed stem cells contain a preservative, it is possible that an allergic reaction may occur during the stem cell infusion. Cell particles in the thawed stem cell product can possibly cause damage to the kidneys, but you will be well hydrated prior to and after the infusion to help prevent this. The preservative in which cells are frozen has a specific smell that makes many patients nauseous, and stays around the room for a couple of days after the stem cell infusion.

Risks of a Urinary Catheter Placement: Placing a urinary catheter to drain urine from the bladder may cause a urinary tract infection. The catheter may also cause bladder spasms and discomfort.

Risks of a Peripheral Intravenous Catheter Placed in a Vein: The risks of this procedure include temporary discomfort from the needle stick, bruising, and infection.

Risks of a CT Scan: You may have a contrast material injected into a vein in your arm. This material may make you feel warm and tingly for a few seconds, which may be uncomfortable. Rarely, patients have an allergic reaction to the contrast material such as rash or coughing. You will be exposed to radiation while having a CT scan. The amount of radiation exposure you receive from this standard diagnostic test is considered small. Such doses of radiation may be harmful, but the risks are so small they are difficult to measure.

MRI Risks: Having an MRI may mean some added discomfort for you. In particular, you may be bothered by feelings of claustrophobia and by the loud banging noise during the procedure.

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Temporary hearing loss has been reported from this loud noise. This is why you will be asked to wear earplugs. At times during the test, you may be asked not to swallow for a while, which may be uncomfortable.

Contrast agent (gadolinium) risks: A few side effects of gadolinium injection such as mild headache, nausea, and local pain may occur. Rarely (less than 1% of the time) low blood pressure and lightheadedness occurs. This can be treated immediately with intravenous fluids. Very rarely (less than on in one thousand), patients are allergic to gadolinium. These effects are most commonly hives and itchy eyes, but more severe reactions have been seen which result in shortness of breath.

Patients with severe kidney disease sometimes have a bad reaction to gadolinium contrast. The condition is called nephrogenic sclerosing fibrosis (NSF). It can cause skin to tighten or scar and can damage internal organs. Sometimes it can be life-threatening. There are no reports of NSF in patients with normal kidney function. Before you have a MRI scan requiring an injection of gadolinium contrast, you will have a blood test in order to check the function of your kidneys. Based on your medical history and the results of the test, a doctor will decide whether it is safe for you to undergo the MRI scans.

Blood/Platelet Transfusion Risks: Blood products come from voluntary donors who are carefully selected and tested, but there are still some risks with any blood transfusion. Occasional risks include fever, allergic reactions and formation of antibodies. Infrequent risks include infections with viruses such as hepatitis and fluid overload. Very rare risks are serious incompatibility reactions and infections other than hepatitis including HIV, the virus that causes AIDS. Complications are uncommon and are usually mild, but may be severe or life threatening.

Bone Marrow Aspiration and/or Biopsy Risks: The potential risks associated with bone marrow examinations include the following: infection; bleeding, discomfort from the needle sticks, allergic skin reaction to iodine (soap used to clean skin) or local anesthesia (numbing medicine); and risk of side effects associated with the anesthesia or the intravenous sedation used during the bone marrow procedure.

Risk to the Unborn Child: The ^{131}I-MIBG treatment poses risks to the unborn child.

Women: ^{131}I-MIBG treatments are hazardous to a growing fetus or a baby. Therefore, if you are pregnant or breast-feeding, you may not take part in this study. It is important that you not become pregnant during this treatment and for 4 months thereafter. If you are sexually active, you (and your partner) should use abstinence or an effective method of contraception that is medically appropriate based upon your personal doctor's recommendation at the time. If you should become pregnant during this treatment program, you should notify your personal doctor and immediately contact Dr. Fitzgerald or his associates for advice.

Women Caretakers: Caregivers (your spouse, parent, other family member, guardian, friend) will be exposed to radiation after you receive ^{131}I-MIBG. The amount of

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radiation will be approximately equivalent to less than one abdominal X-ray or less than 1/3 of a lumbar spine X-ray. Caregivers may not be pregnant while caring for you during this study, because exposure of the fetus to radiation may increase the risk that the unborn child will later develop cancer or other health problems. If your parent/caretaker is pregnant, then special precautions will be used to avoid contact with you during and for 4 weeks after ^{131}I-MIBG therapy. Should your spouse/parent/caretaker become pregnant within 4 weeks after ^{131}I-MIBG therapy, we will immediately contact Dr. Fitzgerald or his associates for advice.

Men: Abnormalities of sperm can be seen for up to 6 months after radiation therapy**,** which could possibly result in malformations in a baby conceived during this time. If you are sexually active, you (and your partner) should use abstinence or an effective method of contraception (based upon your/her personal doctors' recommendations) so as not to cause a pregnancy within 6 months after treatment with ^{131}I-MIBG**7)**

Blood Pressure: High or low blood pressure occurs frequently (10 - 50% of the time), but is usually mild. Treatment for high blood pressure is occasionally required during the infusion of the ^{131}I-MIBG; this might rarely result in dizziness or fainting.

NEW INFORMATION

Any new information developed during the course of this research that may relate to your willingness to participate in this study will be provided to you. If the study design changes, you will be informed and your consent will be re-obtained.

ARE THERE BENEFITS TO TAKING PART IN THE STUDY?

There may or may not be any direct medical benefit to you if you participate in this study. There is a possibility that the radioactive MIBG will cause a decrease in the size of your tumors, or a decrease in symptoms such as pain; however, this possibility cannot be guaranteed. However, even if you do not personally benefit from participating in this study, the results from your treatment could contribute to a better understanding of pheochromocytoma (and other related tumors) that may help patients in the future who have this disease.

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

Your other choices may include:

1. Getting treatment or care for your cancer without being in a study
2. An experimental chemotherapy treatment or another study.
3. Getting comfort care, also called palliative care. This type of care helps reduce pain, tiredness, appetite problems, and other problems caused by the cancer. It does not treat the cancer directly, but instead tries to improve how you feel. Comfort care tries to keep you as active and comfortable as possible.

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WILL MY MEDICAL INFORMATION BE KEPT PRIVATE?

The researcher, Dr. Paul Fitzgerald and his research associates and team members will have access to information about you. A medical record will be created because of your participation in this study. Your consent form and some of your research test results will be included in this record. Therefore, your other doctors may become aware of your participation. Hospital regulations require that all health care providers treat in formation in medical records confidentially. A unique number for each patient will be assigned to all study data. Without identifying you by name, results of this study may be reported in medical journals or at meetings, or to authorized agencies named above. Your name will not be used in any published reports about this study. Unless required by law, no identifying information gained from this study will be released to anyone.

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

- UCSF's Committee on Human Research
- UCSF Comprehensive Cancer Center
- The National Cancer Institute (NCI) and other government agencies, e.g., the Food and Drug Administration (FDA), involved in keeping research safe for people.

WHAT HAPPENS IF I AM INJURED BECASE I TOOK PART IN THIS STUDY?

It is important that you tell your study doctor, Dr. Paul Fitzgerald or his associates, 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 415-665-1136.

> **Treatment and Compensation for Injury:** If you are injured as a result of being in this study, treatment will be available. The costs of such treatment may be covered by the University of California, depending upon a number of factors. The University does not normally provide any other form of compensation for injury. For further information about this, you may call the office of the Committee on Human Research at (415) 476-1814 or write: Committee on Human Research, Box 0962, UCSF, San Francisco, CA 94143.

WILL YOU HAVE TO PAY FOR THIS TREATMENT?

You/your parents and/or your health plan/insurance company will need to pay for all of the costs of treating your cancer in this study. Some health plans will not pay these costs for taking part in studies. You/your parents should check with your health plan/insurance company to find out what they will pay for. If you/your parents have/has any questions regarding financial payment, you/your parent may consult with the pediatric oncology social worker.

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

WILL I BE PAID FOR PARTICIPATING IN THIS STUDY?

I will not be paid for participating in this study.

WHAT ARE MY RIGHTS IF I TAKE PART IN THIS STUDY?

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

We will tell you about new information or changes in the study that may affect your health or your willingness to continue in the study.
In the case of injury resulting from this study, you do not lose any of your legal rights to seek payment by signing this form.

WHO CAN ANSWER MY QUESTIONS ABOUT THE STUDY?

You can talk to your study doctor about any questions, concerns, or complaints you have about this study. Contact Dr. Fitzgerald or his associate at (415) 665-1136.

WHERE CAN I GET MORE INFORMATION?

National Cancer Institutes (NCI's) Cancer Information Service:
1-800-4-CANCER (1-800-422-6237)
CancerTrials: comprehensive clinical trials information **http://cancertrials.nci.nih.gov**
CancerNetTM: accurate cancer information **http://cancernet.nci.nih.gov**

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CONSENT

PARTICIPATION IN RESEARCHIS VOLUNTARY. You have the right to decline to participate or to withdraw at any point in this study without penalty or loss of benefits to which you are otherwise entitled.

You have been given a copy of the consent form and the Experimental Subject's Bill of Rights to keep.

You will be asked to sign a separate HIPAA Authorization Form authorizing access, use, creation, or disclosure of health information about you.

If you wish to be a research subject on this study, you should sign below.

_____
Subject Name (Printed)

Date	Signature of Subject
Date	Signature of Person Obtaining Consent
Date	Translator/Interpreter (if applicable)

OR: The person being considered for this study is unable to consent for himself/herself because he/she is a minor. By signing below, you are giving your permission for your chid to be included in this study.

Date	Signature of Parent or Guardian (if applicable)

Information and Guidelines for I^{131}-Metaiodobenzylguanidine Therapy

APPENDIX I

Patient's Name_____.

The date for your ^{131}I-Metaiodobenzylguanidine (MIBG) treatment has been set for _____. The following information will help you prepare for the treatment and its follow-up.

Before coming to UCSF for MIBG treatment:

You will need to have a variety of tests, procedures and blood tests in the 2-6 weeks before the MIBG treatment date. With the exception of the stem cell harvest, these tests must be done after the last chemotherapy and before the MIBG treatment date.

The tests and procedures that are required for you are outlined below. Please discuss them and their planned dates with your doctor. Please make sure the results are forwarded to us the week before the planned MIBG treatment date.

- Central venous catheter (broviac, port, or peripheral central venous catheter)(if necessary)
- Stem cell harvest (if appropriate)
- X-Ray studies to evaluate the current disease status (*the actual scans must be sent by express delivery or brought to UCSF):*
  - MIBG scan
  - MRI
  - CT scan
  - GFR (or creatinine clearance)
- Bilateral bone marrow aspirate and biopsy with special testing for immunocytology
- Blood tests
  - CBC/differential/platelets (blood counts)
  - AST/Total Bilirubin/Albumin/ALP (liver function tests)
  - BUN/Creatinine/Electrolytes/Calcium/Phosphorous/Magnesium (kidney function)
  - FT4/TSH (gland function)
  - Serum Chromogranin A
  - Serum HCG (if female)
- Urine analysis (kidney function)
- 24-hour urine for fractionated catecholamines, metanephrines, and creatinine
- Genetic tests
- Other_____

We have attached a list of medications that can interfere with the uptake of MIBG in the body. It is important that you do not take any of these medications for up to six weeks before and after

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the MIBG treatment without first consulting with your doctor. (From __/__/____ until __/__/____.)We have sent the same list to your doctor. Be sure you check with your doctor or us if you have any questions about a medication you wish to take.

Our social worker will assist you with information about transportation and housing options while in San Francisco for MIBG consultations and treatment. There are no funds available for housing or transportation.

At UCSF, before hospital admission:

Before admission to the Pediatric Clinical Research Center (PCRC) for MIBG treatment, you will see a doctor in the clinic for a physical exam to be sure everything is set for the treatment. An IV and bladder catheter will be placed by the nurse in the PCRC and will require that you have nothing to eat for four (4) hours before the procedures.

- The date and time for your clinic appointment is_____.

During hospitalization

Upon admission to the Pediatric Clinical Research Center, the nursing staff will instruct you and your caretaker(s) on the care you will need following the MIBG infusion. Because of the frequent exposure of the nursing staff to radiation and the high level surrounding you during therapy, the nurses' contact will be limited to complex medical care so that they are available for you in the event of an emergency. Adult family members or friends will be expected to be present at all times during the hospitalization to:

- assist with hygiene
- give oral medications
- offer and empty bedpans
- assist with meals
- change clothing and bed linens if soiled

We cannot provide MIBG therapy to you without the full involvement and cooperation of adult caregivers.

Your caretaker(s) will be instructed to wear gloves, gowns and shoe covers when caring for you. Additionally, they will be instructed in the use of a Geiger counter to check for contamination with any radioactive substances, and appropriate disposal of protective coverings. Each adult will be allowed to spend an increasing number of minutes each day behind the lead shield in your room.

While you are being treated with MIBG, your caretaker(s) will be exposed to radiation that is approximately equivalent to less than one abdominal X-ray or less than 1/3 of a lumbar spine X-ray.

You will not leave the room during the hospitalization except for scans done in nuclear medicine or for emergency procedures.

You will have a urinary catheter in place for at least 72 hours after the MIBG treatment, to protect the bladder from unnecessary radiation exposure. Extra fluids will also be given intravenously and/or by mouth, in order to dilute the urine radioactivity. The catheter and the extra fluids will be discontinued when the level of radioactivity permits, usually 3-4 days after the treatment.

When the radiation level in your body gets low enough (usually within five days of admission), you will be allowed to leave the hospital. We will give you additional instructions about medications, blood tests, doctor's appointments and any remaining radiation precautions that may be necessary.

After Leaving the Hospital

- You will continue to take medicine by mouth (potassium iodide) to protect the thyroid gland for a total of 45 days post treatment.

- If any extra radiation precautions are necessary, you will be instructed by the Radiation Safety Officer prior to discharge

- You will be given a schedule of required blood tests and follow-up scans. You may require blood product transfusions or re-infusion of your stem cells. This will be discussed with the physicians at UCSF.

Please feel free to call our nurse at 415-514-0238 or our social worker at 415-353-1641 if you have any questions at any time about your trip to UCSF or your MIBG treatment.

YOU have read and agree to the guidelines contained in this letter.

Subject Date

Caretaker Date

Witness Date