PENN MEDICINE
RESEARCH SUBJECT
COMBINED INFORMED CONSENT FORM AND HIPAA AUTHORIZATION

Protocol Title:	A Phase II Pilot Trial of Hydroxychloroquine, Everolimus or the Combination for Prevention of Recurrent Breast Cancer
Sponsor:	Angela DeMichele, MD, MSCE/Penn Medicine
Supplier of Study Drug:	Novartis Pharmaceuticals Corporation
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Emergency Contact:	24 Hour Emergency – Call 215-662-4000 Ask for Oncologist On-Call

Summary

You are being invited to participate in a research study. Your participation is voluntary and you should only participate if you completely understand what the study requires and what the risks of participation are. You are being asked to participate in this research study because you have a history of breast cancer, and you have a positive test for disseminated tumor cells in your bone marrow. This study tests the effects of treatment with hydroxychloroquine and everolimus-- alone and in combination

If you agree to participate you will be assigned to one of four groups: 1) hydroxychloroquine alone, 2) everolimus alone, 3) hydroxychloroquine plus everolimus, or 4) no treatment for 3 months then hydroxychloroquine plus everolimus. You will be asked to complete procedures that are consistent with your typical standard of care treatment and procedures for research purposes. Research procedures include: blood samples and a bone marrow aspirate.

Taking part in this study may or may not make your health better. However, while you may not benefit personally, the knowledge learned from your participation in this research study may benefit other patients in the future. It is possible that your disease and/or health may worsen as a result of participating in this study.

You will receive study treatment for a minimum of 6 months and a maximum of 12 months. After you finish study treatment, a study team member will contact you to ask you questions about your health for 3 years.

The most common side effects associated with hydroxychloroquine include: nausea, vomiting, stomach cramping, diarrhea, and loss of appetite. The most common side effects associated with everolimus include: tiredness, feeling weak, chills, anemia, diarrhea, nausea, vomiting, shortness of breath, cough, loss of appetite, weight loss, swelling, and inflammation of the lungs.

Please review the "What are the possible risks or discomforts?" section below for a complete listing of side effects you may experience as a result of your participation on this study. There is always the possibility that unknown risks and side effects may occur. These may be mild or very serious, and in some cases, may be very serious, long-lasting, or may never go away. There may also be a risk of death.

Other options may be available to you. These include: getting treatment or care for your cancer without being in a study, taking part in another study, or not receiving treatment at this time. Talk to your doctor about your choices before you decide if you will take part in this study.

Please note that there are other factors to consider before agreeing to participate such as additional procedures, use of your personal information, costs, and other possible risks not discussed here. You are free to decline or stop participation at any time during or after the initial consenting process.

Why am I being asked to volunteer?

You are being asked to participate in this research study because you have a history of breast cancer, and you have a positive test for disseminated tumor cells in your bone marrow. Disseminated tumor cells are breast cancer cells that have survived treatment and remain resting in the bone marrow with the potential to develop into a metastatic tumor at some point in the future. Your participation is voluntary, which means you can choose whether or not you want to participate. If you choose not to participate, your clinical care will not be affected. Before agreeing to participate in this research study, it is important that you read the following explanation of the proposed procedures and how long you will be in the study. This document describes the purpose, procedures, benefits, risks, discomforts and precautions of the study. It also describes the alternative procedures that are available to you and your right to withdraw from the study at any time.

Please take time to read the following information carefully. You may wish to discuss it with your family, friends, and your personal doctor (i.e., your family doctor or primary care doctor). If you have any questions, you may ask your study doctor and/or the research team for more information. Take time to decide whether or not you wish to take part. If you decide to participate, you will be asked to sign this form. If you decide to participate, you can change your mind at any time and withdraw from the study without giving a reason.

What is the purpose of this research study? What does this study involve?

The main purpose of this study is to:
1) determine the ability of patients to complete at least 6 months of treatment with hydroxychloroquine, everolimus or the combination without severe side effects.
2) determine the type and degree of side effects in people who have completed treatment for breast cancer.
3) determine how well these drugs do at reducing the number of disseminated tumor cells in the bone marrow.

This research study is a Phase II clinical trial, which tests the safety and benefit of a combination of drugs to learn whether they work for a specific cancer. This research study is testing whether using these drugs to target the disseminated tumor cells in your bone marrow can reduce their number or eliminate them. The drugs being studied are hydroxychloroquine (Plaquenil) and Everolimus (also called by the trade name Afinitor® –Novartis Pharmaceuticals Corporation). Both hydroxychloroquine and Everolimus are pills that will be taken daily. Both are approved by the U.S. Food and Drug Administration (FDA). Hydroxychloroquine is FDA-approved for the treatment of malaria and rheumatoid arthritis but not for the treatment of cancer and therefore is considered "investigational". Everolimus (Afinitor®) has received FDA-approval for:

- the treatment of renal cell (kidney) cancer.

- adults with advanced kidney cancer (Renal Cell Carcinoma).
- patients with subependymal giant cell astrocytoma (SEGA), a brain tumor seen with genetic conditions called tuberous sclerosis complex (TSC) who require therapy, but are not candidates for surgery.
- pancreatic neuroendocrine tumor (PNET) in patients with unresectable, locally advanced, or metastatic disease.
- the treatment of postmenopausal women with advanced hormone receptor-positive, HER2-negative breast cancer (advanced HR+ BC) in combination with exemestane, after failure of treatment with letrozole or anastrozole.
- the treatment of patients with TSC who have renal angiomyolipoma not requiring immediate surgery.
- Also approved, in the U.S., in 2016 for advanced non-functional NET of gastrointestinal (GI) or lung origin.

Both drugs have been given to more than 100,000 patients each worldwide as separate agents, and they have been shown to be safe when combined together in patients with other types of cancer. Everolimus (Afinitor®) has been used to treat patients in clinical studies since 2002 and approximately 112,317 patients (as of 31-Mar-2017) have been enrolled in studies with everolimus (Afinitor®). In this trial hydroxychloroquine and everolimus are being studied as a new way to prevent breast cancer recurrence, a use for which they do not currently have FDA approval.

The reason for using these two drugs is that they may both work against disseminated tumor cells in different and complementary ways. Dormant cancer cells need a protein called mTOR, which feeds the cancer cells and allows them to grow. Everolimus works by blocking mTOR, which starves the cancer cell or limits its ability to grow. Dormant cancer cells also use a process called “autophagy” to generate their own fuel internally, which can allow them to stay in a hibernating state. Hydroxychloroquine may work by preventing autophagy, which leads to starvation of the cells. These drugs may be able to eliminate disseminated tumor cells on their own, but they also may work even better when combined. For example, it is possible that if cells try to overcome the lack of mTOR by using autophagy, and autophagy does not work either, there may be an even greater reduction in the number of disseminated tumor cells.

This study has four study groups known as study “arms”. Two of the groups – Arm C and D – have completed enrollment and are now closed; thus, the study is currently enrolling to the remaining two groups. Each participant will be randomly assigned to one of these study arms.

The treatment arms work as follows:

- Participants on **Arm A** will take hydroxychloroquine at a dose of 600 mg twice a day for 6 months (24 weeks).
- Participants on **Arm B** will take everolimus, 10 mg daily for 6 months (24 weeks).
- *CLOSED* Participants on **Arm C** will take hydroxychloroquine at a dose of 600 mg twice a day and everolimus at 10 mg daily, for 6 months (24 weeks).
- *CLOSED* Participants on **Arm D** will be followed by the study staff without receiving treatment for the first 3 months, and then will start treatment with hydroxychloroquine at a dose of 600 mg twice a day and everolimus at 10 mg daily, for 6 months (24 weeks).

Who is sponsoring this study?

Angela DeMichele, MD, MSCE, the Principal Investigator, is also the sponsor (entity responsible for the design, conduct and regulatory oversight of the study). Novartis Pharmaceuticals Corporation is the supplier of the drug everolimus, and will be providing the drug during this research study. Dr. DeMichele and Penn Medicine will receive payments to cover some of the research costs such as the collecting/reporting of study information associated with the conduct of the study. The U.S. Department of Defense (DoD) is providing funding for some aspects of this research protocol, such as the analysis of research samples (i.e., blood and bone marrow) that are collected throughout the duration of the study.

How long will I be in the study?

Participants in the trial will be on the study treatment for a minimum of 24 weeks (6 months) and a maximum of 48 weeks (12 months). Participants will be followed for an additional 3 years following the completion of the treatment portion of the trial.

What am I being asked to do?

If you meet all of the criteria for being in the study, you will be registered to participate.
Screening Procedures: These procedures are done to evaluate your cancer, overall health, and eligibility. If you have had some of these tests/procedures recently, they may not need to be repeated. These tests and procedures need to be done within 30 days before you receive your first dose of study drug, unless otherwise indicated.

- Demographic information about you will be collected (age, sex, race/ethnicity).
- Your medical history will be examined and you will be asked about medications you are taking.
  - Your study doctor will ask you questions about your health, general condition, complaints, and medications that you are taking or have taken prior to randomization (the day you are assigned to a study arm). It is important that you tell your study doctor about all the medications that you have been taking, including any medications or herbal remedies that you may have bought for yourself.
- A full physical exam including vital signs (height, weight, blood pressure and pulse) will be performed.
- Your ability to get around and perform everyday activities (ECOG performance status) will be assessed.
- A detailed assessment of Hepatitis B/C medical history and risk factors will be done. If you have a positive medical history based on risk factors and/or confirmation of prior HBV/HCV infection, or if your study doctor thinks it is appropriate, Hepatitis B and/or C testing will be done on a small blood sample (about 1 tablespoon of blood).
  - If you test positive for hepatitis B, you may not be allowed into the study. If you test negative for hepatitis B, the study doctor may continue to monitor your blood for the hepatitis B virus and to see if your liver is damaged or inflamed. Your study doctor will inform you if there is a need for treatment. This may mean you are given an anti-viral drug and you will stop taking the study drug.
  - If you test positive for hepatitis C, you will not be allowed into the study. If you test positive for hepatitis C while you are taking study drug, you will need to stop the study drug because the treatment for hepatitis C has serious side effects.
  - If you have a positive test result for Hepatitis B or C, you will be referred to the appropriate physician specialist for counseling and treatment. Also, if you test positive for Hepatitis B or C, by law we have to report the positive test results to the City of Philadelphia Health Department and/or the PA Department of Health. Personal identifiers such as name, sex, date of birth, address, and phone number will be reported. For more information about the requirements reporting infectious diseases to the City of Philadelphia Health Department, please visit https://hip.phila.gov/ReportDisease . For more information about the requirements reporting infectious diseases to the PA Health Department, please visit http://www.health.pa.gov/Your-Department-of- Health/ Offices%20and%20Bureaus/ epidemiology/Pages/Reportable-Diseases.aspx#.V620aZ3D9eU .
- Blood sample (about 1 teaspoon) for pregnancy testing (if you are premenopausal, able to have children). The study doctor or study staff will tell you if the pregnancy test results are positive. The results of the pregnancy testing must be negative in order for you to be in the study.
- Blood sample (about 2 tablespoons of blood) for tests to evaluate your red, white, and platelet blood counts along with blood chemistries to test your general health and organ function.

- A blood sample will be collected for research testing for circulating tumor material.
    - This would not typically be done as a part of your standard of care treatment.
- A bone marrow aspirate (only if not previously done on the PENN-SURMOUNT Screening Study).
    - This would not typically be done as a part of your standard of care treatment.

Procedures associated with the administration of the study drug(s)
When all of the above tests/procedures have been completed, you have been found eligible to enter this study, and you agree to participate, you will be scheduled to receive study drug.
This study has four study groups (two currently are open) known as study "arms". Approximately 60 participants will take part in this trial, with 15 patients receiving treatment on each of the arms. Part of the reason that Arms C and D are now closed is because the investigators determined that the study has enough evidence to show that the combination treatment is tolerable in this patient population.

A computer will assign you to one of the two open treatment arms in the study. This is called randomization. This is done by chance (like the flipping of a coin) because no one knows if one study group is better or worse than the other. You and the study doctor and study staff will know what drugs have been assigned.

You have an equal chance of being in Arm A or B. Neither you nor the study doctor or study staff will be able to pick which study group you are in.

The treatment arms work as follows:

- Participants on **Arm A** will take hydroxychloroquine at a dose of 600 mg twice a day for 6 months (24 weeks).
- Participants on **Arm B** will get everolimus, 10 mg daily for 6 months (24 weeks).
- Arm C is closed
- Arm D is closed

If participants on Arms A or B still have a positive test for disseminated tumor cells after 24 weeks of treatment, they will be allowed to continue with their current treatment and add the other drug (that is, take the combination of hydroxychloroquine and everolimus) for an additional 24 weeks.

If participants on Arm D still have a positive test for disseminated tumor cells after 24 weeks of combination treatment, they will be allowed to continue this treatment for an additional 24 weeks.

The study drugs will be given in 28-day cycles.

If you join this study, you will be given everolimus (Afinitor®) tablets or hydroxychloroquine pills to be taken by mouth. It is very important for you to take the study drug just as the study doctor tells you. Do not skip any doses unless your study doctor tells you to skip doses. If you throw up after taking the study drug, you should NOT take another tablet that day. Let your study doctor know that you got sick. If you do forget to take the study drug one day, do not take any extra doses the next day. Call your study doctor and ask for advice.

You will be given a diary to record when you take your study drugs at home between visits. You will be asked to bring this completed diary and your remaining study drug and/or empty pill bottles to each study visit. When you return this study drug kit and diary, the study team will review everything to make sure you are taking the drugs appropriately and completing this diary as requested.

Study Tests/Procedures
These exams, tests, and procedures are being done to evaluate your health and response to the study drug(s). At each of these study visits you will be asked how you are feeling, if you have had any side

effects, if you may be pregnant, if you have had any medical procedures, and about any medications you are taking. It is important you check with your study doctor before starting any new medications. Taking other drugs (including alcohol, over-the-counter medications, herbal preparations, illegal drugs, or nutritional supplements) may cause additional side effects or even life-threatening reactions when combined with the drugs being used in this study. If you experience side effects, changes in your health and/or changes in medications, please contact your study doctor or a study team member.

You will have the following tests, procedures, and assessments done at the time points indicated below:

During the Treatment Phase, the following tests, procedures, and assessments will be done on Day 1 of each cycle.

- ECOG performance status assessment
- Physical exam including vital signs
- Blood sample (about 2 tablespoons of blood) for blood cell count and blood chemistry testing

Additional blood samples for research testing of circulating tumor material will be collected at the completion of Cycle 3, at the completion of Cycle 6, and at the completion of Cycle 12, if applicable.

Additional bone marrow aspirate will be performed at the end of Cycle 3 and at the end of Cycle 6, and if you continue on treatment, at the end of Cycle 12. Results from the end of Cycle 3 bone marrow test will not be returned to you. You will however receive the results of the end of Cycle 6 bone marrow test and, if applicable, end of C12 bone marrow test, if you choose to receive them.

End of Treatment Visit:
Within about 30 days after your last dose of study drug, you will be asked to come in for an end of treatment (first follow-up) visit. The following tests and procedures will be performed:

- ECOG performance status assessment
- Physical exam including vital signs
- Blood sample (about 2 tablespoons of blood) for blood cell count and blood chemistry testing

Post-Treatment Follow-up Procedures:
You will continue to be followed for up to 3 years after your last dose of study drug. You will be asked to come to the clinic or be seen by your local oncologist once every 6 months for follow-up visits during this time. The following tests and procedures will be performed:

- Physical exam including vital signs
- Blood sample (about 2 tablespoons of blood) for blood cell count and blood chemistry testing
- Blood sample for research testing of circulating tumor material
    - This would not typically be done as a part of your standard of care treatment
    - This will be waived if you are doing follow up with your local provider
- For Participants who have a negative bone marrow test after 6 or 12 cycles of therapy, you will have the option of undergoing a bone marrow aspirate for retesting at the first 6 month follow up visit. You will be able to decide whether or not you would like to receive the results of this bone marrow test.
    - This would not typically be done as a part of your standard of care treatment

What research samples are collected and how will they be used?

Blood and bone marrow samples will be collected in this study to be used for research to learn more about breast cancer and its treatment. The research may identify people who are may be more or less likely to respond to the study treatments. Additionally, these studies will focus on side-effects of treatment, as well as studying the treatment of breast cancer and related diseases. In order to do this, a variety of techniques will be used. This research may include analysis of proteins, RNA and DNA.

Your blood and bone marrow samples contain DNA, which makes up the genes that serve as the "instruction book" for the cells in our bodies. Researchers are interested in the way that genes affect how the body responds to drugs. Using DNA from your blood or tissue sample, researchers will study your entire genetic sequence, known as your genome. The genome sequence will be read and this information will be stored. Your genomic data will be used to find differences and similarities among people with regard to response to or side effects of the study treatment. Your genomic data and health information will be studied along with information from other participants in this study, and it will be stored for future studies by this research team.

In general, genetic testing can be performed on tumor or on “germline DNA”, the DNA that is present in all of your cells, and that can predict your risk of future illness. In this study, genetic testing will be performed on your research samples (including circulating blood markers like circulating tumor DNA, and on any tumor cells found in your bone marrow) to examine the genetic changes that make your cancer unique. Germline testing on your sample may be performed only to help us focus specifically on which genetic changes are specific to your tumor. We will not be performing specific germline testing that could be informative about your risk of future illness. As with the other study results, the genetic testing results from this study will not be placed in your medical record or provided to you or your physician. We are not returning tumor genetic test results to you or your doctor because we do not yet know if these results will have any importance to your health or treatment.

The results of genetic tests performed on this trial are for research only. Neither you nor your study doctor will be notified when research will be conducted or given reports or other information about any research that is done using your samples. Because the research tests on your bone marrow and blood samples collected for this study are not used for regular medical care, the test results will not be put in your medical record.

These samples will be sent to and stored in the laboratory of Dr. Lewis Chodosh at Penn Medicine.

What are my responsibilities?

While you are in the study, you must:

- Follow instructions you are given.
- Come to the study center for all visits with the study doctor or study staff.
- Tell the study doctor or study staff about any changes in your health or the way you feel.
- Tell the study doctor or study staff if you want to stop being in the study at any time.

What are the possible risks or discomforts?

If you choose to take part in this study, there is a risk that:

- You may lose time at work or home and spend more time in the hospital or study doctor’s office than usual
- You may be asked sensitive or private questions which you normally do not discuss, although you may choose not to answer
- The study drugs used in this study may affect how different parts of your body work such as your liver, kidneys, heart, and blood. The study doctor will be testing your blood and will let you know if changes occur that may affect your health.

While on the study, you are at risk for the following side effects. Some of these side effects may be potentially serious or life-threatening, and may include death. You should discuss these with the study doctor. There also may be other side effects that are not known and other very rare side effects that are known but not included in this list. If you experience side effects from the study drug(s), your study doctor may delay or skip a dose of the study drug, or ask you to stop taking study drug. Your doctors may also

give you other drugs to help lessen these side effects. Many side effects go away shortly after the study drug is stopped, but in some cases side effects can be serious, long lasting or permanent.

Hydroxychloroquine

Common side effects:

- Nausea
- Vomiting
- Stomach cramping with or without diarrhea
- Anorexia (loss of appetite)

Less likely side effects:

- Headache
- Dizziness
- Visual problems (e.g. blurred vision, difficulty focusing, seeing halos, flashes, streaks, night blindness, visual field loss, difficulty reading, permanent vision damage) Irritability, Change in eye color
- Photophobia, discomfort or pain to the eyes due to exposure to light
- Ringing in the ears (also called tinnitus) with or without decrease in hearing
- Irritability, nervousness, emotional changes
- Convulsions

Rare but serious side effects:

- Severe allergic reaction requiring immediate medical attention.
- Difficulty breathing
- Increased sensitivity to sunlight
- Abnormal liver function or liver failure Aplastic anemia, a condition that occurs when your body's bone marrow stops producing enough new blood cells, causing fatigue and higher risks of infection and uncontrolled bleeding
- Agranulocytosis, a failure of the bone marrow to make enough neutrophils, a type of white blood cell, and leukopenia, a low count of all white blood cells, both increasing your risk of infection
- Lowered platelet counts, which make it more likely for you to have bruising or bleeding
- Hemolysis, a breakdown of red blood cells, in patients with glucose-6-phosphate deficiency. People known to have this deficiency will not be enrolled in the study.
- Dysfunctional muscle fibers (myopathy) leading to progressive muscle weakness and breakdown of muscle tissue
- Bleaching of hair
- Alopecia, a complete or partial loss of hair
- Pigmentation changes
- Itchy skin (pruritus)
- Heart problems (e.g. decreased heart function, heart failure, irregular heartbeat, sudden cardiac death)
- Stevens-Johnson syndrome, a rare, serious disorder in which skin and mucous membranes react severely to a medication or infection. It often begins with flu-like symptoms, followed by a painful red or purplish rash that spreads and blisters, eventually causing the top layer of skin to die and shed.
- Acute generalized exanthematous pustulosis (AGEP), a rare form of drug hypersensitivity characterized by the rapid appearance of many sterile pimples on the skin, accompanied by fever and sometimes lowered blood counts
- Exfoliative dermatitis, a widespread scaling of the skin, often with itching, skin redness, and hair loss
- Retinopathy, non-inflammatory damage to the retina of the eye

Everolimus

Common side effects (occurring in more than 10% of patients):

- Tiredness or weakness
- Chills
- Anemia (decrease in red blood cells)
- Diarrhea
- Nausea
- Vomiting
- Shortness of breath
- Cough
- Loss of appetite or weight loss
- Swelling, pain, infection in lining of the mouth (ulcers or sores)
- Low grade pneumonitis (inflammation of the lungs), which may require treatment with corticosteroids (medication) or admission to the hospital. Please notify your doctor immediately if you experience sudden shortness of breath or coughing and fever as this could be life-threatening.
- Skin rash which may cause itching
- Headache
- Changes or loss of taste
- High blood sugar or cholesterol
- Decreased albumin levels
- Fluid retention, pain and swelling of arms or legs
- Bleeding of the nose
- Spontaneous bleeding or bruising

Less likely side effects (occurring in 1 to <10% of patients):

- Increased blood lipids (level of fat in the blood)
- Fever
- Joint or abdominal pain
- Increased protein in the urine
- Decreased liver function
- Kidney failure
- Bleeding
- High blood pressure
- Indigestion
- Constipation
- Heartburn
- Difficulty swallowing or dry mouth
- Difficulty sleeping
- Decreased white blood cell count, which may increase the chance of infection
- Decreased platelets
- Decreased phosphorus or potassium in the blood
- Dry skin, acne, skin redness, or nail changes
- Irritability
- Dehydration
- Stomach virus
- Passing gas
- Mouth pain
- Inflammation of the lining of the digestive system and other mucous membranes such as the sinus

- Changes to the levels of blood sugar (glucose), which could lead to diabetes, could occur while taking Everolimus. If you are taking other medicine which may increase blood sugar levels, frequent monitoring may be required.
- Everolimus may contribute to increased levels of an enzyme called blood lactate dehydrogenase which gives information about the health of certain organs.

Rare but serious side effects (occurring in <1% of patients):

- Severe decrease in red blood cells or all blood cells
- Loss of taste
- Rash of small blisters
- Bronchitis
- Coughing up of blood
- Swelling of the dermis (along with subcutaneous tissue, mucosa, and submucosal tissues)
- Severe allergic reaction requiring immediate medical attention.
- Cardiac problems (congestive heart failure, heart attack, chest pain)
- Increased daytime urination
- Impaired wound healing
- Women of child-bearing potential taking Everolimus, changes to your menstrual period (menstruation) may occur. These changes may include: delayed or missing one or more menstrual period (secondary amenorrhea), increased or decreased blood flow during menstruation, or any other irregular change to your menstrual cycle. Also, a hormone called luteinizing hormone (LH) and follicle stimulating hormone (FSH) may be increased due to Everolimus. Fertility in male and female patients may be affected.
- Blood clots
- Angioneurotic edema (swelling or welts beneath the skin, particularly around the eyes and lips) has been seen in a total of 4 patients taking both Everolimus and ACE inhibitors (a class of drugs used to treat high blood pressure). This condition is a known side effect of ACE inhibitors, but because the patients who experienced it had not done so while taking ACE inhibitors alone, Everolimus was thought to be partially responsible.
- Radiation recall syndrome (acute inflammatory skin reaction) may look like a severe sunburn and may blister, peel, and become red, swollen, and painful.

NOTE: Everolimus has been found to make some medications more harmful to your kidneys. If you are taking other drugs known to cause kidney toxicity, your kidney function will be monitored closely.

Everolimus can make patients more likely to have an infection such as pneumonia, a bacterial or fungal infection, or severe pneumonitis (inflammation of the lungs), which may interfere with breathing and may require hospitalization or the administration of oxygen. In some patients infections have been severe, and can even lead to death. You may need to be treated as soon as possible. If you have a temperature of 100.5° F or above, chills, or do not feel well or if you develop new or worsening cough, shortness of breath, difficulty breathing, or wheezing, or other new lung problems, you should stop taking Everolimus and contact your doctor immediately, so that he/she can determine the cause of your new symptoms.

Everolimus can make patients with past hepatitis B or hepatitis C infection more likely to have a flare-up of their hepatitis (called ‘reactivation’). If you have risk factors or a history of hepatitis B or hepatitis C infection, your doctor will monitor you closely throughout the study. If your blood test results show that your hepatitis B or hepatitis C infection has reactivated, you may be asked to take antiviral medication or you may be asked to stop taking Everolimus.

You should not get live vaccines or have close contact with people who have had live vaccines within 7 days of starting Everolimus and while on this study without asking your study doctor.

Some examples of live vaccines include nasal/inhaled flu mist vaccine, measles, mumps, rubella, oral polio, BCG, yellow fever, varicella (Chicken Pox) and typhoid vaccines.

You must not drink grapefruit juice, eat grapefruit, or take grapefruit products while taking Everolimus. You must not eat Seville oranges and star fruit or their products, or drink the juice of these fruits, while taking Everolimus. Some foods like grapefruit juice and Seville oranges, as well as some medications, may interfere with the way your body processes Everolimus. This interference could cause the amount of Everolimus in your body to be higher or lower than expected.

You will be given any new information on Everolimus that may affect your willingness to start or continue in the study as it becomes available.

Other side effects not mentioned above or not observed in previous studies with the drug are possible. There is the possibility that the combination of Everolimus with hydroxychloroquine may increase the severity of some of the listed risks. However, the risks of Everolimus and hydroxychloroquine are non-overlapping, and therefore we do not believe there will be any new side effects associated with the combination of drugs.

Other Study Related Risks

Risks of Blood Draws

Blood samples will be taken for tests throughout this study. The amount of blood to be taken by these blood draws is very small, and may be associated with discomfort and/or bruising at the site where the needle is inserted; and less commonly, fainting, the formation of a small blood clot or swelling of the vein and surrounding tissue, bleeding, and infection.

Risks of Bone Marrow Aspirate and Biopsy

During a biopsy procedure you may feel momentary mild pain (usually a burning/stinging sensation) as the local anesthetic is injected. In addition you may feel pain from the biopsy itself. This pain can sometimes persist for several days after the procedure, and there may be some bruising around the biopsy site. The biopsy procedures are carried out on many patients each day and are generally very safe, but there is a small risk that complications may arise as a result of the biopsy. It is possible that such complications could be serious or life-threatening. It is generally considered a safe procedure, but it is important for you to be aware of the following risks:

- Discomfort or bruising at the biopsy site, which often lasts for 1-4 days after the procedure.
- Bleeding from the biopsy site, which is usually only a small amount that has stopped by the end of the procedure. More serious bleeding is possible but happens rarely.
- Pain, redness or swelling at the biopsy site.
- Infection at the biopsy site, which is very rare
- Reaction to the numbing agent
- Damage to surrounding tissues

Risks of Genetic Research

This research includes genetic testing. Even without your name or other identifiers, your genetic information is unique to you. The researchers believe the chance that someone will identify you is very small, but the risk may change in the future as people come up with new ways of tracing information.

There can be a risk in knowing genetic information. New health information about inherited traits that might affect you or your blood relatives could be found during a research study. Even though your genes are unique, you share some of the same genes with your blood relatives. Although we are not able to know all of the risks from taking part in research on inherited traits, we believe that the risks to you and your family are very low, because your samples will be coded. Research results will not be returned to you or your doctor.

Very rarely health or genetic information could be misused by employers, insurance companies, and others. For example, it could make it harder for you to get or keep a job or insurance, or life insurance companies may charge a higher rate based on this information. We believe the chance these things will happen is very small, but we cannot make guarantees.

A federal law (Genetic Information Non-Discrimination Act, GINA) helps reduce the risk from health insurance or employment discrimination. The law does not include other types of misuse by life insurance or long term care insurance. If you want to learn more about GINA, you can find information about it on the internet or ask the study staff.

Reproductive Risks

Female Participants

You should not become pregnant while on this study and for 8 weeks after your last dose of study treatment because the study drugs could have a negative effect on an unborn baby. In addition, you should not breastfeed while on this study during treatment and for 2 weeks after the last dose as these drugs may also affect a breast-feeding child. Pregnant women and women who are breast-feeding are not allowed to participate in this study. If you become pregnant, you will no longer be able to participate in this study.

If you are able to have children, you must agree to use two medically accepted forms of birth control including condoms, diaphragms, cervical cap, an intra-uterine device (IUD), surgical sterility (tubal ligation or a partner that has undergone a vasectomy), or oral contraceptives, OR you must agree to completely abstain from intercourse during participation in this study and for 8 weeks after your last dose of study treatment. Abstinence at certain times of the cycle only, such as during the days of ovulation, after ovulation and withdrawal are not acceptable methods of birth control. Your study doctor must approve your form of birth control. Ask your study doctor about the contraceptive methods that are available and which might be the best for you.

Even when you use an approved contraceptive method, there is always a small risk that you could still become pregnant. If you do become pregnant during the course of this study or up to 8 weeks after your last dose of study treatment, you must discontinue study treatment, tell the investigator immediately, and consult an obstetrician or maternal-fetal specialist. If you become pregnant while on this study, we will ask permission to collect information about your pregnancy.

Male Participants

You should not father a child while on this study and for 8 weeks after your last dose of study treatment, because the drug involved could have a negative effect on an unborn baby. If your spouse or partner has the potential to become pregnant, you and your partner must use two medically accepted forms of birth control including condoms, diaphragms, cervical cap, an intra-uterine device (IUD), surgical sterility (vasectomy or a partner that has undergone a tubal ligation), or oral contraceptives, OR you must agree to completely abstain from intercourse during participation in this study and for 8 weeks after your last dose of study treatment. Abstinence at certain times of the cycle only, such as during the days of ovulation, after ovulation and withdrawal are not acceptable methods of birth control. Your study doctor must approve your form of birth control. Ask your study doctor about the contraceptive methods that are available and which might be the best for you.

You should also inform your partner of the potential harm to an unborn child. She should know that if a pregnancy should occur during the course of this study or up to 8 weeks after your last dose of study treatment, you will need to report it to the study doctor immediately, and she should promptly notify her doctor. The study doctor will also ask to follow-up on the pregnancy.

Fertility

The potential for everolimus to cause infertility in male and female patients is unknown. However, menstrual irregularities, secondary amenorrhea and associated luteinizing hormone (LH)/follicle stimulating hormone (FSH) imbalance has been observed in female patients receiving everolimus. Blood levels of FSH and LH increased, blood levels of testosterone decreased, and azoospermia have been observed in male patients receiving everolimus.

What if new information becomes available about the study?

During the course of this study, we may find more information that could be important to you (such as new information about how the drug works or newly discovered side effects). If we discover new information about the study that could affect your decision to stay in the study, you will be notified in a timely manner. You will be able to ask questions about this new information and can discuss it with your family, friends, or doctor.

What are the possible benefits of the study?

Taking part in this study may or may not make your health better. However, while you may not benefit personally, the knowledge learned from your participation in this research study may benefit other patients in the future. It is possible that your disease and/or health may worsen as a result of participating in this study.

What other choices do I have if I do not participate?

Your participation in this study is entirely voluntary. Other possible options include:

- Getting treatment or care for your cancer without being in a study.
- Taking part in another study.
- Not receiving treatment at this time.

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

Will I be paid for being in this study?

You will not be paid for taking part in this study.

Will I have to pay for anything?

Novartis Pharmaceuticals Corporation will supply the drug everolimus at no charge while you take part in this study. The cost of hydroxychloroquine will be the responsibility of you and/or your insurance provider. You will be responsible for any deductibles or applicable co-pays for standard tests, exams or procedures, such as office visits, scans and blood work, that are done while you take part in this study. You and/or your insurance provider will be responsible for standard tests, exams or procedures that would be done even if you were not in this study. Please talk to your doctor and study team about putting you in touch with a financial counselor to determine exactly what the deductible and co-pay will be for you; this is highly variable depending on your type of insurance. There will be no charge to you for those laboratory tests and other procedures that are being done specifically for the purposes of this research study.

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

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 or hurt during the study?

If you have a medical emergency during your participation on this study, you should go to the nearest emergency room. You should contact the Principal Investigator or Emergency contact listed on page one

of this form. You may also contact your own doctor, or seek treatment outside of Penn Medicine. Be sure to tell the doctor or his/her staff that you are in a research study being conducted at Penn Medicine. Ask them to call the telephone numbers on the first page of this consent form for further instructions or information about your care.

Penn Medicine will offer you the care needed to treat side effects and/or injuries that occur while you are taking part in this research. We may bill your insurance company or other third parties, if appropriate, for the costs of the care you get for the injury, but you may also be responsible for some of them. There are no plans for Novartis Pharmaceuticals Corporation or Penn Medicine to pay you or give you other compensation for the injury.

You may receive bills for injuries/illnesses that occur during your participation in this study. If you have questions about these bills and whether or not they are covered by the research study, please bring copies of these bills to a member of the study team and they will be able to answer your questions.

Financial compensation for such things as traveling, parking, lost wages, disability or discomfort due to injury is not routinely available.

You will not lose any of your legal rights when you sign this form.

When is the Study over? Can I leave the Study before it ends?

You may receive study treatment for between 6 and 12 months. You will then be followed for an additional 3 years following the completion of the treatment portion of the trial.

You may stop participating at any time. However, if you decide to stop participating in the study, we encourage you to talk to your doctor first. You can also choose to leave the study at any time without giving a reason. It is important to tell the doctor if you are thinking about stopping so any risks for the treatments that you received 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. Leaving the study will not affect your future medical care.

The doctor may stop you from taking part in this study at any time if he/she believes that it is in your best interest, if you do not follow the study rules, or if the study is stopped. If new information becomes available that might affect your choice to stay in the study, your study doctor will notify you as soon as possible.

This study may also be stopped at any time by your study doctor, the study Sponsor, the drug supplier, or the Food and Drug Administration (FDA) without your consent because:

- The Principal Investigator or the sponsor feels that it is in your best interest to discontinue the study. Such an action would not require your consent, but you will be informed if such a decision is made and the reason for this decision.
- You have not followed study instructions, or you become pregnant
- The Sponsor, the study Principal Investigator, or the Food and Drug Administration (FDA) has decided to stop the study due to new information regarding side effects.
- It is determined that you are no longer benefiting from the study therapy
- For any other reason that is not known at this time

If you are removed from the research study, your study doctor will explain to you why you were removed. The study doctor and study team will help arrange for your continued care.

How will my personal information be protected during this study?

If you decide to participate in this study, the study doctor and staff will collect medical and personal information about you as part of completing the study. 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. This study is being overseen by the Food and Drug Administration (FDA); therefore, they may review your research records. Since the Department of Defense (DoD) is providing funding for some parts of this research, the DoD will have access to research records. Please refer to the information below which explains more specifically how your personal information will be protected. If you do not want to allow these uses, you should not participate in this study. Information identifying you will be kept confidential as described below. While collected as part of this study by your study doctor and study team, identifying information (including your name, address, telephone number, medical record number, or any number/codes that will directly identify you) will be kept as confidential as possible and will not be routinely disclosed outside of Penn Medicine. Personal health information that could be used to identify you will not be sent to Novartis Pharmaceuticals Corporation, and/or their designated representatives.

You will be assigned a unique subject registration number upon enrollment. This number and your initials will be used to identify you throughout the course of this study so that your identity is protected. The key to this code (which links your name back to the personal health information collected during this study) will be stored in a secure area and only the Penn Medicine study team will have access to this code. However, some of the study data (e.g. date of birth) could be used in combination with other information, in order to identify you. If you have questions about the specific information that will be released, you should ask your study doctor.

Will information about this study be available to the public?

A description of this clinical trial will be available on http://www.clinicaltrials.gov, as required by US 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 any time.

What may happen to my information collected on this study?

Your identifiable information will be stored indefinitely and may be used for future research purposes. Future researchers may receive information that could identify you. This can be done without again seeking your consent in the future, as permitted by law.

There are no plans to tell you about any of the specific research that will be done. Possible future research may include: studies to learn more about your disease or the treatment you received.

We may share your information with: other research, academic, and medical institutions, other researchers, drug and device companies, biotechnology companies and others.

We will not follow up with you to tell you about the specific research that will be done. We will not give you any results from these studies. It is possible that you may have chosen not to participate in these future research studies, had you been approached for participation.

Penn Medicine will retain all identifiable information that was collected as part of your participation (e.g. name, address, phone number, email address, and medical record number). We will protect your confidentiality by labeling your information with a unique code. The key to this code (which links the information collected on this study back to your name and other identifiable information) will be stored in a secure area and only Penn Medicine personnel will have access to this code. There is a risk of breach of confidentiality (unintentional release of your information). We will do our best to make sure that this doesn't happen.

You will likely not directly benefit from future research with your information. Research with your identifiable information may help others by improving our understanding of health and disease, improving health care and making safer or more effective medical therapies, and developing new scientific knowledge.

If you have questions about the storage of your information, or have changed your mind, you can contact the Principal Investigator at the number listed on the first page of this form. If you change your mind, we will stop any future research with your information however, we will be unable to remove your information from any datasets already under analysis.

Electronic Medical Record and Release of Study Related Information?

What is an Electronic Medical Record?

An Electronic Medical Record (EMR) is an electronic version of your medical chart within a health system. An EMR is simply a computerized version of a paper medical record.

If you have never received care within Penn Medicine and are participating in a Penn Medicine research study that uses Penn Medicine healthcare related services, an EMR will be created for you for the purpose of maintaining any information produced from your participation in this research study. The creation of this EMR is required for your participation in this study. In order to create your EMR, the study team will need to obtain basic information about you that would be similar to the information you would provide the first time you visit a hospital or medical facility (i.e. your name, the name of your primary doctor, the type of insurance you have). If you have been a patient at Penn Medicine in the past, information from your research participation will be added to your existing medical record.

What may be placed in the EMR?

Information related to your participation in the research (e.g., laboratory tests, notes from your physician, imaging studies, and clinical procedures, etc.) will be placed in your EMR maintained by Penn Medicine.

Once placed in your EMR, your information may be accessible to appropriate Penn Medicine workforce members that are not part of the research team. Information within your EMR may also be shared with others who are determined by Penn Medicine to be appropriate to have access to your EMR (e.g. health insurance company, disability provider, etc.).

Penn Medicine also participates in automated information sharing through Health Information Exchanges (HIEs). HIEs securely share parts of your electronic health record, including research information, with other healthcare organizations involved in your care. This information is shared to improve the quality, safety and efficiency of your healthcare. To request that your health information not be shared through HIEs, please call 215-662-4484.

Will I, as a subject, have access to research related information within the EMR?

Please note the following about diagnostic test and/or imaging results:

- The 21st Century Cures Act requires healthcare institutions to allow patients increased access to their electronic medical record. As part of your participation in this research, you will have access to research related information within your EMR through Penn Medicine's patient portal – called MyPennMedicine (MPM).
- Results that may be placed in the medical record: Results from testing conducted in a laboratory or center that is part of Penn Medicine (i.e., the results would have been placed in the medical record, regardless of research participation). Results placed in the medical record are part of the designated record set and you have a right to review these results per HIPAA regulations.
- Results that may not be placed in the medical record: Results from biospecimen testing conducted in a laboratory that is not part of Penn Medicine and/or results from testing conducted in a non-certified laboratory (i.e., the results would not have been placed in the medical record as part of clinical care).

Will I receive the results of research testing that may be relevant to my health?

Clinically relevant research results will be disclosed to you; this will be done in the context of discussion with your study doctor and/or clinical treatment team. Results from clinical testing done as part of this research will be placed in your medical record. Results placed in the medical record and will be available to you per HIPAA regulations, as noted above.

What information about me may be collected, used, or shared with others?

The following personal health information will be collected and used for the purposes of this study.

- Name, address, telephone number, gender, email address, date of birth
- The history and diagnosis of your disease
- Specific information about the therapy you received, including previous treatment(s) you may have had
- Information about other medical conditions that may affect your care
- Medical data including laboratory test results, health status, pathology results, etc
- Information on side effects (adverse events) you may experience, and how these were treated
- Long-term information about your general health status and the status of your disease. This may include information from other health care providers.
- Data that may be related to tissue samples that may be collected from you
- Numbers or codes that will identify you, such as your medical record number
- Information related to study visits and other tests/procedures performed while you are participating on this study.

Why is my personal health information being used?

Your personal contact information is important for the research team to contact you during the study. For this study we may need to contact you via email to provide you information about scheduling, appointments, notes or to send you information about your participation in the study. Email communications are often not secure and may be seen by others as a result. By signing below, you accept this risk. If you wish for us to use a different means to communicate with you during the course of this study please discuss this with the research team and alternative methods can be arranged.

Your personal health information and results of tests and procedures are being collected as part of this research study, and will be used to conduct and oversee this research study, and to help guide your medical care.

Where may my information be stored?

Information related to your participation in clinical research will be contained in a clinical trial management system (CTMS). A clinical trial management system (CTMS) is used to register your information as a participant in a study. This allows for your research data to be entered and stored for the purposes of study operational and financial applications and other activities required as part of the conduct of the research. Once placed in the CTMS your information may be accessible to other authorized personnel at Penn Medicine that support research operations. Your information may be held in other research databases

Who can see or use my information?

Which Penn Medicine personnel may use or disclose my personal health information?

The following individuals may use or disclose your personal health information for this research study:

- The Principal Investigator and the Investigator's study team
- Authorized members of the workforce of the Penn Medicine, and Penn Medicine support offices, who may need to access your information in the performance of their duties (for example: for

research oversight and monitoring, to provide care as part of this study or as part of your routine care, to manage accounting or billing matters, etc.). This includes members of the Institutional Review Board (IRB), an Ethics Committee at Penn Medicine who are responsible for reviewing and overseeing research studies to ensure that they are safe and being well managed.

- Other research personnel with access to the databases for research and/or study coordination and as otherwise approved by the IRB

Who, outside of Penn Medicine, might receive my personal health information?
As part of the study, the Principal Investigator, the study team and others listed above, may disclose your study-related records, including the results of the research study tests and procedures, to those listed below. This study data may be processed and transmitted using secure computer systems. In all disclosures outside of Penn Medicine, you will not be identified by name, medical record number, address, telephone number, or any other direct personal identifier unless disclosure of the direct identifier is required by law. In records and information disclosed outside of Penn Medicine, you will be assigned a unique code number.

Your original medical records also may be reviewed by the sponsor of this study or its designated representatives, the Institutional Review Board overseeing this study, and any of the regulatory or safety oversight organizations outlined below. They may review these records for the purpose of checking data collected for the study, to make sure the study is being done properly, and to analyze the results of the study.

Individuals or organizations responsible for administering the study:

- Angela DeMichele, MD, MSCE (the sponsor of this study) and their designated representatives.
- Novartis Pharmaceuticals Corporation (the supplier of Everolimus) and their designated representatives.
- Authorized representatives of Penn Medicine

Regulatory and safety oversight organizations

- The U.S. Food and Drug Administration (FDA)
- The U.S. Department of Defense (DoD)
- Other regulatory agencies and/or their designated representatives, including international agencies
- Public Health agencies and other government agencies (including non-U.S.) as authorized or required by law

Once your personal health information is disclosed to others outside of Penn Medicine, it may no longer be covered by United States federal privacy protection regulations.

The Principal Investigator or study staff will inform you if there are any additions to the list above during your active participation in the trial. Any additions will be subject to Penn Medicine procedures developed to protect your privacy.

How long may Penn Medicine be able to use or disclose my personal health information?
Your authorization for use of your personal health information for this specific study does not expire. If you sign this form, we will collect your health information until the end of the research study. We may collect some information from your medical records even after you finish taking part in this study or after your death. We will keep all of the information forever in case we need to look at it again. We will protect this information and keep it confidential.

Your information may be held in a research database. However, Penn Medicine may not re-use or re-disclose information collected in this study for a purpose other than this study unless:

- You have given written authorization to do so

- Penn Medicine's Institutional Review Board grants permission after ensuring that appropriate privacy safeguards are in place
- As permitted by law

The data from this study may be published or used for teaching purposes, however you will not be personally identified in any publication. Your identity will remain confidential unless disclosure is required by law.

What if I decide not to give permission to use and give out my health information?
Then you will not be able to be in this research study.

Can I change my mind?
You have the right to withdraw your permission for the use of your personal health information, but if you do so, you must stop taking part in this study. You must do so in writing to the Principal Investigator at the address on the first page. Even if you withdraw your permission, your personal health information that was collected before we received your written request may still be used and disclosed, as necessary for the study. If you withdraw your permission to use your personal health information, you will also be withdrawn from the research study and no new information will be collected. However, even if you do withdraw your permission to use the data about you, we are required by the FDA and other national regulatory authorities to record anything that relates to the safety of the investigational drug under study.

Will I be able to access my research records?
You have the right to see and get a copy of your medical records kept by Penn Medicine. However, you will not be able to review or receive some of your records related to the study until after the entire study has been completed. When the study is over, you may write to the study doctor to ask to see or copy all of your medical information that was collected during the study. You also have the right to say how your medical information may be used, and to have any incorrect data about yourself updated or corrected.

By signing this document you are permitting Penn Medicine to use and disclose personal health information collected about you for research purposes as described above.

Who can I call with questions, complaints or if I'm concerned about my rights as a research subject?

If you have questions, concerns or complaints regarding your participation in this research study you should speak with the Principal Investigator listed on page one of this form. If you have any questions about your rights as a research subject, you may contact the Office of Regulatory Affairs at Penn Medicine with any questions, concerns or complaints by calling (215) 898-2614.

Where can I get more information?

You may call the National Cancer Institute's Cancer Information Service at 1-800-4-CANCER (1-800-422-6237). You may also visit the NCI website 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.

When you sign this form, you are agreeing to take part in this research study. This means that you have read the consent form, the study has been explained to you, your questions have been answered, you have had time to make your decision, and you have decided to volunteer to participate. You have been given the names of study staff that you can contact if you need assistance or if you have any additional questions or concerns. You agree to follow all of the instructions of your study doctor to the best of your ability, and report any changes in your health that may occur during the study.

Your signature also means that you are permitting Penn Medicine to use your personal health information collected about you for research purposes within our institution. You are also allowing Penn Medicine to disclose that personal health information to outside organizations or people involved with the operations of this study.

You agree that your primary care physician can be informed about your participation in this clinical trial.

A copy of this signed and dated consent form will be given to you.

Name of Subject (Print)	Signature of Subject	Date
Name of Person Obtaining Authorization (Print)	Signature of Person Obtaining Authorization	Date

Optional Research Consent

In addition to the main research study, you will also have the option of participating in optional research sub-studies. You may take part in these additional studies if you want to. You can still be a part of the main study even if you say 'no' to taking part in these additional sub-studies. All of the information in the main consent form you signed above (such as your rights as a participant in the study, risks of study procedures, how your medical information will be used, and who may see it) also applies to this optional sub-study research consent form.

Use of leftover biospecimens for research

There may be additional samples of your bone marrow, blood or tissue that remain after this research is complete. We would like to obtain your consent for the use of leftover biospecimens for research. If you agree, these samples will be kept and may be used in research to learn more about cancer and other diseases. This includes leftover blood samples, serum, plasma and buffy coat cells and bone marrow from the samples we collect. We would like to keep this for future research. If you do not consent to the use of leftover samples, these specimens will be discarded

The research that may be done with your, blood samples, and bone marrow is not designed specifically to help you. It might help people who have cancer and other diseases in the future.

Reports about research done with your blood samples, and bone marrow will not be given to you or your doctor. These reports will not be put in your health record. The research will not have an effect on your care. Whatever you decide regarding use of leftover specimens, your participation in the main study will not be affected.

Things to Think About

The choice to let us keep the left over specimens (blood samples, and bone marrow) for future research is up to you. No matter what you decide to do, it will not affect your care. If you decide now that your specimens can be kept for research, you can change your mind at any time. Just contact us and let us know that you do not want us to use your specimens. Then any specimens that remain will no longer be used for research.

In the future, people who do research may need to know more about your health. While the investigator(s) may give them reports about your health, we will not give them your name, address, phone number, or any other information that will let the researchers know who you are.

Sometimes specimens are used for genetic research (about diseases that are passed on in families). Even if your specimens are used for this kind of research, the results will not be put in your health records.

Your specimens will be used only for research and will not be sold. The research done with your specimens may help to develop new products in the future, including some that may be sold and/or make money for others. If this happens, there are no plans to tell you, or to pay you, or to give any compensation to you or your family. Most uses of biospecimens or information do not lead to commercial products or to profit for anyone.

Benefits

The benefits of research using specimens include learning more about what causes cancer and other diseases, how to prevent them, and how to treat them.

Risks

The greatest risk to you is the release of information from your health records. We will do our best to make sure that your personal information will be kept private. The chance that this information will be given to someone else is very small.

Future contact

You may be eligible for future research based upon your participation in this study. Researchers may wish to follow up with you to see how you are doing or may want to offer you the opportunity to join other research studies. Please indicate below whether you are willing to be contacted in the future about other research.

Making your decision

Please circle "yes" or "no" below and initial next to your choice to indicate whether or not you agree to participate in the optional research:

1. My blood samples (plasma, and buffy coat cells) and bone marrow may be kept for use in future research to learn about, prevent, or treat cancer:

Yes **No** **Initials: _____**

2. My blood samples (plasma, and buffy coat cells) and bone marrow may be kept for use in future research to learn about, prevent or treat other health problems (for example: diabetes, Alzheimer's disease, or heart disease):

Yes **No** **Initials: _____**

3. I am willing to be contacted in the future about other research:

Yes **No** **Initials: _____**

When you sign this form, you are confirming if or not you agree to take part in these optional research sub-studies. This means that you have read the consent form, the study has been explained to you, your questions have been answered, you have had time to make your decision, and you have decided if you would like to volunteer to participate. You have been given the names of study staff that you can contact if you need assistance or if you have any additional questions or concerns. You agree to follow all of the instructions of your study doctor to the best of your ability, and report any changes in your health that may occur during the study.

Your signature also means that you are permitting Penn Medicine to use your personal health information collected about you for research purposes within our institution. You are also allowing Penn Medicine to disclose that personal health information to outside organizations or people involved with the operations of this study.

You agree that your primary care physician can be informed about your participation in this sub-study.

A copy of this signed and dated consent form will be given to you.

Name of Subject (Print)	Signature of Subject	Date
Name of Person Obtaining Authorization (Print)	Signature of Person Obtaining Authorization	Date