

6G-09-1

STUDY TITLE: Cilengitide for Subjects with newly Diagnosed Glioblastoma Multiforme and Methylated MGMT Gene Promoter – a Multicenter, Open-label, Controlled Phase III Study, Testing Cilengitide in Combination with Standard Treatment (Temozolomide with Concomitant Radiation Therapy, Followed by Temozolomide Maintenance Therapy) versus Standard Treatment Alone (CENTRIC)

PRINCIPAL INVESTIGATOR: Thomas Chen, MD

EXPERIMENTAL SUBJECT’S BILL OF RIGHTS

You have been asked to participate as a research participant in a medical experiment. Before you decide whether you want to participate in the experimental procedure, you have a right to the following information:

CALIFORNIA LAW REQUIRES THAT YOU MUST BE INFORMED ABOUT:

1. The nature and purpose of the study.
2. The procedures in the study and any drug or device to be used.
3. Discomforts and risks reasonably to be expected from the study.
4. Benefits reasonably to be expected from the study.
5. Alternative procedures, drugs or devices that might be helpful and their risks and benefits.
6. Availability of medical treatment should complications occur.
7. The opportunity to ask questions about the study or the procedure.
8. The ability to withdraw from the study at any time and discontinue participation without affecting your future care at this institution.
9. Be given a copy of the signed and dated written consent form for the study.
10. The opportunity to consent freely to the study without the use of coercion.

I have carefully read the information contained above and I understand fully my rights as a potential subject in this study.

Date: _____ Time _____

Signature: _____
(Research Participant)

Name
PF#
Ward or Clinic

INFORMED CONSENT

6G-09-1

STUDY TITLE: Cilengitide for Subjects with newly Diagnosed Glioblastoma Multiforme and Methylated MGMT Gene Promoter – a Multicenter, Open-label, Controlled Phase III Study, Testing Cilengitide in Combination with Standard Treatment (Temozolomide with Concomitant Radiation Therapy, Followed by Temozolomide Maintenance Therapy) versus Standard Treatment Alone (CENTRIC)

PRINCIPAL INVESTIGATOR: Thomas Chen, MD

DEPARTMENT: Neurological Surgery

24-HOUR TELEPHONE NUMBER: (323) 865-3000

Please take as much time as you need to read the consent form. You may also decide to discuss it with your family, friends, or your doctor. You may find some of the language difficult to understand. If so, please ask questions. If you decide to participate, you will be asked to sign this form.

WHY IS THIS STUDY BEING DONE?

We invite you to take part in a research study because you have recently been diagnosed with glioblastoma (cancerous brain tumor). In addition, you have already had a pre-test (a molecular analysis) done on your brain tumor to see if it showed a certain type of gene, methylation of the MGMT gene, that would potentially qualify you for this study.

The main purpose of this study is to compare standard treatment for glioblastoma (which is radiation therapy and oral chemotherapy with temozolomide (TMZ) to standard treatment plus an experimental drug, cilengitide. The word “experimental” means that cilengitide is not approved by government authorities, such as the Food and Drug Administration.

Cilengitide is being developed to affect the tumor cells and the blood vessels supplying the tumor with nutrients and oxygen. Cilengitide might make brain tumors more responsive to other cancer therapies, such as the standard treatment of radiation therapy and TMZ.

Name
PF#
Ward or Clinic

Other purposes of this study include:

- Looking at the effect of cilengitide on progression of cancer (whether or not it grows, spreads or gets worse) and survival
- Obtaining additional information on the safety and effectiveness of cilengitide when it is used in combination with standard treatment
- Looking at whether “markers” in the blood and/or tumor tissue can predict treatment outcome
- Measuring participants’ quality of life during the study

This study is expected to include about 504 study participants and will be conducted in approximately 150 study centers (hospitals) in more than 20 countries worldwide. About 4 research participants from USC will take part in this study.

The study is being sponsored and paid for by Merck KGaA, Darmstadt, Germany, and its affiliate EMD Serono, Inc., Rockland, MA in USA.

WHAT IS INVOLVED IN THE STUDY?

The standard treatment is about 8 months long. The treatment with cilengitide is about 18 months long.

It is important that you inform the study doctor of any changes in your health whether or not you think that it is related to the study drug or treatment.

You must tell the study doctor about all drugs or medicines you are currently taking. This includes both prescribed medication as well as substances you obtain without prescription, (e.g. herbal medication and vitamin supplements). The study doctor will inform you whether you can continue taking these.

The following products or therapies are not allowed for a certain period of time prior or during the study:

- other chemotherapy,
- biologic agents (such as interferons or interleukins),
- radiation therapy of the head and antiangiogenic therapy.
- Any blood dilution – therapy (called anticoagulation therapy) will be discussed between the study doctor and the coordinating investigator/ sponsor of the study.

The study doctor will discuss with you the details. You must tell the study doctor before making changes to your existing regular medication or taking any new medication, except in an emergency situation. You should also tell the study doctor about any reactions to drugs or allergies that you have had.

You should not have immunizations with live vaccines (like rubella, mumps, measles etc.) while you are having chemotherapy or for 6 months afterwards, unless advised to do so by the study doctor.

Name
PF#
Ward or Clinic

You will be given a contact card which will have all the details you need should you wish to contact the study doctor in an emergency. This should be kept with you at all times. It is important that you follow the study doctor's instructions throughout the study. If you have questions or want further information contact the study doctor.

You will be instructed to go to the Clinical Trials Unit (CTU) at the University Hospital for the following visits:

- Week 1, Day 1
- Week 7, Day 1
- Week 11, Day 1

Before starting treatment

If you decide to take part in this study, the following examination and tests need to be done to make sure you are eligible to take part:

- Medical history and review all medications you take or have taken.
- Physical examination including vital signs and a neurological examination
- Blood tests will be done to see how well your organs are working (about 2 tablespoons for laboratory analysis and marker analysis)
(The marker analysis tests for markers in your blood that might be related to cancer or how the treatment works.)
- Urine analysis
- Blood pregnancy test for females of childbearing potential (about ½ teaspoon).
- A Gadolinium enhanced magnetic resonance imaging (Gd-MRI), will be also performed if it was not performed within 48 hrs after your brain surgery.
- You will also be asked to fill out 2 Quality of Life questionnaires as a measurement of how you are feeling before any study related procedures will be conducted.
- You will also be asked about how your ability to perform daily activities has been affected by your having cancer (this is called your performance status).

If for some reason there is a delay of more than 1 week after these examinations/tests have been performed and the start of study treatment, it will be necessary to repeat a few of the tests.

Study ID: HS-10-00072 Valid From: 8/12/2010 To: 2/24/2011

Name
PF#
Ward or Clinic

Study Treatments:

If you are eligible for the study, you will be randomized into one of the two groups described below. A computer program will assign you to one of the two groups: the standard treatment group (radiation therapy and oral chemotherapy with TMZ) or the cilengitide group (standard treatment plus cilengitide).

You will have an equal chance (50/50) to be placed in either group (standard treatment group or cilengitide group); however neither you nor the study doctor can influence which group you are assigned to. In case of severe side effects or intolerance, treatment will be immediately suspended or stopped.

Participants in both groups will take TMZ. It should be taken on an empty stomach or after a light meal with a glass of water. Do not open or split the capsules. They should be swallowed as a whole and never chewed. If the capsules are accidentally opened or damaged, you should be extremely careful to avoid inhaling the powder in the capsules or getting it on your skin or mucous membranes (in the nose or mouth). The study doctor may also prescribe an anti-nausea medication to be taken 20-30 minutes before the TMZ in order to prevent a sick stomach or vomiting. If you nevertheless vomit up the capsules, do not take more capsules to replace them. Similarly, if you forget to take the TMZ, just take the normal dose the next day. Do not take double the dose.

Standard Treatment (Radiation, Oral Chemotherapy with TMZ):

The standard treatment involves radiation therapy and chemotherapy with TMZ (temozolomide, also known as Temodal®, which is commercially available).

There are two phases to the treatment. Initially you will receive 6-7 weeks of radiotherapy (5 days a week, Monday-Friday for a total of 30 sessions). Each session will last less than a half an hour (30 minutes). During this same 6-7 weeks, you will also take a dose of TMZ by mouth, every day (7 days a week, even on Saturdays and Sundays when you do not have radiotherapy). You will take your last dose of TMZ on the last day of your radiotherapy.

Four weeks later (on Day 1 of Week 11), you will begin a “maintenance cycle” of TMZ. Maintenance cycle means you will take TMZ for 5 consecutive days and then stop. Four weeks later, you will do another maintenance cycle of TMZ (5 consecutive days then stop). There will be 6 maintenance cycles in all, each 4 weeks apart, until Week 34.

Your treatment will be given until Week 34 or until your disease progresses or your treatment needs to be stopped due to safety reasons.

Study ID: HS-10-00072 Valid From: 8/12/2010 To: 2/24/2011

Name
PF#
Ward or Clinic

Standard Treatment plus Cilengitide (Cilengitide Group):

Cilengitide will be given as an intravenous infusion (given through a vein in your arm). Each infusion takes about an hour and you will receive 2 infusions a week.

You will have the cilengitide infusions one week before starting standard therapy. After the first week you will start the standard treatment of radiation and TMZ (radiation 5 days a week and TMZ 7 days a week for 6-7 weeks). On the infusion days, you will take your dose of TMZ about two hours following the infusion. One hour later your radiotherapy will start. The entire process will take approximately 5 hours.

On days when you do not receive radiotherapy, you will take your dose of TMZ capsules within 1 hour after finishing the cilengitide infusion. On days when you do not receive radiotherapy or cilengitide, you will take your dose of TMZ capsules in the morning.

When you are done with the standard treatment, you will continue to receive cilengitide 2 times a week for the next 10 months.

At the end of the 10 months, if your cancer has not grown, spread or gotten worse, and the study doctor thinks it may be beneficial to you, you will have the option of continuing to receive cilengitide.

Extended ECG recordings will be performed and blood samples to determine the amount of cilengitide in the blood will be collected at certain time points. Blood samples will be drawn before the start of the first cilengitide infusion and at 30 minutes, 1 hr, 1.5 hrs, 2 hrs, 4 hrs and 6 hours after the start of cilengitide infusion. At each time point about one teaspoon of blood (about 2 tablespoons total) will be collected.

You will wear a small portable ECG monitor (holter) for 7 hours that provides continuous monitoring of your ECG parameters. The ECG data will be analyzed and interpreted centrally by experienced cardiologists, without knowing your personal data. Continuous ECG determination by using this Holter ECG equipment will start 1 hour before cilengitide infusion in week -1, day 1 and will stop 6 hours after start of infusion.

Study ID: HS-10-00072 Valid From: 8/12/2010 To: 2/24/2011

Name
PF#
Ward or Clinic

Study Procedures:

You will have to come to the site for certain visits to receive your treatment, including radiotherapy, oral chemotherapy and cilengitide infusions (if you are in the cilengitide group), as well as for several examinations and observations.

The following things will be checked or done during your study visits:

- Physical examination
- Vital signs
- Performance status,
- Other medications you might be taking,
- Blood and Urine testing.
 - About 1 tablespoon of blood will be taken weekly (week 1-6) for various weekly blood tests.
 - About 2 ½ teaspoons of additional blood will be drawn up to three more times during your treatment for marker analysis.
- Neurological examinations will be performed 9 times during your treatment.
- An electrocardiogram (ECG)

- A Gd-MRI will be performed 4 times during this phase of the study. Once you begin to respond to the treatment, another Gd-MRI will be done within 1 month in order to confirm the response.
- You will be asked to complete 2 Quality of Life questionnaires at 5 different visits during the study.
- At every visit you will be asked about any possible side effects you are experiencing.

Cilengitide Group

The following additional things will be checked or done during your study visits in the maintenance treatment phase with Cilengitide:

- Physical examination will be performed
- Vital signs
- Performance status,
- Other medications you might be taking,
- Blood drawn and Urine collected for testing.
- Every fourth week between week 10 and 34, you will have blood drawn (about 1 tablespoon) each time.
- Neurological examinations will be performed 11 times.
- A Gd-MRI 3 times during this phase of the study.
- Furthermore at 6 different visits during the study, you will be asked to complete 2 Quality of Life questionnaires.
- At every visit you will be asked about any possible side effects you are experiencing.

Study ID: HS-10-00072 Valid From: 8/12/2010 To: 2/24/2011

Name
PF#
Ward or Clinic

- Blood for pharmacokinetic (PK) research will be drawn. This type of blood test show how cilengitide acts in the body in terms of how long it stays active, how it is spread throughout the body, and how the drug gets out of the body. This type of testing is part of the cilengitide group. Blood for PK testing will be taken at 3 visits during the study. This blood will be taken at the end of your cilengitide infusion and then 2-8 hours later (at each time point about 1 teaspoon).

At the End of Study Treatment

At the end of your study treatment, you will return for an end of treatment visit. The purpose of this visit is to check on your safety and to see if there has been any change in your tumor since your last dose of the study drug. At this visit the following procedures will be done:

- Blood will be drawn for laboratory and marker analysis (about 5 ½ teaspoons)
- Vital signs,
- Physical and Neurological examination;
- Gd-MRI;
- Performance Status;
- Questions about Concomitant Medications;
- 2 Quality of Life Questionnaires;
- Urine Testing;
- Blood Pregnancy Tests for female research participants (about ½ teaspoon);
- Evaluation of side effects that you have experienced.

End of Study Treatment to Study Termination

About 4 weeks after the end of your treatment or after being permanently discontinued from the study for any other reason, you will have a final visit. The following procedures will be performed:

- Physical exam
- Blood tests (about 1 tablespoon).
- Side effects will be recorded,
- If needed, another ECG and chest-X-ray will be performed.
- You will be asked to fill-out the quality of life questionnaires.

After that, similar clinical follow-up visits will be scheduled every 3 months (or more frequently if needed). In addition to the above procedures, the following will also be performed:

- Brain MRIs,
- Neurological Evaluation,
- Recording your performance status.

Name
PF#
Ward or Clinic

Final Study Visit

When your disease progresses or when you withdraw your consent you will return for a final study visit. The following procedures will be done:

- Blood will be drawn for tests (1 tablespoon in total will be taken).
- Vital signs will be taken
- Physical and Neurological examination;
- Gd-MRI will be performed
- Performance status will be assessed.
- Questions about other medications you have taken;
- 2 Quality of Life Questionnaires;
- Urine will be collected for testing;
- An evaluation of side effects that have occurred.

Follow Up Contact

On a periodic basis after your final study visit, you will be telephoned by the study staff or asked during your routine visits in the hospital about how you are doing and which (if any) anticancer treatments you have received. This will last for at least 3 years from the time you start the study. Please inform the study doctor if your contact information changes.

If you stopped participating in the study before your disease progressed, then the follow up contact will focus on getting essential information about the status of your disease until it progresses, including information about any imaging you may have had done.

INFORMATION ABOUT SAMPLES COLLECTED AS PART OF THIS RESEARCH:

As part of this clinical study, we plan to perform additional cancer research on some of your blood samples and on the tumor tissue obtained at your initial surgery (or subsequent surgeries). From this research, we might learn more about your disease and/or how certain anticancer treatments work. In the future, this may help to predict which research participants might benefit most from certain anticancer treatments.

A total of no more than 5 additional blood samples (each a little less than 1 tablespoon, or in total about 4 tablespoons) will be collected throughout the study. These samples will be stored and tested in the future. Your samples will be identified by a unique numerical code for the study and your personal information will be protected. The samples will be stored for at least 12 years after the end of the study.

The individual results of research done on your blood and tumor tissue samples will not be available to either yourself or the study doctor.

Name
PF#
Ward or Clinic

The results of the research (which will not identify you) will be the property of the Sponsor and only authorized individuals will have access to this data. The results of research done with your blood and tumor tissue samples will not be given to you or your doctor. These results will not be put in your health record and will not have an effect on the care you receive.

The decision about whether to let us keep your blood and tumor tissue samples 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 blood and tumor tissue samples can be kept for research, you can change your mind at any time. If you do not want your identifiable samples to be kept, please inform the study doctor. You are still free to withdraw at any time and without giving a reason and without penalty or loss. We will then use the data and samples collected up to your withdrawal and will keep your tumor tissue sample for potential re-testing of the biochemical modification of the specific genetic region in your tumor. If you do not want your samples to be kept, please inform the study doctor to make a specific request for the samples to be destroyed.

Please read each sentence below and think about your choice. After reading each sentence, mark "Yes" or "No". If you have any questions, please talk to your doctor or nurse. No matter what you decide to do, it will not affect your care.

1. My tissue may be kept for use in future research on the type of disease I have.

Yes _____ No _____ Initials _____

2. My blood may be kept for use in future research on the type of disease I have

Yes _____ No _____ Initials _____

WHAT ARE THE POSSIBLE RISKS AND DISCOMFORTS?

In a research study like this one, every risk or side effect cannot be predicted. Each person's reaction to a test drug or procedure may be different. You may have a side effect or be at risk for symptoms, illnesses and/or complications that could not be predicted by the study doctor or the sponsor. Talk to the study doctor or study nurse about all of your side effects.

You may experience intolerance or an allergic reaction to any part of the study treatment and in rare cases, study treatment may lead to severe complications requiring hospitalization and may be fatal (causing death). In case of severe side effects or intolerance, treatment will be immediately suspended or stopped.

Name
PF#
Ward or Clinic

Cilengitide:

Cilengitide has so far been administered to several hundred research participants with varying cancer diagnoses in various clinical trials.

Single cases of potentially severe bleeding events have been reported in research participants treated with cilengitide in clinical studies. Based on the data from research participants treated in clinical studies thus far, there seems to be no increased risk factor for bleeding, but because cilengitide works by preventing the formation of new blood vessels, clotting and/or bleeding events might be expected with cilengitide treatment. You will be closely monitored for bleeding and/or clotting events.

With the currently available data, the following side effects have been observed in research participants in other clinical trials treated with cilengitide. Some of the side effects might possibly be related to other chemotherapy give at the same time or related to the disease itself; however, it may be possible that the side effects were enhanced by the cilengitide.

The most frequent side effects reported in other clinical trials with cilengitide were:

- nausea
- vomiting
- fatigue
- anorexia
- diarrhea
- lethargia (a degree of inactivity and unresponsiveness approaching or verging on unconscious)
- constipation
- headache
- tumor bleeding
- chest pain
- paraesthesia (a feeling of “pins and needles” or hands/feet going to sleep)
- stomatitis (red, swelling inflammation of your mouth)
- increase of liver enzymes
- shortness of breath

The following serious adverse events were observed around the same time as the use of cilengitide and were assessed to be possibly related to cilengitide:

- anaphylactic (allergic) reaction
- decreased red and white blood cells
- decreased platelets (also associated with bleeding of the kidney and brain)
- headache
- nausea
- vomiting
- diarrhea
- dehydration

Name
PF#
Ward or Clinic

- decreased potassium, sodium, and phosphate in the blood
- weight loss
- increased weakness
- hypotension (low blood pressure)
- increased shortness of breath
- urinary tract infection
- pneumonia
- infection of bile duct
- fever
- ulcer of the duodenum (small intestine)
- deep vein thrombosis (blood clot in your vein)
- pulmonary embolism (bloodclot that forms in your leg and travels to your lung)
- epistaxis (nose bleed)
- bleeding in the brain
- gastrointestinal bleeding
- myocardial infarction (heart attack)
- cerebral infarction (death of part of the brain from a lack of oxygen-carrying blood)
- renal insufficiency (kidney failure)
- lung edema (fluid in your lungs)
- lymph node enlargement
- pain
- pain in joints and muscles
- exanthema (rash)
- erysipelas (bacterial infection on face and lower extremities)

There have also been deaths, for which a possible relationship to cilengitide could not be excluded.

Radiation therapy:

Radiotherapy uses ionizing radiation similar to X-rays. It is delivered by special machines emitting the radiation focused on the tumor and the surrounding cells. It is given in a total of 30 sessions of a few minutes duration each. In order to deliver the radiation the same way every day, your head needs to be fixed in the same position. Before beginning this treatment, a mask will be fitted to your face and head. Radiation therapy may cause redness or soreness of the skin of the irradiated area (similar to a sun burn), hair loss, fatigue, difficulty with concentration, headache, and a dry mouth. During radiation treatment, it may be necessary to use medication (steroids) to minimize side effects of the radiation therapy. Rarely, late reactions to radiation therapy may occur. These consist of mental slowing and memory disturbances. Very seldom, a severe localized reaction of the brain, so called radionecrosis may develop and might require repeat surgery.

Study ID: HS-10-00072 Valid From: 8/12/2010 To: 2/24/2011

Name
PF#
Ward or Clinic

Temozolomide or TMZ (Temodal[®], Temodar[®]):

The most common side effects associated with TMZ, especially on the first day of each cycle are:

- nausea
- vomiting
- headache
- feeling tired
- loss of appetite
- hair loss
- constipation

The study doctor can prescribe medicines that may help reduce some of these.

TMZ also can reduce the number of certain types of blood cells, which can have serious effects. White blood cells are needed to fight infections. Lowering of white blood cells could result in a serious infection with a potential outcome of death. Platelets are needed in the normal course of blood clotting. Lowering of platelets does not allow your blood to clot normally, which can result in bleeding episodes. The study doctor will check your blood periodically while you are taking TMZ to see if these side effects are occurring. Research participants age 70 or older, women, and research participants who have had chemotherapy or radiation therapy may be more likely to have their blood cells affected.

The combination of corticosteroid therapy (cortisone-like medication often prescribed for the initial management of brain tumors) and a low white cell count may make you more susceptible to certain lung infections; therefore preventive antibiotics are often prescribed. In general, after you stop taking TMZ, your blood and bone marrow function should recover.

Rarely, other side-effects have been reported such as liver function disturbances. If these reactions are severe it may be necessary to discontinue treatment.

MRI:

You will have extra MRI scans of the brain during the study that would not be part of normal care. You should discuss the risks of MRI scans with the study doctor.

The gadolinium contrast agent used with MRIs has known risks. The most common are:

- strange tastes
- changes in smells
- injection site reactions
- nausea
- generalized feeling of warmth
- headache
- dizziness

Name
PF#
Ward or Clinic

Subjects with kidney disease who receive gadolinium-based contrast agents are at potential risk for developing Nephrogenic Systemic Fibrosis (NSF). NSF may result in fatal or debilitating systemic fibrosis affecting the skin, muscle, and internal organs.

There is also the risk of serious, life-threatening, fatal, allergic type reactions. Although these are not expected with the use of gadolinium contrast agents, they can happen unexpectedly.

Blood Draw:

There is a risk of discomfort, bruising, and possible infection from having blood samples taken or insertion of the needle/catheter into the vein for the study therapy administered.

EKG:

You may experience a slight pinching sensation during the removal of the ECG leads from the skin of your chest. You may also experience minor skin irritation at the sites of the ECG leads.

WHAT ABOUT PREGNANCY?

The study treatment can harm to an unborn child; therefore you must not take part in this study if you are pregnant, breast-feeding or you intend to become pregnant or intend to father a child during the treatment and for a safety period of 6 months after treatment. For this reason, all female participants must have a pregnancy test before taking part, during, and at the end of the study.

You and your partner must agree to use a reliable form of contraception during the trial. Discuss with the study doctor required methods of contraception. This should be continued for at least 6 months after the treatment has finished.

If you or your partner does become pregnant during the course of the study or within 6 months of stopping the treatment, you must inform the study doctor **immediately**.

If you become pregnant you may be referred to a specialist for counseling on the possible risks to your unborn baby and arrangements will be offered to monitor the health of both yourself and your unborn baby. Your permission may also be requested to collect information about your health and that of the baby.

If you are male and your partner becomes pregnant, it is recommended that your partner agrees to medical monitoring during her pregnancy and for the baby after it is born, as the risk to your partner and you baby is unknown. Your partner will be asked to sign a consent form to allow medical supervision. You and your partner's permission may also be requested to collect information about her health and that of the baby.

Study ID: HS-10-00072 Valid From: 8/12/2010 To: 2/24/2011

Name
PF#
Ward or Clinic

WHAT ARE THE POSSIBLE BENEFITS OF TAKING PART IN THIS STUDY?

There is no guaranteed benefit from taking part in this study. If your treatment works it may keep your cancer from temporarily growing, which may allow you to live longer. Even if you do not benefit personally from this study, the information gained may help in the treatment of other cancer research participants in the future.

There is no benefit to you by the additional research that may be done with your stored blood and tumor tissue samples. However, this may help to find out new information about markers in the disease and/or how certain anticancer treatments work and this might allow us to predict which research participants will respond to which type of anti-cancer treatments. Therefore this may allow us to better and individually select certain anti-cancer treatments in the future.

WHAT OTHER OPTIONS ARE THERE?

You can receive standard treatment without being in the study. If you do not want to participate in this study, the study doctor can explain what alternative treatments or other clinical trials are available to you. You should discuss the alternatives including their risks and benefits with your doctor before you make your decision about taking part in this study.

WILL YOUR INFORMATION BE KEPT PRIVATE?

The investigator and the Institutional Review Board (IRB) will keep your records private as far as the law allows. The IRB is a research review board that is made up of professionals and community members who review and monitor research studies to protect the rights and welfare of research participants. Officials sent by the Food and Drug Administration (FDA), other appropriate government agencies, the sponsor and representatives of the sponsor may look at your research records and medical records. Your records will be kept confidential unless the law requires us to share these records. We may publish the information from this study in journals or present it at meetings. If we do, we will not use your name.

WHAT ARE THE COSTS?

All research tests and procedures provided to you for this study are being paid for by the sponsor and you and/or your health plan or insurance company will not be charged for the cost of any research tests or procedures that are being done only for this study. Should you require any routine tests or procedures to treat your illness that are not related to this study that you would normally receive if you were not participating in this study you and/or your health plan/insurance company will be billed for the costs of the routine tests and procedures in the same way as if you were not in a research study. You will also be responsible for any co-payments and deductibles that are standard for your health plan/insurance coverage. Some health plans will not pay these costs for people taking part in studies. Check with your health plan or insurance company to find out what they will pay for. If you have any questions about which tests or procedures will be billed to you and/or your health plan/insurance company, ask the study doctor.

Study ID: HS-10-00072 Valid From: 8/12/2010 To: 2/24/2011

Name
PF#
Ward or Clinic

You will not be paid for taking part in this study. Your blood samples will be used for research purposes which are related to developing new and better treatments for cancer research participants. They will not be sold. Research performed on your sample may also lead to the development of treatments, devices, or new drugs that may be marketed and sold commercially. There will be no payment or patents to you if products are commercialized or developed from research on your samples. All rights on the results will remain the property of the sponsor.

The experimental drug, Cilengitide, will be provided by the sponsor free of charge while you are participating in this study.

ARE THERE ANY PAYMENTS TO YOU FOR TAKING PART IN THE STUDY?

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

WHAT HAPPENS IF YOU GET INJURED OR NEED EMERGENCY CARE?

It is important that you tell your study doctor, **Dr. Thomas Chen**, 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 at (323) 865-3000.

If you get sick or are physically injured as a direct result from your participation in this study, emergency medical care/treatment will be provided to you. The sponsor will pay for the costs of your immediate medical treatment for this sickness or physical injury as long as the study has been performed in accordance with any applicable law and regulation, and the terms of the protocol (study plan). No other form of compensation will be provided for injuries resulting from your personal conduct or participation in activities outside of the scope of the study protocol (study plan). No financial compensation will be provided for such things as lost wages, disability or discomfort, losses claimed by spouses or family members, medical expenses due to treatment of any underlying or unrelated condition.

However, by signing this form you have not given up any of your legal rights.

WILL YOU RECEIVE NEW INFORMATION ABOUT THIS STUDY?

During the study, we may learn new things about the risks or benefits of being in the study. If we do, we will share this information with you. You might change your mind about being in the study based on this information. If new information is provided to you, we will ask for your agreement to continue taking part in this study.

Study ID: HS-10-00072 Valid From: 8/12/2010 To: 2/24/2011

Name
PF#
Ward or Clinic

UNDER WHAT CIRCUMSTANCES CAN YOUR PARTICIPATION BE TERMINATED?

If you do not follow the investigator's instructions, if your disease gets worse, or if the sponsor closes the study, you may be removed from the study. If this happens, the investigator will discuss other options with you.

WHAT ARE YOUR RIGHTS AS A PARTICIPANT AND WHAT WILL HAPPEN IF YOU DECIDE NOT TO PARTICIPATE?

Your participation in this study is voluntary. Your decision whether or not to take part will not affect your current or future care at this institution. You are not waiving any legal claims or rights. If you do decide to take part in this study, you are free to change your mind and stop being in the study at any time.

WHOM DO YOU CALL IF YOU HAVE QUESTIONS OR PROBLEMS?

You may contact _____ at _____ with any questions, concerns, or complaints about the research or your participation in this study. If you feel you have been hurt by taking part in this study, please contact Thomas Chen, MD at (323) 865-3000. If you have questions, concerns, or complaints about the research and are unable to contact the research team, or if you want to talk to someone independent of the research team, please contact the Institutional Review Board (IRB) Office at 323-223-2340 between the hours of 8:00 AM and 4:00 PM. (Fax: 323-224-8389 or email at irb@usc.edu). If you have any questions about your rights as a research participant, please also contact the Institutional Review Board Office at the numbers above or write to the Institutional Review Board at the LAC+USC Medical Center, General Hospital, 1200 North State Street, Suite 4700, Los Angeles, CA 90033.

Study ID: HS-10-00072 Valid From: 8/12/2010 To: 2/24/2011

Name
PF#
Ward or Clinic

UNIVERSITY OF SOUTHERN CALIFORNIA/KENNETH NORRIS, JR. COMPREHENSIVE CANCER CENTER
 USC/Norris Comprehensive Cancer Center - 1441 Eastlake Ave., Los Angeles, CA 90033 Tel. (323) 865-3000
 Los Angeles County/USC Medical Center - 1200 N. State St., Los Angeles, CA 90033 Tel. (323) 226-6395
 USC/University Hospital – 1500 San Pablo St., Los Angeles, CA 90089-9177 Tel. (323) 442-8500

AGREEMENT:

I have read (or someone has read to me) the information provided above. I have been given a chance to ask questions. All my questions were answered. I have decided to sign this form in order to take part in this study.

Name of Research Participant	Signature	Date (& Time) of Signature
------------------------------	-----------	----------------------------

Name of Witness	Signature	Date (& Time) of Signature
-----------------	-----------	----------------------------

I have personally explained the study to the research participant and answered all questions. I believe that he/she understands the information described in this informed consent and freely consents to participate.

Name of Investigator/Person Obtaining Informed Consent	Signature	Date (& Time) of Signature
--	-----------	----------------------------

If applicable:

I have verbally translated this informed consent document to the research participant.

Name of Translator	Signature	Date (& Time) of Signature
--------------------	-----------	----------------------------

Study ID: HS-10-00072 Valid From: 8/12/2010 To: 2/24/2011

Name

PF#

Ward or Clinic