

6G-09-1
PHARMACOGENETICS

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)

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

INFORMED CONSENT

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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?

In addition to the procedures described in the main Informed Consent Form for this study, all participants are being asked to consider taking part in pharmacogenetic analyses (genetic research).

We intend to use your donated blood sample for pharmacogenetic research, the purpose of which is to identify if there are genetic markers which may help in predicting the response to treatment with cilengitide.

Genetic and pharmacogenetic research are important ways to try to understand the role of genes in human disease and their impact on drug treatment.

1. Genetic and pharmacogenetic research serves a number of purposes. These include medical and public health knowledge, the development of new drugs, tests and treatments. Information gained from tests of your genetic material (DNA) will be used for research by the sponsor's scientists.
2. Information obtained during the pharmacogenetic analyses will be used for exploratory purposes, and will not have a direct clinical impact or a prognostic value, therefore you will not receive any results. The sample is not labeled with your name and any other person's name, neither your initials nor the exact date of your birth will be part of the code.

If you are concerned about a potential genetic disease or problem, you and your doctor might choose to test specifically for it. You should discuss this option with your doctor or genetic counselor.

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3. Even though your name will not be connected to the blood sample, other information about you might still be connected. For instance, information about race, ethnicity, sex, your medical history, and so forth might be available to scientists studying your blood. Such information might be important for research or public health. It is possible that genetic information might come to be associated with your racial or ethnic group.
4. Following completion of this present study, all remaining de-identified biological material (blood) will be kept for a maximum of 5 years. After this period of 5 years, all the samples will be destroyed or new ethical committee approval will be obtained. Your samples will be stored at Merck KGaA in Darmstadt, Germany during this period.
5. 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?

If you decide to participate in this additional experimental procedure, an additional volume of about 1 teaspoon of blood would be taken at the first scheduled visit or at the next scheduled visit, when a blood sample is scheduled to be taken for routine safety tests.

Your samples will be used for the purpose of the present study, and for no other purpose (this information may be used with information from other studies conducted with the same drug). Testing will be performed only if it is believed that these results may benefit the further development of cilengitide. In that case, the blood will be tested to find out the genetic make-up of a specific region of one of your chromosomes and to determine the structure of a specific gene within that region. The information resulting from the testing will be used anonymously – your identity will not be revealed. The data will not be de-coded unless specifically required by Regulatory Authorities or if you wish to withdraw your consent, so we can specifically delete your samples.

WHAT ARE THE POSSIBLE RISKS AND DISCOMFORTS?

The needle stick that is part of this blood draw may cause local pain, bruising and swelling. Some people may also experience light-headedness, dizziness and rarely fainting or a local infection.

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

There is no immediate benefit to you by taking part in this additional research. However, the information gained may help in the treatment of cancer in the future.

WHAT OTHER OPTIONS ARE THERE?

You do not have to take part in this substudy.

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), the sponsor and the sponsor's representatives, 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.

The pharmacogenetic blood samples will be double-coded. This means that they will be given a first code assigned to you at the start of trial (your coded trial subject number). For the pharmacogenetic analyses the sponsor's staff will randomly assign a second code (double-coding) to these samples which will never be disclosed to your study doctor/staff. Only your study doctor/staff can link your identity to your trial subject number. No one else has this key. The link between your study subject number and the second code is only known by identified authorized personnel at the sponsor's. By these means, the scientists who perform the pharmacogenetic analyses only have access to the second code, therefore they have no key either to your study subject number or to your identity. This extra level of security will help protect your confidentiality and anonymity at all time.

WHAT ARE THE COSTS?

You and/or your health plan or insurance company will not be charged for you taking part in pharmacogenetic analyses (genetic research). However, you will still be responsible for any co-payments and deductibles that are standard for your health plan/insurance coverage.

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.

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

Your participation in this additional study is voluntary. You do not have to participate in this additional study in order to participate in the main study on cilengitide. Your decision whether or not to take part in this additional study 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.

Any genetic data generated from sample analysis prior to the completion of the analysis will be deleted unless this information has already been published or merged into larger databases where extraction is not possible. If you wish to withdraw your consent at any time please contact your study doctor who will take the appropriate measures to deal with your request.

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.

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
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Name of Witness	Signature	Date (& Time) of Signature
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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
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If applicable:

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

Name of Translator	Signature	Date (& Time) of Signature
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