THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center

Informed Consent

INFORMED CONSENT/AUTHORIZATION FOR PARTICIPATION IN RESEARCH WITH OPTIONAL PROCEDURES

Phase Ib Study of Erlotinib Prior to Surgery in Patients with Head and Neck Cancer
2008-0137

Subtitle: 2008-0137

Study Chair: Xiuning Le

1. _____ _____
Participant's Name Medical Record Number

You are being asked to take part in this clinical research study at The University of Texas MD Anderson Cancer Center ("MD Anderson"). This consent form explains why this research study is being done and what your role will be if you choose to take part. This form also describes the possible risks connected with being in this study. After reviewing this information with the person responsible for your enrollment, you should know enough to be able to make an informed decision on whether you want to take part in the study.

You are being asked to take part in this study because you have head and neck cancer and you are scheduled to have surgery.

DESCRIPTION OF RESEARCH

2. PURPOSE OF STUDY

The goal of this clinical research study is to learn the effects of the standard dose of erlotinib and the higher dose of erlotinib on biomarker levels in patients with head and neck cancer. Biomarkers are chemical "markers" in the blood and/or tissue that may be related to your response to the study drug. The safety of the drug will also be studied.

3. DESCRIPTION OF STUDY

The Study Drug

Erlotinib is designed to block the activity of a protein found on the surface of many tumor cells that may control tumor growth and survival. This may stop tumors from growing.

Screening Tests

Before you can be enrolled on this study, you will have what are called "screening tests". These tests will help the doctor decide if you are eligible to take part in the study. The following tests and procedures will be performed:

- Your complete medical history (including smoking history) will be recorded.
- You will have a physical exam, including measurement of vital signs (blood pressure, heart rate, temperature, and breathing rate).
- Blood (2 teaspoons) will be drawn for routine tests, to check your blood clotting and liver function.
- You will be asked how well you are able to perform the normal activities of daily living (performance status evaluation).
- You will be asked about any side effects you may be experiencing.
- You will have a computed tomography (CT) scan or magnetic resonance imaging (MRI) scan to check the status of the disease.
- Women who are able to have children must have a negative blood (about 1 teaspoon) pregnancy test.

A tissue sample from your original tumor biopsy will be collected to check the status of the disease and to check for biomarkers. If there is not enough of the tumor sample or if a tissue sample is not available, you will have a CT-guided tumor biopsy or a punch biopsy.

To perform a CT-guided biopsy, a tissue sample is withdrawn from an organ or suspected tumor mass using a very thin needle and a syringe. The needle is guided while being viewed by the doctor on a CT (computed tomography) scan or an imaging scan.

To perform a punch biopsy, the area of the tumor will be numbed with a local anesthetic and a small cut will be made to remove all or a piece of the area affected by the disease.

Study Groups

If you are found to be eligible to take part in this study, you will be randomly assigned (as in the toss of a coin) to receive erlotinib at either the standard dose or the high dose. There is an equal chance of being assigned to either group. If you are assigned to the high dose group and you are a current smoker, you will receive

an even higher daily dose of erlotinib. Both you and your study doctor will know which group you are in.

Study Drug Administration
Group 1 will take 1 tablet of erlotinib once a day, every day leading up to surgery.

Group 2 will take 2 tablets once a day, every day leading up to surgery. Depending on your assigned dose level, the 2 tablets may contain the same drug amount or 2 different drug amounts.

Erlotinib should be taken at the same time of day, 1 hour before or 2 hours after a meal. Each dose should be taken with 8 ounces of water. You should not consume grapefruit or grapefruit juice while on this study.

If you vomit after taking the medication, you can take another dose again, but only if the vomited tablet(s) can be seen and counted (in other words, they have not been digested yet).

Study Visits
Every 2 weeks, you will have a study visit. The following tests and procedures will be performed:

- Your medical history will be recorded.
- You will have a physical exam, including measurement of your vital signs.
- Blood (about 2 teaspoons) will be drawn for routine tests.
- You will be asked about any side effects you may be experiencing.
- You will have a CT scan or MRI to check the status of the disease within 1 week before the surgery.

Within one week before your surgery, you will also have blood (about 2-3 teaspoons) drawn to check your blood clotting function.

Length of Study
You will be on study for at least 2-3 weeks up to the day before surgery. You may be on study for up to 8 weeks if there is a delay in surgery.

After you have completed the study, you will have surgery to remove your tumor. During your surgery, a sample of your tumor tissue that is already being removed will be collected to check for biomarkers.

Follow-up
Within 30 days after your surgery, you will be contacted by phone to be asked you about any side effects you have experienced. The phone call will last about 10 minutes.

This is an investigational study. Erlotinib is FDA approved and commercially

available for the treatment of non-small cell lung cancer and pancreatic cancer (first-line therapy in combination with gemcitabine). Its use in this study is investigational.

Erlotinib will be provided to you free of charge. While you are on study, any tests or procedures performed for research purposes only will be paid for by the study.

Up to 55 patients will be enrolled in this study. All will be enrolled at M. D. Anderson.

4. RISKS, SIDE EFFECTS, AND DISCOMFORTS TO PARTICIPANTS

While on this study, you are at risk for side effects. These side effects will vary from person to person. The more commonly occurring side effects are listed in this form, as are rare but serious side effects that the drug is known to cause. You should discuss these with the study doctor. You may also want to ask about uncommon side effects that have been observed in small numbers of patients but are not listed in this form. Many side effects go away shortly after treatment is stopped, but in some cases side effects may be serious, long-lasting or permanent, and may even cause death.

Erlotinib Side Effects

Likely (occurring in more than 20% of patients)

● fatigue ● skin rash ● diarrhea	● loss of appetite ● nausea ● vomiting	● difficulty breathing ● cough

Erlotinib may likely cause an increased risk of infection, such as pneumonia. This infection may occur anywhere. It may become life-threatening. Symptoms of infection may include fever, pain, redness, and difficulty breathing.

Common (occurring in 3-20% of patients)

● acne ● itching and/or dry skin ● mouth blisters/sores ● weight loss	● abdominal pain ● abnormal liver tests (possible yellowing of the skin and/or eyes)	● eye disorders (such as painful red eyes and/or dry eyes) ● lung inflammation and/or damage (possible difficulty breathing)

Rare but serious (occurring in fewer than 3% of patients)

● skin disorders (possible blistering and/or peeling	● stomach and/or small intestine ulcer (possible	● vomiting of blood ● liver damage

of the skin) ● severe skin damage (possibly resulting in inflammation of the bowel and/or loss of a large portion of skin) ● low blood levels of potassium (possible weakness)	bleeding) ● digestive system bleeding ● bright red, tarry, or coffee ground-like blood in the stool ● hole in the intestines (possibly leaking contents into the abdomen)	● liver failure ● kidney failure ● liver and kidney failure resulting in death ● sores and/or a small hole in the front part of the eye ● painful torn eardrum ● hearing loss ● damage of the small airways with difficulty breathing

Erlotinib hydrochloride may interact with warfarin (Coumadin®), a drug used to decrease blood clotting. You should inform your doctor if you are taking this drug. Erlotinib hydrochloride may also interact with certain other medications/substances. These include Diflucan (fluconazole), Tagamet (cimetidine), erythromycin, St. John's wort, and grapefruit juice. Because of these interactions, and others that are not listed here, you should tell the study doctor about all medications, herbal remedies, vitamins, and supplements you may be taking.

Erlotinib may interact with certain statin drugs (drugs usually given to lower your cholesterol) and cause rare episodes of rhabdomyolysis (breakdown of muscle tissue, which can cause kidney failure).

Surgery may cause pain, bleeding from the incision, delayed wound healing, and/or infection. It may cause an abnormal passage that connects an abscess, cavity, or hollow organ to the body surface. It may also cause bone damage. You will sign a separate consent form for your surgery.

Biopsies may cause pain, bruising, bleeding, redness, low blood pressure, swelling, and/or infection at the site of the biopsies. An allergic reaction to the anesthetic may occur. A scar may form at the biopsy site.

Blood draws may cause pain, bleeding, and/or bruising. You may faint and/or develop an infection with redness and irritation of the vein at the site where blood is drawn. Frequent blood collection may cause anemia (low red blood cell count), which may create a need for blood transfusions.

This study may involve unpredictable risks to the participants.

Pregnancy Related Risks

4a. Because taking part in this study can result in risks to an unborn or breastfeeding baby, you should not become pregnant, breastfeed a baby, or father a child while on this study. You must use birth control during the study if

you are sexually active.

Birth Control Specifications: Women who are able to become pregnant must agree to use adequate birth control (hormonal or barrier method of birth control; abstinence) before starting the study and during your whole participation on study. Male participants must agree to use effective birth control or abstinence. Males: Tell the doctor right away if your partner becomes pregnant or suspects pregnancy.

Females: If you are pregnant, you will not be enrolled on this study. If you become pregnant or suspect that you are pregnant, you must tell your doctor right away.

Getting pregnant may result in your removal from this study.

5. POTENTIAL BENEFITS

Erlotinib may help to control the growth of your tumor. Future patients may benefit from what is learned. There may be no benefits for you in this study.

6. ALTERNATE PROCEDURES OR TREATMENTS

You may choose not to take part in this study. You may choose to have surgery without receiving any earlier treatment. You may choose to receive other investigational therapy, if available. You may choose not to have treatment for cancer at all. In all cases, you will receive appropriate medical care, including treatment for pain and other symptoms of cancer.

OPTIONAL PROCEDURES FOR THE STUDY

You will be asked to have extra blood drawn for biomarker testing and for storage in a research blood bank at M. D. Anderson for use in future research related to cancer. Biomarkers are chemical "markers" that may be related to your response to the study drug. If you agree, blood (5-6 teaspoons each time) will be drawn during the Screening Visit, after 2 weeks of treatment, and within 2 weeks before your surgery. This blood will be used for biomarker testing and storage in a research blood bank at M. D. Anderson for use in future research related to cancer.

You will be asked to allow leftover samples of your tumor tissue to be used for biomarker testing and for storage in a research tissue bank at M. D. Anderson for use in future research related to cancer.

If you also agree, samples of your leftover tumor tissue will be used for biomarker analysis and storage in a research tissue bank at M. D. Anderson for use in future research related to cancer.

Some of these samples will be taken from tissue either left over from previous procedures or left over from the screening biopsy (if a screening biopsy is necessary). Other samples that will be banked will be taken from the tissue left over after your scheduled surgery.

Before your blood and/or tissue can be used for research, the people doing the research must get specific approval from the Institutional Review Board (IRB) of M. D. Anderson. The IRB is a committee made up of doctors, researchers, and members of the community. The IRB is responsible for protecting the participants involved in research studies and making sure all research is done in a safe and ethical manner. All research done at M. D. Anderson, including research involving your blood and tissue from this bank, must first be approved by the IRB.

Your samples will be given a code number. No identifying information will be directly linked to your samples. Only the researcher in charge of the bank will have access to the code numbers and be able to link the samples to you. This is to allow medical data related to the samples to be updated as needed. Other researchers using your samples will not be able to link this data to you.

You do not have to agree to take part in the optional procedures in order to receive treatment on this study.

Optional Procedure Risks:

Blood draws may cause pain, bleeding, and/or bruising. You may faint and/or develop an infection with redness and irritation of the vein at the site where blood is drawn. Frequent blood collection may cause anemia (low red blood cell count), which may create a need for blood transfusions.

M. D. Anderson and others can learn about cancer and other diseases from your banked blood and/or tissue. In the future, people who may do research with these samples may need to know more information about your health. This information may be collected from your medical record. M. D. Anderson will make reasonable efforts to preserve your privacy, but cannot guarantee complete privacy. Sometimes your samples may be used for genetic research about diseases that are passed on in families. If the samples were used for this kind of research, your samples will be coded as mentioned above. M. D. Anderson will not be able to give you, your family, or your doctor the reports about the research done with these samples, and these reports will not be put in your medical record. If this information were released, it could be misused. Such misuse could be distressing, and it could cause you or your family members to have difficulty obtaining insurance coverage and/or a job.

If you agree now to allow leftover blood and/or tissue to be stored in a research tissue bank, and then later change your mind, the leftover materials will no longer be collected for storage. Any of your blood and/or tissue still in the tissue bank will no longer be used for research and will be removed from the tissue bank and destroyed.

However, if any of your de-identified blood and tissue was already released for research purposes before you withdrew consent, M. D. Anderson will not be able to destroy it.

Optional Procedure Benefits:
There are no benefits to you for taking part in the optional procedures. Future patients may benefit from what is learned.

Optional Procedure Alternatives:
Treatment with the study drug may be given without taking part in the optional procedures.

CONSENT/PERMISSION/AUTHORIZATION FOR OPTIONAL PROCEDURES

I elect to ____ or not to ____ allow extra blood to be drawn for biomarker testing and to be stored in a research blood bank for use in future research related to cancer as an optional procedure.
Participant's Initials _____

I elect to ____ or not to ____ allow leftover tissue to be collected for biomarker testing and to be stored in a research blood and tissue bank for use in future research related to cancer as an optional procedure.
Participant's Initials _____

Additional Information

7. You may ask the study chair any questions you have about this study. You may contact the study chair, Dr. Xiuning Le, at 713-792-6363. You may also contact the Chair of MD Anderson's Institutional Review Board (IRB - a committee that reviews research studies) at 713-792-2933 with any questions that have to do with this study or your rights as a study participant.

8. Your participation in this research study is strictly voluntary. You may choose not to take part in this study without any penalty or loss of benefits to which you are otherwise entitled. You may also withdraw from participation in this study at any time without any penalty or loss of benefits. If you withdraw from the study, data collected about you up to the time you withdrew may have to remain in the study database for inclusion in the data analysis. If you decide you want to stop taking part in the study, it is recommended for your safety that you first talk to your doctor. If you withdraw from this study, you can still choose to be treated at MD Anderson.

9. This study or your participation in it may be changed or stopped at any time by the study chair, OSI Pharmaceuticals, the U.S. Food and Drug Administration (FDA), the Office for Human Research Protections (OHRP - a regulatory agency that oversees research in humans), or the IRB of MD Anderson.

10. You will be informed of any new findings that might affect your willingness to continue taking part in the study.

11. MD Anderson will take appropriate steps to keep your personal health information private. However, there is no guarantee of absolute privacy. Federal agencies (such as the FDA and the OHRP), OSI Pharmaceuticals, OSI Pharmaceutical's agents, and the IRB of MD Anderson might review your record to collect data or to check that the research is being done safely and correctly. In some situations, FDA could be required to reveal the names of participants.

12. MD Anderson may benefit from your participation and/or what is learned in this study.

13. This study is supported by: OSI Pharmaceuticals.

14. The MD Anderson Conflict of Interest policy states that MD Anderson employees may not serve as the study chair or co-chair on a research study if they have received funds that are greater than the amount allowed by the policy or own stock in the sponsoring or supporting companies.

    The MD Anderson Conflict of Interest policy and the IRB require that you be told about significant financial relationships that the study staff and MD Anderson officials may have with the study sponsor(s).

At this time, no significant financial relationships with the study sponsor(s) have been disclosed by any of the study staff.

15. In a medical emergency, you may be cared for by someone who has a financial interest with the study sponsor(s). If you have any questions about this, you may call the IRB at 713-792-2933.

STUDY COSTS AND COMPENSATION

If you suffer injury as a direct result of taking part in this study, MD Anderson health providers will provide medical care. However, this medical care will be billed to your insurance provider or you in the ordinary manner. You will not be reimbursed for expenses or compensated financially by MD Anderson or OSI Pharmaceuticals for this injury. You may also contact the Chair of MD Anderson's IRB at 713-792-2933 with questions about study-related injuries. By signing this consent form, you are not giving up any of your legal rights.

Certain tests, procedures, and/or drugs that you may receive as part of this study may be without cost to you because they are for research purposes only. However, your insurance provider and/or you may be financially responsible for the cost of care and treatment of any complications resulting from the research tests, procedures, and/or drugs, including hospitalization, nausea, vomiting, low blood cell counts, and dehydration. Standard medical care that you receive under this research study will be billed to your insurance provider and/or you in the ordinary manner. Before taking part in this study, you may ask about which parts of the research-related care may be provided without charge, which costs your insurance provider may pay for, and which costs may be your responsibility. You may ask that a financial counselor be made available to you to talk about the costs of this study.

There are no plans to compensate you for any patents or discoveries that may result from your participation in this research.

You will receive no compensation for taking part in this study.

Authorization for Use and Disclosure of Protected Health Information:

A. During the course of this study, the research team at MD Anderson will be collecting information about you. This information may include your medical history, study schedule, and the results of any of your tests, therapies, and/or procedures. The purpose of collecting and sharing this information is to learn about how the study procedures may affect the disease and any study-related side effects. Your doctor and the research team may share your study information with the parties named in Section E below.

B. If you refuse to provide authorization to disclose your protected health information, you will not be able to participate in this research study.

C. Your protected health information will be protected according to state and federal law. However, there is no guarantee that your information will remain confidential, and it may be re-disclosed at some point.

D. All identifying information such as your name and address will be kept private. This information may be kept at MD Anderson forever. You will be assigned a code number so that your name will not be used. The research team at MD Anderson will be able to link the code number to your name. In some instances, in order to ensure the scientific value of the study, the parties named in Section E below will be able to view your study record but will not be permitted to copy any identifying information contained in your record.

E. The following parties may view your identifying information:

- OSI Pharmaceuticals
- OSI Pharmaceutical's agents
- The FDA
- The OHRP
- The IRB of MD Anderson
- Officials of MD Anderson
- Clinical study monitors who verify the accuracy of the information
- Individuals with medical backgrounds who determine the effect that the study procedures may have on the disease
- Individuals who put all the study information together in report form

F. You have the right to see and reproduce your records related to the research study, and ask for corrections, for as long as this information is held by the study chair and/or MD Anderson. However, in some studies, in order to ensure the scientific value of the study, participants are not able to view or reproduce their study records until the research has been completed with all participants in the study. If possible for this study, your doctor will be able to discuss your clinical test results with you.

G. There is no expiration date for the use of your protected health information. You may withdraw your authorization to share your protected health information at any time in writing. Instructions on how to do this can be found in the MD Anderson Notice of Privacy Practices (NPP). You may contact the IRB Staff at 713-792-2933 with questions about how to find the NPP. If you withdraw your authorization, you will be removed from the study and the study chair and staff will no longer use or disclose your protected health information in connection with this study, unless the study chair or staff needs to use or disclose some of your research-related protected health information to preserve the scientific value of the study. The parties listed in Section E above may use any study data that were collected before you canceled your authorization.

H. Information about this research study may be submitted to ClinicalTrials.gov, a publicly available online database managed by the U. S. National Institutes of Health (NIH). None of your identifying information will be submitted to ClinicalTrials.gov. If information from this study is submitted, none of it will be able to be directly linked to you.

CONSENT/AUTHORIZATION
(Adult Participants Only)

I understand the study. I have had a chance to read the consent form for this study, or have had it read to me. I have had a chance to think about it, ask questions, and talk about it with others as needed. I give the study chair permission to enroll me on this study. By signing this consent form, I am not giving up any of my legal rights. I will be given a signed copy of this consent document.

SAMPLE -- NOT FOR USE IN CONSENTING PATIENTS _____ _____
SIGNATURE OF PARTICIPANT DATE

WITNESS TO CONSENT
I was present during the explanation of the research to be performed under Protocol **2008-0137**.

SAMPLE -- NOT FOR USE IN CONSENTING PATIENTS _____ _____
SIGNATURE OF WITNESS TO THE VERBAL CONSENT PRESENTATION (OTHER THAN PHYSICIAN OR STUDY CHAIR) DATE

A witness signature is only required for vulnerable adult participants. If witnessing the assent of a pediatric participant, leave this line blank and sign on the witness to assent page instead.

RELATIONSHIP TO PARTICIPANT **SAMPLE -- NOT FOR USE IN CONSENTING PATIENTS**

PERSON OBTAINING CONSENT
I have discussed this clinical research study with the participant and/or his or her authorized representative, using language that is understandable and appropriate. I believe that I have fully informed this participant of the nature of this study and its possible benefits and risks and that the participant understood this explanation.

SAMPLE -- NOT FOR USE IN CONSENTING PATIENTS _____ _____
SIGNATURE OF STUDY CHAIR OR PERSON AUTHORIZED TO OBTAIN CONSENT DATE

Translator

I have translated the above informed consent as written (without additions or subtractions) into _____ and assisted the people
(Name of Language)
obtaining and providing consent by translating all questions and responses during the consent process for this participant.

SAMPLE -- NOT FOR USE IN CONSENTING PATIENTS

NAME OF TRANSLATOR | SIGNATURE OF TRANSLATOR | DATE

☐ Please check here if the translator was a member of the research team. (If checked, a witness, other than the translator, must sign the witness line below.)

SAMPLE -- NOT FOR USE IN CONSENTING PATIENTS

SIGNATURE OF WITNESS TO THE VERBAL TRANSLATION (OTHER THAN TRANSLATOR, PARENT/GUARDIAN, OR STUDY CHAIR) | DATE