Study Title for Study Participants: Testing the combination of afatinib and cetuximab compared to afatinib alone in newly diagnosed EGFR mutation positive, advanced stage non-small cell lung cancer

http://www.ClinicalTrials.gov: S1403, "A Randomized Phase II Trial of Afatinib Plus Cetuximab Versus Afatinib Alone in Treatment-Naive Patients with Advanced, EGFR Mutation Positive Non-Small Cell Lung Cancer (NSCLC) (BI 1200.124)"

This is a clinical trial, a type of research study. Your study doctor will explain the clinical trial to you. Clinical trials include only people who choose to take part. Please take your time to make your decision about taking part. You may discuss your decision with your friends and family. You can also discuss it with your health care team. If you have any questions, you can ask your study doctor for more explanation.

What is the usual approach to my advanced EGFR mutation positive non-small cell lung cancer?

You are being asked to take part in this study because you have newly diagnosed or recurrent non-small cell lung cancer which has spread to other parts of your body and has an EGFR (epidermal growth factor receptor) genetic mutation. An EGFR mutation is a change in a gene called EGFR. EGFR allows cells to grow and divide. People who are not in a study are usually treated with either the drug erlotinib or afatinib alone. Talk to your study doctor regarding your options.

What are my other choices if I do not take part in this study?

If you decide not to take part in this study, you have other choices. For example:

- you may choose to have the usual approach described above
- you may choose to take part in a different study, if one is available
- or you may choose not to be treated for cancer but you may want to receive comfort care to relieve symptoms.

Why is this study being done?

The purpose of this study is to compare any good and bad effects of using afatinib along with cetuximab to using afatinib alone. The addition of cetuximab to the usual afatinib could shrink your cancer, but it could also cause side effects. This study will allow the

researchers to know whether this different approach is better, the same, or worse than the usual approach. T There will be about 212 people taking part in this study. The study will be considered positive if the study approach delays disease progression. Afatinib is already FDA-approved for use in advanced non-small lung cancer and cetuximab is FDA-approved for treating other types of cancer, but using them together is considered investigational.

What are the study groups?

This study has two study groups.

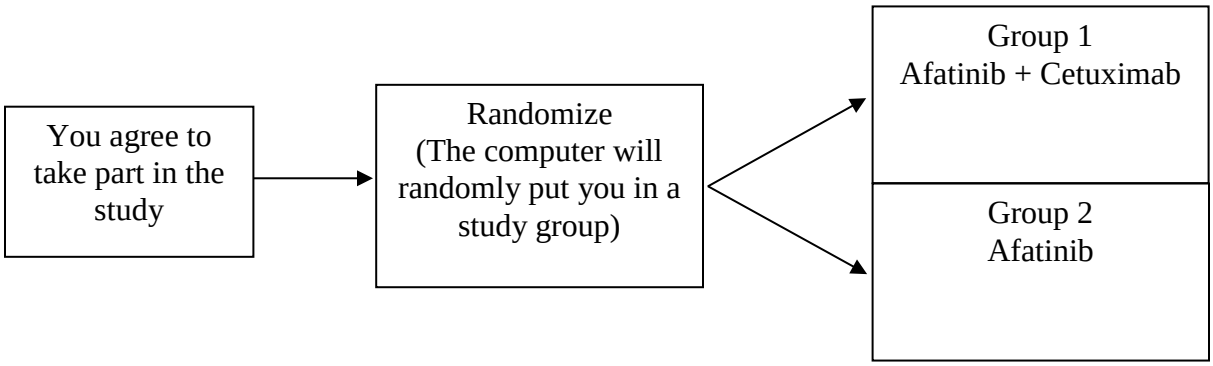
If you are in Group 1, you will receive the study drugs afatinib and cetuximab. The combination of the two drugs is considered investigational. Once every two weeks you will receive cetuximab which will be given into a vein. Before receiving cetuximab, you will receive diphenhydramine hydrochloride (Benadryl) to help prevent a hypersensitivity reaction. You will also take one afatinib tablet every day. Afatinib is to be taken by mouth on an empty stomach (at least one hour before eating or two hours after a meal). Every 28 days is considered a "cycle."

If you are in Group 2, you will receive afatinib alone. You will take one afatinib tablet every day. Afatinib is to be taken by mouth on an empty stomach (at least one hour before eating or two hours after a meal). Every 28 days is considered a "cycle."

To help keep track of the number of tablets you take and any side effects, you will need to keep a pill diary. The pill diary is called an Intake Calendar and you will need to bring it and the pill container with you for your follow-up visits. You should complete the pill diary daily.

A computer will by chance assign you to treatment groups in the study. This is called randomization. This is done by chance because no one knows if one study group is better or worse than the other.

Another way to find out what will happen to you during this study is to read the chart below. Start reading at the left side and read across to the right, following the lines and arrows.



How long will I be in this study?

You will receive study treatment (afatinib with cetuximab OR afatinib alone) until your disease gets worse or the side effects become too severe. If you stop taking the study treatment before your cancer gets worse, follow up exams will be every eight weeks until your cancer gets worse or three years from beginning the study (whichever comes first). After you are finished taking the study treatment, the study doctor will ask you to visit the office for follow up exams every six months for up to three years from beginning the study.

What extra tests and procedures will I have if I take part in this study?

Most of the exams, tests, and procedures you will have are part of the usual approach for your cancer. However, there are some extra tests that you will need to have if you take part in this study.

Before you begin the study:

You may need to have the following extra test to find out if you can be in the study:

- ECHO/MUGA scan and ECG to check for adequate cardiac function

If the exams, tests, and procedures show that you can take part in the study, and you choose to take part, then you will need the following extra tests and procedures.

- Researchers will use samples of your tissue and blood to learn what makes EGFR mutation positive tumors sensitive to and resistant to cetuximab and afatinib. The tissue and blood submissions are required because the research on them is an important part of the study.

  The tissue samples will be taken from a surgery or a biopsy that you have already had.

  The blood samples will be taken at three time points: before you begin the study treatment, before you begin Cycle 3 of study treatment, and if your disease gets worse. About two tablespoons of blood will be needed at each time.

  Your privacy is very important and the researchers will make every effort to protect it. Results of tests done on your tissue and blood will be identified by a unique code and the list that links the code to your name will be kept separate from your sample and health information.

  The results of tests done on your tissue and blood are not part of normal clinical decision making, and will not be made available to you or your study doctor.

Neither you nor your health care plan/insurance carrier will be billed for the collection of your tissue and blood.

What possible risks can I expect from taking part in this study?

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 doctor's office than usual**
- **You may be asked sensitive or private questions which you normally do not discuss**

The 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. There is also a risk that you could have side effects from the study drugs/study approach.

Here are important points about side effects:

- **The study doctors do not know who will or will not have side effects.**
- **Some side effects may go away soon, some may last a long time, or some may never go away.**
- **Some side effects may interfere with your ability to have children.**
- **Some side effects may be serious and may even result in death.**

Here are important points about how you and the study doctor can make side effects less of a problem:

- **Tell the study doctor if you notice or feel anything different so they can see if you are having a side effect.**
- **The study doctor may be able to treat some side effects.**
- **The study doctor may adjust the study drugs to try to reduce side effects.**

The tables below show the most common and the most serious side effects that researchers know about. There might be other side effects that researchers do not yet know about. If important new side effects are found, the study doctor will discuss these with you.

Possible side effect of Afatinib (all patients in Group 1 and Group 2)

COMMON, SOME MAY BE SERIOUS In 100 people receiving afatinib, more than 20 and up to 100 may have:
• **Diarrhea, nausea** • **Sores in the mouth which may cause difficulty swallowing** • **Tiredness** • **Infection** • **Rash**

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving afatinib, from 4 to 20 may have:
• **Swelling and redness of the eye** • **Redness and pain around lips** • **Constipation, heartburn, vomiting** • **Fever** • **Weight loss, loss of appetite** • **Dehydration** • **Pain** • **Changes in taste** • **Kidney damage which may require dialysis** • **Cough, shortness of breath, stuffy nose** • **Nose bleed** • **Dry skin** • **Itching, acne** • **Change in or loss of some or all of the fingernails or toenails**
RARE, AND SERIOUS In 100 people receiving afatinib, 3 or fewer may have:
• **Liver damage which may cause yellowing of eyes and skin, swelling** • **Change in heart function** • **Damage to the lungs which may cause shortness of breath** • **Redness, pain or peeling of palms and soles** • **Severe skin rash with blisters and peeling which can involve mouth and other parts of the body**

Possible Side Effects of Cetuximab (all patients in Group 1)
(Table Version Date: May 28, 2013)

COMMON, SOME MAY BE SERIOUS **In 100 people receiving Cetuximab, more than 20 and up to 100 may have:**
• **Change in nails** • **Swelling and redness of the area of radiation** • **Rash, itching, dry skin, acne** • **Dehydration, weight loss, loss of appetite** • **Sores in mouth which may cause difficulty swallowing** • **Constipation, diarrhea, vomiting, nausea** • **Difficulty sleeping** • **Headache, tiredness** • **Pain** • **Fever** • **Infection, especially when white blood cell count is low** • **Cough, shortness of breath**

OCCASIONAL, SOME MAY BE SERIOUS **In 100 people receiving Cetuximab, from 4 to 20 may have:**
• **Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat** • **Confusion, depression, worry** • **Fainting** • **Severe blood infection** • **Blood clot which may cause swelling, pain, shortness of breath**

RARE, AND SERIOUS **In 100 people receiving Cetuximab, 3 or fewer may have:**
• **Scarring of the lungs** • **Kidney damage which may require dialysis** • **Heart stops beating**

Let your study doctor know of any questions you have about possible side effects. You can ask the study doctor questions about side effects at any time.

Reproductive risks: You should not get pregnant, breastfeed, or father a baby while in this study or for two weeks after your last afatinib dose and 2 months after your last cetuximab dose if in Group 1. The drugs used in this study could be very damaging to an unborn baby. Check with the study doctor about what types of birth control, or pregnancy prevention, to use while in this study.

What possible benefits can I expect from taking part in this study?

It is not possible to know at this time if the study drugs/study approach is better than the usual approach so this study may or may not help you. This study will help researchers learn things that will help people in the future.

Can I stop taking part in this study?

Yes. You can decide to stop at any time. If you decide to stop for any reason, it is important to let the study doctor know as soon as possible so you can stop safely. If you stop, you can decide whether or not to let the study doctor continue to provide your medical information to the organization running the study.

The study doctor will tell you about new information or changes in the study that may affect your health or your willingness to continue in the study.

The study doctor may take you out of the study:

- If your health changes and the study is no longer in your best interest

- If new information becomes available
- If you do not follow the study rules
- If the study is stopped by the sponsor, IRB or FDA.

What are my rights in this study?

Taking part in this study is your choice. Participation is voluntary. No matter what decision you make, and even if your decision changes, there will be no penalty to you. You will not lose medical care or any legal rights.

For questions about your rights while in this study, you may contact the Operations Office of the National Cancer Institute (NCI) Central Institutional Review Board (CIRB) at 888-657-3711.

What are the costs of taking part in this study?

The afatinib and cetuximab will be supplied at no charge while you take part in this study whether you are in Group 1 or Group 2. The cost of getting the cetuximab ready and giving it to you is not paid by the study sponsor so you or your insurance company may have to pay for this. It is possible that these drugs may not continue to be supplied while you are on the study. Although not likely, if this occurs, your study doctor will talk to you about your options.

You and/or your health plan/insurance company will need to pay for all of the other costs of treating your cancer while in this study, including the cost of tests, procedures, or medicines to manage any side effects, unless you are told that certain tests are supplied at no charge. Before you decide to be in the study, you should check with your health plan or insurance company to find out exactly what they will pay for.

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

What happens if I am injured or hurt because I took part in this study?

If you are injured or hurt as a result of taking part in this study and need medical treatment, please tell your study doctor. Contact information for your study doctor is listed on the consent cover page. The study sponsors will not offer to pay for medical treatment for injury. Your insurance company may not be willing to pay for study-related injury. If you have no insurance, you would be responsible for any costs.

If you feel this injury was a result of medical error, you keep all your legal rights to receive payment for this even though you are in a study.

No funds have been set aside to compensate you in the event of injury.

Who will see my medical information?

Your privacy is very important to us and the researchers will make every effort to protect it. Your information may be given out if required by law. For example, certain states require doctors to report to health boards if they find a disease like tuberculosis. However, the researchers will do their best to make sure that any information that is released will not identify you. Some of your health information, and/or information about your specimen, from this study will be kept in a central database for research. Your name or contact information will not be put in the database.

There are organizations that may inspect your records. These organizations are required to make sure your information is kept private, unless required by law to provide information. Some of these organizations are:

- Montana Cancer Consortium
- The study sponsor, SWOG, and any drug company supporting the study.
- The Institutional Review Board, IRB, is a group of people who review the research with the goal of protecting the people who take part in the study.
- The Food and Drug Administration and the National Cancer Institute in the U.S., and similar ones if other countries are involved in the study.
- Qualified representative(s) of the Pharmaceutical Collaborator(s).
- Qualified representative(s) of the National Clinical Trial Network member with whom your institution is affiliated (ALLIANCE, ECOG-ACRIN, NRG, or SWOG).

Where can I get more information?

You may visit the NCI Web site at http://cancer.gov/ for more information about studies or general information about cancer. You may also call the NCI Cancer Information Service to get the same information at: 1-800-4-CANCER (1-800-422-6237).

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

Who can answer my questions about this study?

You can talk to the study doctor about any questions or concerns you have about this study or to report side effects or injuries. Contact information for your study doctor is listed on the consent cover page.

OPTIONAL STUDIES SECTION

This part of the consent form is about optional studies that you can choose to take part in. You will not get health benefits from any of these studies. The researchers leading this optional study hope the results will help other people with cancer in the future.

The results will not be added to your medical records, nor will you or your study doctor know the results.

You will not be billed for these optional studies. You can still take part in the main study even if you say 'no' to any or all of these studies. If you sign up for but cannot complete any of the studies for any reason, you can still take part in the main study.

Circle your choice of "yes" or "no" for each of the following studies.

1. Future contact

   Occasionally, researchers working with SWOG may have another research idea that relates to people who were on a SWOG study. In some cases, to carry out the new research, we would need to contact participants in a particular study. You can agree or not agree to future contact.

   I agree to allow my study doctor, or someone approved by my study doctor, to contact me regarding future research involving my participation in this study.

   Yes **No**

2. Biobanking for Possible Future Research

   Researchers are trying to learn more about cancer, diabetes, and other health problems. Much of this research is done using samples from tissue, blood, urine, or other fluids. Through these studies, researchers hope to find new ways to prevent, detect, treat, or cure health problems.

Some of these studies may be about genes. Genes carry information about features that are found in you and in people who are related to you. Researchers are interested in the way that genes affect how your body responds to treatment.

As mentioned in the main portion of the consent, samples of your tissue and blood will be used to study what makes EGFR mutation positive tumors sensitive to and resistant to cetuximab and afatinib. In this section of the consent, the researchers are asking your permission to store and use your samples and related health information (for example, your response to cancer treatment, results of study tests and medicines you are given) for medical research. The research that may be done is unknown at this time. Storing samples for future studies is called "biobanking". The Biobank is being run by SWOG and is supported by the National Cancer Institute.

What is involved?

If you agree to take part, here is what will happen next:

1) Your samples and some related health information may be stored in the Biobank, along with samples and information from other people who take part. The samples will be kept until they are used up.
2) Qualified researchers can submit a request to use the materials stored in the Biobank. A science committee at SWOG and/or the National Cancer Institute will review each request. There will also be an ethics review to ensure that the request is necessary and proper. Researchers will not be given your name or any other information that could directly identify you.
3) 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.
4) Some of your genetic and health information may be placed in central databases that may be public, along with information from many other people. Information that could directly identify you will not be included.

What are the possible risks?

1) There is a risk that someone could get access to the personal information in your medical records or other information researchers have stored about you.
2) There is a risk that someone could trace the information in a central database back to you. 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.
3) In some cases, this information could be used to make it harder for you to get or keep a job or insurance. There are laws against the misuse of genetic information, but they may not give full protection. There can also 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 study. The researchers believe the chance these things will happen is very small, but cannot promise that they will not occur.

How will information about me be kept private?

Your privacy is very important to the researchers and they will make every effort to protect it. Here are just a few of the steps they will take:

1) When your sample(s) is sent to the researchers, no information identifying you (such as your name) will be sent. Samples will be identified by a unique code only.
2) The list that links the unique code to your name will be kept separate from your sample and health information. Any Biobank and *SWOG* staff with access to the list must sign an agreement to keep your identity confidential.
3) Researchers to whom SWOG sends your sample and information will not know who you are. They must also sign an agreement that they will not try to find out who you are.
4) Information that identifies you will not be given to anyone, unless required by law.
5) If research results are published, your name and other personal information will not be used.

What are the possible benefits?

You will not benefit from taking part. The researchers, using the samples from you and others, might make discoveries that could help people in the future.

Are there any costs or payments?

There are no costs to you or your insurance. You will not be paid for taking part. If any of the research leads to new tests, drugs, or other commercial products, you will not share in any profits.

What if I change my mind?

If you decide you no longer want your samples to be used, you can call the study doctor, who will let the researchers know. Contact information for your study doctor is listed on the consent cover page. Then, any sample that remains in the bank will no longer be used and related health information will no longer be collected. Samples or related information that have already been given to or used by researchers will not be returned.

What if I have more questions?

If you have questions about the use of your samples for research, contact the study doctor. Contact information for your study doctor is listed on the consent cover page.

My samples and related information may be kept in a Biobank for use in future health research.

Yes **No**

THIS IS THE END OF THE SECTION ABOUT OPTIONAL STUDIES.

Signature:

This study has been explained to me, and I have been told what my enrollment in the study involves. I have read all pages of this consent and have had my questions answered to my satisfaction at this time. I consent to participate in this study and any additional studies where I circled 'yes'. I understand that by signing this form I have not given up any of my legal rights. I will be given a copy of this consent form. I may also request a copy of the protocol (full study plan).

Participant Signature: _____

Date: _____

Signature of Person Obtaining Consent: _____

Date: _____

Time of consent: _____ (AM) (PM)
(Required for initial consent only)