Study Title for Study Participants: Testing the combination of trametinib and docetaxel in advanced non-small cell lung cancer

Official Study Title for Internet Search
on http://www.ClinicalTrials.gov: S1507, "A Phase II Trial of Trametinib with Docetaxel in Patients with KRAS Mutation Positive Non-Small Cell Lung Cancer (NSCLC) and Progressive Disease Following One or Two Prior Systemic Therapies"

What is the usual approach to advanced non-small cell lung cancer?

You are being asked to take part in this study because you have non-small cell lung cancer with a KRAS mutation that has spread to other parts of your body or has come back, after one or two prior treatments. People who are not in a study are usually treated with other FDA approved drugs such as nivolumab, pembrolizumab, or atezolizumab. All of these drugs have been shown to help people with your type of cancer live longer. Your doctor can explain which option may be best for you.

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 test any good and bad effects of the combination of trametinib and docetaxel in patients with KRAS mutant lung cancer. Docetaxel is FDA-approved to treat your type of cancer but trametinib is not. However, trametinib is FDA-approved to treat other cancers. The combination of the two drugs is considered investigational. These drugs could shrink your cancer by about one-third in size but they could also cause side effects. Researchers hope to learn if this combination will shrink cancer in at least 37% of patients. There will be about 53 people taking part in this study.

What are the study groups?

All study participants will get the same study intervention. Trametinib is a tablet that you will take once every day by mouth on an empty stomach, either 1 hour before or 2 hours after food. Your study doctor will tell you how many tablets to take. You will also receive docetaxel once every three weeks. You may also be given filgrastim and pegfilgrastim if your docetaxel dose is

75 mg/m^2 to help prevent low blood counts. It will be given to you in the clinic through a tube in your vein (intravenous or IV).

How long will I be in this study?

You will receive the study treatment as long as the side effects are not too great and your disease does not get worse. After you finish the study treatment, your doctor will continue to watch you for side effects and follow your condition for three years from the time you started the study.

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 that 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 effects of docetaxel

COMMON, SOME MAY BE SERIOUS In 100 people receiving docetaxel, more than 20 and up to 100 may have:
• **Swelling of the body** • **Hair loss** • **Change in nails** • **Rash, itching** • **Vomiting, diarrhea, nausea, constipation** • **Sores in mouth which may cause difficulty swallowing** • **Infection, especially when white blood cell count is low** • **Anemia which may require blood transfusions** • **Bruising, bleeding** • **Tiredness** • **Numbness and tingling of the arms and legs** • **Fever** • **Absence of menstrual period** • **Swelling and redness of the arms, leg or face** • **Pain** • **Watering, itchy eyes**

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving docetaxel, from 4 to 20 may have:
• **Severe skin rash with blisters and peeling which can involve inside of mouth and other parts of the body** • **Belly pain** • **Kidney damage which may require dialysis** • **Blood clot which may cause swelling, pain, shortness of breath** • **Abnormal heart rate** • **Shortness of breath, wheezing** • **Chest pain**
RARE, AND SERIOUS **In 100 people receiving docetaxel, 3 or fewer may have:**
• **Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat** • **Cancer of bone marrow (leukemia) caused by chemotherapy**

Docetaxel may cause you to become intoxicated from the alcohol it contains. You should avoid driving, operating machinery, or performing other activities that are dangerous within one to two hours after the infusion of docetaxel. In addition, some medications, such as pain relievers and sleep aids, may interact with the alcohol in the docetaxel infusion and worsen the intoxicating effects. Less than 3% of people may experience scarring and thickening or inflammation of the tissue around the air sacs of the lungs.

Possible Side Effects of Filgrastim

COMMON, SOME MAY BE SERIOUS In 100 people receiving Filgrastim, more than 20 and up to 100 may have:
• **Nausea, vomiting** • **Pain in bone**

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving Filgrastim, from 4 to 20 may have:
• **Anemia which may cause tiredness, or may require transfusion** • **Damage to the lungs which may cause shortness of breath** • **Internal bleeding which may cause coughing up blood** • **Swelling or tenderness of vessels**

RARE, AND SERIOUS In 100 people receiving Filgrastim, 3 or fewer may have:
• **Rupture of the spleen leading to bleeding in the belly**

Possible Side Effects of Pegfilgrastim

COMMON, SOME MAY BE SERIOUS In 100 people receiving Pegfilgrastim, more than 20 and up to 100 may have:
• **Pain in bone**

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving Pegfilgrastim, from 4 to 20 may have:
• **Anemia which may cause tiredness, or may require transfusion** • **Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat** • **Damage to the lungs which may cause shortness of breath**

RARE, AND SERIOUS In 100 people receiving Pegfilgrastim, 3 or fewer may have:
• **Rupture of the spleen with bleeding in the belly**

Possible side effects of trametinib

COMMON, SOME MAY BE SERIOUS In 100 people receiving trametinib dimethyl sulfoxide (GSK1120212B), more than 20 and up to 100 may have:
• **Diarrhea, nausea** • **Tiredness** • **Swelling of the body** • **Skin changes including rash, acne**

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving trametinib dimethyl sulfoxide (GSK1120212B), from 4 to 20 may have:
• **Anemia which may require blood transfusion** • **Abnormal heartbeat** • **Blurred vision or other visual disturbances** • **Dry eye, mouth, skin** • **Swelling of the eye** • **Pain** • **Constipation, heartburn, vomiting** • **Sores in the mouth which may cause difficulty swallowing** • **Chills, fever** • **Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat** • **Infection** • **Change in heart function** • **Loss of appetite, dehydration** • **Dizziness, headache** • **Cough, shortness of breath** • **Hair loss, itching** • **Change in or loss of some or all of the finger or toenails** • **High blood pressure which may cause headaches, dizziness, blurred vision** • **Bleeding**

RARE, AND SERIOUS In 100 people receiving trametinib dimethyl sulfoxide (GSK1120212B), 3 or fewer may have:
• **Heart failure which may cause shortness of breath, swelling of ankles, and tiredness** • **Changes in the eyes (blood clot or retinal detachment) which may cause blindness** • **Blood clot which may cause swelling, pain, shortness of breath** • **A tear or hole in the bowels that may require surgery** • **Damage to muscle which may cause muscle pain, dark red urine** • **Damage to the lungs which may cause shortness of breath** • **Redness, pain or peeling of palms and soles**

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 become pregnant or father a baby while on this study and for at least 4 months following completion of treatment because the drugs in this study can affect an unborn baby. Women should not breastfeed a baby while on this study and for at least 4 months following completion of treatment. It is important you understand that you need to use birth control while on this study and for at least 4 months following completion of treatment. Check with your study doctor about what kind of birth control methods to use and how long to use them. Some methods might not be approved for use in this study. Women who become pregnant or think they might be pregnant must inform their treating physician immediately. Pregnancy requires a woman to come off protocol treatment immediately.

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

This study has only a small chance of helping you because we do not know if the study approach is effective. This study may help researchers learn things that may help other 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. 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?

Trametinib will be supplied at no charge while you take part in this study. It is possible that the trametinib 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.

Docetaxel and filgrastim/pegfilgrastim are commercially available.

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 the docetaxel and filgrastim pegfilgrastim tests, procedures, or medicines to manage any side effects, unless you are told that certain tests are supplied at no charge. The cost of getting the filgrastim and/or pegfilgrastim 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. The cost of getting the docetaxel 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.
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 (Southwest Oncology Group), and Novartis the drug company are 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 National Clinical Trial Network member with whom your institution is affiliated (ALLIANCE, ECOG-ACRIN, or NRG Oncology).

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 these optional studies hope the results will help other people with cancer in the future.

The results will not be added to your medical records and you or your study doctor will not 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. Optional Sample Collections for Laboratory Studies and/or Biobanking for Possible Future Studies

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.

If you choose to take part, samples of your blood and tissue from a previous surgery or biopsy may be collected. The research that may be done on your blood and tissue is unknown at this time. The researchers ask your permission to store and use your samples and related health information. Storing samples for future studies is called "biobanking". The Biobank is being run by SWOG and supported by the National Cancer Institute.

What is involved?

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

1) About *two teaspoons* of blood will be collected from a vein in your arm at three points in time: before you begin the study treatment, six weeks after you begin the study treatment, and when you stop the study treatment. These blood draws will take place at the same times that you are receiving other blood draws for the study. Also, a sample from the tissue that was collected at the time of your surgery or biopsy will be sent to the Biobank. This tissue already exists so you will not need another biopsy or surgery for this purpose.
2) Qualified researchers can submit a request to use the materials stored in the Biobanks. A science committee at the clinical trials organization, and/or the National Cancer
3) 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.
4) 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.
5) 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.

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.

3) Common side effects of a blood draw are a small amount of bleeding at the time of the procedure, pain at the blood draw site, which can be treated with regular pain medications, and bruising. Rarely, an infection can 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 samples are 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. Patients who withdraw their consent will have the option of having their specimen destroyed.

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.

Please circle your answer to show whether or not you would like to take part:

SAMPLES FOR FUTURE RESEARCH STUDIES:

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)

Specimen Consent Supplemental Sheets

How are Specimens Used for Research?

Where do specimens come from?

A specimen may be from a blood sample or from bone marrow, skin, toenails or other body materials. People who are trained to handle specimens and protect donors' rights make sure that the highest standards of quality control are followed by SWOG. Your doctor does not work for SWOG, but has agreed to help collect specimens from many patients. Many doctors across the country are helping in the same way.

Why do people do research with specimens?

Research with specimens can help to find out more about what causes cancer, how to prevent it, how to treat it, and how to cure it. Research using specimens can also answer other health questions. Some of these include finding the causes of diabetes and heart disease, or finding genetic links to Alzheimer's.

What type of research will be done with my specimen?

Many different kinds of studies use specimens. Some researchers may develop new tests to find diseases. Others may develop new ways to treat or even cure diseases. In the future, some of the research may help to develop new products, such as tests and drugs. Some research looks at diseases that are passed on in families (called genetic research). Research done with your specimen may look for genetic causes and signs of disease.

How do researchers get the specimen?

Researchers from universities, hospitals, and other health organizations conduct research using specimens. They contact SWOG and request samples for their studies. SWOG reviews the way that these studies will be done, and decides if any of the samples can be used. SWOG gets the specimen and information about you from your hospital, and sends the specimen samples and some information about you to the researcher. SWOG will not send your name, address, phone number, social security number or any other identifying information to the researcher.

Will I find out the results of the research using my specimen?

You will not receive the results of research done with your specimen. This is because research can take a long time and must use specimen samples from many people before results are known. Results from research using your specimen may not be ready for many years and will not affect your care right now, but they may be helpful to people like you in the future.

Why do you need information from my health records?

In order to do research with your specimen, researchers may need to know some things about you. (For example: Are you male or female? What is your race or ethnic group? How old are you? Have you ever smoked?) This helps researchers answer questions about diseases. The information that will be given to the researcher may include your age, sex, race, diagnosis, treatments and family history. This information is collected by your hospital from your health record and sent to SWOG. If more information is needed, SWOG will send it to the researcher.

Will my name be attached to the records that are given to the researcher?

No. Your name, address, phone number and anything else that could identify you will be removed before they go to the researcher. The researcher will not know who you are.

How could the records be used in ways that might be harmful to me?

If your confidential genetic information is discovered, you may suffer from genetic discrimination. Genetic discrimination occurs if people are treated unfairly because of differences in their genes that increase their chances of getting a certain disease. In the past, this could have resulted in the loss of health insurance or employment. Because of this, The Genetic Information Nondiscrimination Act of 2008, also referred to as GINA, was passed by Congress to protect Americans from such discrimination. The new law prevents discrimination from health insurers and employers. This act was signed into federal law on May 21, 2008, and went into effect May 2009. This law does not cover life insurance, disability insurance and long-term care insurance.

While this study has safeguards in place to protect your confidential genetic information and to make it extremely unlikely that your identity would be connected with any special studies that are performed on your tissue, it is possible that this information could be discovered by someone who is unauthorized to have access to it.

How am I protected?

SWOG is in charge of making sure that information about you is kept private. SWOG will take careful steps to prevent misuse of records. Your name, address, phone number and any other identifying information will be taken off anything associated with your specimen before it is given to the researcher. This would make it very difficult for any research results to be linked to you or your family. Also, people outside the research process will not have access to results about any one person which will help to protect your privacy.

What if I have more questions?

If you have any questions, please talk to your doctor or nurse, or call our research review board at 888-657-3711.