

## Kansas City Clinical Oncology Program

### Randomized, Phase III, Double-Blind Placebo-Controlled Trial of Sunitinib (NSC #736511, IND #74019) as Maintenance Therapy in Non-Progressing Patients following an Initial Four Cycles of Platinum-Based Combination Chemotherapy in Advanced, Stage IIIB/IV Non-Small Cell Lung Cancer

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.

You are being asked to take part in this study because you have advanced stage non-small cell lung cancer that has been treated by chemotherapy.

#### Why is this study being done?

The purpose of this study is to determine whether or not giving you a drug called sunitinib after you respond to chemotherapy (your tumor shrinks or stops growing) will help your tumor continue to shrink, or stay the same. Sunitinib is experimental (investigational) in the treatment of non-small cell lung cancer. Standard treatment for your type of cancer after you receive initial treatment would be to consider therapy with pemetrexed, which is FDA approved for treatment after chemotherapy (also called maintenance therapy), or to stop chemotherapy treatment. In this study, you will get either the sunitinib or the placebo (a substance that looks like sunitinib, but contains no medication). You will not get both.

#### How many people will take part in the study?

About 244 people will take part in this study.

#### What will happen if I take part in this research study?

##### **Before you begin the study**

You will need to have the following examinations, tests or procedures to find out if you are eligible for the study. None of these examinations, tests or procedures are experimental, they are part of regular cancer care and may be done even if you do not join the study. If you have had some of them recently, they may not need to be repeated. This will be up to your study doctor.

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- You will be asked to give your medical history and have a physical examination
- Blood tests (about 2 tablespoons of blood will be drawn)
- Pregnancy test for women of child-bearing potential
  
- CT scan or MRI scan of your chest and other organs in your chest area (special x-rays that use computerized images to determine the extent of the tumor and to make measurements of the tumors)
- Bone scan or PET scan (special x-rays that look at your entire body to see if the cancer has spread to any other parts of your body)
- MRI scan of the brain (special x-rays that use computerized images to see if the cancer has spread to your brain)

The following tests are required before you begin the study to make sure it is safe for you to be treated on this study. They are not part of regular cancer care:

- EKG (a test also known as an electrocardiogram that examines the heart rhythm)
- TSH (a test also known as thyroid-stimulating hormone that tests your thyroid function)

### **Treatment During the Study**

If you agree to participate you will be put into one of the two groups described below. You will receive either sunitinib or placebo. The group you are put into will be chosen by randomization. Randomization means that you are assigned to a group by chance. The treatment group you are assigned to is chosen by a computer. You will have an equal chance of being put into either of the two treatment groups. Neither you nor your doctor will choose, or know which groups you will be assigned to. When neither the doctor nor the patient knows what the treatment is, this is called a “double blind” study. However, your treatment information will be available to your doctor in case of emergency.

#### Treatment:

#### **Group 1: Sunitinib**

If you are placed in group 1, you will be asked to swallow three sunitinib capsules daily.

#### **Group 2: Placebo**

If you are placed in group 2, you will be asked to swallow three placebo capsules daily.

Patients in both group 1 and group 2 will receive the study treatment as long as the cancer is not growing or there are no serious side effects from the medication.

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The following medications should not be taken for 2 weeks before you start treatment, and while you are taking the study drug: ketoconazole, itraconazole, diltiazem, clarithromycin, erythromycin, verapamil, delavirdine, indinavir, saquinavir, ritonavir, atazanavir, nelfinavir, rifampin, rifabutin, carbamazepine, phenobarbital, phenytoin, St. John's Wort, efavirenz, tipranavir, and certain drugs for heart rhythm disturbances (such as terfenadine, quinidine, procainamide, sotalol, probucol, bepridil, indapamide or flecainide). Also, please review with your doctor all medications that you are currently taking to avoid possible drug interactions. Please speak with your study doctor before starting or changing medications.

### **Testing and visits while receiving study treatment**

During the time that you are receiving study treatment you will need the following tests and procedures during the study. They are part of regular cancer care.

- Physical examination every 3 weeks
- Blood tests, every 3 weeks
- CT scan of your chest and other nearby organs every 6 weeks (2 cycles) to see if your cancer is shrinking or growing

You may also need other scans if your doctor thinks that your cancer is spreading.

### **Testing and visits after study treatment has been completed**

After you are done with the study treatment, you will have a physical examination and CT scan of your chest and nearby organs every 3 months for the first year, then every 6 months for 2 years from study entry.

## **Can I stop being in the study?**

Yes. You can decide to stop at any time. Tell the study doctor if you are thinking about stopping or decide to stop. He or she will tell you how to stop safely.

It is important to tell the study doctor if you are thinking about stopping so any risks from the sunitinib or placebo can be evaluated by your doctor. Another reason to tell your doctor that you are thinking about stopping is to discuss what followup care and testing could be most helpful for you.

The study doctor may stop you from taking part in this study at any time if he/she believes it is in your best interest; if you do not follow the study rules; or if the study is stopped.

## **What side effects or risks can I expect from being in the study?**

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You may have side effects while on the study. Everyone taking part in the study will be watched carefully for any side effects. However, doctors don't know all the side effects that may happen. Side effects may be mild or very serious. Your health care team may give you medicines to help lessen side effects. Many side effects go away soon after you stop taking the sunitinib or placebo. In some cases, side effects can be serious, long lasting, or may never go away.

You should talk to your study doctor about any side effects that you have while taking part in the study.

The risks and side effects related to sunitinib are listed below. If you are randomized to the placebo you will not be receiving the active drug sunitinib. Sometimes, even while taking placebo, people experience side-effects. These side-effects may or may not be due to the placebo. Some side-effects for patients on placebo may or may not be similar to the side effects of sunitinib.

### **Sunitinib (or Placebo)**

#### **Likely**

- Feeling tired.
- Nausea, vomiting, or diarrhea.
- Sores in the mouth or throat, or other places in the gut such as the rectum
- Loss of appetite, taste changes.
- Stomach pain.

#### **Less Likely**

- Lowered white blood cell count that may lead to infection. Should this occur, it can be treated with antibiotics and maybe a reduction in the amount of drug given to you.
- Lowered platelets which may lead to an increase in bruising or bleeding. Should this occur, it can be treated with blood products (transfusions) and maybe a reduction in the amount of drug given to you.
- Lowered red blood cells which may cause anemia, tiredness, or shortness of breath. Should this occur, it can be treated with blood products (transfusions) and maybe a reduction in the amount of drug given to you.
- High blood pressure.
- Fever.
- Difficulty in sleeping or falling to sleep
- Chills
- Weight loss

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- Change in hair color
- Dry skin
- Hair loss
- Lightening of the skin
- Skin rash with the presence of macules (flat discolored area) and papules (raised bumps)
- Swelling or blistering of the skin on the palms of the hands or soles of the feet
- Irritation of the stomach lining
- Low thyroid function
- Constipation
- Dehydration
- Feeling of fullness
- Dry mouth
- Excess passing of gas
- Heartburn
- Nose bleed
- Swelling of the arms and/or legs
- Abnormal liver function as seen on a blood test
- Low levels of a blood protein called albumin
- Abnormal blood level that might be a sign of digestive or pancreas problems
- Increased blood level of a substance normally eliminated by the kidneys into the urine
- Decreased blood phosphate level
- Abnormal blood test of bone health (the blood test is called alkaline phosphatase)
- Increased blood levels of uric acid (a waste material from food digestion)
- Swelling of the nerve in the back of the eye responsible for vision
- Pain in arms, back, chest, legs, joints, muscles, or mouth
- Headache
- Cough
- Shortness of breath
- Dizziness
- High blood levels of an enzyme found in muscles (called creatinine phosphokinase)

**Rare but Serious**

- Changes and irregularities in heart rhythm.

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- Perforation (a hole) in the stomach or intestine, or other organs, which may be fatal.
- Decrease in the ability of the heart to pump blood
- Abnormal clotting of blood in small blood vessels
- A syndrome that includes high blood pressure with headache, confusion, seizures and/or loss of vision.
- Swelling of a part of the eye
- Decrease in vision
- Severe reaction of the skin and gut lining that may include rash and shedding or death of tissue.
- Liver failure, which may lead to death

**Secondary malignancies:** A number of established chemotherapeutic agents have an inherent risk of causing secondary cancers and/or leukemia. Certain agents in use today, not currently known to be associated with this risk may be shown at a later time to result in the development of these secondary cancers and/or leukemia.

**Reproductive risks:** Because the drugs in this study can affect an unborn baby, you should not become pregnant or father a baby while on this study. You should not nurse your baby while on this study. You will be asked to practice appropriate contraceptive measures while you are on this study. Appropriate methods of birth control include abstinence, oral contraceptives, implantable hormonal contraceptives (Norplant), or double barrier method (diaphragm plus condom). Ask about counseling and more information about preventing pregnancy.

For more information about risks and side effects, ask the researcher or your regular doctor.

## Are there benefits to taking part in the study?

Taking part in this study may or may not make your health better. While doctors hope that the sunitinib will be more useful against cancer compared to the usual treatment, there is no proof of this yet. We do know that the information from this study will help doctors learn more about sunitinib as a treatment for cancer. This information could help future cancer patients.

## What other choices do I have if I do not take part in this study?

Your other choices may include:

- Getting treatment or care for your cancer without being in a study
- Getting treatment with pemetrexed
- Taking part in another study
- Getting no treatment

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- Getting comfort care, also called palliative care. This type of care helps reduce pain, tiredness, appetite problems and other problems caused by the cancer. It does not treat the cancer directly, but instead tries to improve how you feel. Comfort care tries to keep you as active and comfortable as possible.

Talk to your doctor about your choices before you decide if you will take part in this study.

## Will my medical information be kept private?

We will do our best to make sure that the personal information in your medical record will be kept private. However, we cannot guarantee total privacy. Your personal information may be given out if required by law. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used.

Organizations that may look at and/or copy your medical records for research, quality assurance, and data analysis include:

- Cancer and Leukemia Group B (CALGB)
- Pfizer, Inc (the manufacturer of sunitinib)
- The National Cancer Institute (NCI) and other government agencies, like the Food and Drug Administration (FDA), involved in keeping research safe for people

If your doctor is participating in this study through the Cancer Trials Support Unit (the CTSU is a clinical trials mechanism sponsored by the NCI to provide greater access to phase III trials), a record of your progress will also be kept by the CTSU. If your record is used or disseminated for such purposes, it will be done under conditions that will protect your privacy to the fullest extent possible consistent with laws relating to public disclosure of information and the law-enforcement responsibilities of the agency.

The CALGB has received a Certificate of Confidentiality from the federal government, which will help us to protect your privacy. The Certificate protects against the involuntary release of information about you collected during the course of the study. The researchers involved in this project may not be forced to identify you in any legal proceedings (criminal, civil, administrative, or legislative) at the federal, state, or local level. However, some information may be required by the Federal Food, Drug, and Cosmetic Act, the U.S. Department of Health and Human Services, or for purposes of program review or audit. Also, you may choose to voluntarily disclose the protected information under certain circumstances. For example, if you or your guardian requests the release of information about you in writing (through, for example, a written request to release medical records to an insurance company), the Certificate does not protect against that voluntary disclosure.

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## What are the costs of taking part in this study?

The sunitinib will be provided free of charge by the Division of Cancer Treatment and Diagnosis, NCI (National Cancer Institute) while you are participating in this study. It is possible that the supply of sunitinib that has been supplied to the NCI could run out. If this happens, your study doctor will discuss with you how to obtain additional sunitinib from the manufacturer and you may be asked to pay for it. You and/or your health plan/ insurance company will need to pay for some or all of the costs of treating your cancer in this study. The costs of the EKG and TSH tests necessary for your participation in this study will be reimbursed by Pfizer, Inc, and you will not be billed for these tests. Taking part in this study may or may not cost your insurance company more than the cost of getting regular cancer treatment.

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

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

It is important that you tell your study doctor, \_\_\_\_\_  
[investigator's name(s)], 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/her at \_\_\_\_\_  
[telephone number].

You will get medical treatment if you are injured as a result of taking part in this study. You and/or your health plan will be charged for this treatment. The study will not pay for medical treatment.

## What are my rights if I take part in this study?

Taking part in this study is your choice. You may choose either to take part or not to take part in the study. If you decide to take part in this study, you may leave the study at any time. No matter what decision you make, there will be no penalty to you and you will not lose any of your regular benefits. Leaving the study will not affect your medical care. You can still get your medical care from our institution.

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

A Data Safety Monitoring Board will be regularly meeting to monitor safety and other data related to this study. The Board members may receive confidential patient information, but they will not receive your name or other information that would allow them to identify you by name.

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In the case of injury resulting from this study, you do not lose any of your legal rights to seek payment by signing this form.

### Who can answer my questions about the study?

You can talk to your study doctor about any questions or concerns you have about this study. Contact your study doctor \_\_\_\_\_ [name(s)] at \_\_\_\_\_ [telephone number].

For questions about your rights while taking part in this study, call the Kansas City Clinical Oncology Program Institutional Review Board (a group of people who review the research to protect your rights) at 816-823-0560.

### Related research studies

**Please note: The following section of the informed consent document is about additional research studies that are being done with people who are taking part in the main study. You may take part in these additional studies if you want to. You can still be part of the main study even if you say “no” to taking part in any of these additional studies.**

The results of these research studies will not be provided to you or your doctor, nor will the results have any affect on your treatment. It is unlikely that what we learn from these studies will have a direct benefit to you. However, the information learned from these studies may benefit other patients in the future. The results of these studies may be published, but individual patients will not be identified in these publications.

There will be no charge to you for participating in these research studies. Your samples will only be used for research and will not be sold. The research done with your sample may help to develop new products in the future.

The greatest risk to you is the release of information from your health records. We will do our best to make sure that your personal information will be kept private. The chance that this information will be given to someone is very small.

If you decide now to participate and then change your mind at any time about participating in these studies for any reason, you should contact your institution and let them know that you do not want the researchers to use your sample. The sample then will no longer be used for research. It will either be destroyed or returned to your institution for storage. The sample will also be returned to your institution upon request if needed for any other medical or legal reasons.

Please mark your choice by saying “yes” or “no” to each of the following:

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**Quality of Life:**

Part of this trial is to examine the effect of sunitinib on your quality of life. You will be given questionnaires that will ask about your physical symptoms and functioning, mood and your social life. You will be asked to fill out these questionnaires before you begin treatment, and then every three weeks while you are being treated on this study. At the beginning of the study, you will also be asked about your background, including your marital and educational status, and how many people live with you. It should take approximately 15 minutes to fill out these questionnaires.

This information will help doctors better understand how patients feel during treatments and what effects the medicines are having. In the future, this information may help patients and doctors as they decide which medicines to use to treat cancer.

1) I choose to take part in the Quality of Life Study and agree to complete the Quality of Life questionnaires.

\_\_\_\_\_ Yes                      \_\_\_\_\_ No                      \_\_\_\_\_ Initials

**Studies on Blood Specimens**

Another part of this trial is to study the proteins and DNA in your blood to determine whether or not it has certain characteristics that may make you more likely to respond to drugs like sunitinib. Some of these characteristics may be inherited through your family, and could be passed to your children. These are also called genetic studies.

The blood for this study (about 2 teaspoons) will be obtained before you receive treatment, and then the first and second time you have your doctor's visits (at 3 weeks and at 6 weeks). Analysis of your blood will be done at a CALGB approved laboratory. In order to study the genes, DNA must be removed from your blood sample. DNA is the substance that makes up your genes. Genes are the units of inheritance that are passed down from generation to generation. They are responsible for eye color, hair color, blood type, and hundreds of other traits.

There are specific risks associated with genetic studies. To help you make your decision, additional information about participation in genetic studies is included below. The information identifies how your personal information will be protected by the CALGB and its researchers.

**Safeguards of Confidentiality in Studies Involving Genes (Genetic Studies):**

It is possible to use blood samples to study many different kinds of genes. The CALGB recognizes this possibility and will take the following steps to protect

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your privacy and to protect you from having your sample tested for any genetic changes not directly related to cancer:

- Blood samples will be stored at a CALGB laboratory. The CALGB Statistical Center will perform all analyses of data and store all study results. Your blood sample will not be stored with your name on it. Instead, it will be labeled with a special CALGB identification number. The only location where your special identification number will be stored is at the CALGB Statistical Center. The greatest effort will be made to see that all personal information that can identify you is kept under conditions that protect your privacy.
- Information about your participation in this study and results of any tests performed on your sample will be kept only at the CALGB Statistical Center at Duke University. This information will not be made available to your doctors or to individual researchers at CALGB. Test results from this study will not be put in your medical records. All study information, including test results, is stored under conditions that limit access in order to protect the privacy of the people participating in this study.
- Your blood will be used only for the study of genes involved in cancer.
- There are no absolute legal protections against discrimination on the basis of genetic information. Instances are known in which a patient has been required to provide genetic information before applying for health insurance and/or a job. Since neither you nor your physician will be notified of the results of this test, it is unlikely that any discrimination could take place.

The same precautions to protect your privacy will be in place for such future studies. Future investigators will receive blood samples with the special CALGB identification number only, and your blood sample will not be identified with your name. These future investigators must apply to the CALGB and have their research project reviewed and approved by the CALGB.

If you decide now to give a sample of blood and then change your mind at any time about participating in the study, just contact your institution and let them know that you do not want the researchers to use your sample. The results from these studies may be published, but individual patients will not be identified in the publications.

2) My specimen(s) may be used for the research described above.

\_\_\_\_\_ Yes                      \_\_\_\_\_ No                      \_\_\_\_\_ Initials

**Storage of Your Specimens:**

We would like to keep any blood specimens that are left over for future research. If you agree, these specimens will be kept and may be used in research to learn more about cancer and other diseases.

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The research that may be done with your specimens is not designed specifically to help you. It might help people who have cancer and other diseases in the future. Reports about research done with your specimens will not be given to you or your doctor. These reports will not be put in your health record. The research will not have an affect on your care. The choice to let us keep left over specimens for future research is up to you.

You have the right to receive the planned therapy on this study without allowing your specimens to be stored for future research. Please read the sentences below and think about your choice. After reading the sentence, please mark your choice. **No matter what you decide to do, it will not affect your care.**

- 3) My specimen(s) may be kept for future use in research to learn about, prevent, or treat cancer.

\_\_\_\_\_ Yes                      \_\_\_\_\_ No                      \_\_\_\_\_ Initials

- 4) My specimen(s) may be kept for future use in research to learn about, prevent, or treat other health problems (for example: diabetes, Alzheimer disease, and heart disease).

\_\_\_\_\_ Yes                      \_\_\_\_\_ No                      \_\_\_\_\_ Initials

- 5) My doctor or someone from CALGB may contact me in the future to ask me to take part in more research.

\_\_\_\_\_ Yes                      \_\_\_\_\_ No                      \_\_\_\_\_ Initials

### Where can I get more information?

You may call the National Cancer Institute's Cancer Information Service at:

1-800-4-CANCER (1-800-422-6237) or TTY: 1-800-332-8615

You may also visit the NCI Web site at <http://cancer.gov/>

For NCI's clinical trials information, go to: <http://cancer.gov/clinicaltrials/>

For NCI's general information about cancer, go to <http://cancer.gov/cancerinfo/>

You will get a copy of this form. If you want more information about this study, ask your study doctor.

### Release

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By signing this form you authorize KCCOP to access and obtain information that is required for the study. This may include your medical records, labs, radiologic films and reports and pathology specimens. This authorization to disclose your medical records shall not expire, even upon death, unless specifically revoked in writing by you.

### Signature

I have been given a copy of all 13 pages of this form. I have read it or it has been read to me. I understand the information and have had my questions answered. I agree to take part in this study.

Participant \_\_\_\_\_

Date \_\_\_\_\_

Signature of Person Obtaining Consent \_\_\_\_\_

Date \_\_\_\_\_

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