

KANSAS CITY CLINICAL ONCOLOGY PROGRAM

Phase III randomized study of sorafenib (IND 69896, NSC 724772) plus doxorubicin versus sorafenib in patients with advanced hepatocellular carcinoma (HCC)

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 primary liver cancer also known as hepatocellular carcinoma for which you need treatment.

Why is this study being done?

The purpose of this study is to compare the effects (good and bad) of the drug sorafenib with the combination of sorafenib plus doxorubicin on you and your advanced primary liver cancer to find out which is better. In this study, you will get either the combination of sorafenib plus doxorubicin or you will receive sorafenib alone. At the present time, sorafenib is approved by the Food and Drug Administration (FDA) for the treatment of hepatocellular carcinoma. Doxorubicin is a marketed drug. It has been used in the treatment of a lot of different cancers, including hepatocellular cancer, but is not specifically FDA approved for hepatocellular cancer. The use of the combination of sorafenib and doxorubicin is not approved by the FDA for hepatocellular carcinoma.

How many people will take part in the study?

480 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 exams, tests or procedures to find out if you can be in the study. These exams, tests or procedures are part of regular cancer care and may be done even if you do not join the study. Depending on when you last had them, you may need to repeat some of these tests:

- Electrocardiogram (ECG) to test your heart function and rhythm.

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- CT and/or MRI scan of your chest, abdomen, and pelvis to provide pictures and check the size(s) of the tumor(s).
- If for any reason a biopsy of your tumor is unavailable, your doctor will ask you to consider having one before the start of the study, to confirm that you have primary liver cancer.
- A test (MUGA) to check the pumping function of your heart. A MUGA test involves a small amount of contrast material given in your vein and special scanners and cameras take pictures of your heart.
- Physical Exam including blood pressure, pulse, height, weight, assessment of your functional level (performance status) and medical history will be obtained. During the exam, your doctor will measure and record cancers that can be seen or felt.
- A pregnancy test, if you are a woman who can get pregnant.
- Blood tests (3-4 teaspoons).

You must stop taking all anti-cancer medicines. If you take St. John's Wort, you must stop taking it at least 4 weeks before enrolling on this study. Give your doctor a list of every drug you take. He or she will tell you what you can continue to take.

If the exams, tests and procedures show that you can be in the study, and you choose to take part, you will be registered/randomized to the study.

During the study ...

You will be "randomized" into one of the study groups described below. Randomization means that you are put into a group by chance. A computer program will place you in one of the study groups. Neither you nor your doctor can choose the group you will be in. You will have an equal chance of being placed in any group.

- **If you are in Group 1 (called "Arm A")** you will take sorafenib by mouth with a glass of water twice a day, 12 hours apart. You can take it without food or with a low or moderate fat meal. You will take the sorafenib tablets every day as your doctor tells you at each visit. You will be asked to record the day, number of pills taken and time of each dose of sorafenib on a medication calendar. You will be asked to bring the calendar and any unused tablets to your doctor every 6 weeks.

You will also get doxorubicin. It will be given through a needle in your vein once every 3 weeks for 6 cycles. A cycle lasts 21 days (or 3 weeks). In some cases, more than 6 cycles of doxorubicin may be given. Your doctor may decide to give you doxorubicin in the hospital. This may require an over-night stay. Your doctor will discuss this with you before you start treatment.

You will take sorafenib as long as you continue to benefit from therapy. You will receive sorafenib even if the doxorubicin has been stopped due to side effects.

- **If you are in Group 2 (often called "Arm B")** you will take sorafenib by mouth with a glass of water twice a day, 12 hours apart. You can take it without food or with a low or moderate fat meal. You will take the sorafenib tablets every day as your doctor tells you at each visit. You will be asked to record the day, number of pills taken and time of each dose of sorafenib on a medication calendar. You will be asked to bring the calendar and any unused tablets to your doctor every 6 weeks. You will take sorafenib as long as you continue to benefit from therapy.

Each treatment group will receive treatment over 3 weeks. This 3-week period is called "a cycle."

ARM A:

	Week 1	Week 2	Week 3		
Doxorubicin	X			Repeated a total of 6 times, then:	Sorafenib only, twice a day, every day
Sorafenib	Twice a day, every day				

ARM B:

	Week 1	Week 2	Week 3...
Sorafenib only	Twice a day, every day		

During the time that you are receiving study treatment, you will need the following tests and procedures that are part of regular cancer care. However, they may be done more often because you are in this study:

- A brief medical history and physical examination, blood pressure (Day 1 of each cycle), weight, and test to measure functional level (performance status).
- Blood tests (3-4 teaspoons) every 3 weeks.
- If you are randomized to Arm A, a test (MUGA) to check the pumping function of your heart (usually every 6 weeks). However, if you are receiving doxorubicin for more than 6 cycles, a MUGA may be done every 9 weeks.
- At regular intervals throughout the duration of the trial (usually every 6 weeks), measurements of the growth or shrinkage of your tumor(s) will be made from CT and/or MRI scans. These scans are like X-rays for which an injection of a dye (non-radioactive) is given before the tests are done.

At each visit you must let your doctor know what other drugs, whether prescribed or bought from a pharmacy, you are taking or have taken since the last visit. If you are unsure about taking a particular drug please check first with your doctor. It is recommended that you keep a list of drugs you are taking and bring it with you to each visit.

You must also let your doctor know immediately if there are any major changes in your health between visits and if you have any concerns regarding the study. If you see another doctor/nurse/health care person you must tell them you are taking part in this study and that

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they can contact your doctor for information. If you are admitted to a hospital between study visits you must inform your doctor as soon as possible.

How long will I be in the study?

You will continue to receive study treatment until your doctor feels you are no longer benefiting from treatment or you experience side effects that prevent you from continuing. After you finishing taking the study drugs, the doctor will continue to follow your progress every 3 months for one year and then every 6 months for two years for a total of 3 years.

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 sorafenib plus doxorubicin or soafenib can be evaluated by your doctor. Another reason to tell your doctor that you are thinking about stopping is to discuss what follow-up 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 by the researchers.

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

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 sorafenib plus doxorubicin or sorafenib. In some cases, side effects can be serious, long lasting, or may never go away. There also is a risk of death.

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

Risks and side effects related to the treatments being studied include:

Arm A (Sorafenib plus Doxorubicin)

Likely:

- Lowered white blood cell count (neutrophils/granulocytes) that may lead to infection
- Decreased number of a type of white blood cell (lymphocyte)

- Decreased number of blood cells that help to clot blood, which may lead to an increase in bruising or bleeding
- Lowered red blood cells which may cause anemia, tiredness, or shortness of breath
- Low levels of a blood protein called albumin
- Decreased blood levels of calcium, sodium, and phosphate
- Abnormal blood tests that could be a sign of liver problems (AST, ALT, alkaline phosphatase, bilirubin)
- Abnormal blood level of a bone enzyme
- Abnormal blood tests that could be a sign of kidney problems
- Abnormal blood level that might be a sign of digestive or pancreas problems
- Blood test that shows a problem with blood clotting
- High blood sugar level
- Nausea and vomiting
- Loss of appetite
- Heartburn
- Hair loss
- Fatigue
- Skin rash
- Inflammation of the skin on the palms of the hands and soles of the feet
- Diarrhea
- Belly pain
- Weight loss

Less Likely:

- Abnormal digestive enzyme level
- Decreased blood potassium level
- Low blood sugar level
- Decreased blood level of carbon dioxide
- Increased blood levels of calcium, potassium, sodium, and/or uric acid (a waste material from food digestion)
- Abnormal blood test that could be a sign of liver problems (GGT)
- Fever with dangerously low white blood cell count
- Formation or presence of a blood clot inside a blood vessel that can break loose and plug another blood vessel
- Decrease in a part of red blood cells that carries oxygen in the body
- High blood pressure
- High cholesterol
- Tingling and redness in the hands and feet
- Change in color or loosening of fingernails and toenails
- Inflammation or damage to the skin around the IV tubing
- Allergic reaction
- Irregular heartbeat
- Fever

- Trouble sleeping
- Dry skin
- Itching
- Constipation
- Irritation or sores in the lining of the digestive tract
- Irritation or sores in the mouth or throat
- Bleeding of the digestive tract
- Bleeding of the urinary tract
- Bleeding of the male or female reproductive tract
- Bleeding of the respiratory tract
- Nose bleed
- Infection
- Swelling of the arms and legs
- Dizziness
- Condition of the nervous system that causes numbness, tingling, burning
- General pain, including pain of the back, chest, legs, joint, muscle, and headache
- Cough
- Shortness of breath
- Collection of fluid between the thin layers of tissue (pleura) lining of the lung and the wall of the chest cavity
- Voice changes, laryngitis, hoarseness
- Kidney failure
- You may experience red colored urine within 24 hours of being treated with doxorubicin.
- Fluid collection in the abdomen
- Muscle spasms

Rare but Serious:

- Heart damage, which could decrease the heart's ability to pump blood
- Severe damage to tissue if doxorubicin leaks out of blood vessel
- Decreased blood supply to the heart/heart attack
- Rarely, sorafenib can cause holes (perforations) in the digestive tract, which can be life-threatening. Tell your doctor or nurse right away if you have any severe stomach (abdominal) pain, especially if you also have nausea, constipation, fever, or any other symptom.
- Bleeding into the brain or spinal cord
- Collection of symptoms including headache, confusion, seizures, and vision loss associated with X-ray findings
- Serious potentially life-threatening type of allergic reaction that may cause breathing difficulty, dizziness, low blood pressure, and loss of consciousness
- Severe reaction of the skin and gut lining that may include rash and shedding or death of tissue
- Potentially life-threatening condition affecting less than 10% of the skin in which cell death causes the epidermis (outer layer) to separate from the dermis (middle layer)

- Collection of signs and symptoms that indicate sudden heart disease in which the heart does not get enough oxygen. Sudden symptoms such as chest pain, shortness of breath, or fainting could indicate heart disease and should be reported right away. Signs such as abnormal EKG and blood tests can confirm damage to the heart.

In about 20 patients who have received both drugs, an increase in the amount of doxorubicin in the blood was noted. Having an increased blood level of doxorubicin might cause side effects to be more common or serious. Also, in a previous study in which about 50 patients received the combination of sorafenib and doxorubicin, there was an increased risk of heart toxicity on MUGA scans, but not necessarily associated with symptoms. The current study will be monitoring toxicity very carefully.

Arm B (Sorafenib)

Likely:

- Abnormal blood tests that could be a sign of liver problems (AST, ALT, alkaline phosphatase, bilirubin)
- Abnormal blood level of a bone enzyme
- Abnormal blood tests that could be a sign of kidney problems
- Abnormal blood level that might be a sign of digestive or pancreas problems
- Blood test that shows a problem with blood clotting
- Low levels of a blood protein called albumin
- Decreased number of a type of white blood cell (lymphocyte)
- High blood sugar level
- Decreased number of blood cells that help to clot blood, which may lead to an increase in bruising or bleeding
- Decreased blood levels of calcium, sodium, and phosphate
- Fatigue
- Hair loss
- Skin rash
- Inflammation of the skin on the palms of the hands and soles of the feet
- Loss of appetite
- Diarrhea
- Nausea
- Belly pain
- Weight loss

Less Likely:

- Decrease in a part of red blood cells that carries oxygen in the body
- Lowered white blood cell count (neutrophils/granulocytes) that may lead to infection
- Fever with dangerously low white blood cell count
- Abnormal blood test that could be a sign of liver problems (GGT)
- Decreased blood potassium level
- Decreased blood level of carbon dioxide

- Increased blood levels of calcium, potassium, sodium, and/or uric acid (a waste material from food digestion)
- Low blood sugar level
- High blood pressure
- High cholesterol
- Formation or presence of a blood clot inside a blood vessel that can break loose and plug another blood vessel
- Fluid collection in the abdomen
- Fever
- Dry skin
- Itching
- Constipation
- Irritation or sores in the lining of the digestive tract
- Irritation or sores in the mouth or throat
- Vomiting
- Bleeding of the digestive tract
- Bleeding of the urinary tract
- Bleeding of the respiratory tract
- Bleeding of the male or female reproductive tract
- Nose bleed
- Infection
- Swelling of the arms and legs
- Dizziness
- Condition of the nervous system that causes numbness, tingling, burning
- General pain, including pain of the back, chest, legs, joint, muscle, and headache
- Trouble sleeping
- Cough
- Shortness of breath
- Voice changes, laryngitis, hoarseness
- Kidney failure
- Muscle spasms

Rare but Serious:

- Heart damage, which could decrease the heart's ability to pump blood
- Decreased blood supply to the heart/heart attack
- Rarely, sorafenib can cause holes (perforations) in the digestive tract, which can be life-threatening. Tell your doctor or nurse right away if you have any severe stomach (abdominal) pain, especially if you also have nausea, constipation, fever, or any other symptom.
- Bleeding into the brain or spinal cord
- Collection of symptoms including headache, confusion, seizures, and vision loss associated with X-ray findings

- Serious potentially life-threatening type of allergic reaction that may cause breathing difficulty, dizziness, low blood pressure, and loss of consciousness
- Severe reaction of the skin and gut lining that may include rash and shedding or death of tissue
- Potentially life-threatening condition affecting less than 10% of the skin in which cell death causes the epidermis (outer layer) to separate from the dermis (middle layer)
- Collection of signs and symptoms that indicate sudden heart disease in which the heart does not get enough oxygen. Sudden symptoms such as chest pain, shortness of breath, or fainting could indicate heart disease and should be reported right away. Signs such as abnormal EKG and blood tests can confirm damage to the heart.

Reproductive risks: You should not become pregnant or father a baby while on this study because the drugs in this study can affect an unborn baby. Women should not breastfeed a baby while on this study. It is important you understand that you need to use birth control while on this study. Check with your study doctor about what kind of birth control methods to use and how long to use them. Since the effects of some of these drugs may continue after you stop taking them, these instructions should be followed for at least 30 days after you stop taking study medications. When you are no longer taking the study drugs, ask your doctor when it might be safe to become pregnant or to become a new father.

For more information about risks and side effects, ask your study 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 sorafenib plus doxorubicin will be more useful against cancer compared to the commonly used sorafenib, there is no proof of this yet. We do know that the information from this study will help doctors learn more about sorafenib plus doxorubicin 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
- Taking part in another study
- Getting no treatment
- 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)
- The National Cancer Institute (NCI) and other government agencies, like the Food and Drug Administration (FDA), involved in keeping research safe for people
- Bayer/Onyx Pharmaceuticals, the makers of sorafenib

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 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.

What are the costs of taking part in this study?

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. Some health plans will not pay these costs for people taking part in studies. Check with your health plan or insurance company to find out what they will pay for. Taking part in this study may or may not cost your insurance company more than the cost of getting regular cancer treatment.

The NCI will supply the sorafenib at no charge while you take part in this study. The NCI does not cover the cost of getting the sorafenib ready and giving it to you, so you or your insurance company may have to pay for this. Even though it probably won't happen, it is possible that the manufacturer may not continue to provide the sorafenib to the NCI for some reason. If this were to occur, other possible options are:

- You might be able to get the sorafenib from the manufacturer or your pharmacy but you or your insurance company may have to pay for it.
- If there is no sorafenib available at all, no one will be able to get more and the study would close.

If a problem with getting sorafenib occurs, your study doctor will talk to you about these options.

Since the drug doxorubicin is commercially available, either you or your insurance will be billed for it.

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

For more information on clinical trials and insurance coverage, you can visit the National Cancer Institute's Web site at <http://cancer.gov/clinicaltrials/understanding/insurance-coverage>. You can print a copy of the "Clinical Trials and Insurance Coverage" information from this Web site.

Another way to get the information is to call 1-800-4-CANCER (1-800-422-6237) and ask them to send you a free copy.

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.

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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.

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 816-823-0555.

RELATED STUDIES

Please note: The following section of the informed consent form 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 a part of the main study even if you say “no” to taking part in any of these additional studies.

You are being asked to contribute some of your blood and related information for these additional studies. This can help researchers learn more about how to prevent, diagnose and treat cancer and other diseases. Please read this form carefully, and ask questions on anything you do not understand.

These additional studies include research on the genetic material you have inherited and can be passed down to your children (these are often called “genetic” studies). Other studies include changes that may have occurred after you were born and are not inherited. These may include changes that happen in your body before, during and after you receive treatment.

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 from 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.

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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.

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

Imaging companion study:

As part of the evaluation of the effectiveness of the chemotherapy treatments used in this trial, we would like to collect CT scan images that are obtained during the normal course of your therapy. CT scans, which provide measurements of the growth or shrinkage of your tumor(s), will be performed prior to study treatment and every 6 weeks during therapy.

- 1) I agree to take part in the CT imaging study described above.
 Yes No

Studies on blood:

In addition to the treatment study, the researchers would also like to collect additional samples of your blood. We would like to collect samples of blood to see if the levels of different types of proteins and/or hepatitis virus in your blood tell which patients will do better or worse after receiving sorafenib and doxorubicin or sorafenib alone. Smaller studies of these tests have shown that measuring the levels of these proteins may help predict which patients will do better or worse. In the future, this information could be used to help doctors decide how well a new drug might work for hepatocellular carcinoma.

Approximately 2 teaspoons of additional blood at the beginning of the study, 2 teaspoons of blood every three weeks for the first six cycles and then every other cycle during the study, and 2 teaspoons of blood at the end of treatment would be collected.

- 2) I agree that my specimen may be used for the research studies described above.
 Yes No

Genetic studies on blood cells:

Researchers at special CALGB laboratories wish to determine whether there is a relationship between genes and response to treatment and treatment outcomes, and side effects. No research studies will be performed that can knowingly reveal genetic information that might be of risk to you or to your family.

In order to study genes, the 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.

New scientific tools will now allow researchers to look at your whole DNA, not just one part or one gene. This kind of research can provide information to researchers about the development of cancer and response to treatment. It can also provide information about a variety of other conditions and diseases, including heart disease, diabetes and Alzheimer’s disease.

Because the information gained in these genetic studies can be very useful to the research community, the National Institutes of Health (NIH) has requested that these data be placed in a central database housed at the NIH. The goal is to speed up the process for discovery of new treatments, prevention and diagnosis of disease. Researchers must get approval from the NIH before they can access the research results and health-related information from your specimen.

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All information will be coded with a unique number. Researchers will not have access to your identity; they will only see coded information.

Participation in this additional research study would require an additional sample of blood (about 2 teaspoons).

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. Below are some of the steps we have taken to protect your privacy and confidentiality:

- 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 name and special identification number will be stored together 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. 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 the study.
- The Cancer and Leukemia Group B has received a Certificate of Confidentiality from the federal government, which will help us to protect your privacy. More information about the Certificate can be found in the paragraph "Will my medical information be kept private?"
- A federal law (Genetic Information Non-Discrimination Act, GINA) will help lower the risk from health insurance or employment discrimination on the basis of genetic information. The federal law does not include other types of misuse by life insurance, long-term care or disability insurance. If you want to learn more about the GINA Law, which will go into effect in 2009, you can find information about it on the internet or ask the study staff. In addition to the federal law, some states have laws that also help protect against genetic discrimination.

While we believe that the risks to you and your family are very low, we cannot tell you exactly what all of the risks are from taking part in genetic research studies. Your privacy and confidentiality will be protected to the fullest extent possible.

You have the right to receive the planned therapy on this study without participating in the proposed research study on your blood sample. Please read the sentence below and think about

your choice. After reading the sentence, please mark your choice, sign your name, and provide the current date. **No matter what you decide to do, it will not affect your care.**

- 3) I agree that my blood specimen may be used for the genetic research studies described above.

_____ Yes _____ No

Storage of your blood:

The researchers would also like to store any portion of the blood that is not used up by the related studies described above. These samples may be stored indefinitely. You can still take part in the treatment study, and the research studies described above without giving your consent for your samples to be stored.

It is not possible for you or the CALGB to know what studies of cancer may be appropriate in the future. We ask that you give permission in advance for other studies to be performed using the blood without being re-contacted to give permission for each test.

- 4) My blood may be kept for future unknown use in research to learn about, prevent, treat, or cure cancer.

_____ Yes _____ No

- 5) My blood may be kept for research about other health problems (for example: causes of diabetes, Alzheimer's disease and heart disease).

_____ Yes _____ No

- 6) Someone may contact me in the future to ask me to take part in more research.

_____ Yes _____ No

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

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.

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

Signature

I have been given a copy 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 _____