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## CONSENT FORM

**CIRB E2805: ASSURE: Adjuvant Sorafenib or Sunitinib for Unfavorable Renal Carcinoma.**

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## **CIRB E2805: ASSURE: Adjuvant Sorafenib or Sunitinib for Unfavorable Renal Carcinoma**

You are being asked to take part in this study because you have kidney cancer which has just been removed or is about to be removed and is thought to be at high risk of recurrence.

### **WHY IS THIS STUDY BEING DONE?**

This research is being done because there is no effective therapy to prevent recurrence of kidney cancer.

Sunitinib and sorafenib are drugs which have been approved by the FDA for use in advanced kidney cancer, but not in the setting of kidney cancer which has been completely removed.

The purpose of this study is to determine if either sunitinib or sorafenib can prevent recurrence of your kidney cancer and to compare the effects (both good and bad) of the sunitinib and the sorafenib with placebo (pills that look like the study drugs, but are inactive or do not contain the drug) on you and your kidney cancer to see which is better. It is not known whether the benefits of taking either sunitinib or sorafenib will outweigh the risks.

### **HOW MANY PEOPLE WILL TAKE PART IN THE STUDY?**

About 1923 people will take part in this study.

### **WHAT IS INVOLVED IN THIS STUDY?**

**If you agree to take part in this study, you will take sorafenib or a matching placebo by mouth every day for 6 weeks and sunitinib or a matching placebo by mouth every day for 4 weeks followed by a 2 week break. This regimen is called a cycle. You will follow 9 cycles of this treatment for approximately one year. During this time, you will undergo routine physical exams, blood tests, CT scans, and heart scans to make sure you are tolerating the study medication and to make sure your kidney cancer has not returned. After you have completed approximately one year of therapy, you will stop taking the study medications but will continue to be followed for possible side effects from the therapy and to detect possible recurrence of your cancer. You will continue to be followed for 10 years.**

### **BEFORE YOU BEGIN THE STUDY**

You will need to have the following exams, tests, and procedures to find out if you can be in the study. Most of these exams, tests or procedures 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.

- Physical examination
- Blood tests (1 tablespoon)
- Pregnancy test, if you are a female of childbearing potential.
- [Deleted in Addendum #6]
- MUGA scan or Echocardiogram if MUGA scan not available
- CT and/or MRI scans
- Have blood pressure checked
- Have an EKG performed
- You will also fill out two “Quality of Life” forms. We want to know your view of how your life has been affected by this cancer and its treatment. These “Quality of Life” forms look at how you are feeling physically and emotionally during your cancer treatment. They also look at how you are able to carry out your day-to-day activities. This information will help doctors better understand how patients feel during treatments and what effects the medicines are having. All of this information will be completely confidential. In the future, this information may help patients and doctors as they decide which medicines to use to treat cancer. If any questions make you feel uncomfortable, you may skip those questions and not give an answer.

### **DURING THE STUDY**

**If you take part in this study, you will have the following test and procedures (some of these tests would be done even if you did not take part in the study):**

- A physical examination by your study doctor every 6 weeks (every cycle of treatment).
- Blood pressure monitoring every week for the first 6 weeks and then every 6 weeks (every cycle of treatment).
- Laboratory tests every 6 weeks (every cycle of treatment) to ensure that bone marrow, remaining kidney, liver, and other vital organs remain healthy. These tests measure the levels of various enzymes, proteins and other compounds found in your blood.
- A pill count with your study coordinator every 6 weeks (every cycle of treatment).
- Pregnancy test, if you are a female of childbearing potential.
- CT scan of the chest, abdomen and pelvis with IV and oral contrast every 4.5 months (every 3 cycles of treatment). Equivalent scans may be substituted in certain circumstances. These would consist of a CT scan of the chest without any contrast and MRI scans of the abdomen and pelvis with contrast.
- While you are on treatment, a MUGA (Multi Gated Acquisition) scan will be performed 3 months, 6 months, and 12 months from the day you start cycle 1 study medication. If you stop treatment before you get the 12 month scan, a scan will be performed at the end of treatment instead. A MUGA scan will also be performed at any time you develop

certain symptoms that may indicate problems with your heart (such as shortness of breath or swelling in the ankles). A MUGA scan is used to evaluate how your heart is working. If your test scan is abnormal, you will have another one 3 months later. Your study doctor may also recommend further evaluation or treatment if it is deemed necessary based on the scan results or your overall condition.

- Some of these tests would be done even if you do not take part in the study
- If you agree to take part in this study before you have your surgery for removal of your kidney cancer, you will be asked to allow some of your kidney tumor to be collected and sent to ECOG for special studies to learn more about risk of recurrence.
- If you agree to participate in this study after you have already had surgery to remove your kidney tumor, then slides and paraffin blocks of your kidney cancer will be sent to ECOG to confirm what type of kidney cancer you have as well as possibly perform other tests on the tissue to better determine likelihood for recurrence.
- You will also fill out two "Quality of Life" forms at two occasions during treatment: approximately 10 weeks from starting treatment and approximately 22 weeks from starting treatment. The QOL forms will take about 30 minutes to complete. You will be given these forms before you begin study treatment and then you will fill them out at home 4 weeks after the start of cycle 2 and cycle 4. If you lose these forms, please notify your doctor's office and the forms can be mailed, e-mailed or faxed to you. When you have finished filling out these forms, you will mail them to your doctor's office in a pre-stamped envelope. If you need help filling out these forms, please contact your study doctor's office for help.

You will be "randomized" into one of the three study groups described below. This means that you will be placed into one of the study groups by chance using a computer program. There is an equal possibility that you will be placed into any of the three study groups, and neither you nor your study doctor can choose the group you will be in. Due to the fact that this is a blinded study, you and your study doctor will also not know to which of the three groups you are assigned at randomization. This information will not be provided to you or your doctor even after completing treatment, unless your cancer returns.

Depending on which study group you are placed in, you will take one of the following combinations:

- Sorafenib and placebo capsules that look like sunitinib
- OR sunitinib and placebo tablets that look like sorafenib
- OR a combination of placebo capsules and tablets that look like sunitinib and sorafenib (but contain no active drug) for about one year

### **Central Review**

While you are on study, samples of your tissue may be sent to a central laboratory to be examined by a central reviewer. This review is to confirm the results of the local laboratory review.

### STUDY CHART

You will receive a kit containing one bottle of sunitinib or matching placebo capsules, one bottle of sorafenib or matching placebo tablets, and a "Patient Medication Calendar." To help you identify your two drugs, the sorafenib bottle will have a blue label and the sorafenib column on the "Patient Medication Calendar" will be colored blue. In addition, the sunitinib bottle will have an orange label and the sunitinib column on the "Patient Medication Calendar" will be colored orange. Each kit will contain enough study medication for 6 weeks (42 days). This 6 week period of time is called a "cycle" and you will complete a maximum of 9 of these 6 week cycles (a total of 54 weeks or slightly more than 1 year) for this protocol.

During each cycle you will take 2 tablets from the sorafenib bottle (the bottle with the blue label) once daily for each of the 42 days of the cycle, unless your study doctor tells you otherwise. You will also take 3 capsules from the sunitinib bottle (the bottle with the orange label) every day for the first 28 days of the cycle, unless your study doctor tells you otherwise. If you have not experienced any moderate or higher side effects while taking study medication, you will begin taking a higher dose for both medications at the beginning of either your second or third cycle. Also, your doctor can consider increasing your dose if you have ONLY moderate side effects but are feeling well. While on the higher dose you will take 2 tablets from the sorafenib bottle each morning and 2 tablets in the evening for each of the 42 days of the cycle, unless your study doctor tells you otherwise. You will also take 4 capsules from the sunitinib bottle every day for the first 28 days of the cycle, unless your study doctor tells you otherwise. For the last 14 days of the cycle, you will not take any capsules from the sunitinib bottle, although you will continue to take tablets from the sorafenib bottle. These last 14 days are marked out with an "XXXXX" on the "Patient Medication Calendar" to help you remember to stop taking the capsules for those days. Each time you take any of your study medications, you should drink a full 8 ounce glass of water. The pills may be taken without regards to meals. However, if taken with a meal, the meal should be moderate to low-fat.

The chart below shows you what will happen during Cycle 1 and future treatment cycles. The left-hand column shows the day in the cycle and the right-hand column tells you what to do on that day.

**PRE-TREATMENT & CYCLE 1**

DAY	WHAT YOU DO
Up to 4 weeks before being randomized	<ul style="list-style-type: none"> <li>• Have physical exam at your study doctor's office.</li> <li>• Get routine blood tests.</li> <li>• Have blood pressure checked.</li> <li>• Get MUGA scan.</li> <li>• Have CT and/or MRI scans performed.</li> <li>• Have an EKG performed.</li> <li>• Take pregnancy test (if you are a woman of childbearing potential.)</li> <li>• Have bone scan performed if you have bone pain or a rising level of alkaline phosphatase.</li> </ul>
Within 2 weeks before starting study medication	<ul style="list-style-type: none"> <li>• Complete and return the two "Quality of Life" Forms at your study doctor's office. If you cannot complete these forms at your study doctor's office, you must complete them at home or over the telephone with your study doctor's office. These forms must then be returned to your study doctor's office by mail in a pre-stamped envelope or in person at your office visit on Day 1 of Cycle 1. If you need help filling out these forms, please contact your study doctor's office for help.</li> <li>• Receive the "Quality of Life" Forms that you will need to fill out during Cycles 2 and 4.</li> </ul>
Day 1	<ul style="list-style-type: none"> <li>• Begin taking study medications as shown on your "Patient Medication Calendar." Record the day of the week, date, number of tablets or capsules taken and time taken.</li> <li>• Have your blood pressure checked. If blood pressure recording is not done in your study doctor's office, you will be required to phone in your blood pressure reading. Results must be phoned in to your study doctor's office within 24 hours of when the blood pressure recording occurred.</li> </ul>
Days 2-42	<ul style="list-style-type: none"> <li>• Keep taking study medications as shown on your "Patient Medication Calendar." Record the day of the week, date, number of tablets or capsules taken, and time taken. Call your study doctor at _____ [<i>insert phone number</i>] if you do not know what to do.</li> </ul>
Day 8, 15, 22, 29 & 36	<ul style="list-style-type: none"> <li>• Have your blood pressure checked. If blood pressure recording is not done in your study doctor's office, you will be required to phone in your blood pressure reading. Results must be phoned in to your study doctor's office within 24 hours of when the blood pressure recording occurred.</li> </ul>

**CYCLES 2 THROUGH 9**

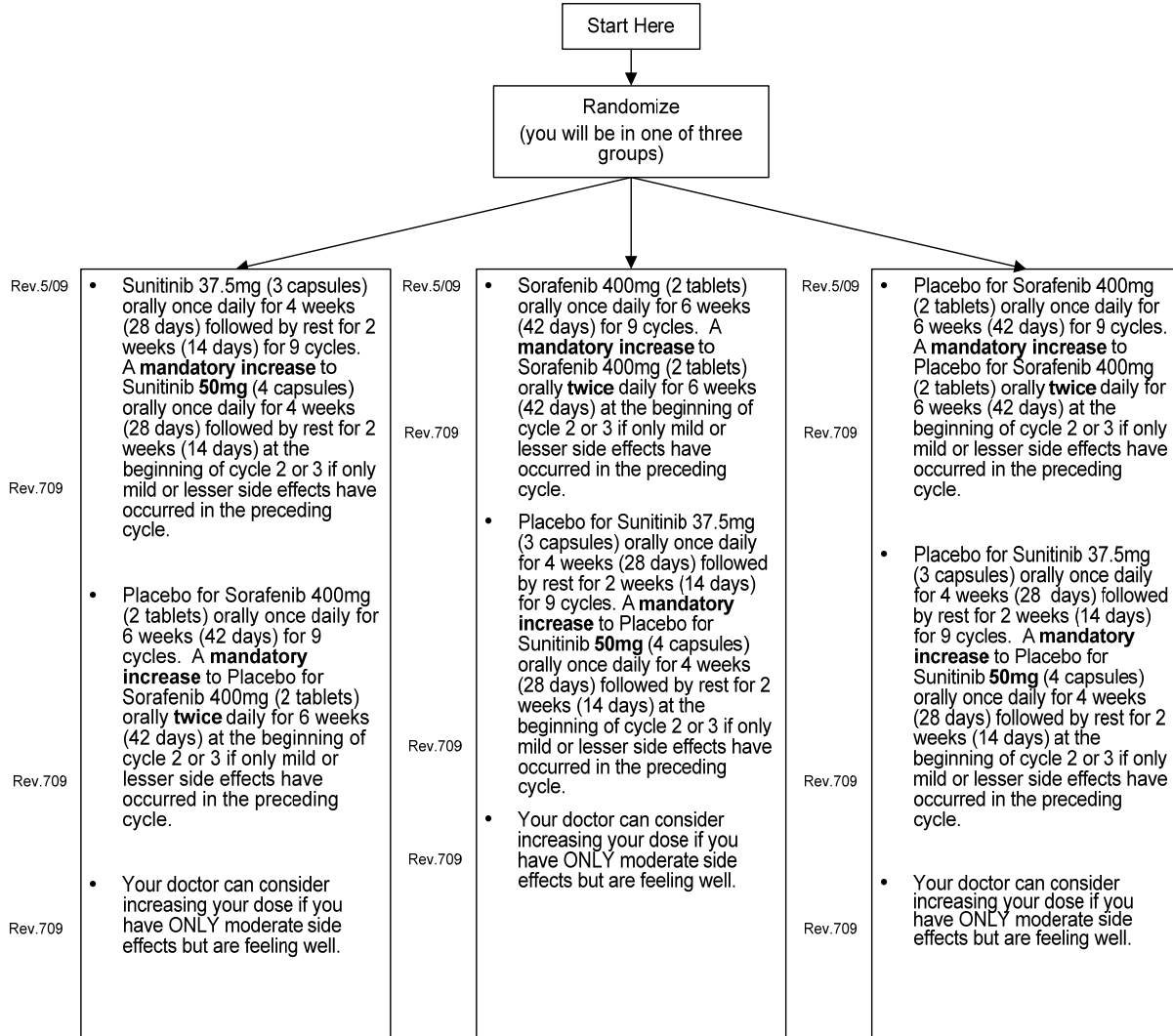
DAY	WHAT YOU DO
Day 1	<ul style="list-style-type: none"> <li>• Return to your study doctor's office at <i>[insert appointment time]</i> for all necessary tests and to begin the current cycle.</li> <li>• Return the completed pill calendar and the pill bottles containing any unused pills from the previous cycle.</li> <li>• Get routine blood tests and physical exam every cycle (more if your study doctor tells you to).</li> <li>• Have blood pressure checked.</li> <li>• Get routine CT scans and/or MRIs every 3 cycles (more if your study doctor tells you to).</li> <li>• Start new pills.</li> <li>• Get MUGA scan at 3 months, 6 months, and 12 months from the day you started Cycle 1 study medication or at the end of treatment (if you stop treatment early), and in cases where you have symptoms. If the last scan is abnormal, it will be repeated 3 months later.</li> <li>• Have bone scan performed if you have bone pain or a rising level of alkaline phosphatase.</li> </ul>
Days 2-42	<ul style="list-style-type: none"> <li>• Keep taking study medications as shown on your "Patient Medication Calendar". Record the day of the week, date, number of tablets or capsules taken, and time taken. Call your study doctor at the number listed on the cover page if you do not know what to do.</li> <li>• Complete the two "Quality of Life" Forms on Day 28 of Cycle 2 and Day 28 of cycle 4. If you stop treatment early, you will complete these forms at week 10 and week 22 after the day you started Cycle 1 study medication. If you lose these forms, please notify your doctor's office and the forms can be mailed, e-mailed or faxed to you. Mail the completed forms to your study doctor's office in the pre-stamped envelope provided to you. If you need help filling out these forms, please contact your study doctor's office for help.</li> </ul>

**FOLLOW UP**

LENGTH OF TIME	WHAT WILL HAPPEN
For 10 years from date of registration	<ul style="list-style-type: none"> <li>• All patients, including those who stop protocol treatment, will be followed for relapse and for length of survival.</li> </ul>
Every 6 months until you have been on the study for 2 years, then every year after that (until disease recurrence)	<ul style="list-style-type: none"> <li>• Return to your study doctor's office at <i>[insert appointment time]</i> for all necessary tests.</li> <li>• Get routine CT and/or MRI scans.</li> <li>• Have bone scan performed if you have bone pain or a rising level of alkaline phosphatase.</li> <li>• Get routine blood tests and physical Exam.</li> </ul>
At disease recurrence	<ul style="list-style-type: none"> <li>• Have biopsy to confirm disease recurrence</li> </ul>

### STUDY PLAN

Another way to find out what will happen to you during the study is to read the chart below. Start reading at the top and read down the list, following the lines and arrows.



## **HOW LONG WILL I BE IN THE STUDY?**

You will receive study medication for 54 weeks (about 1 year). You will continue to be followed for an additional 9 years for a total study duration of 10 years to look at the long-term effects of the study. During this follow-up period, you will be assessed for length of survival every 3 months, every 6 months or every 12 months depending on the length of time that has passed from entering the study. You will also be assessed on an annual basis for relapse.

Your study doctor may decide to take you off this study if you experience severe side effects from the drugs or your kidney cancer returns.

If you experience any problems possibly related to treatment those will also be reported.

You may stop participating at any time. However, if you decide to stop participating in the study, we encourage you to talk to your study doctor first.

## **WHAT ARE THE RISKS OF THE STUDY?**

While on the study, you are at risk for the following side effects. The drugs sunitinib and sorafenib may cause some, all, or none of the side effects listed. You should discuss these with your study doctor. There may also be other side effects that we cannot predict. Other drugs will be given to make side effects less serious and less uncomfortable. Many side effects go away shortly after the sunitinib or sorafenib is stopped, but in some cases side effects can be serious, long-lasting, permanent, or life-threatening. Death is rare, but possible.

Your study doctor will check you closely to see if any of these side effects are occurring and routine blood tests will be done to monitor the effects of treatment.

### **Risks and side effects related to the sorafenib and/or sunitinib include those which are:**

#### **Likely:**

- Belly pain
- Diarrhea
- Nausea or the urge to vomit
- Fatigue or tiredness
- Liver damage
- Jaundice
- Kidney damage
- Increased INR (measure of the ability of the blood to clot properly) which increases the risk of bleeding
- Inflammation of the pancreas that can cause abdominal pain, and difficulty digesting fats
- Lowered platelet count that might interfere with clotting (may make you more likely to bruise or bleed)
- Weight loss
- Loss of appetite
- Increased blood sugar level

- Decreased levels of a blood protein called albumin that could cause swelling
- Decreased blood level of calcium
- Decreased blood level of sodium
- Hair loss
- Swelling and redness of the skin on the palms of the hands and soles of the feet
- Skin rash
- Taste changes
- Irritation or sores in the lining of the anus that can cause pain or bleeding
- Irritation or sores in the lining of the mouth that can cause pain
- Irritation or sores in the lining of the rectum that can cause pain or bleeding
- Irritation or sores in the lining of the small bowel that can cause pain or bleeding
- Vomiting
- Irritation or sores in the lining of the voice box that can make it hard or painful to talk
- Irritation or sores in the lining of the throat that can cause pain and make it hard to swallow

**Less Likely:**

- Lack of enough red blood cells (anemia)
- Fever associated with dangerously low levels of a type of white blood cell (neutrophils)
- Fluid collection in the abdomen
- Constipation
- Bleeding in some organ(s) of the digestive tract
- Irritation or sores in the lining of the anus
- Irritation or sores in the lining of the mouth
- Irritation or sores in the lining of the rectum
- Irritation or sores in the lining of the small bowel
- Fever
- Increased blood level of cholesterol
- Decreased blood level of carbon dioxide
- Increased blood level of calcium
- Increased blood level of potassium
- Increased blood level of sodium
- Decreased blood sugar level
- Decreased blood level of potassium
- Vomiting
- Infection
- Tests that show a problem in blood clotting
- Bone pain
- Muscle spasms

- Inflammation (swelling and redness) or degeneration of the peripheral nerves (those nerves outside of brain and spinal cord) causing numbness, tingling, burning
- Sudden or traumatic injury to the kidney
- Blood in the urine
- Bleeding in the kidney
- Presence of blood in a fallopian tube (tube between ovary to uterus [womb])
- Bleeding in the ovary
- Bleeding in the prostate
- Bleeding in the spermatic cord (a structure resembling a cord that suspends the testis within the scrotum and contains the vas deferens [the tube that carries sperm] and other vessels and nerves)
- Bleeding in the testis
- Bleeding in the uterus (womb)
- Bleeding in the vagina
- Bleeding in the respiratory tract
- Irritation or sores in the lining of the voice box that can make it hard or painful to talk
- Irritation or sores in the lining of the throat that can cause pain and make it hard to swallow
- Voice change
- Itching
- Formation of a blood clot that breaks loose and is carried by the blood stream to plug another blood vessel
- Abnormally low level of thyroid gland hormone that can cause fatigue
- Temporary loss or changes in vision
- Swelling or feeling of fullness and tightness in the abdomen (belly)
- Dry mouth
- Heartburn
- Excess passing of gas
- Irritation of the stomach lining that can cause pain, nausea and vomiting
- Mouth pain
- Chills
- Swelling of the arms and/or legs
- Chest pain
- Liver damage
- Jaundice
- Muscle damage
- Kidney damage
- Inflammation of the pancreas that can cause abdominal pain, and difficulty digesting fats
- Lowered white blood cell count (may make you more likely to get infections)
- Lowered platelet count that might interfere with clotting (may make you more likely to bruise or bleed)
- Weight loss
- Dehydration (when your body does not have as much water and fluid as it should)
- Increased blood level of uric acid, a waste material from food digestion

- Decreased levels of a blood protein called albumin that could cause swelling
- Joint pain
- Back pain
- Muscle pain
- Leg and/or arm pain
- Dizziness (or sensation of lightheadedness, unsteadiness, or giddiness)
- Headache or head pain
- Difficulty sleeping or falling asleep
- Cough
- Shortness of breath
- Nose bleed
- Hair loss
- Dry skin
- Swelling and redness of the skin on the palms of the hands and soles of the feet
- Skin rash
- Changes in hair color
- Lightening of the skin
- High blood pressure

**Rare but Serious:**

- 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.
- Heart attack caused by a blockage of a blood vessel supplying part of the heart
- Hole in a part(s) of the digestive tract
- Serious potentially life-threatening type of allergic reaction that may cause breathing difficulty, dizziness, low blood pressure, and loss of consciousness
- Bleeding in the brain
- 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)
- A disorder in which blood clots form within small blood vessels
- Decrease in heart's ability to pump blood
- Swelling of a portion of the inner eye
- Reduction in quality or strength of vision
- Gastrointestinal perforation: A tear or hole in the stomach or gut that can lead to serious complications and may require surgery to repair
- Liver failure, which may be severe and may lead to death
- Irregular heart beat
- Brain damage
- Abnormal changes in the brain that can cause a collection of symptoms including headache, confusion, seizures, and vision loss associated with MRI imaging findings (RPLS)
- Severe reaction of the skin and gut lining that may include rash and shedding or death of tissue

### **Other instructions:**

You should not take the following medications or foods within two weeks before randomization or during the period of time on this study that you are taking study medication:

- Grapefruit or grapefruit juice
- St. Johns Wort
- Certain drugs for epilepsy (phenytoin, carbamazepine or phenobarbital)
- Ketoconazole,
- Dexamethasone
- Certain drugs for heart rhythm disturbances (terfenadine, quinidine, procainamide, sotalol, probucol, bepridil, indapamide or flecainide)
- Rifampin
- Haloperidol
- Risperidone

Also, please review with your doctor all medications that you are currently taking to avoid possible drug interactions

**No side effects are expected for placebo.**

**Reproductive risks:** You should not become pregnant or father a baby while on this study because the drugs in this study can affect a fetus and cause serious birth defects. 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. Some methods might not be approved for use in this study. Some of the drugs used in the study may make you unable to have children in the future. For more information about risks and side effects, ask your study doctor. If you become pregnant while participating in this study, inform your study doctor immediately.

### **ARE THERE BENEFITS TO TAKING PART IN THE STUDY?**

If you agree to take part in this study, there may or may not be direct medical benefits to you.

The possible benefits of taking part in the study may be the same as receiving no treatment without being in the study or may decrease the likelihood that your kidney cancer returns.

We hope the information learned from this study will benefit other patients with kidney cancer in the future.

### **WHAT OTHER CHOICES DO I HAVE IF I DO NOT TAKE PART IN THIS STUDY?**

Instead of being in the study, you have this option:

No therapy at this time, with monitoring for return of your kidney cancer.

## **WILL MY MEDICAL INFORMATION BE KEPT PRIVATE?**

The Eastern Cooperative Oncology Group (ECOG) is conducting this study. ECOG is a cancer group that conducts studies for the National Cancer Institute. Your study doctor is a member of ECOG or another group that is participating in this study. To help protect your privacy, ECOG has obtained a Confidentiality Certificate from the Department of Health and Human Services (DHHS).

With this Certificate, ECOG cannot be forced (for example, by court subpoena) to disclose information that may identify you in any federal, state or local civil, criminal, administrative, legislative or other proceedings. Disclosure will be necessary, however, upon request of DHHS for audit or program evaluation purposes.

You should understand that a Confidentiality Certificate does not prevent you or a member of your family from voluntarily releasing information about you or your involvement in this research. Note, however, that if an insurer or employer learns about your participation and obtains your consent to receive research information, then ECOG may not use the Certificate of Confidentiality to withhold this information. This means that you and your family must also actively protect your privacy.

You should also understand that your study doctor and ECOG may take steps, including reporting to authorities, to prevent you from seriously harming yourself or others. Finally, the Certificate does not prevent the review of your research records under some circumstances by certain organizations for an internal program audit or evaluation. Organizations that may inspect and/or copy your research records for quality assurance and data analysis include groups such as:

- Eastern Cooperative Oncology Group (ECOG)
- National Cancer Institute (NCI)
- Food and Drug Administration (FDA)
- Other regulatory agencies and/or their designated representatives
- Drug manufacturers, and/or their representatives
- Central Laboratories, tissue banks and/or representatives
- Cancer Trials Support Unit (CTSU), a research group sponsored by the National Cancer Institute (NCI) to provide greater access to cancer trials

## **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 Division of Cancer Treatment and Diagnosis, NCI, will provide you with sorafenib or placebo tablets and sunitinib or placebo capsules free of charge for this study. Every effort will be made to ensure adequate supplies of sorafenib, sunitinib and their matching placebos for the duration of the study, free of charge to all participants. If sorafenib or sunitinib should become commercially available for this indication, there is a remote possibility that you may be asked to purchase subsequent supplies. Your study doctor will discuss this with you should this situation arise.

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 if you feel that you have been injured because of taking part in this study. You can tell the study doctor in person or call him/her at the number listed on the cover page.

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 AS A PARTICIPANT?**

Taking part in this study is voluntary. You may choose not to take part, or you may leave the study at any time. Leaving the study or choosing not to take part will not result in any penalty or loss of benefits to which you are entitled.

We will tell you about new information that may affect your health, welfare, or willingness to stay in this study.

A Data Safety and Monitoring Board, which is an independent group of experts, will be reviewing the data from this research throughout the study.

### **WHOM DO I CALL IF I HAVE QUESTIONS OR PROBLEMS?**

For questions about the study or a research-related injury, contact your study doctor at the number listed on the cover page.

For questions about your rights as a research participant, contact the MultiCare Health System Investigational Review Board which is a group of people who review the research to protect *your rights*) at 253-403-3877.

### **SCIENTIFIC STUDIES**

This study includes one or more laboratory tests that will analyze a small sample of tissue, blood, and urine. The tissue samples will be collected from the biopsy that you had at the time of your diagnosis and at recurrence and fresh tissue will also be collected if you go on the study prior to surgery. At least ten teaspoons of urine will be collected prior to surgery, at cycle 1 day 1 before treatment, month 3, month 6, and recurrence. Five to six teaspoons of blood will be collected by inserting a needle into a vein at several times throughout the study: at prior to surgery, cycle 1 day 1 before treatment, cycle 2 day 1, month 6 and at recurrence.

The tissue, blood, and urine will be sent to laboratories where tests will be performed. Researchers will perform these tests in order to understand how you and your disease respond to therapy. They hope this will help them better understand your type of cancer. The results from these tests will not be sent to you or your study doctor, and they will not be used in planning your care. These tests are only for research purposes.

### **Making Your Choice**

Please read the sentence below and think about your choice. After reading the sentence, circle "Yes" or "No." No matter what you decide to do, it will not affect your care. You can participate in the treatment part of the study without participating in the research studies. If you have any questions, please talk to your study doctor or nurse, or call our research review board at 253-403-3877.

I agree to participate in the scientific laboratory tests that are being done as part of this study
<b>Yes    No</b>

## **PHARMACOGENETIC AND PHARMACOKINETIC LABORATORY STUDIES**

When a patient receives a treatment for cancer, how effective the treatment may be depends on how the drugs act in both normal and cancer tissue. People differ in how their bodies breakdown and absorb drugs. Side effects are often different between patients. Different cancers also may respond differently to the same drug. It is important to understand the differences between people and cancers so that patients can be treated with the most effective treatment with the fewest number of side effects.

Pharmacogenetics is the study of genetic differences (which may be inheritable) that effect response to drugs. Specimens for these types of studies will be collected once or twice. Pharmacokinetics is the study of the processes by which a drug is absorbed, distributed, metabolized (broken down or changed) and eliminated by the body. Pharmacokinetic studies require specimens to be taken several times during, and perhaps after, the treatment.

The purpose of the laboratory studies described below is to investigate how sorafenib affects your cancer and how your body breaks down this drug. Patients with different types of cancers (bladder cancer, gastric cancer, lymphoma, lung cancer, melanoma, and renal cancer) and who are being treated with sorafenib or placebo are being asked to participate in these studies.

### **PHARMACOGENETIC STUDIES**

The studies will look at differences in certain proteins and genes (DNA) that are known to be affected by or involved in processing sorafenib/placebo. Also, some studies will be a general search to look for other markers or genes that may predict response to sorafenib/placebo. If you agree to participate in these studies, two tubes of blood (1-2 tablespoons) will be collected (usually before you start treatment, but may be collected anytime). The samples of your tumor tissue, if available, will also be used in these studies. An additional biopsy is not necessary.

There are some risks from participating in genetic research. Your genetic information is unique to you, but you do share some genetic information with your family members. Although rare, there are examples where health insurers or employers have denied insurance or employment based on results from genetic testing. Many states currently have laws to protect against genetic discrimination by employers or insurance companies. Currently there is no federal law that prohibits such misuse or discrimination.

How we will address these risks: We have several safeguards in place to prevent misuse of research results by any third party including insurers or employers: your research results will not be sent to you or your doctor and will not be placed in your medical record; insurers or employers will not be authorized to view any research records; and all information will be coded. As stated before, we also have a Certificate of Confidentiality from the US government, which protects your information from forced disclosure by civil, criminal, administrative, legislative or other proceeding. We believe that the risks to you and your family are very low.

I agree to participate in the protein and DNA studies that are being done as part of this treatment trial. *(If you do not want your specimens used for genetic research, answer "No")*

**Yes    No**

### **PHARMACOKINETIC STUDIES**

*[LIMITED INSTITUTION (centrifuge and -70°C freezer (preferred) available)]*

This study also includes additional laboratory tests that will analyze small samples of blood collected before you begin treatment and at various times during your treatment. 2-3 extra tubes of blood, approximately 2 tablespoons, will be collected each time using a needle inserted into the vein. The blood will be collected just before you take sorafenib/placebo for the first time, one hour after your first dose of sorafenib/placebo, and before you take your first daily dose of sorafenib on days 8, and 15, and before your treatment on cycles 2 and 3. Researchers will perform these tests in order to monitor the blood level of the drug to help them understand how sorafenib is absorbed and distributed in the body.

I agree to participate in the blood drug levels study that is being done as part of this treatment trial.

**Yes    No**

## **WILL ANY OF THE SAMPLES (E.G., TISSUE) TAKEN FROM ME BE USED FOR OTHER RESEARCH STUDIES?**

### **About Using Tissue for Research**

Biological samples like tissue, blood and urine are often referred to as “specimens.” If you participate in the laboratory studies and central review associated with this protocol, some of the specimens obtained will be sent to central laboratories for analysis.

We would like to keep some of the tissue, blood and urine that may be left over for future research. If you agree, this tissue, blood and urine will be kept and may be used in research to learn more about cancer and other diseases. This tissue, blood and urine will be given only to researchers approved by the Eastern Cooperative Oncology Group (ECOG). Any research done on the tissue, blood and urine also must be approved by the researcher’s Institutional Review Board.

Your tissue, blood and urine may be helpful for research, whether you do or do not have cancer. The research that may be done with your tissue, blood and urine will probably not help you. It might help people who have cancer and other diseases in the future.

Reports about the research done with your tissue, blood and urine will not be given to you or to your study doctor. These reports will not be put into your health record. The research will not have an effect on your care.

### **Things to Think About**

The choice to let us keep the leftover tissue, blood and urine for future research is up to you. No matter what you decide to do, it will not affect your care, and you may still take part in the Eastern Cooperative Oncology Group study.

If you decide now that your tissue, blood and urine can be kept for research, you can change your mind at any time. Just contact your study doctor and let him or her know that you do not want us to use your tissue. Then the tissue, blood and urine will no longer be used for research.

In the future, people who do research may need to know more about your health. When the Eastern Cooperative Oncology Group gives them reports about your health, it will not give them your name.

Sometimes tissue, blood and urine used for genetic research (about disease that are passed on in families). Even if your tissue, blood and urine are used for this kind of research, the results will not be put into your health records.

Your tissue, blood and urine will be used only for research, and it will not be sold. You will not be paid for allowing your leftover tissue, blood and urine to be used in research, even though the research done with your tissue, blood and urine may help to develop new products in the future. Similarly, there will be no cost to you for any tissue, blood and urine collected and stored by the Eastern Cooperative Oncology Group.

It is possible that, at some time in the future, as part of deciding on which therapy to give you, a new test might become available that could be done on some of the tissue, blood and urine that is now thought of as “leftover.” This situation is unusual, but it could happen. In order to see that not all of this leftover tissue, blood and urine is used up, the Eastern Cooperative Oncology Group will take care to see that some of your cancer tissue, blood and urine is stored for 10 years so it is available if you or your study doctors should need it.

This will depend upon the amount of leftover tissue, blood and urine that is submitted for this study. There may not be any leftover tissue, blood and urine to store.

#### **Benefits**

The benefits of research using tissue, blood and urine include learning more about what causes cancer and other diseases, how to prevent them, how to treat them, and how to cure them.

#### **Risks**

There are very few risks to you. The greatest risk is the release of information from your health records. The Eastern Cooperative Oncology Group will protect your records so that your name will be kept private. The chance that this information will be given to someone else is very small.

**There can be a risk to you if your samples or information are improperly shared or used.** The chance of this happening is very small. We have many protections in place to lower this risk. See the section, “How will the information related to your specimens be protected?”

**There can be a risk in knowing genetic information.** While we believe that the risks to you and your family are very low, we are not able to know all of the risks from taking part in genetic research studies. Your privacy will be protected to the fullest extent possible.

Certain health concerns that affect you and your blood relatives might be found as inherited traits are studied. Even though your genes are unique, you share some of the same genes with your blood relatives. While very rare, information could be misused by employers, insurance companies, and others. For example, life insurance companies may charge a higher rate based on this information.

There is a national effort to share genetic testing results and related information among researchers. If this type of testing is done with your specimens in the future, coded data would be sent to a central database kept by the NCI. The NCI would determine which researchers may look in this database.

Some states have laws to protect against genetic discrimination [*list appropriate state information if your state has such laws*]. A new federal law called GINA, or the Genetic Information Non-Discrimination Act should help lower the risk from unfair health insurance or employment policies. The law does not include other types of misuse by life insurance or long term care insurance. To learn more about the GINA Law, please check the Internet or ask the study staff.

## **HOW WILL INFORMATION RELATED TO YOUR SPECIMENS BE PROTECTED?**

We have many ways to protect the information related to your specimens:

1. Your specimens and information receive a unique code. Researchers only receive coded specimens and information, and will not be able to see the key that links the code to you. Only approved people in ECOG can match you to the code on your specimens and related information.
2. Strict security safeguards are in place to reduce the chance of misuse or unplanned release of information. Steps we take include password protected access to databases and keeping freezers that contain specimens in a locked area.
3. Before specimens are given to researchers, studies are reviewed for the quality of the science and for patient protection. To make sure the research follows the rules of ECOG and state or federal laws, records from research studies can be reviewed by ECOG, by the sponsor, and by government agencies.
4. If research results are published, your name or other personal information will not be given.
5. ECOG also has a Certificate of Confidentiality from the U.S. Department of Health and Human Services. What this means is that ECOG cannot be forced to disclose your identity to any third party. It is possible that for some criminal proceedings, the Certificate of Confidentiality could be over-ridden.

### **Making Your Choice**

The choice to take part is up to you. If you decide not to let us store and use your specimens, you will still receive medical care. You are able to take part in other research studies.

To learn more, ask the study staff or visit <http://www.cancer.gov>.

If you decide that your samples can be kept, you may change your mind at any time. Contact the study staff at your hospital and let them know that you do not want your samples and related information used for research [*Insert contact number*]. Then, any samples and information that remain in the bank will no longer be used. Samples or information that have already been given to or used by researchers cannot be returned or destroyed.

Read each sentence below and circle "Yes" or "No." For questions about this study or if you have an injury while samples are collected, please talk to your study staff. For questions about your rights as a person taking part in a study, contact the Institutional Review Board at [*insert IRB contact information*].

Thank you for considering whether to allow your samples to be banked for future research.

<p><b>My specimens may be kept for use in research to learn about, prevent, treat, or cure cancer. This may also include research on inherited traits.</b></p> <p style="text-align: center;">Yes    No</p>
<p><b>My specimens may be kept for use in research about other health problems (for example, causes of diabetes, Alzheimer's disease, and heart disease). This may also include research on inherited traits.</b></p> <p style="text-align: center;">Yes    No</p>
<p><b>My study doctor (or someone from the Eastern Cooperative Oncology Group) may contact me in the future to ask me to take part in more research.</b></p> <p style="text-align: center;">Yes    No</p>

### 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/](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.

### SIGNATURE

I have been given a copy of all 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.

Signature of Patient

or Patient's Legal Representative: \_\_\_\_\_ Date: \_\_\_\_\_

Printed Name of Legal Representative (if any): \_\_\_\_\_

Representative's Authority to Act for Patient: \_\_\_\_\_

Signature of Person

Obtaining Permission: \_\_\_\_\_ Date: \_\_\_\_\_

Printed Name of Person Obtaining Permission: \_\_\_\_\_

**EASTERN COOPERATIVE ONCOLOGY GROUP (ECOG)  
Authorization (Permission) to Use or Disclose (Release)  
Identifiable Health Information for Research**

**Participant's Name:** \_\_\_\_\_

**Birth Date:** \_\_\_\_\_

**1. What is the purpose of this form?**

The Eastern Cooperative Oncology Group (ECOG), is an organization that does research to learn about the causes of cancer, and how to prevent and treat cancer. Researchers would like to use your health information for research. This information may include data that identifies you. Please carefully review the information below. If you agree that researchers can use your personal health information, you must sign and date this form to give them your permission.

**2. What personal health information do the researchers want to use?**

The researchers want to copy and use the portions of your medical record that they will need for their research. If you enter an ECOG research study, information that will be used and/or released may include the following:

- the history and diagnosis of your disease;
- specific information about the treatments you received, including previous treatment(s) you may have had;
- information about other medical conditions that may affect your treatment;
- medical data, including laboratory test results, tumor measurements, CT scans, MRIs, x-rays, and pathology results;
- information on side effects (adverse events) you may experience, and how these were treated;
- long-term information about your general health status and the status of your disease;
- data that may be related to tissue and/or blood samples that may be collected from you; and
- numbers or codes that will identify you, such as your social security number and medical record number.

You may request a blank copy of the ECOG data forms from the study doctor or his/her research staff to learn what information will be shared.

**3. Why do the researchers want my personal health information?**

The Northwest CCOP will collect your health information and share it with the ECOG Biostatistical Center and the ECOG Operations Center if you enter a cooperative group research study. The ECOG centers will use your information in their cancer research study, **E2805 - A Randomized, Double-Blind Phase III Trial of Adjuvant Sunitinib versus Sorafenib versus Placebo in Patients with Resected Renal Cell Carcinoma**. The purpose of this study is to determine if either Sunitinib or Sorafenib can prevent recurrence of your kidney cancer and to compare the effects (both good and bad) of the Sunitinib and the Sorafenib with Placebo (inactive agent) on you and your kidney cancer to see which is better.

**4. *Who will be able to use my personal health information?***

The Northwest CCOP will use your health information for research. As part of this research, they may give your information to the following groups taking part in the research. The Northwest CCOP may also permit the following groups to come in to review your original records that are kept by the Northwest CCOP so that they can monitor their research study:

- the ECOG Operations Center;
- the ECOG Biostatistical Center;
- the Cancer Trials Support Unit (CTSU) or designees, a research group sponsored by the National Cancer Institute that supports the research of ECOG;
- Public Health agencies and other government agencies (including non-U.S.) as authorized or required by law;
- other people or organizations assisting with ECOG research efforts. This may include drug manufacturers, drug companies that may provide partial support for the study, drug distributors, and/or their designees (Pfizer, Bayer Corp./Onyx Pharmaceuticals); and
- central laboratories, central review centers, and central reviewers. The central laboratories and review agencies may also give your health information to those groups listed in the bullets above.

**5. *How will information about me be kept private?***

ECOG will keep all patient information private to the extent possible, even though ECOG is not required to follow this federal privacy rule. Only researchers working with ECOG or authorized by ECOG will have access to your information.

ECOG will not release personal health information about you to others except as authorized or required by law. However, once your information is given to other organizations that are not required to follow federal privacy laws, we cannot assure that the information will remain protected.

**6. *What happens if I do not sign this permission form?***

If you do not sign this permission form, you will not be able to take part in the research study for which you are being considered.

**7. *If I sign this form, will I automatically be entered into the research study?***

No, you cannot be entered into any research study without further discussion and separate consent. After discussion, you may decide to take part in the research study. At that time, you will be asked to sign a specific research consent form.

**8. *What happens if I want to withdraw my permission?***

You can change your mind at any time and withdraw your permission to allow your personal health information to be used in the research. If this happens, you must withdraw your permission in writing. Beginning on the date you withdraw your permission, no new personal health information will be used for research. However, researchers may continue to use the health information that was provided before you withdrew your permission.

If you sign this form and enter the research study, but later change your mind and withdraw your permission, you will be removed from the research study at that time.

To withdraw your permission, please contact the person below. He/she will make sure your written request to withdraw your permission is processed correctly.

Karyn Hart, RHIT, CCRP  
Program Coordinator  
Northwest CCOP  
315 Martin Luther King Jr., Way  
Tacoma, WA 98405  
(253) 403-1461

**9. How long will this permission last?**

If you agree by signing this form that researchers can use your personal health information, this permission has no expiration date. However, as stated above, you can change your mind and withdraw your permission at any time.

**10. What are my rights regarding access to my personal health information?**

You have the right to refuse to sign this permission form. You have the right to review and/or copy records of your personal health information kept by **the Northwest CCOP**. You do not have the right to review and/or copy records kept by ECOG or other researchers associated with the research study.

**Signatures**

I agree that my personal health information may be used for the research purposes described in this form.

**Signature of Patient**  
**or Patient's Legal Representative:** \_\_\_\_\_ **Date:** \_\_\_\_\_

**Printed Name of Legal Representative (if any):** \_\_\_\_\_

**Representative's Authority to Act for Patient:** \_\_\_\_\_

**Signature of Person Obtaining Permission:** \_\_\_\_\_ **Date:** \_\_\_\_\_

**Printed Name of Person Obtaining Permission:** \_\_\_\_\_