Testing the Addition of the Drug Nivolumab Before and After Surgery for Renal Cell Cancer

Official Study Title for Internet Search on http://www.ClinicalTrials.gov/: EA8143: A Phase 3 RandOmized Study Comparing PERioperative Nivolumab vs. Observation in Patients with Renal Cell Carcinoma Undergoing Nephrectomy (PROSPER RCC)

What is the usual approach to my type of kidney cancer?

You are being asked to take part in this research study because you have cancer in your kidney, which is planned to be removed by a surgeon. The standard treatment for your disease is to remove the kidney or part of the kidney that contains the cancer by surgery. You are then monitored after surgery with imaging scans and exams to watch for any possible signs of recurrence (close observation). As of November 2017, the FDA also approved the use of sunitinib malate (Sutent®) to treat some patients with high risk types of kidney cancer after surgery even if no signs of cancer on imaging. High risk is defined as stage 3 or 4 clear cell kidney cancer that was fully removed by surgery. The FDA decision was based on two big randomized studies that evaluated giving patients sunitinib after their kidney was removed. One large study did not observe any clinical benefits compared to placebo, but a second smaller study showed that taking one year of sunitinib after surgery could delay the time to the cancer returning by over 1 year in some patients. However, sunitinib has not been proven to increase overall survival and can potentially decrease quality of life during that year due to side effects of the drug. Choosing close observation or one year of sunitinib instead of this trial are options that you and your doctor(s) should discuss so that you can make a fully informed decision that is best for you.

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

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

- You may choose one of the approaches described above
- You may choose to take part in a different research study, if one is available
- Or you may choose not to be treated for your cancer and only receive supportive care to relieve symptoms

Why is this study being done?

The purpose of this study is to compare any good and bad effects of using nivolumab (also known as OPDIVO®), before and after the kidney cancer surgery to using the usual approach of surgically removing the kidney cancer followed by standard post-operative follow-up and monitoring. Nivolumab is a drug that may help stimulate your immune system to attack any cancer cells that may remain after surgery. The addition of nivolumab to the usual surgery

could prevent your cancer from returning but it could also cause side effects. This research study will allow researchers to find out whether this different treatment is better, the same, or worse than the usual treatment for kidney cancer that has been removed, but is at risk for coming back. The study drug, nivolumab, is already FDA-approved for patients who have kidney cancer that has spread outside of the kidney to other organs or lymph nodes. The use of nivolumab in this study is investigational (not approved by the FDA) for your early stage of cancer where we do not know for sure if the disease has spread outside of the kidney. This research study will allow the researchers to know whether this different approach is better, the same, or worse than the usual approaches. To be better, the study drug should improve how long you are able to live without any signs or symptoms of your cancer compared to the usual approaches.

There will be about 805 people taking part in this research study.

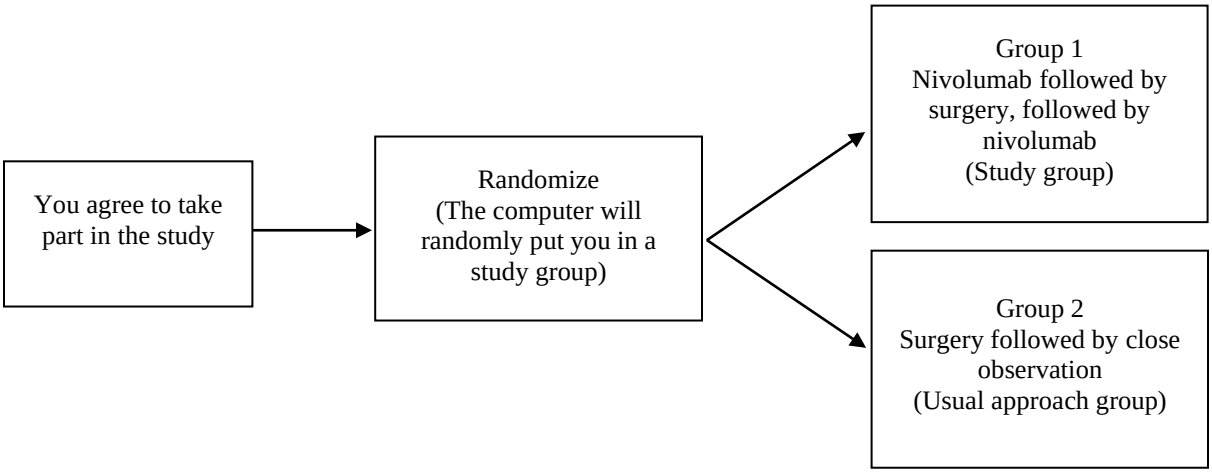
What are the study groups?

This research study has two study groups.

- If you are assigned to Group 1, you will get the study drug, nivolumab before and after surgery for a total of 10 doses. Nivolumab will be administered by an intravenous (IV) infusion over 30 minutes once before surgery. After recovering from surgery, you will receive nivolumab monthly for 9 months of treatment after surgery. Treatment will continue for a maximum of 9 months after surgery (9 doses of nivolumab) or until you have intolerable side effects, your cancer returns, or you decide to stop.
- A cycle is a term used to describe the schedule your course of treatment will follow. Each cycle is 4 weeks long.While you are on this study you will receive nivolumab on the first day of each cycle. There will be one cycle prior to your surgery. After your surgery there will be 9 cycles. There will be a total of 10 cycles.
- If you enrolled on an earlier version of the study, you may have received more frequent dosing of nivolumab. Going forward starting on the next odd cycle, you will receive the rest of your dosing on an every 4 week schedule for a total of 9 months from when you started after surgery.
- If you are assigned to Group 2, you will undergo surgery to remove the kidney cancer, followed by standard post-operative follow-up monitoring for return of the cancer with radiology scans, doctor’s visits, bloodwork and physical exams. You will not receive nivolumab and you will not receive placebo.

A computer will assign you by chance to one of the two groups in the research study. This is called randomization. This is done by chance because no one knows if one study group is better or worse than the other. You will have an equal (50%) chance of being placed in either group. You and your doctor will be informed of your group.

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



How long will I be in this study?

If you are in Group 1, you will receive 1 dose of the nivolumab prior to surgery. Then, starting at least 4 weeks after your surgery, you will receive nivolumab once every 4 weeks for 9 months. You will receive nivolumab 9 times after your surgery. If you are in Group 1 you will not receive any more than 10 doses of nivolumab unless you started in an earlier version of the study. Patients, who started in an earlier version of the study, may have received more frequent dosing of nivolumab but all will have the same amount over the course of the study. After you finish taking nivolumab, your doctor will continue to monitor you for side effects and follow your condition for up to 10 years. This follow-up will include CT or MRI scans of your chest and abdomen, blood work, and physical exams to monitor your status for up to 6 years from the day you join the study. You are being asked to return for this monitoring 20 and 40 weeks after you join the study, twice a year for years 2 – 3, and once a year for years 4 – 5. After you have been on the study for 6 years you may be asked to return for a physical exam to monitor your status as clinically indicated once a year for years 6 – 10.

If you are in Group 2, you will be monitored after surgery, which is the usual approach for this disease. Your doctor will follow your condition for up to 10 years. This follow-up will include CT or MRI scans of your chest and abdomen; blood work, and physical exams to monitor your status for up to 6 years from the day you join the study. You are being asked to return for this monitoring 20 and 40 weeks after you join the study, twice a year for years 2 – 3, and once a year for years 4 – 5. After you have been on the study for 6 years you may be asked to return for a physical exam to monitor your status as clinically indicated once a year for years 6 – 10.

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

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

Before you begin this study:

- For this trial, your disease must be confirmed by a biopsy if you are in Group 1. It is necessary to perform a biopsy in all cases of cancer before you receive a drug for the cancer. Biopsies are increasingly being performed to determine the type of kidney cancer and gain valuable information about your tumor /prior to surgery. However, if this was not done as part of your usual care, this biopsy must be done before you receive treatment on this trial. Before having this procedure, you will be asked to indicate that you understand the nature of the surgical procedure to be performed and that you give your permission for the procedure. This permission is indicated by signing a consent form provided by your study doctor.
- If you had samples of your tumor tissue collected during your surgery and/or diagnostic biopsy, these tissue samples will be sent to a central laboratory to be examined by a central pathology reviewer. This review will be done for all participants and will be used to confirm the results of the local institutional review for this study only. The results of this review will not be returned to your doctor and will not impact your care.
- Your tumor tissue will also be sent for research testing on this protocol. The study researchers would like to test your tumor for levels of PD-L1, a kind of marker found in your tumor and other tissue markers found in your tumor.
- The tests are for research purposes only and the results will not be given to you or your doctor and will not affect your care. The tissue samples are required because the research on these samples is an important part of the study.
- Your radiology images will be collected.
- You may be asked to answer questionnaires about your quality of life while on this study. The purpose is to see how the side effects of treatment might be different in the 2 groups from the patient's point of view. If you are in Group 1, you may be asked to fill out the questionnaires before you begin treatment with nivolumab. If you are in Group 2, you may be asked to fill out the questionnaires before your surgery.

  NOTE: *New patients will no longer be required to fill out the questionnaires. Since the QOL study component has reached its accrual goal, new patients are unable to participate in this QOL sub-study.*

During the study:

- At times, you may be asked to answer questionnaires about your quality of life while on this study. The purpose is to see how the side effects of treatment might be different in the 2 groups, from the patient's point of view. Patients may also be asked to fill out the questionnaires before surgery, 8 weeks after surgery, and 20 weeks, 40 weeks, 54 weeks and 2 years after joining the trial. You may also be asked to complete questionnaires if your disease returns. You may feel uncomfortable answering some of the questions, and you can skip any you do not want to answer. It would take about a half hour in total to complete the questionnaires at each time point. Copies of your imaging scans taken during the study will be collected for future research.

- If you are in Group 1, blood samples will be collected for research studies as described below. These research studies are required if you participate in this trial. The tests are for research purposes only and the results will not be given to you or your doctor and will not affect your care.

  The blood samples will be collected by using a needle to draw some blood from a vein in your arm. There can be mild pain or some bleeding and bruising when blood is drawn. Rarely, an infection can happen where the needle was placed. Feeling dizzy or fainting can also happen, but should only last a few minutes after blood is drawn.

- In patients receiving nivolumab, approximately two (2) teaspoons of blood will be collected before treatment on day 1 of cycles 1, 2, 3, 5, 7; just prior to the end of treatment on cycles 2, 5, and 7, and at your first two (2) follow-up visits, approximately 6 weeks post discontinuation of nivolumab and approximately three (3) months from first follow-up visit.

  The blood samples will be sent to research laboratories to study the levels of drug in the blood and to see if your body is building antibodies to nivolumab. Researchers will perform these tests in order to understand the differences in the way the body handles certain drugs and to monitor the level of drug to help them understand how the study drug is absorbed and distributed in the body as well as how your disease responds to the treatment. These studies may help explain why some people respond to treatment and why others do not benefit.

  Your privacy is very important and the researchers will make every effort to protect it. Your test results will be identified by a unique code and the list that links the code to your name will be kept separate from your samples and health information. Neither you nor your health care plan/insurance carrier will be billed for the collection of the blood samples that will be used for this study. The samples of blood are required because the research on these blood samples is an important part of the study.

- After you have been on the study for 6 years you will be asked to return for a physical exam to monitor your status once a year for years 6 – 10, if your doctor determines that continued monitoring is necessary.

At the end of this consent, in the *Additional Studies* section, you will be asked if additional blood and tissue samples as well as imaging may be submitted for research studies.

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

If you choose to take part in this research study, there is a risk that:

- You may lose time at work or home and spend more time in the hospital or doctor's office than usual.
- You may be asked sensitive or private questions which you normally do not discuss.
- The study drug may not be better, and could possibly be worse, than the usual approach for your cancer.

- There is a risk of delaying a potentially curative surgery and the delay may not benefit you.
- This study involves undergoing a series of CT scans, which may lead to an increase in secondary cancer risk of 0.05%.
- If you are in Group 1, and disease has not already been confirmed by a biopsy, you will need to undergo a biopsy before you are assigned treatment. Common risks involved in collecting a new biopsy could include bleeding, pain, and/or infection
- There is a risk that someone could get access to the personal information in your medical records or other information that researchers have kept about you. Someone might be able to trace this information back to you. The researchers believe the chance that someone will identify you is very small, but the risk may change in the future as people come up with new ways of tracing information. In some cases, this information could be used to make it harder for you to get or keep a job.

There are laws against misuse of genetic information, but they may not give full protection. The researchers believe the chance these things will happen is very small, but cannot promise that they will not occur.

The drug used in this research study, nivolumab, may affect how different parts of your body work such as your liver, kidneys, lungs and blood. The study doctor will be examining you and testing your blood and will let you know if changes occur that may affect your health. These risks are described in more detail below.

There is also a risk that you could have other side effects from the study drug.

Here are important points about side effects:

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

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

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

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

Possible Side Effects of Nivolumab

(Table Version Date: December 2, 2020)

Special precautions

Side effects of Nivolumab may happen anytime during treatment or even after your treatment has ended. Some of these problems may happen more often when Nivolumab is used in combination with ipilimumab. **Call or see your healthcare provider right away if you develop any problems listed below or the symptoms get worse.**

COMMON, SOME MAY BE SERIOUS

In 100 people receiving Nivolumab, more than 20 and up to 100 may have:

- Tiredness

OCCASIONAL, SOME MAY BE SERIOUS

In 100 people receiving Nivolumab, from 4 to 20 may have:

- Anemia which may require blood transfusion
- Swelling and redness of the eye
- Pain
- Diarrhea, nausea
- Dry mouth
- Fever
- Swelling and redness at the site of the medication injection
- Bruising, bleeding
- Pain or swelling of the joints
- Loss of appetite
- Reaction during or following a drug infusion which may cause fever, chills, rash

Nivolumab may cause your immune system to attack normal organs and cause side effects in many parts of the body. These problems may include but are not limited to:

- Lung problems (pneumonitis and pleural effusion). Symptoms may include: new or worsening cough, chest pain, shortness of breath.
- Intestinal problems (colitis) that can rarely lead to tears or holes in your intestine. Signs and symptoms of colitis may include: diarrhea or increase in bowel movements, blood in your stools or dark, tarry, sticky stools, severe belly pain or tenderness.
- Skin: itching; rash, blisters including inside the mouth; loss of skin pigment
- Liver problems (hepatitis) which can cause liver failure. Signs and symptoms of hepatitis may include: yellowing of your skin or the whites of your eyes, severe nausea or vomiting; drowsiness; pain in the right upper belly

OCCASIONAL, SOME MAY BE SERIOUS

In 100 people receiving Nivolumab, from 4 to 20 may have:

- Hormone gland problems (especially the thyroid, pituitary and adrenal glands, and pancreas). Signs and symptoms may include: headaches that will not go away or unusual headaches, extreme tiredness or changes in mood or behavior; decreased sex drive; weight loss or weight gain; excessive thirst or urination; dizziness or fainting.

RARE, AND SERIOUS

In 100 people receiving Nivolumab, 3 or fewer may have:

- Dry eyes
- Sores in the mouth which may cause difficulty swallowing
- A syndrome starting with flu-like symptoms and followed by swelling, tenderness which may cause blurred vision, ringing in the ears, changes in hair or hair loss
- Swelling of the bowels

Nivolumab may cause your immune system to attack normal organs and cause side effects in many parts of the body. These problems may include but are not limited to:

- Visual disturbances which may cause double vision, blurred vision, or loss of vision with a chance of blindness
- A condition with high blood sugar which leads to tiredness, frequent urination, excessive thirst, headache, nausea and vomiting, and can result in coma
- Kidney problems, including nephritis and kidney failure requiring dialysis. Signs of kidney problems may include: decrease in the amount of urine, blood in your urine, ankle swelling.
- Heart problems including swelling and heart failure. Symptoms and signs of heart problem may include: Shortness of breath, swelling of the ankle and body.
- Problem of the muscle, including swelling, which can cause muscle pain and severe muscle weakness sometimes with dark urine
- Swelling of the brain (meningitis/encephalitis) which may cause: headache, stiff neck confusion, sleepiness, seizures or injury to the brain which may cause headache, blindness (also known as Reversible Posterior Leukoencephalopathy Syndrome)
- Problem of the nerves that can cause paralysis. Signs and symptoms may include: numbness, tingling of hands and feet; weakness of the arms, legs and facial muscle movement
- Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat
- Complications associated with stem cell transplant using donor stem cells (allogeneic stem cell transplant). These complications are caused by attack of donor cells on the host organs (inducing liver, skin and gut damage), and can lead to death. If you are

RARE, AND SERIOUS In 100 people receiving Nivolumab, 3 or fewer may have:
considering an allogeneic stem transplant after participating in this study, please tell your doctor that you have received Nivolumab therapy, since the risk and severity of transplant-associated complications may be increased.

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

Reproductive risks:

You should not get pregnant, breastfeed, or father a baby while in this study and for at least 5 months for a woman and 7 months for a man after the last dose of nivolumab. The potential harm of nivolumab to an unborn baby is not known. Avoiding sexual activity is the only certain method to prevent pregnancy. However, if you choose to be sexually active, you must agree to use at least **one highly effective** method of contraception or **two forms of effective** contraception methods during the study and continuing for 5 months for a woman and 7 months for a man after the last dose of the study drug. Check with the study doctor about what types of birth control, or pregnancy prevention, to use while in this study. If you choose to be sexually active during the study, you must accept that pregnancy could still result, exposing you or your sexual partner to potential loss of pregnancy as well as other unknown effects on the developing unborn baby. Female participants who suspect they may be pregnant, and male participants who suspect their partner may be pregnant must contact their treating physician immediately. If a woman becomes pregnant while on this study or within 100 days after the last dose of study drug, she will be asked for information concerning the outcome of her pregnancy. If a female partner of a male patient becomes pregnant while the male patient is on the study or within 100 days after the last dose of study drug, the male patient must notify the investigator. Pregnancy testing will be performed before each nivolumab infusion in female patients with reproductive potential.

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

It is not possible to know at this time if the study drug is better than the usual care for this cancer so this research study may or may not help you. But, this research study will help researchers learn things that will help people in the future.

Can I stop taking part in this study?

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

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

The study doctor may take you out of the study:

- If your health changes and the study is no longer in your best interest
- If new information becomes available
- If you do not follow the study rules
- If the study is stopped by the sponsor, Institutional Review Board (IRB) or FDA.

What are my rights in this study?

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

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

What are the costs of taking part in this study?

The nivolumab will be supplied at no charge while you take part in this research study. If nivolumab is approved in the adjuvant setting prior to the study closure, you will continue to receive nivolumab from the study supply until you complete your planned study doses. It is possible that the nivolumab may not continue to be supplied while you are on the study. Although not likely, if this occurs, your study doctor will talk to you about your options.

If you are in Group 1 your disease needs to be confirmed by a biopsy before you receive study treatment. A biopsy will be performed to confirm your disease if you did not have a biopsy as part of your usual care before study entry. If a biopsy is required to confirm your disease after you enter the study and it is not part of your usual care, this study will reimburse your hospital for the performance of this biopsy. If the procedure is done as part of your standard care, you or your health plan/insurance will need to pay for these costs.

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

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

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

If you are injured or hurt as a result of taking part in this study and need medical treatment, please tell your study doctor. Contact information for your study doctor is listed on the consent cover page. The study sponsors will not offer to pay for medical treatment for injury.

Your insurance company may not be willing to pay for study-related injury. If you have no insurance, you would be responsible for any costs.

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

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

Who will see my medical information?

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

The ECOG-ACRIN Cancer Research Group is conducting this study. ECOG-ACRIN is a cancer research group that conducts studies for the National Cancer Institute. Your doctor is a member of ECOG-ACRIN or another group that is participating in this study. To help protect your privacy, ECOG-ACRIN has obtained a Confidentiality Certificate from the Department of Health and Human Services (DHHS). With this Certificate, ECOG-ACRIN 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 proceeding. Disclosure will be necessary, however, upon request of DHHS for audit or program evaluation purposes.

There are organizations that may inspect your records. These organizations are required to make sure your information is kept private, unless required by law to provide information. Organizations that may inspect and/or copy your research records for quality assurance and data analysis include groups such as the study sponsor – ECOG-ACRIN and its approved designees:

- Montana Cancer Consortium
- The study sponsor; ECOG-ACRIN
- Bristol-Myers Squibb, the drug company supporting the study.
- Southwest Oncology Group (SWOG), Alliance for Clinical Trials in Oncology (ALLIANCE), Canadian Cancer Trials Group (CCTG), NRG Oncology Foundation.
- Alpha Oncology.
- The Institutional Review Board (IRB) is a group of people who review the research with the goal of protecting the people who take part in the study.
- The Food and Drug Administration and the National Cancer Institute in the U.S, and similar regulatory bodies in other countries that are involved in the study.

Where can I get more information?

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

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

Who can answer my questions about this study?

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

Additional Studies Section:

This section is about optional studies you can choose to take part in.

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

The results will not be added to your medical records and you or your study doctor will not know the results.

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

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

Optional Imaging Research Study

Researchers are trying to learn more about cancer and other health problems. Much of this research is done using imaging technology. Through these studies, researchers hope to find new ways to prevent, detect, treat, or cure health problems.

At this time, we are requesting that you consent to undergo two additional scans (once at the beginning of the study and once after 40-weeks on the study) for research on how renal cell carcinoma and immunotherapy (Group 1) versus not receiving immunotherapy (Group 2) affects bone quantity, or bone density, during your time on this study. The scan would only be used for research and not to guide your medical care.

Additionally, we are requesting that you allow the storage of these images to be used for this research. This storage will be done securely through an image exchange software application.

What is involved if you agree to take part in this study?

If you choose to take part in this study, here is what will happen next:

1. You will have an extra dual energy x-ray absorptiometry (DXA) scan, at the beginning of the study as well as at the end of the study (40-weeks). This scan is already used in routine medical care to measure bone strength and health. In this study, the scan would be done at a different time in your treatment than it would be if you were getting usual care.
2. If you agree to have this extra scan at the beginning of the study as well as at the end of the study (40-weeks), it would involve changing into an examination gown and lying on your back on a padded table. Your legs will rest on a small foam block to measure your spine density. For the hip bone density test, you will lie flat, and one leg will be turned inward slightly and held with a Velcro strap. The forearm scan involves sitting upright while the DXA operator places your non-dominant arm on a small table where it will be held with a Velcro strap. The DXA machine is open to the air and quiet. The exam is painless. You will be asked to lie still and breathe normally. Each scan takes about 5-10 minutes. The DXA operator will be in the room with you the whole time.

What are the possible risks in taking part in this imaging research study?

1. This study involves exposure to radiation from x-rays or gamma rays. This radiation exposure is for research purposes only and is not part of your medical care. X-rays and gamma rays can damage cells, but at low doses the body is usually able to repair these cells. All people are exposed to natural sources of radiation during their daily life. Common sources of radiation are the sun, outer space, air, food, and soil. The radiation exposure that you will get on this research study is less than the amount that the average person in the United States gets from natural sources over 108 days. Ask your study doctor if you would like to learn more about this type of scan.
2. There is a risk that someone could get access to the personal information in your medical records or other information researchers have stored about you.
3. There is a risk that someone could trace the information in a central database back to you. Even without your name or other identifiers, the researchers believe the chance that someone will identify you is very small, but the risk may change in the future as people come up with new ways of tracing information.

When my images are used for research, how will information about me be kept private?

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

1. When your images are sent to the researchers, no information identifying you (such as your name) will be sent. Images will be identified by a unique code only.
2. Information that identifies you will not be given to anyone, unless required by law.
3. There is a risk that someone could trace the information in a central database back to you. Even without your name or other identifiers, the researchers believe the chance that

someone will identify you is very small, but the risk may change in the future as people come up with new ways of tracing information.

What are the Possible Benefits of taking part in this imaging research study?

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

Are there any costs or payments associated with taking part in this imaging research study?

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

What if I change my mind about taking part in this imaging research study?

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

What if I have more questions?

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

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

IMAGING RESEARCH STUDY:

Will you undergo x-ray absorptiometry (DXA)scans for this research study?

I choose to take part in the imaging study and will have the experimental x-ray absorptiometry (DXA) scans.

YES **NO**

Optional Sample Collections for Laboratory Studies and/or Bio-banking for Possible Future Studies

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

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

If you choose to take part in the optional study section "SAMPLES FOR THE LABORATORY STUDIES" below, additional tumor and normal tissue from your surgical biopsy, as well as tumor tissue from the biopsy collected to confirm if your cancer has returned, if available, will be submitted for research to test your tumor for levels of PD-L1 and other tissue markers found in your tumor. Up to one (1) tablespoon of blood will also be collected and submitted for research to test your blood for levels of bone markers

If you choose to take part in the optional study section "SAMPLES FOR FUTURE RESEARCH STUDIES" below, additional tumor tissue from your diagnostic biopsy and up to eight (8) tablespoons of blood samples will be submitted. Additionally, the researchers ask your permission to store and use your samples and related health information (for example, your response to cancer treatment, results of study tests and medicines you are given) for medical research. The research that may be done is unknown at this time. Storing samples for future studies is called "bio-banking". The Biobank is being run by ECOG-ACRIN and supported by the National Cancer Institute.

What is involved if you provide your samples for research?

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

1. Depending on the optional studies in which you choose to take part, up to nine (9) tablespoons of blood will be collected from a vein in your arm prior to the start of any study treatment, prior to your surgery, at week 40 from randomization, and at recurrence (if your cancer gets worse). These samples will be sent to the Biobank for research. The blood samples will usually be collected at the same time as the blood collected for your clinical tests to monitor your health. In most cases an additional needle stick will not be required to collect the blood samples.
2. Depending on the optional studies in which you choose to take part, additional samples from the tumor tissue that was collected prior to your surgery, at the time of your surgery, and to confirm if your cancer has returned will be sent to the Biobank for research. Any tumor tissue leftover after the central review and laboratory research studies will also be kept for future research studies.
3. Your samples and some related health information will be sent to a researcher for use in the study described above. Remaining samples may be stored in the Biobank, along with samples from other people who take part. The samples will be kept until they are used up.
4. Only qualified researchers can submit a request to use the materials stored in the Biobanks. A committee of experts at ECOG-ACRIN, and/or the National Cancer Institute, will review each request to use the samples for research. All research projects that use these samples will be reviewed by an ethics or institutional review board to ensure that the request is necessary and proper. Researchers will not be given your name or any other information that could directly identify you.

5. Neither you nor your study doctor will be notified when research will be conducted or given reports or other information about any research that is done using your samples. Results from the research may be placed in centralized storage systems called databases. It is possible that some of your genetic information and your health information may be placed in these databases. It is also possible that some of these databases may be public. Information that could directly identify you will not be included.

What are the possible risks in providing your samples for research?

1. The most common risks related to drawing blood from your arm are brief pain and possibly a bruise.
2. There is a risk that someone could get access to the personal information in your medical records or other information researchers have stored about you.
3. There is a risk that someone could trace the information in a central database back to you. Even without your name or other identifiers, your genetic information is unique to you. The researchers believe the chance that someone will identify you is very small, but the risk may change in the future as people come up with new ways of tracing information.
4. In some cases, this information could be used to make it harder for you to get or keep a job or insurance. There are laws against the misuse of genetic information, but they may not give full protection. There can also be a risk in knowing genetic information. New health information about inherited traits that might affect you or your blood relatives could be found during a study. The researchers believe the chance these things will happen is very small, but cannot promise that they will not occur.

When my samples are used for research, how will information about me be kept private?

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

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

What are the Possible Benefits of allowing my samples to be used for research?

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

Are there any costs or payments associated with providing my samples for research?

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

What if I change my mind about allowing my samples to be used for research?

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

What if I have more questions?

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

Please circle your answers to show whether or not you would like to take part in each option:

SAMPLES FOR THE LABORATORY STUDIES:

May we have samples of your tumor tissue and blood for laboratory research studies?

- **I agree to have my samples collected and I agree that my samples and related information may be used for the laboratory studies described above.**

YES **NO**

SAMPLES FOR FUTURE RESEARCH STUDIES:

May we have samples of your tumor tissue and blood for research?

- **I agree to provide additional specimens for research.**

YES **NO**

May we keep any tumor tissue and blood leftover after the central review and laboratory research studies for future research?

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

YES **NO**

THIS IS THE END OF THE SECTION ABOUT OPTIONAL STUDIES.

My signature agreeing to take part in the main study

I have read this consent form or had it read to me. I have discussed it with the study doctor and my questions have been answered. I will be given a signed copy of this form. I agree to take part in the main study and any additional studies where I circled 'yes.'

Participant Signature: _____

Date: _____

Signature of Person Obtaining Consent: _____

Date: _____

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