

Kansas City Clinical Oncology Program

S0931, "EVEREST: EVERolimus for Renal Cancer Ensuing Surgical Therapy, a Phase III Study"

This is a clinical trial, a type of research study. Your study doctor will explain the clinical trial to you. Clinical trials include only people who choose to take part. Please take your time to make your decision about taking part. You may discuss your decision with your friends and family. You can also discuss it with your health care team. If you have any questions, you can ask your study doctor for more explanation.

You are being asked to take part in this study because you have cancer of the kidney that has been surgically removed.

Why is this study being done?

The purpose of this study is to see whether treatment with everolimus after surgery for kidney cancer will increase the time without cancer returning. The current standard treatment after surgery is careful monitoring with no immediate treatment. Studies suggest that one way kidney cancer may grow is through chemical signaling through a protein named "mTOR". Everolimus is a drug that stops signaling through mTOR and may therefore stop the growth of kidney cancer. Everolimus is a drug currently approved for the treatment of patients with advanced or metastatic kidney cancer. It is considered investigational for use after surgery. In this study, you will get either everolimus or placebo (a pill with no medication). You will not get both.

How many people will take part in the study?

About 1170 people will take part in this study.

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

Before you begin the study ...

You will need to have the following exams, tests or procedures to find out if you can be in the study. These exams, tests or procedures are part of regular cancer care and may be done even if you do not join the study. If you have had some of them recently, they may not need to be repeated. This will be up to your study doctor.

- Medical history including screening for hepatitis B and C risk and physical examination,

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- Blood tests for blood counts and to test your kidney and liver function,
- Blood tests to check your blood sugar (glucose) and lipids (cholesterol and triglycerides),
- CT scan to assess your disease.

During the study ...

If the exams, tests and procedures show that you can be in the study, and you choose to take part, then you will need the following tests and procedures. They are part of regular cancer care.

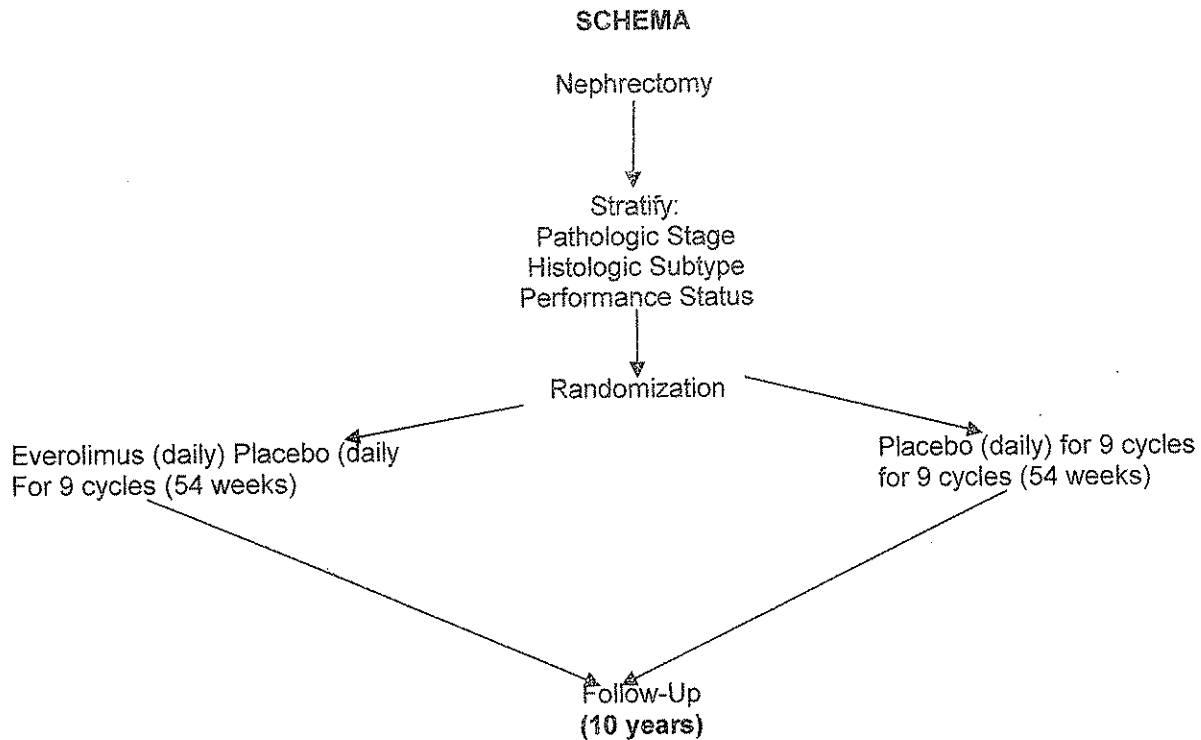
- History and physical exam at Week 4,
- Physical exam every six weeks,
- Blood tests for blood counts and to test your kidney and liver function every six weeks,
- Blood tests to check your blood sugar (glucose) and lipids (cholesterol and triglycerides),
- CT scan to assess your disease every eighteen weeks.

You will be "randomized" into one of the study groups described below. Randomization means that you are put into a group by chance. It is like flipping a coin except that a computer program will place you in one of the study groups. Neither you nor your doctor can choose the group you will be in. You will have an equal chance of being placed in either group. Once you have been placed into one of the groups, neither you nor your doctor will know which group you are in. The treatment in each group will be identical except that half of the patients will receive the investigational drug everolimus and half will take an identical placebo pill. Placebo pills do not contain any medication. These pills will look just like the pills containing everolimus, however, there should not be any side effects.

You will take two pills once a day by mouth with a glass of water. The study drug should be taken on an empty stomach either 1 hour before or 2 hours after meals. Tablets must be swallowed whole and not chewed or crushed. Due to interaction with everolimus, you must not consume grapefruit or grapefruit juice while on study.

You will record the number of pills you take each day and any side effects you experience on a calendar. For the first 6 weeks, your doctor's office will call you to see how you are doing on the weeks that you don't have visits scheduled. You should bring your calendar with you each time you have a doctor's visit. During your visits, your pills will be counted and your calendar reviewed. For this study, each six-week treatment period is called a cycle. Treatment will continue for nine cycles (54 weeks) as long as you are able to tolerate treatment and your cancer hasn't returned. All treatment can be given without being admitted to a hospital.

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How long will I be in the study?

You will be asked to take the study drug for nine six-week cycles, or until your side effects become too great, or until your cancer returns. While you are receiving study treatment, you will need to come to the clinic for doctor visits every six weeks for the first 54 weeks while on treatment. After you are finished with the study treatment, you will return to the clinic with scans every six months for the first two years and then yearly thereafter until 10 years after registration.

Can I stop being in the study?

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

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

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

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

You may have side effects while on the study. Everyone taking part in the study will be watched carefully for any side effects. However, doctors don't know all the side effects that may happen. Side effects may be mild or very serious. Your health care team may give you

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medicines to help lessen side effects. Many side effects go away soon after you stop taking the study drug. In some cases, side effects can be serious, long lasting, or may never go away. There also is a risk of death.

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

Risks and side effects related to the study drug include those which are:

Likely

- Lowered red blood cells which may lead to anemia, tiredness or shortness of breath
- An increase in the amount of cholesterol in your blood
- An increase in the amount of triglycerides (fat) in your blood
- An increase in your blood sugar
- Lowered white blood count which may increase the risk of infection
- An increase of creatinine, a substance normally eliminated by the kidneys into the urine
- Mouth or lip sores
- Infections
- A decrease in phosphate in your blood
- Lack or loss of strength
- Fatigue
- Cough
- Diarrhea
- Rash
- Nausea
- Loss of appetite
- Swelling of the hands and/or feet
- An increase in aspartate transaminase (AST) or alanine transaminase (ALT), enzymes that when present in the blood in high levels may indicate liver dysfunction
- Difficult or labored breathing
- Lowered platelets which may lead to an increase in bruising or bleeding

Less Likely

- Vomiting
- Fever
- Inflammation of the lining of the body cavities
- Headache
- Nosebleed
- Inflammation of the lungs (pneumonia)
- Itching
- Dry skin

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- Altered taste
- Pain in arms and legs
- Weight loss
- Pain in the abdomen
- Inability to sleep
- Dry mouth
- Fluid in the space around the lungs resulting in shortness of breath (requiring drainage or additional treatment)
- Dizziness
- Chest pain
- Hemorrhoids
- Hand-foot syndrome (reported as palmar-plantar erythrodysesthesia syndrome)
- Nail disorder
- A sensation of prickling, tingling, or creeping on the skin
- Abnormal redness of the skin due to inflammation
- Nail Changes (brittleness)
- Skin lesion
- Difficulty swallowing
- Chills
- Sore throat
- Puffy eyes
- High blood pressure
- Renal failure
- Rapid heart beat
- Runny Nose
- Inflammation of the skin resembling acne
- Jaw pain
- Bleeding
- Increase in bilirubin, a reddish yellow pigment that occurs in bile and blood and causes jaundice if accumulated in excess
- Worsening of existing diabetes
- Inflammation of the inner surface of the eyelids
- Congestive cardiac failure
- Diabetes

Reproductive risks: You should not become pregnant or father a baby while on this study and for at least 8 weeks following completion of therapy because the drugs in this study can affect an unborn baby. Women should not breastfeed a baby while on this study and for at least 8 weeks following completion of therapy. 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.

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The study drug may interact with other medications. You should tell your study doctor about all medications (over the counter, herbal, and prescription) you are currently taking and check with your study doctor before beginning any new medications.

Vaccines help protect people from certain illnesses. There is a chance that receiving everolimus could interfere with any vaccinations you receive. Some vaccines are made from live bacteria or live viruses. You cannot receive this kind of vaccine (for example FluMist™ or BCG) for seven days prior to going on study or during the study.

For more information about risks and side effects, ask your study doctor.

Are there benefits to taking part in the study?

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

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

Your other choices may include:

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

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

Will my medical information be kept private?

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

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

- SWOG
- Qualified representative from Novartis Pharmaceuticals (manufacturer of everolimus)
- The National Cancer Institute (NCI) and other government agencies, like the Food and Drug Administration (FDA), involved in keeping research safe for people
- The Cancer Trials Support Unit (CTSU), a research group sponsored by the National Cancer Institute (NCI) to provide greater access to cancer trials.

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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.

Administration of the drug will be charged in the usual way. The parts of the research consisting of keeping research records will be paid by those organizing and conducting the research. The research requires that you receive certain standard medical tests and examinations. These standard tests and examinations will be charged in the usual way. Novartis Pharmaceuticals will supply the investigational agent everolimus or placebo at no charge while you take part in this study. Novartis Pharmaceuticals does not cover the cost of getting the everolimus or placebo ready and giving it to you, so you or your insurance company may have to pay for this.

Even though it probably won't happen, it is possible that Novartis Pharmaceuticals may not continue to provide the everolimus or placebo for some reason. If this would occur, other possible options are:

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

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

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

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

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

It is important that you tell your study doctor, _____ [investigator's name(s)], if you feel that you have been injured because of taking part in this study. You can tell the doctor in person or call him/her at _____ [telephone number].

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

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

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

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

A Data Safety and Monitoring Board, an independent group of experts, will be reviewing the data from this research throughout the study. We will tell you about important new information from this or other studies that may affect your health, welfare, or willingness to stay in this study.

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

Who can answer my questions about the study?

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

For questions about your rights while taking part in this study, call the Kansas City Clinical Oncology Program Institutional Review Board (a group of people who review the research to protect your rights) at 913-948-5588

Future Contact

I agree to allow my study doctor, or someone approved by my study doctor, to contact me regarding future research involving my participation in this study.

Yes No

Consent Form for Use of Specimens for Research

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About Using Specimens for Research

If you agree, a sample of your blood and tumor tissue will be sent to an outside lab for research purposes to study the biology of your cancer and how everolimus works. The blood samples will be obtained to measure the level of everolimus in your blood. We will see if those levels correspond to the risk of getting certain side effects. In the tumor samples we will measure the levels of certain proteins to see if they predict how well everolimus will work. The blood sample (about 3 ½ teaspoons) will be collected before you begin study treatment, before Cycles 2 and 3, when you go off protocol treatment, and if your cancer recurs. The blood sample must be taken before your daily dose of study drug. The tumor tissue sample will be taken from your kidney cancer specimen (obtained from your recent operation). (You will not need to have another surgery for this purpose.) These collections are optional. The research that will be done with your blood and tissue is not designed specifically to help you. It might help people who have cancer and other diseases in the future. Reports about research done with your blood and tissue will not be given to you or your doctor. These reports will not be put in your health record. The research will not have an effect on your case.

As described above, some of your tumor and blood samples will be sent to a lab to study the biology of your cancer. Your tissue and blood ("specimens") will be kept at the following location:

SWOG Solid Tumor Specimen Repository:
University of Colorado HSC at Fitzsimons
Department of Pathology
RC-1 South, Room L18-5400A
12801 East 17th Avenue
Aurora, CO 80045
Contact: Miguel Martinez
Phone: 303/724-3086
E-mail: Miguel.martinez@ucdenver.edu

We would like to keep some of the specimens that are left over for future research. If you agree, these specimens will be kept and may be used in research to learn more about cancer and other diseases. Please read the information sheet called "How are Specimens Used for Research" to learn more about specimen research.

The research that may be done with your specimens is not designed specifically to help you. It might help people who have cancer and other diseases in the future.

Reports about research done with your specimens will not be given to you or your doctor. These reports will not be put in your health record. The research will not have an effect on your care.

Things to Think About

The choice to let us keep the left over specimens for future research is up to you. No matter what you decide to do, it will not affect your care.

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If you decide now that your specimens can be kept for research, you can change your mind at any time. Just contact us and let us know that you do not want us to use your specimens. Then any specimens that remain will no longer be used for research.

In the future, people who do research may need to know more about your health. While SWOG may give them reports about your health, it will not give them your name, address, phone number, or any other information that will let the researchers know who you are.

Sometimes specimens are used for genetic research (about diseases that are passed on in families). Even if your specimens are used for this kind of research, the results will not be put in your health records.

Your specimens will be used only for research and will not be sold. The research done with your specimens may help to develop new products in the future.

Benefits

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

Risks

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

Making Your Choice

Please read each sentence below and think about your choice. After reading each sentence, circle "Yes" or "No." If you have any questions, please talk to your doctor or nurse, or call our research review board at IRB's phone number.

No matter what you decide to do, it will not affect your care.

1. **My specimens may be kept for use in research to learn about, prevent, treat or cure cancer.**
Yes No

2. **My specimens may be kept for use in research about other health problems (for example: diabetes, Alzheimer's disease, or heart disease).**
Yes No

3. **Someone may contact me in the future to ask me to allow other uses of my specimens.**
Yes No

If you decide to withdraw your specimens from a SWOG Specimen Repository in the future, a written withdrawal of consent should be submitted through your study doctor to

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the SWOG Operations Office. Please designate in the written withdrawal whether you would prefer to have the specimens destroyed or returned to the study doctor.

Where can I get more information?

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

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

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

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

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

Release

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

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

Signature

I have been given a copy of all 14 pages of this form. I have read it or it has been read to me. I understand the information and have had my questions answered. I agree to take part in this study.

Participant _____

Date _____

Signature of Person Obtaining Consent _____

Date _____

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Specimen Consent Supplemental Sheets

How are Specimens Used for Research?

Where do specimens come from?

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

Why do people do research with specimens?

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

What type of research will be done with my specimen?

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

How do researchers get the specimen?

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

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

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

Why do you need information from my health records?

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

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

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

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

Sometimes, health records have been used against patients and their families. For example, insurance companies may deny a patient insurance or employers may not hire someone with a certain illness (such as AIDS or cancer). The results of genetic research may not apply only to you, but to your family members too. For disease caused by gene changes, the information in one person's health record could be used against family members.

How am I protected?

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

What if I have more questions?

If you have any questions, please talk to your doctor or nurse, or call our research review board at 913-948-5588

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