NCI Community Oncology Research Program – Kansas City (NCORP-KC)

RTOG 0924

Androgen Deprivation Therapy and High Dose Radiotherapy With or Without Whole-Pelvic Radiotherapy in Unfavorable Intermediate or Favorable High Risk Prostate Cancer: A Phase III Randomized Trial

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 prostate cancer.

Why is this study being done?

The purpose of this study is to compare the effects of hormone therapy (androgen deprivation) and radiation therapy to the prostate gland and seminal vesicles with hormone therapy and radiation therapy to the whole pelvic body area on you and your prostate cancer to find out which is better.

There are 2 treatment groups in this study:
1) Patients who receive hormone therapy plus radiation therapy to the prostate gland and seminal vesicles (two small glands behind the prostate)
2) Patients who receive hormone therapy plus radiation therapy to the whole pelvis

If you agree to participate in this study, you will receive one of these 2 treatments.

How many people will take part in the study?

About 2,580 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.

- History and physical exam, including a digital rectal exam (DRE) and an assessment of your ability to carry out activities of daily living (which will include questions such as whether you are able to feed, bathe, and dress yourself)
- Blood tests to determine your PSA (prostate-specific antigen) and for blood count. The PSA value is a number that helps determine the aggressiveness of your prostate cancer.
- A CT (Computed Tomography) scan or MRI (Magnetic Resonance Imaging) of your pelvis and abdomen to determine if there is any evidence of cancer spread to the pelvic lymph nodes. A CT scan is a study using x-rays to look at one part of your body. An MRI is imaging using a strong magnetic field to look at one part of your body.
- A bone scan to determine if the cancer has spread to the bones

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.

- Transrectal ultrasound assessment of the prostate (brachytherapy patients only)
- Blood test to measure liver function

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

If you are in group 1 (often called "Arm 1"): You will receive radiation treatments to the prostate gland and seminal vesicles once daily, 5 days a week, Monday through Friday, for a total of 44 treatments if treated with external beam radiation alone. Each radiation treatment will take approximately 20 minutes but may be specific to the center in which you are being treated. If you choose to receive brachytherapy (permanent or temporary radiation seed implant) as a boost, the total number of daily external beam treatment sessions will be 25. The logistics of the brachytherapy implant procedure (if you have chosen to undergo this type of treatment) should be thoroughly reviewed by your treating physician.

You also will receive hormone therapy for 4, 6 months or 32 months (either 4 months total of LHRH agonist/antagonist and anti-androgen pills or 6 months total of LHRH agonist/antagonist and anti-androgen pills or 32 months of LHRH agonist and 6 months of anti-androgen pills; the duration of hormone therapy will be determined by your doctor). Hormone therapy will begin 2 months before the start of the radiation treatments. There are two parts to the hormone therapy. You will take injections of a luteinizing hormone releasing hormone (LHRH) agonist/antagonist, either under the skin or in the muscle (typically every 1 to 3 months), and you will take a pill, either flutamide three times per day or bicalutamide once per day. The injected LHRH agonist/antagonist will reduce the amount of circulating testosterone and the pill will interfere with the action of any remaining testosterone.

If you are in group 2 (often called "Arm 2"): You will receive radiation treatments to the whole pelvis once daily, 5 days a week, Monday through Friday, for a total of 25 treatments. Each radiation treatment will take approximately 20 minutes but may be specific to the center in which you are being treated. If you choose to receive brachytherapy (permanent or temporary radiation seed implant), the total number of daily treatment sessions will be 25. If you are treated with external beam as a boost you will receive a total of 44 treatments. The logistics of the brachytherapy implant procedure (if you have chosen to undergo this type of treatment) should be thoroughly reviewed by your treating physician.

You also will receive hormone therapy for 4, 6 months or 32 months (either 4 months total of LHRH agonist/antagonist and anti-androgen pills or 6 months total of LHRH agonist/antagonist and anti-androgen pills or 32 months of LHRH agonist/antagonist and 6 months of anti-androgen pills; the duration of hormone therapy will be determined by your doctor). Hormone therapy will begin 2 months before the start of the radiation treatments. There are two parts to the hormone therapy. You will take injections of a luteinizing hormone releasing hormone (LHRH) agonist/antagonist, either under the skin or in the muscle (typically every 1 to 3 months), and you will take a pill, either flutamide three times per day or bicalutamide once per day. The injected LHRH agonist/antagonist will reduce the amount of circulating testosterone and the pill will interfere with the action of any remaining testosterone.

During treatment:

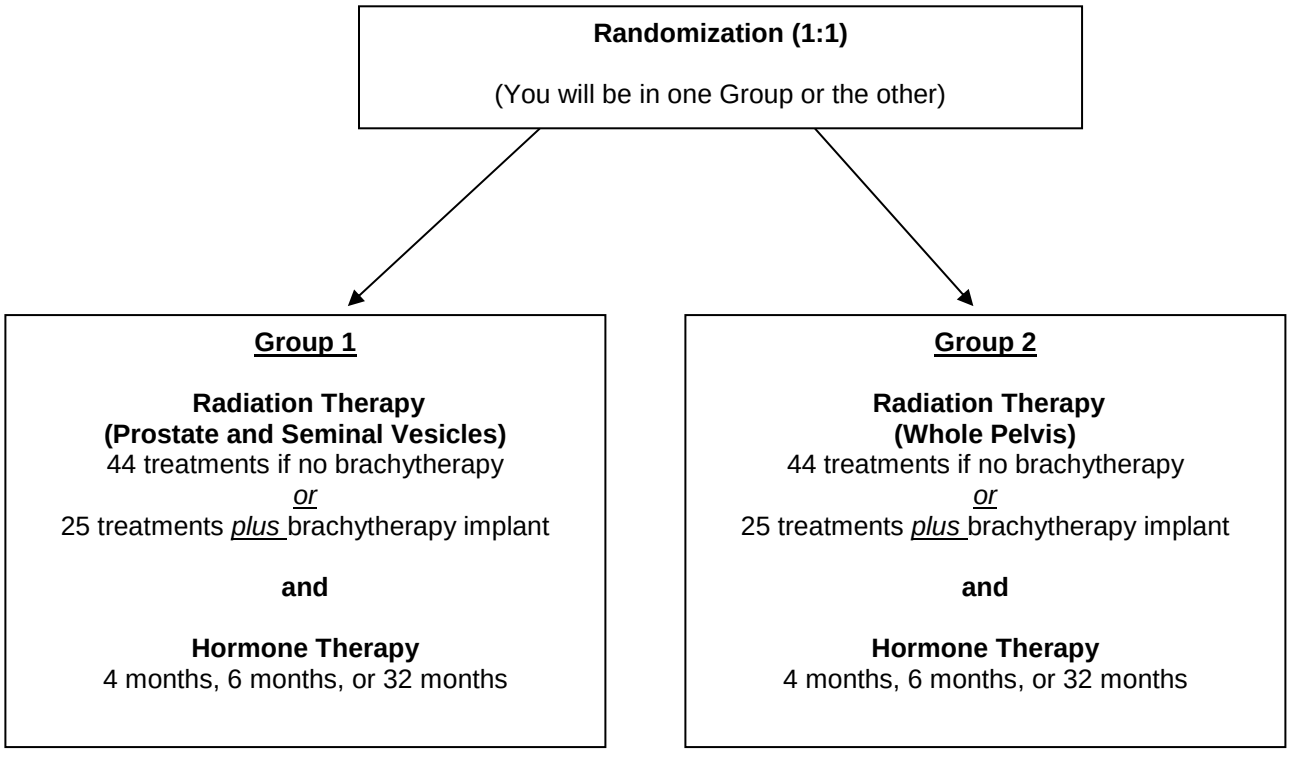
- You will be seen weekly during treatment for 1) a physical exam, 2) to be examined for your ability to carry out activities of daily living (which will include questions such as whether you are able to feed, bathe, and dress yourself), and 3) to check for any side effects that you may be experiencing as a result of the treatment.
- You will have blood tests as clinically needed

When you are finished receiving therapy you will need these tests and procedures:

- Every 3 months for the first year, every 6 months for years 2 through 5, and then yearly after year 5:
    - A physical assessment, including a digital rectal exam (DRE) and an assessment of your ability to carry out activities of daily living (which will include questions such as whether you are able to feed, bathe, and dress yourself)
    - You will be assessed for any side effects that you may be experiencing as a result of the treatment
- Additional testing (for example, pelvic/abdominal CT or MRI scans; blood tests for blood count) may be ordered as deemed clinically appropriate by your treating physician.

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 44 radiation treatments over approximately 2 months. If you choose to receive the brachytherapy implant, you will receive 25 daily treatments plus the implant procedure over a timeframe of

approximately 6 weeks. Hormone therapy will last 4 months, 6 months or 32 months (the duration of hormone therapy will be determined by your doctor).

After you are finished receiving therapy, the study doctor will ask you to visit the office for follow-up exams every 3 months for the first year, every 6 months for years 2 through 5, and then yearly after year 5. The study doctors would like to keep track of your medical condition by seeing you every year for your lifetime.

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 radiation and hormone therapy can be evaluated by him/her. Another reason to tell your study 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, researchers don't know all the side effects that may happen. Side effects may be mild or very serious. These side effects may be related either to the radiotherapy, hormonal therapy, or both. There are several radiotherapy options allowed on this study in the form of external beam radiation, low dose rate brachytherapy, and high dose rate brachytherapy. Each of these options may be associated with subtle differences in their side effect profiles. ***The type of radiotherapy you receive on this study is a choice to be made between you and your physician.*** Your health care team may give you medicines to help lessen side effects. Many side effects go away soon after you stop radiation or hormone therapy. In some cases, side effects can be serious, long lasting, or may never go away.

You should talk to your study doctor about any side effects that you have while taking part in the study.
Risks and side effects related to the *radiation therapy* include those which are:

Likely

- Increased urinary frequency or urgency
- Burning or discomfort/straining with urination
- Increased frequency of bowel movements or change in stool consistency
- Increased straining/discomfort with bowel movements
- Mild fatigue

Less Likely

- Rectal bleeding (usually mild)
- Chronic bowel/bladder symptoms as described above
- Temporary blockage of urination requiring use of a catheter
- Erectile dysfunction

Rare but serious

- Permanent rectal or bladder injury requiring surgery for treatment

Risks and side effects related to the *hormone therapy* include those which are:

Likely

- Hot flashes
- Erectile dysfunction
- Loss of libido
- Mild fatigue
- Breast tenderness or mild enlargement
- Diarrhea
- Decrease in bone mineral density [Note: Patients who receive long-term hormone therapy (32 months) may be at higher risk for a decrease in bone mineral density]

Less Likely

- Headaches
- Bone/joint pain
- Liver toxicity (detected on a blood test) requiring reduced dose or stopping treatment
- Severe fatigue
- Skin rash/hives
- Swelling
- Infection
- Nausea
- Bruising
- Bleeding
- Mood swings
- Increased urination
- Decrease in bone mineral density [Note: Patients who receive short-term hormone therapy (4 to 6 months) may be at lower risk for a decrease in bone mineral density]
- There may be increased risk of rectal or bladder side effects as a result of the interaction between the hormone therapy and the external beam radiation therapy.

Rare, But Serious

- Severe allergic reaction
- Increased long-term risk of cardiovascular disease
- Increased long-term risk of developing diabetes
- Death due to heart disease

For patients undergoing brachytherapy, risks associated with aspects of an invasive procedure such as those associated with anesthesia, infection, and bleeding must be considered and discussed with your treating physician. If permanent seed brachytherapy is used, there is a possibility of loss or migration of seeds leading to areas of under- or overdosage in certain parts of the prostate or elsewhere. Rectal or bladder complications may occur if these organs are affected because of seed misplacement.

Patients receiving treatment with LHRH agonists should undergo periodic monitoring of blood glucose and/or glycosylated hemoglobin (HbA1c) for signs of developing diabetes or worsening of blood glucose control in patients with diabetes, and also for the signs and symptoms suggestive of the development of cardiovascular disease.

Reproductive risks: You should not father a baby nor donate sperm while on this study or during the first 3 months after the completion of therapy because the radiation and drugs in this study can affect an unborn baby. 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 and radiation used in this study may make you unable to have children in the future.

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. Information from this study will help researchers learn more about the addition of whole pelvic radiation therapy to hormone therapy as a treatment for prostate 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; this could include the following options, either alone or in combination with each other:
  - o Radiation therapy (external beam radiation therapy and/or brachytherapy)
  - o Radiation therapy plus hormone therapy
  - o Hormone therapy
  - o Surgery
- Taking part in another study
- Getting no treatment

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

Will my medical information be kept private?

Data are housed at NRG Oncology in a password-protected database. 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:

- NRG Oncology
- The National Cancer Institute (NCI) and other government agencies involved in keeping research safe for people, like the Food and Drug Administration (FDA)
- The Cancer Trials Support Unit (CTSU), an organization sponsored by the NCI to provide greater access to cancer trials
- VisionTree Software, Inc.

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.

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.

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

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

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

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

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

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

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

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

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 _____ *[name of center]* Institutional Review Board (a group of people who review the research to protect your rights) at _____ *(telephone number). [Note to Local Investigator: Contact information for patient representatives or other individuals in a local institution who are not on the IRB or research team but take calls regarding clinical trial questions can be listed here.]*

*You may also call the Operations Office of the NCI Central Institutional Review Board (CIRB) at 888-657-3711 (from the continental US only). *[*Only applies to sites using the CIRB.]*

Please note: This section of the informed consent form is about additional research that is being done with people who are taking part in the main study. You may take part in this additional research if you want to do so. You can still be a part of the main study even if you say 'no' to taking part in this additional research.

Quality of Life Study

Note to Institutions: On 3/9/15, the quality of life (QOL) component of RTOG 0924 closed to patient enrollment, as the substudy met its patient enrollment goal. New patients will not be offered the opportunity to participate in this substudy. Institutions should follow their local IRB policy regarding removal of the QOL text below from the sample consent.

We want to know your view of how your life has been affected by cancer and its treatment. This "quality of life" study looks at how you are feeling physically and emotionally during your cancer treatment. It also looks 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. In the future, this information may help patients and doctors as they decide which medicines to use to treat cancer.

You will be asked to complete four questionnaires with questions about your symptoms (urine, bowel, and fatigue) and your sense of wellbeing (mood, sleep and daily activity) at the following times: *before you begin protocol treatment; during the week prior to radiation therapy; and 6 months, 1 year, and 5 years after therapy starts*. In addition, you will be asked to complete the questionnaire about your fatigue, mood, sleep and daily activity at the following times: *during the last week of radiation therapy and 3 months after completing radiation therapy*. It will take about 15 minutes to fill out the questionnaires. If any questions make you feel uncomfortable, you may skip those questions and not give an answer.

If you agree to participate in the quality of life study, you will be required to have blood drawn *before you start radiation therapy treatment and during the last week of radiation therapy treatment*. Each blood draw will be about 2 tablespoons; the blood will be used to learn more about changes in your body that are related to the symptoms you may be having. You may change your mind about completing the questionnaires and having blood drawn at any time.

<u>Optional Online Completion of QOL Questionnaires</u>
In the past, patients often have filled out quality of life questionnaires on paper. NRG Oncology is working with a company, VisionTree Software, Inc., that has a web site where patients can fill out these questionnaires anywhere there is a computer with Internet access. This option is being offered as some patients may find it more convenient to fill out the forms electronically from any location, including home. When you log on to the web site, it will take you through the process of completing the questionnaires step by step. You will need an e-mail address that you agree to use for this purpose. The e-mail address is needed to identify you on the VisionTree web site and for e-mail reminders that will be sent to you when the questionnaires are due. Your e-mail address will be used for the purpose of this study only, not for mail or marketing purposes.

If you are interested in filling out quality of life questionnaires electronically but do not have an e-mail address, you may obtain one (quickly and for no charge at web sites such as Yahoo!, Hotmail, or AOL). You will only be sent e-mail reminders at the time that the questionnaires are due (a maximum of 3 e-mail reminders per time point).

Your access to the VisionTree web site is password protected and secure. You can use your e-mail address to retrieve your password if you forget it or lose your login card. You will receive a login card either by regular mail or e-mail, and it will include the information you need to log in to the VisionTree web site the first time. You can choose to complete the questionnaires online or on paper. The choice is up to you. If any questions make you feel uncomfortable, you may skip those questions and not give an answer. You may change your mind about completing the questionnaires at any time and you may choose to discontinue answering the questionnaires altogether at any time.

Just like in the main study, we will do our best to make sure that your personal information will be kept private.

Please circle your answer.

I choose to take part in the quality of life study. I agree to fill out the quality of life questionnaires and have blood drawn.

YES **NO**

I choose to use the VisionTree Software. I agree to fill out the Quality of Life Questionnaires electronically using the VisonTree web site.

YES **NO**

You can say "yes" or "no" to the following study. Below, please mark your choice for the study.

About Using Tissue, Blood, and Urine for Research

You are going to have a biopsy (or surgery) to see if you have cancer. Your doctor will remove some body tissue to do some tests. The results of these tests will be given to you by your doctor and will be used to plan your care.

We would like to keep some of the tissue that is left over for future research. If you agree, this tissue will be kept and may be used in research to learn more about cancer and other diseases.
In addition to the tumor tissue, we would like to collect some blood and urine. If you agree, you will have blood drawn before you start radiation therapy treatment and during the last week of radiation therapy treatment. We would like to keep about 2 tablespoons of blood at each of these times for future research. Urine will be collected before you start radiation therapy treatment. This blood and urine will be kept to be used in research to learn more about cancer and other diseases.

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 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 tissue, blood, and urine 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 tissue, blood, and urine for future research is up to you. No matter what you decide to do, it will not affect your care or your participation in the main part of the 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 us and let us know that you do not want us to use your tissue, blood, and urine. Then any tissue that remains will no longer be used for research and will be returned to the institution that submitted it and any blood or urine that remains will be destroyed.

In the future, people who do research may need to know more about your health. While the doctor/institution 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 tissue, blood, and urine are used for genetic research (about diseases 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 in your health records.

Your tissue, blood, and urine will be used only for research and will not be sold. The research done with your tissue, blood, and urine are may help to develop new treatments for cancer in the future.

Benefits

The benefits of research using tissue, blood, and urine 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.

Some of your genetic and health information may be placed in central databases that may be public, along with information from many other people. Information that could directly identify you will not be included. The samples are given a code to protect your privacy before they are used. Any related information given to researchers will also be coded. Researchers will receive the code instead of any information that might directly identify you.

There can 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 research study. Even though your genes are unique, you share some of the same genes with your blood relatives.

Although we are not able to know all of the risks from taking part in research on inherited traits, we believe that the risks to you and your family are very low, because your samples will be coded. Research results will not be returned to you or your doctor.

Very rarely health or genetic information could be misused by employers, insurance companies, and others. For example, life insurance companies may charge a higher rate based on this information.

Some states have laws to protect against genetic discrimination [list appropriate state information if your state has such laws]. A federal law called the Genetic Information Non-Discrimination Act, or GINA is in effect. This law does not allow discrimination by insurers or employers. The law does not include other types of misuse by life insurance, disability, or long term care insurance. To learn more about the GINA Law, please ask your study doctor.

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 888-657-3711.

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, or treat cancer, as follows:

- Tissue ☐Yes ☐ No
- Blood ☐Yes ☐ No
- Urine ☐Yes ☐ No

2. My specimens may be kept for use in research to learn about, prevent or treat other health problems (for example: diabetes, Alzheimer's disease, or heart disease), as follows:
   - Tissue ☐Yes ☐ No
   - Blood ☐Yes ☐ No
   - Urine ☐Yes ☐ No

3. Someone may contact me in the future to ask me to take part in more research.
   ☐Yes ☐ No

Where can I get more information?

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

1-800-4-CANCER (1-800-422-6237)

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://www.cancer.gov/cancertopics/**

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 NCORP-KC 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 12 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.

Print patient's name_____

Patient's signature_____

Date of signature_____

Print name of person(s) conducting the informed consent discussion

_____

Signature of person(s) conducting the informed consent discussion

_____

Date of signature_____