NRG ONCOLOGY
Radiation Therapy Oncology Group

RTOG 0534

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A Phase III Trial Of Short Term Androgen Deprivation With Pelvic Lymph Node Or Prostate Bed Only Radiotherapy (SPPORT) In Prostate Cancer Patients With A Rising PSA After Radical Prostatectomy

Amendment 9: March 1, 2019

RTOG 0534

Informed Consent Template for Cancer Treatment Trials
(English Language)

A Phase III Trial Of Short Term Androgen Deprivation With Pelvic Lymph Node Or Prostate Bed Only Radiotherapy (SPPORT) In Prostate Cancer Patients With A Rising PSA After Radical Prostatectomy

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 had surgery to remove your prostate and your study doctor has recommended radiation therapy because your blood level of Prostate Specific Antigen (PSA) has been going up. (The PSA is a value that helps determine the aggressiveness of your prostate cancer.)

Why is this study being done?

The purpose of this study is to compare the effects, good and/or bad of three treatment methods on participants and their cancer.

External beam radiation therapy is one of the standard treatments for men with prostate cancer who have a rising PSA after surgery. Different methods of radiation therapy are used, and it is not known which one is best. Most commonly, the area where the prostate was originally located before being removed (the prostate bed) is treated, without treating the lymph nodes in the pelvis. Prostate cancer can spread to the lymph nodes. There is some evidence in men who have not had surgery that radiotherapy to the pelvic lymph nodes may stop the cancer from spreading under some conditions. Since treating the pelvic lymph nodes can result in increased side effects, the benefit of this method of radiation therapy needs to be tested.

Prostate cancer feeds on male hormones, such as testosterone. Drugs that reduce or block testosterone (hormone therapy) can cause some prostate cancer cells to die and others to become sick so that they don't grow. Some patients treated with a combination of these drugs and radiation have a greater chance of not having the cancer return when compared to men treated with radiation alone. These studies were done in men who did not have surgery. Since hormone therapy can result in increased side effects, the benefit of combining hormone therapy with radiation therapy needs to be tested.

There are 3 treatment groups in this study:
1) Patients who receive radiation therapy to the prostate bed only;
2) Patients who receive hormone therapy for 4 to 6 months plus radiation therapy to the prostate bed;
3) Patients who receive hormone therapy for 4 to 6 months plus radiation therapy to the prostate bed and to the pelvic lymph nodes.

If you agree to participate in this study, you will receive one of these 3 treatments.

How many people will take part in the study?

About 1,764 people will take part in this study.

What will happen if I take part in this research study? (01/8/09) (3/24/10)

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.

- Review of the tissue from your prior surgery to remove your prostate to determine your Gleason score (a value that helps determine the aggressiveness of your prostate cancer)
- 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).
- You will be asked to fill out a questionnaire on urinary symptoms and function called the American Urological Association Symptom Index (AUA SI).
- A blood test to determine your PSA (a value that helps determine the aggressiveness of your prostate cancer). About 2 teaspoons of blood will be drawn from a vein. At least two PSA tests spaced by 2 months must be obtained after surgery to remove the prostate. Your study doctor also may draw another PSA before the start of treatment for a baseline value.
- Other blood tests (for blood count, liver function, and to measure testosterone)
- A CT (Computed Tomography) scan or MRI (Magnetic Resonance Imaging) of your pelvis 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.
- A CT scan with an urethrogram or an MRI for radiation treatment planning may be ordered; for a urethrogram, a tube is placed into the opening of the canal (at the end of the penis) from which urine is emptied from the body. Dye is injected, and images are taken.

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 a one in three 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 bed once daily, 5 days a week, Monday through Friday, for a total of 36 to 39 treatments (the exact number will be decided by your study doctor). Each radiation treatment will take 15-30 minutes.

If you are in group 2 (often called "Arm 2"): You will receive radiation treatments to the prostate bed once daily, 5 days a week, Monday through Friday, for a total of 36 to 39 treatments (the exact number will be decided by your study doctor). Each radiation treatment will take 15-30 minutes.

You also will receive hormone therapy for 4 to 6 months (the exact length will be decided by your doctor). The 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 either under the skin or in the muscle, and you will take a pill, either flutamide three times per day or bicalutamide once per day. The pills will be taken for at least 4 of the 6 months.

If you are in group 3 (often called "Arm 3"): You will receive radiation treatments to the pelvic lymph nodes and prostate bed once daily, 5 days a week, Monday through Friday, for 25 treatments. From that point on, the radiation treatments will target the prostate bed only, 5 days per week, for another 11-14 treatments. The total number of radiation treatments will be 36 to 39 treatments (the exact number will be decided by your study doctor). Each radiation treatment will take 15-30 minutes.

You also will receive hormone therapy for 4 to 6 months (the exact length will be decided by your study doctor). The 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 either under the skin or in the muscle, and you will take a pill, either flutamide three times per day or bicalutamide once per day. The pills will be taken for at least 4 of the 6 months.

After entering the study and prior to radiotherapy: (1/8/09)
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 if you are randomized to receive hormone therapy (Groups 2 and 3). They are part of regular cancer care.

- After 2 months of hormone therapy and before radiation therapy, blood will be drawn (for a blood count, liver function, and to measure testosterone and PSA).
- After 2 months of hormone therapy and before radiation therapy, you will be requested to fill out an American Urological Association Symptom Index (AUA SI) questionnaire.

During Radiation Therapy: (1/8/09)

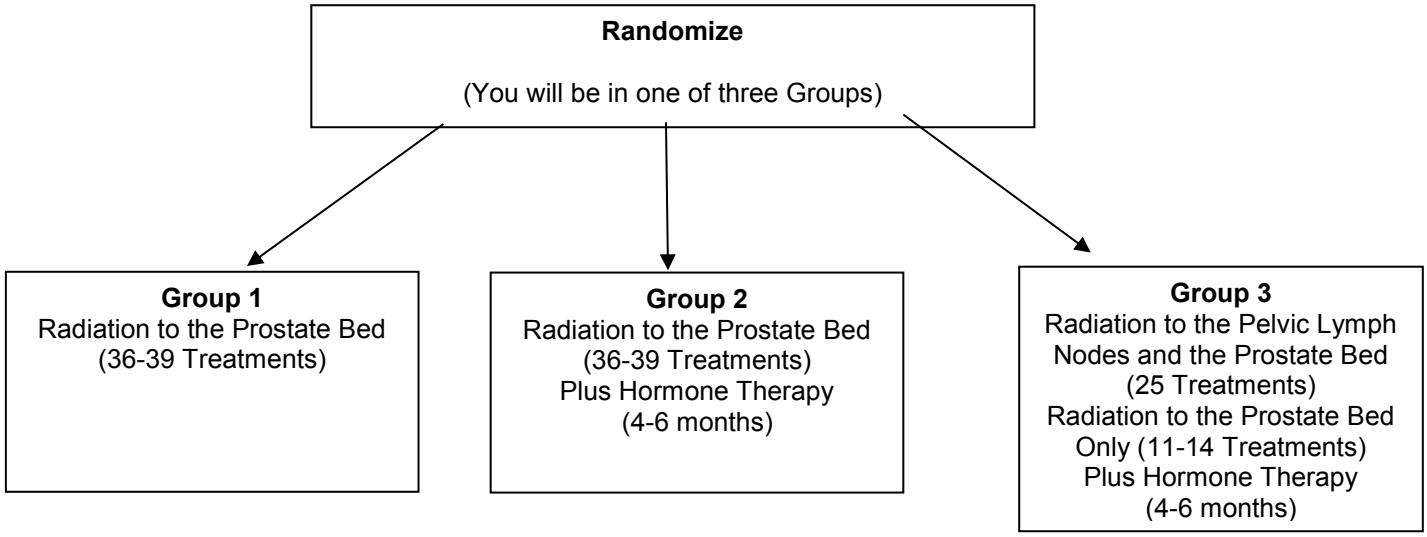
- Weekly during radiation therapy: History and physical exam, including an assessment of your ability to carry out activities of daily living, and assessment of any side effects you may be experiencing from the treatment
- Blood will be drawn during the 6th (last) week of radiotherapy (for a blood count, liver function and to measure testosterone).
- You will be asked to fill out an American Urological Association Symptom Index (AUA SI) questionnaire in the 6th week of radiation therapy.

When you are finished receiving radiation: (1/8/09)
You will need these tests and procedures:

- At 6 weeks (1.5 months), 3, and 6 months following the completion of radiation: blood tests to measure liver function; at 3 and 6 months following the completion of radiation: blood will be drawn for blood count
- At 3, 6, and 12 months following the completion of radiation, every 6 months for the next 6 years, and then annually: History and physical exam, including a digital rectal exam (DRE), an assessment of your ability to carry out activities of daily living, an assessment of any side effects from the treatments, and an AUA-SI questionnaire.
- A PSA and testosterone will be checked at 6 weeks (1.5 months), 3 months, 6 months, 9 months, and 12 months following completion of radiotherapy; at 3-month intervals for the next year; and then at 6-month intervals thereafter.
- If something is felt in the prostate bed that is suspicious for recurrence, your study doctor will request a needle biopsy to evaluate this.
- If your PSA rises at any time after completion of treatment, your study doctor may order a bone scan and CT scan or MRI of the abdomen and pelvis.

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? (1/8/09)

You will receive 36–39 radiation treatments over 7–8 weeks. Hormone therapy, if given, will last 4–6 months. After you are finished receiving radiation therapy, the study doctor will ask you to visit the office for follow-up exams at 3, 6, and 12 months after radiotherapy, then every 6 months for the next 6 years, and annually thereafter. 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 (if given) 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?

(1/8/09) 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. 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 (if given). In some cases, side effects can be serious, long lasting, or may never go away. In addition, some of the side effects may be life threatening and, in rare instances, may cause death. The risks of side effects related to the radiation may be higher in group 3, which includes the treatment of the pelvic lymph nodes.

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 (1/8/09)
- Tanning, redness, or darkening of skin in treatment area
- Rash, itching or peeling of skin
- Temporary hair loss in the treatment area
- Temporary fatigue
- Abdominal cramps
- Frequent bowel movements, sometime with urgency, or diarrhea
- Rectal cramps and irritation with pain on defecation
- Mild rectal bleeding that does not require treatment
- Bladder irritation with a stinging sensation
- Frequency or urgency of urination
- Small amounts of blood in the urine

Less Likely
- Urinary obstruction requiring the placement of a temporary urinary catheter and/or dilatation because of stricture (narrowing)
- Less ability to control urine (increased incontinence)
- Inability to achieve an erection (inability of the penis to become hard)
- Rectal bleeding that requires medication or laser treatment to stop

Rare but serious (1/8/09)
- Injury to the bladder, urethra, bowel, or other tissues in the pelvis or abdomen requiring additional procedure or surgery, such as a colostomy (bag for stool).
- Intestinal obstruction requiring surgery

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

Likely (1/8/09)
- Hot flashes
- Inability to achieve an erection (inability of the penis to become hard)
- Loss of sex drive
- Mood swings
- Muscle loss, weakness and fatigue
- Mild anemia (drop in red blood cell count)
- Weight gain
- Bone weakening

Less Likely (1/8/09)
- Significant bone loss (osteopenia or osteoporosis) which could result in fracture
- Significant anemia
- Blood sugar problems (diabetes)
- High fats and cholesterol in your blood (hyperlipidemia)
- Blood vessel disease (arteriosclerosis, heart failure)
- Fluid retention and ankle swelling (edema)
- Breast enlargement and tenderness
- Difficulty with calculations and memory (verbal recall, cognition)

Rare and Possibly Serious (11/23/11)

- Liver damage (hepatitis)
- Flare up in arthritis
- Bone fracture
- Depression
- Increased long-term risk of developing diabetes
- Increased long-term risk of cardiovascular disease
- Death due to heart disease

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 cessation of therapy because the drugs and radiation 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. It is not known whether the combination of radiation to the prostate bed plus hormone therapy is better than radiation to the prostate bed alone. Also, it is not known whether radiation to the pelvic lymph nodes and prostate bed plus hormone therapy is better than radiation to the prostate bed only combined with hormone therapy. We do know that the information from this study will help researchers learn more about how best to treat men who have a rising PSA after surgery to remove their prostate. 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 External beam radiation therapy (typically, to the prostate bed)
    - o External beam radiotherapy plus hormone therapy
    - o Hormone therapy
- Taking part in another study
- Getting no treatment (With this choice, your tumor could continue to grow and your disease could spread)

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? (12/31/14)

Data are housed at NRG Oncology Statistics and Data Management Center 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 Central Institutional Review Board (CIRB) and the Food and Drug Administration (FDA)
- The Cancer Trials Support Unit (CTSU), a research group sponsored by the National Cancer Institute (NCI) to provide greater access to cancer trials [for CTSU participants only]

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.

[Note to Informed Consent Authors: the above paragraph complies with the new FDA regulation found at 21 CFR 50.25(c) and must be included verbatim in all informed consent documents. The text in this paragraph cannot be revised.]

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 Safety Monitoring Board will be regularly meeting to monitor safety and other data related to this study. The Board 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. You can still be a part of the main study even if you say 'no' to taking part in this additional research.

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

(12/10/13) *Note to Institutions: On March 22, 2012, the Quality of Life (QOL) Substudy of RTOG 0534 closed to patient enrollment, as the substudy met its patient enrollment goal. After closure to enrollment of the QOL substudy, new patients will not be offered the opportunity to participate in the following part of the RTOG 0534 study. Institutions should follow their local IRB policy regarding removal of the QOL study text from the sample consent.*

Quality of Life (QOL) Study

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 and how your cancer and cancer treatment may affect your thinking skills (neurocognitive part of QOL study).

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 some questionnaires at the following time points:

- 4 questionnaires immediately before you enroll in the study
- 4 questionnaires during week 6 of radiation therapy
- 4 questionnaires at year 1 and year 5

<u>Neurocognitive Part of QOL Study</u>
You will be asked to take part in a test of your thinking skills at the following time points:

- immediately before you enroll in the study
- during week 6 of radiation therapy
- at year 1 and year 5

It takes about 25 minutes to fill out the questionnaires and about 20 minutes to complete the test of thinking skills.

If any questions make you feel uncomfortable, you may skip those questions and not give an answer.

If you decide to take part in this study, the only things you will be asked to do is fill out the questionnaires and take part in the test of thinking skills. You may change your mind about completing the questionnaires or the test of thinking skills at any time, and you may chose to stop answering the questionnaires or taking part in the test of thinking skills 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.

YES **NO**

I choose to take part in the neurocognitive portion of the Quality of Life Study. I agree to take part in a test of my thinking skills.

YES **NO**

Use of Tissue, Blood, and Urine for Research

About Using Tissue, Blood, and Urine for Research (11/16/15)

You have had surgery to remove your prostate and your cancer. Your doctors have removed and examined some of this tissue to look at the amount and grade of the cancer and to see if the cancer extended outside of the prostate. The results of these tests will be given to you by your study doctor and will be used to plan your care.

We would like to keep some of the tissue that is left over from your surgery 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. An information sheet about using tissue for research is available to all at the following web site: http://www.cancer.gov/cancertopics/factsheet/clinicaltrials/donating-tissue-research

In addition, if you agree to participate in this part of the study, you will have blood drawn and urine collected before you start radiation therapy. Urine will also be collected at year 5 post treatment. Blood will also be drawn during the 6th week of radiation therapy, at 3, 6, and 12 months in year 1, then yearly for 6 years after completion of treatment. We would like to keep about two tablespoons of blood (all time points) and 5 tablespoons of urine (all time points prior to treatment completion, and at 5 years after completion of treatment) for future research. If you agree, 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. The research that may be done 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 study 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, blood, or urine that remains will no longer be used for research and will be returned to the institution that submitted it.

In the future, people who do research may need to know more about your health. While the study 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 is 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 may help to develop new products in the future.

Benefits

The benefits of research using tissue 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 study 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 tissue, blood, and urine may be kept for use in research to learn about, prevent, or treat cancer.

Yes **No**

2. My tissue, blood, and urine 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).

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? (11/23/11)

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://cancer.gov/cancerinfo/**

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

Signature

I have been given a copy of all _____ *[insert total of number of pages]* **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 _____