Consent and Authorization to participate as a Research Subject in:

Docetaxel and Carboplatin for patients with metastatic prostate cancer and DNA-Repair Deficiencies

SUMMARY OF STUDY: Docetaxel is a standard treatment for metastatic prostate cancer, but carboplatin is only used for certain types of prostate cancer. Studies have shown that the combination of docetaxel with carboplatin can be very effective for a group of prostate cancer patients who have certain kinds of DNA damage. All patients who qualify for this study will receive the combination of the two drugs for 10 cycles (though some may stop early and others may continue with the treatment if it is of benefit to them).

We are inviting you to be in a research study. The purpose of this Consent Form is to give you the information you will need to help you decide whether to be in the study. Please read this form carefully.

You may ask questions about the purpose of the research, what we would ask you to do, the possible risks and benefits, your rights as a volunteer, and anything else about the research or this form that is not clear.

Your participation in this study is entirely voluntary. Please take as much time as you need to discuss the study with your doctors, family, and friends. The decision to participate or not is yours. If you choose to participate, you have the right to withdraw from the study at any time.

Principal Investigator:
Bruce Montgomery, MD

Research Staff:
Stephen Plymate, MD, Investigator
Elahe Mostaghel, MD, PhD Investigator
Akemi Miyamoto, Coordinator
Jessica Maes, Coordinator
Ronda Ramsey, Coordinator

Study Title:
A Phase 2 Study of Docetaxel and carboplatin for treatment of patients with metastatic castration-resistant prostate cancer and germline or somatic DNA repair deficiency

This study is being conducted by the Genitourinary Oncology Research Group through a grant from the Prostate Cancer Foundation and the Department of Defense.

1. Who can I contact with questions while I am in this research study?

During business hours (8:00 a.m. – 4:30 p.m.), please call the Research Coordinator at (206) 277-5598 or Principal Investigator at (206) 559-5058. After business hours (nights and weekends), please call (206) 762-1010 and ask the operator to page the on-call Medical Oncology Resident.

The study researcher(s) listed above must be contacted immediately if:

- You think you may have been harmed or injured as a direct result of this research.
- You have any questions regarding your medical care issues.

You may also contact the Institutional Review Board (IRB) at (206) 277-1715 if you:

- Would like to speak with a neutral party who is not involved with this study.
- Have questions, concerns, or complaints about the research.
- Would like to verify the validity of the study.
- Have questions about your rights as a research subject.

2. What is the purpose of this research study?

Docetaxel is one of the standard treatments for metastatic castration-resistant prostate cancer (mCRPC). Carboplatin is normally only used for certain kinds of prostate cancer, but certain kinds of DNA damage can make tumors especially sensitive to carboplatin. For example, the function of the proteins encoded by the BRCA1 and BRCA2 genes is to repair cell damage, keeping cells healthy and growing normally. However, if these genes have abnormalities or mutations that have been passed from generation to generation, they will not function normally and the risk of cancer increases.

Research studies have shown that combining carboplatin with docetaxel has proven to be effective for some patients. The purpose of the study is to evaluate the safety and effectiveness of the combination of docetaxel and carboplatin for patients with mCRPC and certain kinds of DNA damage or mutations.

Throughout this Consent Form, the combination of carboplatin and docetaxel will be referred to as the "study drug" since carboplatin is not normally used for mCRPC and combining it with docetaxel has not yet been approved for marketing in the United States by the Food and Drug Administration (FDA) for mCRPC.

For purposes of this study, we will be enrolling patients who have the following:

- Metastatic castration-resistant prostate cancer
- Cancer progression after any number of first-line treatments
- Mutations in DNA-repair genes in either their tumor(s) or in their germline DNA *OR* patterns of DNA damage in their tumors that suggest that the tumor cannot repair DNA damage

If you are eligible for this study, we will treat you with a combination of carboplatin and docetaxel every 21 days. You will need to remain on treatment for 10 cycles for 6 months unless you experience unacceptable toxicity or your tumor progresses. If you respond well to treatment, you may be able to stop treatment early or we may treat you with additional cycles, which would increase the duration of your study participation.

We are planning to treat up to 20 subjects from Veterans Affairs Puget Sound Health Care System (VA Puget Sound) and may need to consent up to 67 Veterans in order to find 20 who will qualify for this study because we anticipate a significant screening failure rate.

3. What will I be asked to do in this research study?

You will need to go to VA Puget Sound Health Care System for all of your study procedures.

Most of the procedures are standard care for patients who are receiving chemotherapy. You are not consenting to any standard care procedures by signing this Consent Form.

For research purposes only, we will be isolating cell-free circulating tumor DNA from your blood, which will be drawn at the same time as blood drawn for standard care purposes whenever possible. "Cell-free circulating tumor DNA" (ctDNA) are small pieces of dying tumor cells which have been released into the bloodstream. Numerous studies have shown that ctDNA in plasma or serum has the clinical potential to be a more specific tumor marker for the diagnosis and prognosis, as well as the early detection, of cancer. Whole genome sequencing may be performed on these samples.

A chart of study procedures is attached to the end of the Consent Form for your convenience.

Screening Visit

At the Screening Visit, the following will occur:

- We will review this Consent Form, which you will sign after all your questions and concerns have been answered.
- We will collect your medical history.
- We will review your medications (including over-the-counter drugs, prescriptions, and supplements).
- We will give you a physical exam and check your vital signs.
- We will assess your general well-being and ask you questions about your daily activities.
- We will draw your blood (2-3 tablespoons) for standard care purposes and in order to isolate ctDNA for research purposes.
- We will schedule you for the following if you have not had one in the last 4 weeks:
  - Computed tomography (CT) scan or magnetic resonance imaging (MRI) scan of your pelvis/abdomen
  - Chest X-ray or chest CT scan
  - Bone scan

If we determine that you are still eligible for the study, you will begin treatment.

Treatment Period

On Day 1 of every 21-day cycle, we will:

- Check your vital signs.
- Draw your blood (2-3 tablespoons) for standard care purposes and in order to isolate ctDNA for research purposes.
- Check for side effects (adverse events).
- We will review your medications (including over-the-counter drugs, prescriptions, and supplements).
- Administer treatment (combination of carboplatin and docetaxel).

If needed at this time:

- You will need to have a CT or MRI scan of your abdomen/pelvis and an X-ray or CT scan of your chest every 3 months, or as clinically indicated.
- If bone lesions are present, you will need to have a bone scan every 3 months, at development of progression, or as clinically indicated.

Termination Visit

At this visit, the following will occur:

- We will give you a physical exam and check your vital signs.
- We will assess your general well-being and ask you questions about your daily activities.
- We will draw your blood (2-3 tablespoons) for standard care purposes and in order to isolate ctDNA for research purposes.

Genitourinary Repository

We will be isolating ctDNA from your blood, which will be drawn whenever possible at the same time as blood drawn for standard care purposes. We will label the research blood samples with a study code; no identifiers will be used (such as your name, date of birth, or social security number). Whole genome sequencing may be performed on these samples.

We will store data and the research blood samples in the Genitourinary Repository. If you have a lesion that can be biopsied, we may ask you if you would be willing to have a biopsy of your metastatic lesion before treatment and another biopsy after disease progression for the repository.

We will give you a Consent Form, which will explain this information in further detail, for the Genitourinary Repository.

4. What are some risks of joining this research study?

The drugs in this study may involve risks that are currently unknown. We may need to contact you if we learn of a new study risk, even if you have completed the study. If any of the risks included in this Consent Form become significantly updated during this study, we may ask you to sign an updated Consent Form to document that this new information has been explained to you. You will have the right to decide either to continue with the research study or to withdraw.

Below are study-related risks that are known at this time:

- **Risks of blood draw.** Possible side effects of drawing blood include faintness, inflammation of the vein, brief pain, bruising, or bleeding at the puncture site. There will also be a risk of infection, but we will take precautions by keeping the puncture site clean and dry.

- **Confidentiality of genetic testing.** In general, potential risks of genetic testing may include breach of confidentiality, which may lead to discrimination in the areas of employment, insurability, social stigmatization, or psychological stress caused by disclosure of adverse information to you or your family. In the past, people were concerned that genetic information might be used to discriminate against anyone found to be at risk for a genetic disease. While very few cases of discrimination actually occurred, the risk is now even less because of the passage of the federal Genetic Information Nondiscrimination Act (GINA). GINA makes it illegal for health insurance companies to use genetic information to make enrollment or coverage decisions. It also makes it illegal for employers to use genetic information in making decisions about hiring, firing, promotion, compensation, or other employment decisions. The protections of GINA do not include protections from genetic discrimination in life, disability, or long-term care insurance.

- **Confidentiality of DNA sample.** There is a risk that someone could use information from the sample you submitted, via DNA, to identify you if it were matched with another DNA sample provided by you. However, any user of this sample must agree not to use it for that purpose.

The combination of drugs used in this study, docetaxel (Taxotere) and carboplatin (Paraplatin), are synthetic antineoplastic agents extensively used in the treatment of solid tumors. Commercial sources will be used for this study. Both docetaxel and carboplatin are approved by the Food & Drug Administration (FDA).

Possible side effects of docetaxel

Likely side effects (occurred in more than 20% of patients):

- Hair thinning and loss
- Skin and nail changes
- Fluid retention (swelling)
- Mouth sores
- Diarrhea
- Nausea and vomiting

Less likely side effects (occurred in less than 20% of patients):

- Nervous system changes, including numbness and tingling
- Liver abnormalities
- Weakness, muscle soreness and aches

Rare but serious side effects (occurred in less than 3% of patients):

- Allergic reaction
- Life-threatening infection
- Severe fluid retention (swelling)

Possible side effects of carboplatin

Likely side effects (occurred in more than 20% of patients):

- Salt imbalance (sodium, magnesium, calcium, potassium abnormalities)
- Vomiting
- Low blood counts
- Decreased kidney function

Less likely side effects (occurred in less than 20% of patients):

- Abdominal pain and nausea
- Allergic reaction
- Numbness and tingling

Rare but serious side effects (occurred in less than 3% of patients):

- Life-threatening infection

5. What are some benefits of joining this research study?

There may be no direct benefit to you by participating in this study. However, we may be able to identify clinically important results from your DNA test results which may, in turn, help your doctor in pursuing a treatment that may have a higher likelihood of working for you. In any event, by participating, you will be making a meaningful contribution in helping researchers learn about other treatment options for people with mCRPC in the future.

6. Are there other ways I could receive these benefits?

This study is voluntary and for research purposes only. The alternative to the study is to not take part in it.

7. Who will see my information and where will it be stored?

Your research information will be kept confidential. However, some data will be shared, communicated, or stored during or after this research study.

If we learn you intend to harm yourself or others, we must report this information to appropriate authorities.

The access to your records, including your medical records, could be either for study-related purposes or to make sure your study record meets all legal, compliance, and administrative requirements. The reviewers will protect your privacy.

The Medical Monitor, Dr. Wu, will review safety and toxicity data for all subjects undergoing chemotherapy on this study.

To make sure no one other than study personnel can match you to your data, we will use a unique study code instead of identifying information such as your name or social security number. The key to the code will be stored separately from the data in a locked office at the VA Puget Sound and/or on a secure Research drive.

Safekeeping of study data

The data that we collect for this study will be kept confidential. Your paper study chart will include identifying information because it is not feasible to de-identify all study paper data. Identifiable data will be stored in a locked file cabinet in an office that will be locked when unoccupied and accessible only to study staff. Any paper study documents we have received or created will be secured in locked file cabinets accessible only to study staff. Any electronic study records will be kept in electronic folders on the secure VA network with access to the specific folders restricted to designated study staff.

Offsite data transmittal

Some of your data will be shared with other VA researchers, including Dr. Matthew Rettig and the research team at the VA Greater Los Angeles Healthcare System and Dr. Alva and his research team at the VA Ann Arbor Healthcare System who are collaborators in this study. Data will be shared via secure portal (VA's VIReC REDCap system), secure fax, tracked mail, encrypted email, Safe Access File Exchange (SAFE), or other method approved by the Information System Security Officer (ISSO).

Several genetic databases, such as the National Institutes of Health (NIH) Genomic Data Repository, GenBank, and National Cancer Foundation (NCF), are available to help researchers understand different diseases. These databases contain DNA code and medical information from participants who have various diseases. As part of this study, we may release DNA code and information about your medical condition into relevant genetic databases to be stored indefinitely in order to help researchers understand the relationship between DNA and diseases. The genetic databases would not contain names, addresses, or other information that could be used to identify you.

The DNA code in a genetic database cannot be used by itself to identify any specific person. A researcher who already has DNA code about you could use information from a genetic database to

learn more about you. Once we release information to a genetic database, we no longer have any control over the use of this information.

After study completion

Once this study is completed, we will not use the study code linking you to your data for any additional research. We will store the code linking you to your data in a secure database or in a locked filing cabinet in accordance with the VA records retention policy (which will be a minimum of 6 years after the study has been completed). We will keep your coded data indefinitely.

In the future, researchers may write about the information collected from this research study. Any future publications or articles will not include any identifying information about you without your approval in writing. Neither you nor your family will gain financially from discoveries made using the information and specimens you provide.

We would like to use your data and specimens in future research on cancer. If you agree, we will have you sign a separate Consent Form for the Genitourinary Repository.

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

8. What are some other things to think about before I decide to join this research study?

The VA requires some Veterans to pay co-payments for medical care and services. You will still have to pay these co-payments for all standard care medications and procedures (chemotherapy, imaging, blood testing) if applicable. You will not be charged for any study-related procedures, such as the ctDNA and biopsy collections.

9. What will happen if I decide I don't want to be in this research study later?

You do not have to take part in this study. If you are in this study, you can withdraw at any time. If you decide not to participate or to withdraw, no action will be taken against you; for instance, you will not lose your VA benefits.

You may be withdrawn from the study if the Investigators believe it is in your best interest.

If you decide to withdraw from the study, no new information will be collected from you; however, the study information, specimens, and data already collected will continue to be part of the analyses unless you request that we destroy your stored specimens or unpublished data related to these samples. If you decide to withdraw, or if you are terminated from the study, a person from the study team may need to meet with you to discuss the steps that are necessary to end your participation in the study.

10. What will happen if I am hurt in this research study?

If you are injured as a result of participation in a VA-approved research study, the VA will provide you with the necessary medical treatment. You will not be charged for this treatment. Veterans who are injured because of being in this study may receive payment under Title 38, United States Code, Section 1151. Veterans or non-Veterans who are injured may receive payment under the Federal Tort Claims Act.

Neither the Prostate Cancer Foundation, the Department of Defense, nor the VA is obligated to reimburse medical expenses due to your non-compliance with study procedures as described in this Consent Form or otherwise communicated to you by study personnel.

You do not waive any legal rights by signing this Consent Form.

11. Health Information Portability and Accountability Act (HIPAA)

There are rules to protect your private health information. Federal laws, state laws, and the federal medical law known as the HIPAA Privacy Rule also protect your privacy. By signing this Consent Form, you provide your permission, called your "authorization," for the use and disclosure of information protected by the HIPAA Privacy Rule.

The research team working on the study will collect information about you. This includes things learned from the procedures described in this Consent Form. They may also collect other information including your name, address, date of birth, and information from your medical record such as HIV status; drug, alcohol, or sexually transmitted disease treatment; genetic test results; or mental health treatment.

The following list of people or groups may know that you are in this study. They may have access to your research records, which may include your medical records:

- Research team members
- The Prostate Cancer Foundation and the Department of Defense, the sponsors of this study
- Seattle Institute for Biomedical and Clinical Research (the nonprofit institute that works with VA Puget Sound to conduct research) will administer study funds
- Other federal agencies including, but not limited to, the Food and Drug Administration (FDA), the Office for Human Research Protection (OHRP), the VA Office of Research Oversight (ORO), the VA Office of the Inspector General (OIG), and the Government Accountability Office (GAO)
- The VA committees that oversee research
- Dr. Wu, Chief of Oncology at the VA Puget Sound Health Care System, will be the Medical Monitor for all sites
- Laboratory staff in the lab that will be performing the genetic sequencing
- Investigators at other VAs who have similar studies at the VA Greater Los Angeles Healthcare System (Dr. Rettig) and the VA Ann Arbor Healthcare System (Dr. Alva)
- Databases such as the National Institutes of Health (NIH) Genomic Data Repository, GenBank, and National Cancer Foundation (NCF)

Your health information disclosed pursuant to this authorization may no longer be protected by federal laws or regulations and may be subject to re-disclosure by the recipient.

You can revoke this authorization in writing at any time. To revoke your authorization, you must write to the Release of Information Office at this facility or you can ask a member of the research team to give you a form to revoke the authorization. Your request will be valid when the Release of Information Office receives it. If you revoke this authorization, you will not be able to continue to participate in the study. This will not affect your rights as a VHA patient to treatment or benefit outside of the study.

If you revoke this authorization, Dr. Montgomery and his research team can continue to use information about you that was collected before receipt of the revocation. The research team will not collect information about you after you revoke the authorization.

Treatment, payment, or enrollment/eligibility for benefits cannot be conditioned on your signing this authorization. This authorization will expire at the end of the research study unless revoked prior to that time.

12. What am I agreeing to by signing this form?

I have read or have had read to me all of the above. The study has been explained to me, including a description of what the study is about and how and why it is being done. All of my questions have been answered. I have been told of the risks and/or discomforts I may encounter in the study, of the possible benefits of the study, and of the other choices of treatment that are available to me.

My rights as a research subject have been explained to me and I voluntarily consent to participate in this study. I will receive a copy of this Consent Form.

I agree to participate in this research study as described in this document.

_____ _____

Subject Signature Date

_____

Print Name of Subject

Procedure	Pre-Screening[8]	Screening (within 30 days prior to Day 1)[1]	Day 1 of Every Cycle[2]	Termination visit[5]
Informed Consent	X (pre-screen)	X (main)		
Medical History		X		
Physical exam		X		X
Vital Signs		X	X	X
ECOG performance status		X		X
CBC (w/ platelets & differentials)		X	X	X
Serum chemistry & electrolytes[3]		X	X	X
Hepatic function[4]		X	X	X
PSA		X		X
CT or MRI of pelvis/abdomen[6]		X		
Bone scan[7]		X		
Chest film or chest CT[6]		X		
Docetaxel and carboplatin			X	
Adverse Events			X	X
Concomitant Medications		X	X	
Cell free DNA collection		X	X	X
DNA sequencing for signature analysis	X[8]			