Informed consent statement: All eligible patients provided written informed consent prior to enrollment and participation in the trial.

Corresponding Author

Nawaid Usmani

Signature: _____ Date: November 14, 2015

BIOLOGICAL INVESTIGATIONS IN ACTIVE SURVEILLANCE

(A study looking at new tests to monitor prostate cancer in patients that choose not to have immediate treatment)

CONSENT FORM

This form is part of the process of informed consent. It is designed to explain this research study and what will happen to you if you choose to be in this study.

If you would like to know more about something mentioned in this consent form, or have any questions at anytime regarding this research study, please be sure to ask your doctor or nurse. Read this consent form carefully to make sure you understand all the information it provides. You will get a copy of this consent form to keep. You do not have to take part in this study and your care does not depend on whether or not you take part.

Your doctor has given us permission to ask you to be in this study.

Your participation in this study is entirely voluntary. Please take your time to make your decision. It is recommended that you discuss with your friends and/or family about whether to participate in this study.

"WHY IS THIS STUDY BEING DONE?"

You are being asked to take part in this study because you have prostate cancer. Some men that are diagnosed with prostate cancer are thought to have such a slow growing cancer (called an indolent cancer) that their cancer does not require immediate treatment, as it is unlikely that this cancer will cause problems within the patients' lifetime. This is true for your situation.

Instead of treating your prostate cancer, it is recommended that your prostate cancer be monitored with various tests to detect if it grows or becomes more aggressive. The standard follow-up for your situation would involve regular digital rectal examinations, blood tests (testing for prostate specific antigen or PSA), and prostate biopsies on a pre-defined schedule. If any of these assessments suggests that the prostate cancer is growing, then a treatment would be recommended with the intent of curing you of your prostate cancer.

This study is looking at new tests that may provide additional information about prostate cancers. This study plans to perform these tests on a schedule to determine if these tests can find the prostate cancer. It will also attempt to determine when the prostate cancer shows signs of growing or becoming more aggressive. This study is being done because the standard tests that are used to monitor prostate cancers are not fully accurate and it is hoped that better tests can be found to monitor these prostate cancers. If this study is successful, it may give future patients with prostate cancer more peace of mind that their prostate cancer is being monitored in a safe and accurate manner.

"WHAT DO WE HOPE TO LEARN?"

We hope to learn whether or not additional tests may be helpful in monitoring prostate cancers that are not initially treated. The tests that this study will use include high field strength MRI scans (or magnetic resonance imaging scans), PET scans (or positron emission tomography scans), and a biomarker called the TMPRSS2:ETS gene rearrangement. These tests have been chosen due to promising results that were found with these tests in detecting aggressive signs of prostate cancer in previous studies.

The primary purpose of this study is to determine the feasibility of a larger study that uses these tests to monitor prostate cancer in patients with slow growing cancers. This study will also try to find the best parameters to perform these tests when monitoring prostate cancers. Finally, this study will also begin to estimate the ability of these tests to detect prostate cancers and signs suggestive of aggressive cancers.

This is a feasibility study; this means that it is a small-scale version of a trial done in preparation for a larger study. Feasibility studies are used to develop and test the adequacy of research instruments, which is what we are attempting to do.

"WHAT IS INVOLVED IN THIS STUDY?"

In this study, we will follow you on a fixed schedule to monitor your prostate cancer. You will be followed to see whether or not there are any signs of the prostate cancer growing with these tests. All of these tests will be performed while you are followed for your prostate cancer as an out-patient, as none of these tests will require hospitalization. The schedule for the tests is listed below:

Year 1	Month 0	Month 3	Month 6	Month 9	Month 12
Digital rectal examination (DRE)	X	X	X	X	X
Blood test (PSA – prostate specific antigen *add GFR Month 0 and 12)	X*	X	X	X	X*
Prostate biopsy (including tissue for biomarker test)	X				X
MRI scan (magnetic resonance imaging)	X				X
PET scan (positron emission tomography)	X				X

Years 2 and 3	Month 18	Month 24	Month 30	Month 36	Month 42
Digital rectal examination (DRE)	X	X	X	X	X
Blood test (PSA – prostate specific antigen *add GFR Month 24 and 36)	X	X*	X	X*	X
Prostate biopsy (including tissue for biomarker test)		X		X	
MRI scan (magnetic resonance imaging)		X		X	
PET scan (positron emission tomography)		X		X	

Years 4 and 5	Month 48	Month 54	Month 60
Digital rectal examination (DRE)	X	X	X
Blood test (PSA – prostate specific antigen *add GFR Month 48 and 60)	X*	X	X*
Prostate biopsy (including tissue for biomarker test)	X		X
MRI scan (magnetic resonance imaging)	X		X
PET scan (positron emission tomography)	X		X

"HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?"

About 26 people will take part in this study in Alberta.

"WHAT WILL MY PARTICIPATION INVOLVE?"

If you take part in this study, you will have a number of tests and procedures done to monitor your prostate cancer. These are listed above in the table in the section "What is involved in this study?"

If you choose not participate in this study, most physicians would recommend the following tests and procedures as part of standard care:

Year 1	Month 0	Month 3	Month 6	Month 9	Month 12
Digital rectal examination (DRE)	X	X	X	X	X
Blood test (PSA – prostate specific antigen)	X	X	X	X	X
Prostate biopsy	X				X

Years 2 and 3	Month 18	Month 24	Month 30	Month 36	Month 42
Digital rectal examination (DRE)	X	X	X	X	X
Blood test (PSA – prostate specific antigen)	X	X	X	X	X
Prostate biopsy				X	

Years 4 and 5	Month 48	Month 54	Month 60
Digital rectal examination (DRE)	X	X	X
Blood test (PSA – prostate specific antigen)	X	X	X
Prostate biopsy			X

MRI (magnetic resonance imaging):

You will be asked to come to the Cross Cancer Institute at least 30 minutes before your appointment time and you will have to stay in the department for 2-3 hours for the scan and the IV fluids after the scan. An intravenous (IV) line will be inserted into a vein in your arm. You will also be asked to ensure that your bladder and rectum are empty for this scan. About 15 minutes before your scan, you will be given an injection of Buscopan® to help slow down your bowels and allow for clear pictures of the prostate to be taken. You will then have your MRI scan, during which a second injection of gadolinium will be given into your intravenous to help see your prostate clearly. After the MRI scan, you will be hydrated with intravenous normal saline (salt solution) to minimize the risk of kidney damage from the contrast that is used, over a period of 2-3 hours usually.

PET Scan (positron emission tomography):

You will be asked to come to the Department of Oncologic Imaging at least 30 minutes before your appointment time and you will have to stay in the department for up to two hours. You will not have anything to eat for twelve hours before your appointment, but may sip water to satisfy your thirst. You should take your normal medications as required. When you arrive for your appointment you sign a separate consent form for the PET scan aspect of the study and you will be asked to fill out a clinical questionnaire that will take about five minutes to complete.

You may be given an oral medication (Ativan ®) that is placed under your tongue to help you relax and reduce muscle activity. If you choose to receive Ativan, you should make arrangements for someone to take you home since the drug may not have worn off by the time the PET scan is completed.

An intravenous (IV) line will be inserted into a vein in your arm. You will lie down on the PET scanning table, and a small amount (about one teaspoon) of the ^{11}C-Choline solution will be injected through the IV in your arm. The scan will start right away. You will need to lie still and quietly on the scan table for 40 – 60 minutes while the machine moves over your lower abdomen and pelvic area.

After the scan, you will be helped down from the table and your IV will be removed. You will be asked to urinate completely and told to drink plenty of water for the next few hours.

Prostate Biopsies and Pathology Review:
Prostate biopsies are performed by either a urologist or a radiologist. The biopsies require a visit to your local hospital and take approximately 20 to 45 minutes to perform. Using an ultrasound in the rectum, a biopsy of the prostate is taken. The biopsies may cause discomfort.

All or some of your tumour will be removed by biopsy. Some of this tumour tissue will be examined by a pathologist to help make your diagnosis. The remaining tumour tissue is stored in the pathology department. If you participate in this study, this tissue will be sent to a study pathologist for review and research investigation associated with this protocol. This will include testing for the TMPRSS2:ETS gene rearrangement. You will not have to provide any other tissue. After the study testing is finished, any tissue left will be destroyed.

"HOW LONG WILL I BE INVOLVED IN THE STUDY?"

You may be in this study for as long as 5 years. If this study is successful and a larger study is developed, then you will have the option of joining the larger study after your first five years of follow-up.

"WHAT ARE THE SIDE EFFECTS?"

Every medical test including the standard tests have potential side effects, which your doctor will explain to you. It is important that you know and understand the possible side effects of the tests used in this study.

Blood test (PSA – prostate specific antigen and GFR):
You may feel some discomfort from the needle when blood is drawn. There is also a small risk of fainting, swelling, bruising, bleeding or (rarely) local infections at the site of the needle punctures which will be used for taking blood samples.

Prostate biopsies (including tissue for biomarker testing):
The biopsies may cause discomfort. Other risks associated with having a biopsy include possible bleeding or infection at the biopsy site. Less than 2% of patients are expected to experience any significant bleeding or infection related to having a biopsy. A five day course of antibiotics will be given with each set of biopsies to minimize the chance of infection.

MRI (magnetic resonance imaging):
MRI scanning is a way to examine the body without X-rays. Instead, it uses a large magnet, radio-waves, and a computer to scan your body and give us information about your tumor. The scan itself does not have any side effects. Some medical devices, such as cardiac pacemakers, cochlear implants, or surgical clips can interfere with the study or be hazardous. We will discuss this matter with you in detail prior to scanning to ensure you do not have any of these medical devices. Those who suffer from claustrophobia may feel anxiety with the scan as it is taken with the patient in a relatively small space. Very rarely, people may experience a transient tingling sensation in their extremities, dizziness, or a warming sensation during the scan.

The following are the side effects of each drug used for the MRI scans. These side effects may or may not be more severe when the drugs are taken together.

Drug	Route	Common (greater than 10% of cases)	Uncommon/Rare (less than 5% of cases)
Buscopan®	IM/IV	▪ dry mouth ▪ changes in vision (difficulty focusing) ▪ difficulty urinating	▪ dizziness ▪ flushing ▪ allergic reactions
Gadolinium	IV		▪ damage to the kidneys ▪ allergic reactions

IM = Intramuscular (in a muscle)
IV = Intravenous (into a vein)

If you decide to participate in this study, you will first have an intravenous (IV) started in your right fore-arm. This is for the injection of the contrast during the MRI scan. Prior to the MRI you will be given an

intramuscular injection of Buscopan®. This medication will be given to slow down movement in your bowels and ensure that clear pictures of the prostate can be taken with the MRI and MRSI scans. This medication is generally well tolerated, although some patients experience a dry mouth, changes in their vision (difficulty focusing on objects), and/or difficulty with urination. Rarely, Buscopan® can cause dizziness, flushing or allergic reactions.

During the MRI there will be an injection of contrast (called gadolinium) into the IV tubing. This will allow us to see the prostate cancer better on the MRI scans. The injection is very safe, although there is a very small chance of the contrast causing kidney damage or an allergic reaction to this contrast. To minimize the risk of kidney damage, you will be hydrated with intravenous normal saline (salt solution) over a period of 2-3 hours after the MRI which will help eliminate the contrast from your body.

You may feel some discomfort from the needle when these injections are given. There is also a small risk of fainting, swelling, bruising, bleeding or (rarely) local infections at the site of the needle punctures which will be used for giving your study injections.

PET scans (positron emission tomography):
In the following table are the side effects of each drug used in the PET scans. You may or may not be given Ativan®. ^{11}C-Choline is the chemical used in the PET scans. These are the side effects we know about at present that could happen at a dose of ^{11}C-Choline 1000 times more than you will be receiving. However, there may be other side effects we do not know about yet.

Drug	Route	Common (greater than 10% of cases)	Uncommon/Rare (less than 10% of cases)
^{11} C-Choline	IV	None known.	None known from radioactive ^{11}C-Choline; bruise or very rarely infection at the site of injection. The radiation dose to which you will be exposed is comparable to the exposure of about 1/6th that of a normal CT scan.
Ativan®	SL	▪ Clumsiness ▪ Dizziness ▪ Sleepiness ▪ Unsteadiness ▪ Weakness	▪ Abdominal cramps ▪ Blurred vision ▪ Confusion ▪ Convulsions ▪ Dry mouth ▪ Forgetfulness ▪ Hallucinations ▪ Headache ▪ Memory loss ▪ Racing heartbeat / palpitations ▪ Shaking / slurred speech ▪ Sore breast ▪ Staggering / trembling ▪ Trouble breathing ▪ Urination problems

IV = Intravenous (into a vein) SL = Sublingual (under the tongue)

As part of your PET scan, you will have a CT scan. There is a potential risk of radiation exposure from these CT scans, however, this risk is considered small. The amount of radiation exposure from one CT scan is about the same as the amount of radiation a person would get from natural surroundings in three years.

If you have any side effects, either those on the list or others, or if you want more information on how the test(s) could affect you, you should call the doctor or nurse in charge of the study. Their telephone numbers are on page 9 of this form.

If we get any new information about the tests in this study, you will be told about them so that you can continue to get the best care possible.

If you have any side effects, either those on the list or others, or if you want more information, you should call the doctor or nurse in charge of the study. Their telephone numbers are on page 9 of this form.

"WHAT ARE THE REPRODUCTIVE RISKS?"

There are no known reproductive risks associated with any of the tests used in this study.

"**WHAT ARE MY RESPONSIBILITIES?"**

You must be willing to attend all scheduled study visits and undergo all of the procedures described above. It is very important that you inform the study doctor or study nurse of any side effects or health problems that you may be experiencing as well as any medications (prescribed or holistic) that you are taking while on this study.

"WHAT ARE MY ALTERNATIVES?"

You may choose not to participate in this study. Your decision not to participate in this study will not compromise the quality of care that you receive from your physician.

As an alternative, you may choose to monitor your prostate cancer with your physician using the standard tests. Another alternative is to choose to treat your prostate cancer with one of the following treatments:

(1) brachytherapy;
(2) external beam radiation therapy;
(3) surgery; or
(4) cryotherapy

"ARE THERE ANY BENEFITS TO PARTICIPATING IN THIS STUDY?"

Participation in this study may or may not be of personal benefit to you. However, based on the results of this study, it is hoped that, in the long-term, patient care can be improved.

"CAN I WITHDRAW FROM THIS STUDY?"

In discussion with you, your doctor at the Cross Cancer Institute, either at his/her own initiative or at the request of the sponsor of this study, may withdraw you from the study at any time if it is in your best interests. Taking part in this study is voluntary; you may withdraw from the study at any time if you wish to do so. If you decide to stop participating in the study, we encourage you to talk to your doctor first.

Your doctor can take you off the study treatment early for reasons such as:

- You are unable to tolerate the study tests.
- New information becomes available that indicates the study tests are no longer in your best interest.
- Your doctor no longer feels this is the best treatment strategy for you.

If you stop early, we would like to keep track of your medical condition indefinitely to look at the long-term effects of the study.

"ARE THERE COSTS TO ME FOR TAKING PART IN THIS STUDY?"

You will not have to pay for the tests that you receive in this study. You will be coming to the Cross Cancer Institute more often than if you were not part of this study. There may be additional costs to you for taking part in this study such as:

- parking
- transportation
- meals
- babysitting, etc.

"WHAT ARE MY RIGHTS AS A PARTICIPANT?"

If you suffer an injury or become ill as a result of participating in this research, you will receive all medical treatments (or services) recommended by your doctors. No compensation will be provided beyond this point. However, it is important to note that nothing said in this consent form alters your legal rights to recover damages (e.g. legal action).

If new information becomes available or there are changes to the study that may affect your health or willingness to continue in the study, you will be told in a timely manner.

"WILL MY PERSONAL INFORMATION BE KEPT CONFIDENTIAL?"

Identifiable health information will be collected from you and from your Provincial Electronic Health Record (NetCare) during this study. This information may be used by the researchers who are carrying out this study, and may be disclosed to others as described below. Any research proposal to use information that identifies you for a purpose other than this study must be approved in advance by the Alberta Cancer Research Ethics Committee.

Direct access to your identifiable health information collected for this study will be restricted to the researchers who are directly involved in this study except in the following circumstances:

Your identifiable health information may need to be inspected or copied from time to time for quality assurance (to make sure the information being used in the study is accurate) and for data analysis (to do statistical analysis that will not identify you). The following organizations may do this inspection:

- Health Canada, the Canadian regulatory body.
- Alberta Cancer Research Ethics Committee, the institutional review board at this centre

- Members of the Regulatory/Audit team at the Cross Cancer Institute, for quality assurance purposes

Any disclosure of your identifiable health information will be in accordance with the Alberta Health Information Act. As well, any person from the organizations looking at your records on-site at the Cross Cancer Institute will follow the relevant Alberta Health Services policies and procedures that control these actions. Any disclosure of your identifiable health information to another individual or organization not listed here will need the approval of Alberta Cancer Research Ethics Committee.

Your identifiable health information collected as part of this study, which includes records of your progress, will be kept confidential in a secure AHS facility.

The researchers who are directly involved in your study may share information about you with other researchers, but you will not be identified in that shared information except by a number. The key that indicates what number you have been assigned will be kept secure by the researchers directly involved with your study and will not be released.

Although absolute confidentiality can never be guaranteed, Alberta Health Services will make every effort to keep your identifiable health information confidential, and to follow the ethical and legal rules about collecting, using and disclosing this information in accordance with the Alberta Health Information Act and other regulatory requirements.

The information collected during this study will be used in analyses and will be published and/or presented to the scientific community at meetings and in journals, but your identity will remain confidential. This information may also be used as part of a submission to regulatory authorities around the world. It is expected that the study results will be published as soon as possible after completion. Your study doctor will be informed of the results of the study once they are known.

"WHO DO I CALL IF I HAVE QUESTIONS OR PROBLEMS?"

For information about your disease and/or research related injury/illness, you may contact the Principal Investigator Dr. Nawaid Usmani at (780) 432-8518, Research Nurse Michelle Encarnacao at (780) 432-8324 or Wanda Gaudon at (780) 577-8029 or page them through the Cross Cancer Institute Switchboard at (780) 432-8771 to answer any questions you have about this study.

If you feel, at any time, that you have not been informed to your satisfaction about the risks, benefits, or alternatives of this study, or that you have been encouraged to continue in this study after you wanted to withdraw, you can call the Patient Representative at (780) 432-8585

UNDERSTANDING OF PARTICIPANTS

I can refuse to take part or withdraw from this study at any time without jeopardizing my health care. If I continue to take part in the study, I will be kept informed of any important new developments and information learned after the time I gave my original consent.

I also give consent for the Principal Investigator and Alberta Health Services (the Custodian) to disclose identifiable health information, as per the Alberta Health Information Act, to the organizations mentioned on the previous pages.

I have read and understood all of the information in this consent form. I have asked questions, and received answers concerning areas I did not understand. I have had the opportunity to take this consent form home for review and discussion. My consent has not been forced or influenced in any way. I consent to participate in this research study. Upon signing this form I will receive a signed copy of the consent.

(PRINT NAMES CLEARLY)

_____	_____	_____
Name of Patient	Signature of Patient	Date
_____	_____	_____
Name of Person Obtaining Consent	Signature of Person Obtaining Consent	Date

Patient Study Number or Hospital Number: _____

Was the patient assisted during the consent process in one of the ways listed below?
□ Yes □ No

If yes, please check the relevant box and complete the signature space below:

□ The consent form was read to the patient, and the person signing below attests that the study was accurately explained to, and apparently understood by the patient.

□ The person signing below acted as a translator for the patient during the consent process.

_____	_____
Signature of person assisting In the consent discussion	Date

Please note: More information regarding the assistance provided during the consent process should be noted in the medical record for the patient if applicable.