BC Cancer Agency
CARE & RESEARCH
An agency of the Provincial Health Services Authority

Subject Information and Main Study Consent Form

[18F]-6-L-Fluoro-Dihydroxy-Phenylalanine (^{18}F-DOPA) in Positron Emission Tomography (PET) Imaging in Neuroendocrine Tumours

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Sponsor: British Columbia Cancer Agency (BCCA)

Emergency Contact Number (24 hours / 7 days a week):

For emergencies only: Call the centre nearest you and ask for your study doctor or, if he or she is not available, ask for your usual oncologist or the oncologist on-call.

Vancouver Centre	(604) 877-6000
Vancouver Island Centre	(250) 370-8000
Fraser Valley Centre	(604) 581-2211
Abbotsford Centre	(604) 851-4710
Centre for the Southern Interior	(250) 862-4000

For non-emergency contact numbers, see under the section heading "Contact" [page 8-9] below.

INVITATION

You are being invited to take part in this research study because you are either diagnosed with or suspected of having a neuroendocrine tumor (NET), and your doctor has determined that you require a scan to provide additional information.

YOUR PARTICIPATION IS VOLUNTARY

Participation in this study is voluntary. You may decide not to participate or to withdraw at any time without any negative consequences to the medical care, education, or other services to which you are entitled or are presently receiving.

Before you give your consent to participate in this clinical trial, please take time to read carefully and consider the following information which describes the purpose and procedures, the possible risks and benefits, and other information about the clinical trial.

You also need to know that there are important differences between being in a research study and being cared for by your doctor. When you participate in a research study, the main goal is to learn things to help other patients in the future. Outside a research study, your doctor's sole goal is to care for your health. Nevertheless, the researchers have a

duty of care to all subjects and will inform you of any information that may affect your willingness to remain in the study.

If you wish to participate in this study, you will be asked to sign this form.

Please take time to read the following information carefully and to discuss it with your family, friends, and doctor before you decide.

WHO IS CONDUCTING THE STUDY?

This study is not receiving funds from an external agency or sponsor.

BACKGROUND

If you agree to participate with this clinical trial, you will undergo a Positron Emission Tomography (PET) scan, using a radio-labeled tracer called ^{18}F-Fluoro-Dihydroxy-Phenylalanine (or ^{18}F-FDOPA). An ^{18}F-FDOPA PET scan combines both a Computerized Tomography (CT) scan and a PET scan done on the same machine during one procedure. For the purposes of the rest of this consent form, we will refer to this combined scan (PET and CT using the ^{18}F-FDOPA radio-labeled tracer) as an ^{18}F-FDOPA PET scan.

Treatment and outcomes for neuroendocrine tumours (NETs) depend largely on accurate diagnosis and staging of the disease. ^{18}F-FDOPA PET scanning may more accurately characterize disease, or determine the stage and sites of recurrent disease in NETs compared with traditional functional imaging procedures using the radiopharmaceuticals ^{123}I-Metaiodobenzylguanidine (MIBG) and ^{18}F-Fluorodeoxyglucose (^{18}F-FDG), or other conventional imaging such as computerized tomography (CT) and magnetic resonance imaging (MRI). The functional information that is obtained from ^{18}F-FDOPA PET, as performed by the BCCA, may have an impact on the management of some patients with neuroendocrine lesions. ^{18}F-FDOPA PET is used for pre-treatment staging of these lesions, to aid in planning of therapy, to monitor the response to therapy and to provide assessment of restaging / recurrence after therapy.

^{18}F-FDOPA is a radio-labeled tracer that will be used in this study when subjects undergo their PET scan. This tracer is taken up by neuroendocrine cells, helping to identify and differentiate malignant tissue from normal tissue. The ^{18}F-FDOPA is considered investigational because its use as a tracer for patients undergoing PET scanning is not yet routinely performed in British Columbia. This is the first time FDOPA PET scans will be used at the BCCA for treatment planning for subjects with neuroendocrine tumours. Although ^{18}F-FDOPA is considered investigational for NETs, it has been used in Parkinson's Disease research at the University of British Columbia (UBC) Hospital for more than 10 years and has been performed on some patients who have a diagnosis of cancer at the BCCA over the past few years. Side effects related to receiving ^{18}F-FDOPA as the tracer for your PET scan as part of this study are unlikely. The ^{18}F-FDOPA that will be used in this study will be manufactured for the BCCA at the Tri-University Meson Facility (TRIUMF) located at UBC.

WHAT IS THE PURPOSE OF THE STUDY?

This is an expanded access study. The purpose of this study is to make ^{18}F-FDOPA PET/CT imaging available to people who may benefit from the scan's findings, and to also collect further data on the effectiveness of ^{18}F-FDOPA PET/CT in neuroendocrine tumours.

The ^{18}F-DOPA is manufactured by TRIUMF for use in subjects undergoing PET scanning at the BCCA – Vancouver Centre. Before Health Canada will approve the use of a new drug (such as ^{18}F-DOPA) they require information to ensure that the new drug is safe and effective. In this clinical trial, the BCCA will study 300 subjects who will undergo ^{18}F-DOPA PET scanning. Information on the safety and efficacy of ^{18}F-DOPA will be submitted to Health Canada to obtain approval for the use of ^{18}F-DOPA at the BCCA. We anticipate that it will take 5 years to enroll 300 subjects and complete this clinical trial.

This clinical trial will also allow us to evaluate ^{18}F-DOPA PET as a diagnostic and decision-making tool in the management of patients diagnosed with, or suspected of having NETs in the province of British Columbia.

WHO CAN PARTICIPATE IN THIS STUDY?

You may participate in this study if:

- You have provided written informed consent.
- You have been referred by your treating doctor.
- You meet the BCCA evidence-based guidelines for ^{18}F-DOPA PET in neuroendocrine tumours (your doctor and the clinical trial team will ensure this).
- You will be able to tolerate the physical / logistical requirements for completing an ^{18}F-DOPA PET scan including lying flat for 30 minutes and tolerating intra-venous (IV) injection of the ^{18}F-DOPA radioactive tracer.

WHO SHOULD NOT PARTICIPATE IN THE STUDY?

You cannot participate in this if:

- You are pregnant.
- Your doctor or the clinical trials staff assess that you are too sick to participate.
- You exceed the safe medical weight limit of the PET bed (204.5 kg) or you cannot fit through the PET machine (diameter 70 cm).

WHAT DOES THE STUDY INVOLVE?

If you agree to participate in this clinical trial, you will undergo the following:

Prior to the procedure:

- If you are breast feeding you will be pre-instructed to withhold breastfeeding for 24 hours after the scan.
- You will be instructed to fast for a minimum of 6 hours prior to your ^{18}F-DOPA PET scan. When your appointment time is booked, the PET staff will make sure you understand when you have to start fasting. You may drink water and take any usual medications prior to your scan.
- If you are a pre-menopausal woman who cannot state with certainty that you are not pregnant, a urine pregnancy test will be performed.

- If you are diabetic, you will be given instructions on how to manage your diabetes on the day of your scan.

When you arrive for the procedure:
- The clinical trials doctor and/or other PET staff will meet with you to answer any questions you might have.
- You will fill out a medical questionnaire that will ask you some routine information and will take about 5-10 minutes to complete.
- You will be weighed and vital signs will be measured (blood pressure, heart rate and blood oxygen saturation).

During the Procedure:
- You will have an IV catheter inserted. At the same time, if you are known to be diabetic, a small amount of blood will be taken to measure your blood glucose level.
- You will receive an IV dose of ^{18}F-DOPA. The injection volume will be very small and it will only take a few seconds to administer through your IV.
- You will rest in a private quiet room for 45 to 60 minutes, to enable the ^{18}F-DOPA to circulate throughout your body.
- You will undergo the ^{18}F-DOPA PET scan, which will take about 30 minutes. You will need to lie still on the scanner bed.
- During the scan, the PET staff will monitor you by direct vision, by video camera and with pulse oximetry (a small clamp that attaches to a finger and measures blood oxygen saturation and heart rate).

After the Procedure:
After the scan is completed, you will be free to leave the BCCA and will be encouraged to drink 3 to 4 extra glasses of water by the end of the day to promote further clearance of the remaining ^{18}F-DOPA tracer from your body. If there are any concerns that your health status has changed during the ^{18}F-DOPA PET scan then a physician will provide a more in-depth assessment, but we do not expect that any subjects will experience any side effects.

Your ^{18}F-DOPA PET scan will be reviewed by a BCCA doctor specialized in PET. The results will be sent to your referring doctor who will contact you about the results

WHAT ARE THE POSSIBLE HARMS AND DISCOMFORTS?
^{18}F-DOPA PET scans are considered very safe procedures with few associated risks. There have never been any reported side effects attributed to the ^{18}F-DOPA tracer. However, it is possible that not all side-effects are known; there could be side effects that are severe, disabling, or irreversible. You might experience some minor discomfort associated with the insertion of the IV catheter. This will be very similar to having a needle for a routine blood test. You may develop a small bruise, however significant bleeding is extremely rare

The amount of radiation exposure that you will encounter during the ^{18}F-DOPA PET scan is equivalent to the amount you would receive from other conventional scans that have been used safely for decades. There is no published data that any side effects in

humans have ever been shown to be directly related to radiation exposure subjects have received from ^{18}F-DOPA PET scans. You are unlikely to have any complications in the future as a result of the ^{18}F-DOPA PET scan.

WHAT ARE THE POTENTIAL BENEFITS OF PARTICIPATING?
There is no guarantee that you will benefit from participating in this clinical trial. ^{18}F-DOPA PET scans may more accurately characterize disease. Your ^{18}F-DOPA PET scan may help your doctor to offer more appropriate treatment for you. Finally, your participation in this clinical trial may allow the investigators to gain valuable knowledge that may benefit others in the future.

WHAT ARE THE ALTERNATIVES TO THE STUDY TREATMENT?
This is a clinical trial and participation is strictly voluntary. If you decide you do not want to participate in this study, your doctor will organize for you to undergo a conventional scan (such as CT or MRI). Participation in this clinical trial will not make you ineligible for other clinical trials.

WHAT IF NEW INFORMATION BECOMES AVAILABLE THAT MAY AFFECT MY DECISION TO PARTICIPATE?
If you choose to enter this study and at a later date a more effective procedure becomes available, it will be discussed with you. You will also be advised of any new information that becomes available that may affect your willingness to remain in this study.

WHAT HAPPENS IF I DECIDE TO WITHDRAW MY CONSENT TO PARTICIPATE?
You may withdraw from this study at any time without giving reasons.

If you choose to enter the study and then decide to withdraw at a later time, all data collected about you during your enrolment in the study will be retained for analysis. It is a legal requirement that these data cannot be destroyed.

CAN I BE ASKED TO LEAVE THE STUDY?
If you are not able to follow the requirements of the study or for any other reason, the study doctor may withdraw you from the study and will arrange for your care to continue. On receiving new information about the treatment, your research doctor might consider it to be in your best interests to withdraw you from the study without your consent if they judge that it would be better for your health.

WILL MY TAKING PART IN THIS STUDY BE KEPT CONFIDENTIAL
Your confidentiality will be respected. However, research records and health or other source records identifying you may be inspected in the presence of the Investigator or his/her designate by representatives of *Health Canada* and the UBC BCCA Research Ethics Board for the purposes of monitoring the research. No information or records that disclose your identity will be published without your consent, nor will any information or records that disclose your identity be removed or released without your consent unless required by law.

You will be assigned a unique study number as a subject in this study. Only this number will be used on any research-related information collected about you during the course of

this study, so that your identity [i.e. your name or any other information that could identify you] as a subject in this study will be kept confidential. Information that contains your identity will remain only with the Principal Investigator and/or designate. The list that matches your name to the unique study number that is used on your research-related information will not be removed or released without your consent unless required by law.

Your rights to privacy are legally protected by federal and provincial laws that require safeguards to insure that your privacy is respected and also give you the right of access to the information about you that has been provided to the sponsor and, if need be, an opportunity to correct any errors in this information. Further details about these laws are available on request to your study doctor.

PRIMARY CARE PHYSICIAN/SPECIALIST NOTIFICATION

Your family physician and other specialists involved in your care will be notified of your participation in the study so that can be provided with proper medical care. Information shared with your physicians may include:

- Tests results
- Reports of operations
- X-rays, other body scans
- Results of your treatment
- Laboratory tests
- Imaging tests/reports

Even after your procedure is complete, information will still be sent on your progress to see how well the procedure worked. If you stop taking part in the study, information will also still be sent because it is important to follow the progress of all people who started out on the study, unless you choose to withdraw your consent for the release of information as well.

AFTER THE STUDY IS FINISHED

You may not be able to receive additional ^{18}F-DOPA PET scans once the clinical trial is complete. Possible reasons for this include: the ^{18}F-DOPA PET may not turn out to be effective or safe; the ^{18}F-DOPA may not be approved for use in Canada; your doctor may not feel it is the best option for you; coverage may not be available for this treatment in British Columbia and you may decide it is too expensive to purchase on your own.

WHAT HAPPENS IF SOMETHING GOES WRONG?

Signing this consent form in no way limits your legal rights against the sponsor, investigators, or anyone else, and you do not release the study doctors or participating institutions from their legal and professional responsibilities.

WHAT WILL THE STUDY COST ME?

Reimbursement:

You will not be paid for participating in this study. There will be no costs to you during the study for medical services or laboratory tests which are needed as part of the study. However, taking part in this study may result in added costs to you, such as travel expenses, parking and meal costs while away from home.

Compensation:
If you are injured as a consequence of participation in the study due to the administration of the study drug or study procedures, your medical condition will be evaluated and medical care will be provided by one of the investigators or you will be referred for appropriate treatment. If you are injured as a result of participating in this study, the costs of your medical treatment will be paid for by your provincial medical plan.

No funds have been set aside to compensate you in the event of injury or illness related to study treatment or procedures.

You do not waive any of your legal rights to compensation by signing this consent form.

The investigators conducting this clinical trial will not receive any personal payments for conducting this clinical trial. In addition, neither the BC Cancer Agency nor any of the investigators or staff conducting this clinical trial will receive any direct financial benefit from conducting this clinical trial.

WHO DO I CONTACT IF I HAVE QUESTIONS ABOUT THE STUDY DURING MY PARTICIPATION?
If you have any questions or desire further information with respect to this clinical trial, or if you experience any side effects, you can talk to your clinical trial doctor, who is:

Dr. _____ Telephone:_____

In the event of a research related injury, please speak to your doctor (indicated above) or (after hours) call the centre nearest you and ask for your doctor or, if he or she is not available, your usual oncologist or the oncologist on call.

Or, you can speak to the doctor who is the principal investigator, Dr. Don Wilson, Medical Director, BCCA Centre for Functional Imaging at (604) 877-6000 ext 5979.

WHO DO I CONTACT IF I HAVE ANY QUESTIONS OR CONCERNS ABOUT MY RIGHTS AS A SUBJECT?
If you have any concerns or complaints about your rights as a research subject and/or your experiences while participating in this study, contact the Research Subject Information Line in the University of British Columbia Office of Research Services by e-mail at RSIL@ors.ubc.ca or by phone at 604-822-8598 (Toll Free: 1-877-822-8598).

SUBJECT CONSENT TO PARTICIPATE

A Phase II Study for the use of [18F]-6-L-Fluoro-Dihydroxy-Phenylalanine (^{18}F-DOPA) in Positron Emission Tomography (PET) Imaging in Neuroendocrine Tumours

SIGNATURES

Subject Consent

My signature on this consent form means:

- I have read and understood the subject information and consent form.
- I have had the opportunity to ask questions and have had satisfactory responses to my questions.
- I understand that my participation in this study is voluntary and that I am completely free to refuse to participate or to withdraw from this study at any time without changing in any way the quality of care that I receive.
- I authorize access to my health record as described in this consent form.
- I understand that I am not waiving any of my legal rights as a result of signing this consent form.

I will receive a signed copy of this consent form including all attachments, for my own records. I consent to participate in this clinical trial.

_____	_____	_____
Subject's Signature	Printed name	Date

_____	_____	_____	_____
Signature of Person Obtaining Consent	Printed name	Study Role	Date

If this consent process has been done in a language other than that on this written form, with the assistance of a translator, indicate:

Language:_____

Was the subject assisted during the consent process in one of ways listed below?

☐ Yes ☐ No [Note: For typical situations where the person conducting the consent discussion simply reads the consent with the subject to ensure that informed consent is properly obtained, check "no".]

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

☐ The consent form was read to the subject, and the person signing below attests that the study was accurately explained to, and apparently understood by, the subject (please check if subject is unable to read).

☐ The person signing below acted as an **interpreter/translator** for the subject, during the consent process (please check if an interpreter/translator assisted during the consent process).

_____	_____	_____
Signature of Person Assisting in Consent Discussion	Printed Name	Date

Where Third Party Consent is Being Obtained

The parent/guardian or legally authorized representative AND investigator are satisfied that the information contained in this consent form was explained to the child/minor to the extent that he/she is able to understand it, that all questions have been answered, and that the child/minor assents (agrees with the decision) to participate in this research.

_____	_____	_____
Parent/Guardian or Legally Authorized Representative's signature	Printed name	Date
_____	_____	_____
Signature of Investigator or Designate	Printed name	Date

SUBJECT'S ASSENT (AGREEMENT) TO PARTICIPATE IN RESEARCH

I have had the opportunity to read this consent form, to ask questions about my participation in this research, and to discuss my participation with my parent(s)/guardian(s) or legally acceptable representative. All my questions have been answered. I understand that I may withdraw from this research at any time, and I will continue to be offered the best available medical care. I will receive a copy of this consent form. I agree to participate in this study.

_____	_____	_____
Subject's Signature	Printed name	Date