Study Information and Consent Form

Official Study Title for Internet Search on http://www.ClinicalTrials.gov:

Evaluation of the safety and sensitivity of ^{68}Ga-DOTATOC PET/CT for imaging NET patients

Clinical Trials Reg # NCT03583528

Functional Imaging, BC Cancer
BC Cancer Research Centre

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Funding Support: BC Cancer Foundation

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) 851-4700
Centre for the Southern Interior	(250) 862-4000
Centre for the North	(250) 645-7300

1. Invitation

You are being invited to take part in this research study because you may have a type of cancer called a neuroendocrine tumor (NET) or a type of cancer that has what is called "somatostatin receptors". To determine the extent of your cancer, some diagnostic scans are in current use (like computed tomography (CT), magnetic resonance imaging (MRI), and somatostatin receptor scintigraphy), but this research project proposes a new type of scan, ^{68}Ga-DOTATOC PET/CT, that may be better than current scans. The goal of this research project is to evaluate the new type of scan.

2. Your participation is voluntary

Your participation is voluntary. You have the right to refuse to participate in this study. If you decide to participate, you may still choose to withdraw from the study at any time without any negative consequences to the medical care, education, or other services to which you are entitled or are presently receiving.

You should be aware that there is a difference for both you and your doctor between being a patient and being a research participant. As a patient all medical procedures and treatments are carried out for your benefit only according to standard accepted practice. As a research participant you and your doctor also must take into account the requirements for the research study. These may include procedures and treatments that are not part of standard practice or are not yet proven. This consent form describes the diagnostic and treatment procedures that are being carried out for research purposes. Please review the consent document carefully when deciding whether or not you wish to be part of the research and sign this consent only if you accept being a research participant.

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.

3. Who is conducting this study?

This study is being conducted by the BC Cancer and funded by the BC Cancer Foundation.

4. Background

NETs are a type of cancer that originates from specific types of cells in your body and are most often seen in the digestive tract, pancreas, and in the lungs, although they may appear anywhere in your body. These tumors are generally slow growing, but some can be aggressive and difficult to treat. Some of these tumors can also produce hormones and proteins that can cause discomfort in people that have them, even when there is little tumor present in the body. It is important to accurately locate where the cancer cells are in the body.

Compared to healthy cells, the surface of these tumor cells has a greater number of special molecules called somatostatin receptors. One type of scan in current use, sometimes called an Octreoscan™, is able to show where in your body the cancer cells are located, so that your treatment can be more accurately determined by your physician or surgeon. This is a test that is sometimes ordered by your physician in addition to other types of scans like CT scan, MRI, or ultrasound.
Another type of nuclear medicine scan that is sometimes used is called a fluorodeoxyglucose positron emission tomography with computed tomography (FDG PET/CT). It makes use of the fact that aggressive cancers need a lot of glucose (a type of sugar your body uses for energy) to find out where the cancer is in your body. For cancers like yours, it can help your doctors determine the aggressiveness of the tumor. It is a standard type of scan that is already approved by Health Canada.

A new type of scan called a ^{68}Ga-DOTATOC PET/CT, which is not yet approved in Canada, but which is in current use in many European countries has been demonstrated in many scientific studies to be more

accurate than other types of scans. It works in the same way as Octreoscan™, but with a different scan technology that is expected to be able to detect even smaller tumors. Even if your cancer is not classified as a NET, some other types of cancer can be detected by ^{68}Ga-DOTATOC PET/CT, and this research project may apply to your cancer too.

We will recruit 400 participants for this research project that will be conducted at BC Cancer.

Health Canada has not approved the sale or use of ^{68}Ga-DOTATOC PET/CT for the diagnosis of NETs or tumors that overexpress somatostatin receptors, although they have allowed its use in this clinical study. ^{68}Ga-DOTATOC PET/CT is currently being used in many European countries.

5. What is the purpose of the study?

The purpose of this study is to assess the safety of the new type of scan (^{68}Ga-DOTATOC PET/CT), for people with your type of cancer and to see if it is better at detecting cancer than tests currently being used in Canada. Even though this type of scan is approved for use in Europe, it is necessary to conduct this study here also to confirm its safety and effectiveness in Canada.

Once the study is complete, if it confirms effectiveness and safety of the new scan type, the results of this research will help to make it available to Canadians and have it eventually approved by Health Canada.

6. Who can participate in this study?

You may be able to participate in this study if*:*

- You have a type of cancer called a NET (or a type of tumor that has a feature called "overexpression of somatostatin receptors").

7. Who should not participate in this study?

You will not be eligible to participate in this study if:

- You are too unwell, or participating in this study would not be in your interest, in the opinion of the study doctor.
- You are not able to tolerate the physical and logistical requirements of completing one PET/CT scan, including have an IV injection of the radioactive tracer into a vein in your arm and lying flat for 30 minutes.
- You are unable to provide written informed consent.
- You weigh over 204.5kg or are unable to fit through the scanner opening (diameter 70cm).

If you are breastfeeding, you can still participate in this study, but you must stop breastfeeding for 12 hours following the ^{68}Ga-DOTATOC and ^{18}F-FDG PET/CT scan.

8. What does the study involve?

If you agree to join this study you will receive a ^{68}Ga-DOTATOC PET/CT scan for the purposes of this study as well as a standard ^{18}F-FDG PET/CT scan. Both PET/CT scans will be performed at BC Cancer. The ^{68}Ga-DOTATOC PET/CT scan is only available in Vancouver, however the ^{18}F-FDG PET/CT scan can be completed in Victoria or Kelowna if that is more convenient to you. These two scans will occur on two

different days at least 1 day and no more than 8 weeks apart. You will be followed on this study for three years after completion of your PET/CT scan.

Consent and Medical History:
Before completing any study procedures, you will meet the research coordinator who will answer all your questions about the study, and obtain your signature for the consent. You will complete a medical history questionnaire at this time as well. This meeting will be done before your first appointment at the PET/CT department.

PET/CT scans:

Prior to the procedure:
- You may take your usual medications as prescribed.
- You are required to fast for 6 hours before the ^{18}F-FDG scan only. There are no dietary restrictions for the ^{68}Ga-DOTATOC scan.
- Please drink 3 to 4 glasses of water within the 2 hours before your PET/CT scan.
- If you are female with potential to get pregnant, a pregnancy test will be performed before starting the procedure.*

When you arrive for the procedure:
- The study doctor and/or a technologist will meet with you to answer any questions.

During the procedure:
- You will have an IV needle inserted into your arm and you will receive a dose of the radioactive tracer (^{18}F-FDG or ^{68}Ga-DOTATOC). The injection volume will be very small and it will only take a few seconds to give.
- There is a waiting period of <u>1 hour</u> so the tracer can circulate throughout your body.
- You will be taken to a designated washroom and asked to void prior to being scanned in order to clear the radioactive tracer from your urinary tract.
- You will undergo the PET/CT scan, which will take about 40 minutes. You will need to lie still on the scanner bed during this time.
- During the scan, a technologist monitors you by direct vision or by video camera.
- If you feel anxious at any time during the scan it can be stopped and you will be brought out of the scanner immediately.

After the procedure:
- After the scan is complete, you can leave the PET scan department. You will be encouraged to drink 3 to 4 extra glasses of water by the end of the day.
- A doctor will provide a more in-depth assessment if there are any concerns that your health status has changed during the PET/CT scan. We do not expect that any participants will experience any side effects.
- Your PET/CT scan will be reviewed by a BC Cancer doctor specialized in PET/CT. The results of the scan will be sent to your referring doctor.

- Your PET/CT scan will also be reviewed by central readers for study purposes only and this information will not be available to you or your referring doctor. No personal information will be transferred to the central readers and you will only be identified by your unique study code.

* The pregnancy test is only completed for the ^{68}Ga-DOTATOC PET/CT scan

24-hour visit or phone call:

- You will be asked to return to the clinic or agree to be contacted by phone approximately 24 hours after your ^{68}Ga-DOTATOC PET/CT scan.
- You will be asked if your health status has changed since receiving the radioactive tracer or if you experienced any undesirable effects following the administration of the ^{68}Ga-DOTATOC.

Follow-up Visits:

A study team member will call you to complete a follow up at 12, 24 and 36 months after the date of your ^{68}Ga-DOTATOC PET/CT scan and inquire about any treatments you may have undergone. Your medical chart will be reviewed to compare your PET/CT scan results to other imaging, as well as any clinical and laboratory tests to evaluate the accuracy of the PET/CT scan (the information obtained from your medical file is detailed below).

Time:

In total, there will be about 6 hours and 30 minutes of extra time required of you to participate in this study:

- Consent and medical history questionnaire – 30 minutes
- Each of the PET/CT scan – 2.5 hours
- Adverse event follow-up phone call – 15 minutes
- The follow-up visits – 15 minutes per visit (3 visits/phone calls)

Use of Data from your Medical File

As stated above, we will obtain data from your medical file for the purpose of this study. We ask for this authorisation for a period of 3 years following the ^{68}Ga-DOTATOC scan so we can follow the progress of your disease and compare it with the results of the scan. Your medical file will only be accessed by research staff and only for the purpose of this study. The information will be stored in BC Cancer computer systems, in a database, in coded form (without any information that can be used to identify you). The following information will be collected from your medical file:

- Year of birth
- Biological sex assigned at birth
- History of suspected or known cancer
- Symptoms related to your cancer
- Laboratory results (hormone or tumor marker levels)
- Pathology reports
- Results of other types of scans (CT, MRI, etc)
- History of treatments and interventions (biopsy, surgery, radiotherapy, chemotherapy)
- Initiation of new treatment after ^{68}Ga-DOTATOC PET/CT scan
- Final diagnosis by your doctor and relevant medical notes
- History of therapy with octreotide and similar medications

Conventional medical imaging tests may be needed in addition to the ^{68}Ga-DOTATOC PET/CT scan. These have often already been done by your doctor before the decision to offer you participation in this study, but may also be done after the ^{68}Ga-DOTATOC PET/CT for logistic reasons. Those scans, which may be a contrast-enhanced CT scan or a MRI, are the same scans that are usually obtained as standard of care for many patients, including non-participants.

Optional Repeat Scans:

A repeat ^{68}Ga-DOTATOC PET/CT may be recommended by the principal investigator or your doctor to obtain more information about your disease. You can have a total of 2 additional scans as part of this study. After a minimum period of 12 weeks, and up to 36 months following the initial ^{68}Ga-DOTATOC PET/CT scan, repeat ^{68}Ga-DOTATOC imaging study may be requested for the following reasons:

- To look for progressive disease to confirm the results of your first ^{68}Ga-DOTATOC PET/CT.
- To look at the response to treatment you may have undergone.
- To look at the progression of unconfirmed ^{68}Ga-DOTATOC findings (no other imaging or biopsy has been completed).

You can decline to undergo the additional scans at any time.

Optional Sub-Studies:

The new scan type proposed in this study can be useful for other research projects. Some of these optional sub-studies may be available for you to participate in.

For each optional study, you will be provided with a separate consent form that describes the details, and which you will be required to sign if you wish to participate. You can take part in the main study and not take part in these optional studies. If you decide not to take part in any or all of the optional studies, your care will not be affected.

If you are eligible for any eventual sub-studies, your treating doctor may propose them to you.

9. What are the possible harms and discomforts?

PET/CT scans are considered very safe procedures with few associated risks. You might experience some minor pain when the IV is inserted into your arm. This will be very similar to having a needle for a routine blood test. You may develop a small bruise, but significant bleeding is extremely rare. Some people feel anxious in the narrow PET/CT scanner. If necessary, your doctor can prescribe you medication to manage this anxiety. Sometimes participants feel tired or have a headache after the scan.

^{68}Ga-DOTATOC and ^{18}F-FDG are radioactive tracers. This means that they emit a small quantity of radiation that is used to create the PET image. The CT scan performed at the same time (CT part of the PET/CT) also emits a small amount of radiation. The amount of radiation you will be exposed to in this study is comparable to that of other diagnostic tests that are used in the standard of care for your type of cancer. In some cases, it is less exposure than some standard of care scans (for example Octreoscan™).

The amounts of radiation exposure from the extra scans performed as part of this study are within the guidelines issued by Health Canada for such research studies. The effects of exposure to low levels of

radiation are expected to be minimal, as your risk level is calculated over your entire lifetime. The main potential risk from exposure to radiation is cancer, and this risk is extremely low for the radiation exposure from this study. This would appear decades from now, if it were to happen at all.

Everyone is exposed to natural radiation occurring in the environment. The radiation comes from radioactive products in natural elements, present in earth's crust, gases in soil and bedrock, in food and water, as well as from cosmic rays to which we are exposed. Radiation exposure is measured in units of milliSievert (mSv). As a reference value, the average radiation exposure in the world is approximately 2.4 mSv per year. In Canada, this ranges from 1.3 mSv (Vancouver) to 4.1 mSv (Winnipeg).

Medical imaging examples:

- Screening mammography – 0.4-0.6 mSv
- CT scan of the abdomen and pelvis – 10 mSv

The additional radiation dose from the ^{68}Ga-DOTATOC PET/CT scan will range between 7.6 to 10.8 mSv. And the additional radiation dose from the ^{18}F-FDG PET/CT scan will range between 8.6 to 11.6 mSv.

For 6 hours following the radiotracer injection (^{68}Ga-DOTATOC and ^{18}F-FDG) your body will give off radiation and can expose people around you. It is important that if you are around any pregnant women or children under the age of 16, you keep an arms-length distance (1 meter) to protect their developing bodies.

Reproductive Risks

Because the effects that ^{68}Ga-DOTATOC and ^{18}F-FDG may have on an unborn child are unknown, you should not be pregnant when the ^{68}Ga-DOTATOC and ^{18}F-FDG scan is performed. To avoid that risk, a pregnancy test will be performed before the tracer is administered to you.

You should not breastfeed your baby in the 12 hours after administration of ^{68}Ga-DOTATOC and ^{18}F-FDG because it is possible the drugs used in this study may be present in your breast milk.

10. What are the potential benefits of participating?

No one knows whether or not you will benefit from this study. There may or may not be direct benefits to you from taking part in this study.

We hope that the information learned from this study can be used in the future to benefit other people with a similar disease.

One of the possible benefits of participating in this study is that the type of scan you will have access to, a ^{68}Ga-DOTATOC PET/CT, may be more able to see cancer in your cells compared to other types of scans currently available in Canada. The increased detection ability may lead to better treatment planning and improve symptoms.

11. What are the alternatives to the study diagnostic procedure?

If you choose not to participate in this study or to withdraw at a later date, the standard diagnostic scans are still available to you and may be offered to you by your doctor. Those tests include (but are not limited to):

- Octreoscan™ scintigraphy (somatostatin receptor scintigraphy)
- Contrast-enhanced CT
- MRI
- Ultrasound imaging

You can discuss these options with your doctor before deciding whether or not to participate in this research project.

12. 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 diagnostic 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.

13. 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 information about you collected up to the point of your withdrawal including, where applicable, information obtained from your biological samples will be retained for analysis in order to protect the integrity of the research, which may benefit future research participants and patients. However, no further information will be collected.

14. How will my taking part in this study be kept confidential?

Federal and provincial privacy laws give safeguards for privacy, security, and authorized access to information. We will not give information that identifies you to anyone without your permission, except as required by law.

However, there is a risk that someone could get access to the information we have stored about you, it could be revealed inappropriately or accidentally, and the risk of someone identifying you may increase in the future as people find new ways of tracing information. Depending on the nature of the information, such a release could upset or embarrass you, or be misused. For example, it could be used to make it harder for you to get or keep a job or insurance. There are laws against this kind of misuse in Canada, but they may not give full protection, and laws in other countries may not be as strict as those in Canada, so when your information and samples are sent to places outside of Canada, you may not be afforded the same rights. We believe the chance these things will happen is very small, but we cannot make guarantees. Your privacy and the confidentiality of your data are very important to us, and we will make every effort to protect these as described below.

Study-related data and coding:

- All information gathered for use in the study is referred to as the 'study-related data'. This data may include your medical records, biological materials, genetic information, completed

questionnaires and/or diaries, etc. The study-related data will be transformed into datasets that can be analyzed. You will be assigned a unique code that will be used to track your study-related data. This unique code does not include any personal information that could identify you, and will be used on all study-related data that leave BC Cancer unless otherwise specified in this form (this is referred to as 'coded data').

- Coded data (including genetic information) from this study may be pooled and shared with researchers from around the world for future studies that are unknown at this time. It may also be added to public databases, published, or presented at scientific meetings. The aim of these future studies is to benefit people by improving our understanding of health conditions like cancer.

Who will know I participated?

- Your family doctor will be notified that you are taking part in this study so that your study doctor and family doctor can provide the proper medical care.
- If required by law, your medical information may also need to be given out. If this should happen, the study doctors and staff will do their best to make sure that any information that is shared will not directly identify you.

Using email:
We are asking study participants to provide a personal email address so that we can communicate with them about the study and their participation. Before you provide your consent, please carefully consider whether this email account is secure, whether other people have access to it or whether you have concerns about the security of any information sent to this account. We will only send your personal information to the email address you have provided to us, and all of the information which you provide to us will be kept confidential by the research team. However, you should be aware that some webmail services (e.g. Gmail, Hotmail, etc.) may store the contents of your email account outside of Canada (for example, in the United States), where privacy and data security standards may be different than they are in Canada. The security of information sent over the internet can also not be guaranteed. The email communications we exchange with you may contain some of your personal information (your name, health information, etc.). Under the *Freedom of Information and Protection of Privacy Act* (British Columbia), we require your consent in order to send your personal information outside of Canada. By providing your email address, you are voluntarily providing your consent for the study team to communicate with you using your email account.

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 that the interpretation of the investigational ^{68}Ga-DOTATOC PET/CT scan will be written in a report that will be included in your medical file at the BC Cancer and will be available to your doctors.

15. Who will have access to your study-related data?

Your signed consent form will be included in your study-related data, and in any electronic medical record(s). Your healthcare team will also be alerted that you are on a study to ensure they can treat you safely according to the study protocol.

Your study-related data will be reviewed by the sponsor of this study, or their representatives at BC Cancer. The BC Cancer Research Ethics Board or regulatory authorities and auditors may also look at your study-related data for the purpose of overseeing the conduct of the study. By signing this form you are authorizing such access. Table 1 sets out the organizations that may access your study-related data and for what purposes.

Table 1: Access to your study-related data

WHO	WHAT	WHERE	PURPOSE
Health Canada	Study-related records and data (including your medical records) that include information that can identify you	Canada	Oversight of the use of drugs in Canada

16. What happens if something goes wrong?

By signing this form, you do not give up any of your legal rights and you do not release the study doctor, participating institutions, or anyone else from their legal and professional duties. If you become ill or physically injured as a result of participation in this study, medical treatment will be provided at no additional cost to you. The costs of your medical treatment will be paid by your provincial medical plan and/or by the study sponsor, the BC Cancer.

17. What will the study cost me?

All research-related medical care and treatment and any related tests that you will receive during your participation in this study will be provided at no cost to you.

Reimbursement

No reimbursement of expense is offered for participation to this study.

Remuneration

You will not be paid for participating in this study.

18. Who do I contact if I have questions about the study during my participation?

- **For questions about the study:** You can ask the study doctor or staff any questions or concerns that you may have about this study.
  STUDY COORDINATOR at 604-877-6000 extension 2818
  If required, the study coordinator can communicate with the study doctor to obtain the requested information.

- **For privacy related questions or questions about your rights as a research participant:** You can contact BC Cancer Research Ethics at reb@bccancer.bc.ca, or 604.877.6284. Please reference the study number H17-00909 when contacting Research Ethics so staff can better assist you.

By signing this form, you do not give up any of your legal rights and you do not release the sponsor, study doctor, participating institutions, or anyone else from their legal and professional duties. If you become ill or physically injured as a result of participation in this study, medical treatment will be provided at no additional cost to you.

You will be given a copy of this signed and dated consent form prior to participating in this study.

19. Signatures

Title: Evaluation of the safety and sensitivity of ^{68}Ga-DOTATOC PET/CT for imaging NET patients

Participant Consent

My signature on this consent form means:

- I have read and understood the information in this consent form.
- I have had enough time to think about the information provided.
- I have been able to ask for advice if needed.
- I have been able to ask questions and have had satisfactory responses to my questions.
- I understand that all of the information collected will be kept confidential and that the results will only be used for scientific purposes.
- I understand that my participation in this study is voluntary.
- I understand that I am completely free at any time to refuse to participate or to withdraw from this study at any time, and that this will not change the quality of care that I receive.
- I authorize access to my health records 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 understand that there is no guarantee that this study will provide any benefits to me.

I will receive a signed copy of this consent form for my own records.

I consent to participate in this study.

Participant 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 an interpreter/translator, indicate:

Language: _____

Was the participant 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 participant 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 participant, and the person signing below attests that the study was accurately explained to, and apparently understood by, the participant (please check if participant is unable to read).

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

Signature of the Person assisting in the consent discussion	Printed name	Date