21-007799

Optimizing Outcomes of Patients with Advanced HCC Undergoing Immunotherapy Through Novel ^{68}Ga PSMA PET Imaging

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RESEARCH PARTICIPANT CONSENT AND PRIVACY AUTHORIZATION FORM

Study Title: Optimizing outcomes of patients with advanced HCC undergoing immunotherapy through novel 68Ga PSMA PET imaging

IRB#: 21-007799

Principal Investigator: Dr. Nguyen Tran and Colleagues

Key Study Information

This section provides a brief summary of the study. It is important for you to understand why the research is being done and what it will involve before you decide. **Please take the time to read the entire consent form carefully and talk to a member of the research team before making your decision.** You should not sign this form if you have any questions that have not been answered.	
It's Your Choice	This is a research study. Being in this research study is your choice; you do not have to participate. If you decide to join, you can still stop at any time. You should only participate if you want to do so. You will not lose any services, benefits or rights you would normally have if you choose not to take part.
Research Purpose	The purpose of this research is to know whether 68Ga-PSMA PET/CT can improve upon the diagnosis and management of hepatocellular carcinoma.
What's Involved	The study includes one blood draw and up to five ^{68}Ga-PSMA PET/CT examinations.
Key Information	Benefits: There is not likely to be any direct benefit to you by participating in the study. However, information we learn from this study may identify tumors that are undetectable on current imaging. Risks: In this study you should consider the following risks. Blood draws and intravenous (IV) infusions carry risks of pain, bruising, light-headedness, and infection. Risks from the imaging may include some discomfort from lying still on the scanner bed for up to 30 minutes.

	Radiation exposure from the CT portion of the PET/CT scans and the imaging agent has a low risk of harmful effects. Small risk of an allergic reaction from the ^{68}Ga-PSMA. The amount of radiation received from the ^{68}Ga-PMSA radiotracer has a low risk of harmful effects. As with all research, there is a chance that confidentiality could be compromised, however, we take precautions to minimize this risk and all other known risks. Costs: You won't need to pay for tests and procedures which are done just for this research study. Alternative Treatments/Procedures: This imaging study is being done to gather information. You can decide not to participate in this study.
Learn More	If you are interested in learning more about this study, read the rest of this form carefully. The information in this form will help you decide if you want to participate in this research or not. A member of our research team will talk with you about taking part in this study before you sign this form. If you have questions at any time, please ask us.

Making Your Decision

Taking part in research is your decision. Take your time to decide. Feel free to discuss the study with your family, friends, and healthcare provider before you make your decision. Taking part in this study is completely voluntary and you do not have to participate.

If you decide to take part in this research study, you will sign this consent form to show that you want to take part. We will give you either a printed or electronic copy of this form to keep.

For purposes of this form, Mayo Clinic refers to Mayo Clinic in Arizona, Florida and Rochester, Minnesota; Mayo Clinic Health System; and all owned and affiliated clinics, hospitals, and entities.

Contact Information

If you have questions about …	You can contact …
▪ Study tests and procedures ▪ Materials you receive ▪ Research-related appointments ▪ Research-related concern or complaint ▪ Research-related injuries or emergencies ▪ Withdrawing from the research study	**Principal Investigator:** Nguyen Tran, M.D. **Phone:** (507) 266-4198 **Study Team Contact:** Maggie Olson Study Coordinator **Phone:** (507) 266-7337 **Institution Name and Address:** Mayo Clinic 200 First Street SW Rochester, MN 55905
▪ Rights of a research participant	**Mayo Clinic Institutional Review Board (IRB)** **Phone:** (507) 266-4000 **Toll-Free:** (866) 273-4681
▪ Rights of a research participant ▪ Any research-related concern or complaint ▪ Use of your Protected Health Information ▪ Stopping your authorization to use your Protected Health Information ▪ Withdrawing from the research study	**Research Participant Advocate (RPA)** **(The RPA is independent of the Study Team)** **Phone:** (507) 266-9372 **Toll-Free:** (866) 273-4681 **E-mail:** researchparticipantadvocate@mayo.edu
▪ Billing or insurance related to this research study	**Patient Account Services** **Toll-Free:** (844) 217-9591

Other Information:
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.

Why are you being asked to take part in this research study?

You are being asked to take part in this research study because you have advanced hepatocellular carcinoma (HCC). The plan is to have about 30people take part in this study at Mayo Clinic.

Why is this research study being done?

The purpose of this research is to find out whether ^{68}Ga-PSMA PET/CT can improve upon the diagnosis and management of hepatocellular carcinoma.

PET stands for Positron Emission Tomography, an imaging test that helps to measure the information about functions of tissues and organs within the body. A PET scan uses a radioactive drug (radiotracer) to show this activity. CT scan uses X-rays to create images of the bones and internal organs within your body.

Combining a PET scan with an MRI or CT scan can help make the images easier to interpret. PET/CT scans are hybrid scanners that combine both of the two modalities into a single scan. This allows images of both anatomy (CT) and function (PET) to be taken during the same examination.

The ^{68}Ga-PSMA PET/CT scan is done with a very small amount of a radioactive tracer called 68-Gallium PSMA. In patients that have been diagnosed with HCC, a protein called prostate-specific membrane antigen (PSMA) appears in large amounts on the surface of the cancerous cells. The PSMA protein was first discovered in human prostate cancer cell lines; however, recent studies have shown that PSMA can also be found on cells of HCC. The healthy cells of the liver do not express the PSMA protein on their surface as much as these cancerous cells.

The radioactive chemical compound (^{68}Ga-PSMA) has been designed to circulate through the body and attach itself to the PSMA protein on HCC cells. A PET/CT scan is then used to detect the location of HCC lesions.

The purpose of this study is to know whether ^{68}Ga-PSMA PET/CT can improve upon the diagnosis and management of hepatocellular carcinoma in the future.

Information you should know

Who is Funding the Study?
Mayo Clinic Karl-Erivan Haub Family Career Development Award is funding this study.

Information Regarding Conflict of Interest:
Your healthcare provider may be referring you to this research study. If your healthcare provider is also an investigator on this study, there is the chance that his or her responsibilities for the study could influence his or her recommendation for your participation. If you prefer, your healthcare provider will be happy to refer you to another investigator on the research study team for you to decide if you want to participate in the study and to see you for the research study activities while you are in the study.

How long will you be in this research study?

It will take you about 2.5 to 3.5 hours each visit to complete this research study. During this time, we will ask you to make up to 5 study visits to Mayo Clinic.

The study will involve up to 5 visits for PSMA PET/CT, the initial imaging will be prior to systemic therapy and during the course of study (after 3, 6, 9, 12 cycles of treatment), or until progression, whichever comes first. Long-term follow up will be done up to 3 years after treatment.

What will happen to you while you are in this research study?

Visit one: Eligibility review and consent

A member of the study team will meet with you in person or by telephone (if you received an email with the consent) to review if you are eligible to participate in the research, review the consent form, and answer any relevant questions. If you choose to sign the consent form, your study coordinator will schedule all research related procedures on your behalf.

Visit two: Screening: blood draw and imaging

The second visit will consist of a research blood draw (about 1 tablespoon) and ^{68}Ga-PSMA PET/CT scan prior to your clinically ordered chemotherapy. You will undergo ^{68}Ga-PSMA PET/CT imaging prior to initiation of immunotherapy to identify if you are PSMA PET/CT positive. The visit will take approximately 3.5 hours. If you have undergone or will undergo a baseline ^{68}Ga-PSMA PET/CT for IRB#20-006433, you may not have to repeat a baseline scan for this study. The study team will use the information gathered from the IRB#20-006433 baseline scan for this study.

Testing for Hepatitis B and Hepatitis C will be tested as part of the blood work. If it isn't known if you have Hepatitis B and/or Hepatitis C, you will need to have a blood (about 1 tablespoon) test done. If your Hepatitis B and/or Hepatitis C test result is positive you will need to have a second test done to make sure the results are the same. The researcher will tell you how to find medical help and counseling as needed, and you may not be able to take part in the study. Your health insurer or you will have to pay for the cost of the repeat test, any follow-up medical care, or counseling.

You do not have to fast for this appointment. You will need to drink plenty of water.

If you are a female of childbearing age, you must have a negative urine pregnancy test within 48 hours prior to your scan in order to participate in this study unless you cannot become pregnant.

<u>Details of the ^{68}Ga-PSMA PET/CT scans are as described below:</u>

The PET/CT scan will be done on the sixth floor of the Charlton Building within four weeks of enrollment. This appointment will last approximately three hours, including a 30-minute nursing assessment, 90 minutes for ^{68}Ga-PSMA uptake, and 30 minutes for the PET/CT scan. You do not have fast for this appointment. You will need to drink plenty of water.

After you check in, a technologist will assess you and, if applicable, perform a pregnancy test. You will be led to an uptake room in which an intravenous catheter (IV) will be placed in a vein in your arm. This catheter will be used to inject ^{68}Ga-PSMA, a radioactive tracer designed to specifically attach itself to the PSMA protein on liver cancer cells. After the radioactive tracer is injected, you will be asked to sit and relax quietly for approximately 90 minutes to allow the drug to circulate through your body. You will be able to bring a book, your phone, music, or any form of entertainment while waiting for the drug to circulate.

Next, a technologist will lead you to the PET/CT scanner. You will be positioned on the scanner bed on your back with your hands by your sides. The technologist will then begin the 30-minute PET/CT scan. During this scan, it is important to stay as still as possible.

After the completion of the PET/CT examination you will need to drink plenty of water and stay near a restroom without extended travel for a few hours.

After the first PET/CT scan it is possible that you may be confirmed as negative at baseline. You will continue with your standard hepatocellular carcinoma management as advised by your clinical physician. Data from your standard of care will be collected as part of this study.

Visit three – six: ^{68}Ga-PSMA PET/CT scan follow-ups

After the first cycle of your clinically ordered therapy, you will undergo routine clinical blood workup and research blood draws at time of the scans. Follow-up PET/CT scans are taken after the third, sixth, ninth, and twelfth cycle of treatment. These research scans follow the exact same procedures as your first imaging appointment. The timeline of the follow-up scans are as detailed below:

- Second scan: After the **3rd cycle** of your clinically ordered treatment
- Third scan: After the **6th cycle** of your clinically ordered treatment
- Fourth scan: After the **9th cycle** of your clinically ordered treatment
- Fifth scan: After the **12th cycle** of your clinically ordered treatment

If your clinical provider stops your clinically ordered therapy prior to the fifth PET/CT scan, you will not have to continue having subsequent research scans. After your final scan, you will enter the long-term follow-up phase of the study.

Long term follow-up:

We will review your medical records for up to 36 months after your clinically ordered treatment. During the long-term follow-up period, you will not have to do any additional scans for the research study. You will be contacted by telephone call every 6 months for 3 years to ask about your health and medications.

We will review pathology samples that were collected as part of your routine care. If there is enough tissue we will use a portion of that sample for PSMA staining.

Tests done only for research purposes are not meant to provide clinical information or help care for you. The results are only important for research. Therefore, the results of tests done with your information and samples will not be provided to you. In the rare event that a finding might affect

the health of you or your family, we will contact you and you can choose whether to receive or refuse the information. If you decide to follow up and further medical testing or care is needed, the costs will be billed to you or your insurance.

What are the possible risks or discomforts from being in this research study?

Intravenous (IV) Line Placement
Intravenous line placement is associated with discomfort and a small risk of bruising or infection at the IV site. To minimize this risk, IV lines will be placed by experienced radiology nurses and technologists who place IV lines.

Possible Claustrophobia (Fear of Small Spaces)
Some people with claustrophobia and others may feel too closed in and may not be able to tolerate CT scanning. If you feel too confined in the CT scanner, you can ask that the scan be stopped after you enter the CT scanner.

PET/CT scan using ^{68}Ga-PSMA
If you take part in this research, you will receive medical imaging studies or procedures that involve exposure to radiation. The amount of radiation from these studies has a low risk of harmful effects.

As with any medication, allergic reactions are a possibility. The risk of an allergic reaction to ^{68}Ga-PSMA is minimal. As with any new or investigational drug, there may be adverse events or side effects that are currently unknown and it is possible that certain unknown risks could be permanent, serious, or life-threatening.

Pregnancy and Fertility
The effect of ^{68}Ga-PSMA on a fetus (developing baby still in the womb), or on a breastfeeding infant is unknown and may be harmful. Because of these risks, women cannot take part in this study if they are pregnant or breastfeeding. If you are a female, you must have a negative urine pregnancy test within 48 hours prior to your scan in order to participate in this study unless you cannot become pregnant.

If you are sexually active and able to become pregnant, you must agree to use one of the birth control methods listed below:

- Hormonal methods, such as birth control pills, patches, injections, vaginal ring, or implants

- Barrier methods (such as a condom or diaphragm) used with a spermicide (a foam, cream, or gel that kills sperm)
- Intrauterine device (IUD)
- Abstinence (no sex)

If you are sexually active, and able to father a child, you must agree to use one of the birth control methods listed below:

- Barrier methods (such as a condom or diaphragm) used with a spermicide (a foam, cream, or gel that kills sperm)
- Hormonal methods used by your partner, such as birth control pills, patches, injections, vaginal ring, or implants
- Intrauterine device (IUD) used by your partner
- Abstinence (no sex)

If your partner thinks she might have become pregnant while you are in the study or for 6 months afterward, you must tell the Principal Investigator immediately. The Principal Investigator may ask for your partner's permission to collect information about the outcome of her pregnancy and her newborn. You won't have to stop taking part in the study if your partner becomes pregnant.

Radiotracer production issues
There is a possibility that the radiochemistry facility will not be able to provide the radiotracer used in this study because of production issues. These issues are possible and may not be known until you have arrived for your study procedure on the planned day of ^{68}Ga-PSMA dosing. We will communicate issues as early as possible to minimize inconvenience to your time. Depending on factors related to your care, your study doctor may schedule another date for your ^{68}Ga-PSMA PET/CT scan administration if you are agreeable.

Blood draw risks
The risks of drawing blood include pain, bruising, lightheadedness, and/or fainting, or rarely, infection at the site of the needle stick.

You should tell your study doctor and the study team of any risks or discomforts you may experience during the study.

As with all research, there is a chance that confidentiality could be compromised; however, we take precautions to minimize this risk.

Are there reasons you might leave this research study early?

You may decide to stop at any time. You should tell your study doctor if you decide to stop and you will be advised whether any additional tests may need to be done for your safety.

In addition, the Principal Investigator or Mayo Clinic may stop you from taking part in this study at any time:

- if it is in your best interest,
- if you don't follow the study procedures,
- if the study is stopped.

If you leave this research study early, or are withdrawn from the study, no more information about you will be collected; however, information already collected about you in the study may continue to be used.

We will tell you about any new information that may affect your willingness to stay in the research study.

What if you are injured from your participation in this research study?

Where to get help:
If you think you have suffered a research-related injury, you should promptly notify the Principal Investigator listed in the Contact Information at the beginning of this form. Mayo Clinic will offer care for research-related injuries, including first aid, emergency treatment and follow-up care as needed.

Who will pay for the treatment of research related injuries?
Care for such research-related injuries will be billed in the ordinary manner, to you or your insurance. Treatment costs for research-related injuries not covered by your insurance will be paid by Mayo Clinic.

What are the possible benefits from being in this research study?

There will be no direct benefit to you if you decide to take part in this study. However, information we learn from this study may identify tumors that are undetectable on current imaging. It is hoped that the study may lead to improvements in the treatment and management of HCC, which will benefit patients like you in the future.

You will be informed about new findings that are related to this clinical trial and that might affect your decision to continue to participate. You may reconsider your decision of further participation in the clinical trial on the basis of such information at any time.

What alternative do you have if you choose not to participate in this research study?

You don't have to be in this study to receive treatment for your condition. If you decide not to take part in this study, you may undergo the routine standard of care treatment available for your HCC. Talk to the study doctor or your doctor if you have any questions about any of these treatments or procedures.

In patients with suspicion of cancer recurrence, there are additional diagnostic tools available. There are other radiolabeled drugs that are approved for PET imaging in HCC. Other diagnostic procedures include MRI imaging (of the spine, the pelvis, and other body regions), contrast-enhanced CT, and bone scintigraphy. Your doctor and/or your investigator can help you decide on other choices for imaging your disease.

What tests or procedures will you need to pay for if you take part in this research study?

You won't need to pay for tests and procedures which are done just for this research study. These tests and procedures are:

- Pregnancy test (if applicable)
- ^{68}Ga-PSMA PET/CT scans
- Research blood draw

- PSMA staining (if applicable)

However, you and/or your insurance will need to pay for all other tests and procedures that you would have as part of your clinical care, including co-payments and deductibles.

If you have billing or insurance questions call Patient Account Services at the telephone number provided in the Contact Information section of this form.

Will you be paid for taking part in this research study?

If you take part in this study, you will not be paid for your participation.

Will your information or samples be used for future research?

Identifiable information such as your name, Mayo Clinic number, or date of birth will be removed from your information or samples collected in this study, allowing the information or samples to be used for future research or shared with other researchers without your additional informed consent.

How will your privacy and the confidentiality of your records be protected?

Mayo Clinic is committed to protecting the confidentiality of information obtained about you in connection with this research study.

In order to protect the confidentiality of your information, study data will be labeled with a unique identifying number (or "code"). Only the study staff at our site will have access to your personal information linking you to your study code. This information will be stored in a secure location on a password protected computer.

During this research, information about your health will be collected. Under Federal law called the Privacy Rule, health information is private. However, there are exceptions to this rule, and you should know who may be able to see, use and share your health information for research and why they may need to do so. Information about you and your health cannot be used in this

research study without your written permission. If you sign this form, it will provide that permission (or "authorization") to Mayo Clinic.

Your health information may be collected from:

- Past, present and future medical records.
- Research procedures, including research office visits, tests, interviews and questionnaires.

Your health information will be used and/or given to others to:

- Do the research.
- Report the results.
- See if the research was conducted following the approved study plan, and applicable rules and regulations.

Your health information may be used and shared with:

- Mayo Clinic research staff involved in this study.
- The sponsor(s) of this study and the people or groups hired by the sponsor(s) to help perform this research.
- The Mayo Clinic Institutional Review Board that oversees the research.
- Federal and State agencies (such as the Food and Drug Administration, the Department of Health and Human Services, the National Institutes of Health and other United States agencies) or government agencies in other countries that oversee or review research.

How your information may be shared with others:

While taking part in this study, you will be assigned a code that is unique to you, but does not include information that directly identifies you. This code will be used if your study information is sent outside of Mayo Clinic. The groups or individuals who receive your coded information will use it only for the purposes described in this consent form.

If the results of this study are made public (for example, through scientific meetings, reports or media), information that identifies you will not be used.

In addition, individuals involved in study oversight and <u>not</u> employed by Mayo Clinic may be allowed to review your health information included in past, present, and future medical and/or research records. This review may be done on-site at Mayo Clinic or remotely (from an off-site location). These records contain information that directly identifies you. However, the individuals will not be allowed to record, print, or copy (using paper, digital, photographic or other methods), or remove your identifying information from Mayo Clinic.

Is your health information protected after it has been shared with others?

Mayo Clinic asks anyone who receives your health information from us to protect your privacy; however, once your information is shared outside Mayo Clinic, we cannot promise that it will remain private and it may no longer be protected by the Privacy Rule.

Your Rights and Permissions

Participation in this study is completely voluntary. You have the right not to participate at all. Even if you decide to be part of the study now, you may change your mind and stop at any time. You do not have to sign this form, but if you do not, you cannot take part in this research study.

Deciding not to participate or choosing to leave the study will not result in any penalty. Saying 'no' will not harm your relationship with your own doctors or with Mayo Clinic.

If you cancel your permission for Mayo Clinic to use or share your health information, your participation in this study will end and no more information about you will be collected; however, information already collected about you in the study may continue to be used.

You can cancel your permission for Mayo Clinic to use or share your health information at any time by sending a letter to the address below:

Mayo Clinic
Office for Human Research Protection
ATTN: Notice of Revocation of Authorization
200 1st Street SW
Plummer Building PL 3-02
Rochester, MN 55905

Alternatively, you may cancel your permission by emailing the Mayo Clinic Research Participant Advocate at: researchparticipantadvocate@mayo.edu.

Please be sure to include in your letter or email:

- The name of the Principal Investigator,
- The study IRB number and /or study name, and
- Your contact information.

Your permission for Mayo Clinic to use and share your health information lasts until the end of this study, unless you cancel it. The study does not end until all data has been collected, checked (or audited), analyzed, and reported. Because research is an ongoing process, we cannot give you an exact date when the study will end. Sometimes this can be years after your study visits and/or activities have ended.

Enrollment and Permission Signatures

Your signature documents your permission to take part in this research.

Printed Name Date (mm/dd/yyyy) Time (hh:mm am/pm)

Signature

Person Obtaining Consent

- I have explained the research study to the participant.
- I have answered all questions about this research study to the best of my ability.

Printed Name Date (mm/dd/yyyy) Time (hh:mm am/pm)

Signature