RA-2021-018

THE QUEEN'S MEDICAL CENTER
HONOLULU, HAWAII

INFORMED CONSENT TO TAKE PART IN A RESEARCH STUDY

Study Name: Clinical trial of biomarkers for predicting immunotherapy response in hepatocellular carcinoma

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Sponsor:	National Cancer Institute Bethesda, MD

Why am I being asked to take part in this research study?

You are invited to take part in this research study because you have hepatocellular carcinoma that will be treated by immunotherapy (a drug that helps your immune system fight cancer). The purpose of this research study is to learn whether a type of medical imaging test called **PET/CT** or a type of genetic blood test called **liquid biopsy** can predict how your cancer is responding to immunotherapy. PET/CT stands for Positron Emission Tomography / Computed Tomography. PET/CT produces images by measuring how the body uses nutrients given in the form of a radioactive drug called a **tracer**. The **tracer** being used for research in this study is called **18F-fluorocholine**. It is approved in some countries for detecting hepatocellular carcinoma. In the United States, the Food and Drug Administration (FDA) allows for 18F-fluorocholine to be used only for research. This research study will be conducted only at The Queen's Medical Center in cooperation with The University of Hawaii Cancer Center.

What is informed consent?

Before you decide whether or not to take part in this study, you must understand its purpose, how it may help, any risks to you, and what you have to do. Your doctor or a study researcher will talk to you about the study and go over information contained in this form. This process is called **informed consent**. This consent form also gives you information about what health information will be collected as part of the research study and how that information will be used or disclosed. If you sign this form you are agreeing to take part in this study and allow the use and disclosure of your medical records, test results, and health information collected in connection with your participation in this study. You will be given a copy of this consent form to keep. If you do not wish to take part in this study, you will continue to receive medical care, but not as part of this study.

Before you learn about the study, it is important that you know the following:

- Taking part in this study is of your own free will. You have rights that cannot be taken away by signing this consent form.
- You may decide not to take part in the study or stop being in the study at any time without it making any difference to your care now or in the future, or to any benefits that you are allowed.
- If the study changes in any way which could make a difference to your taking part, you will be told about the changes. You may be asked to sign a new consent form.

Why is this study being done?

The purpose of this research study is to find out if an 18F-flurocholine (FCH) **PET/CT** and **liquid biopsy** can predict which patients will benefit most from immunotherapy and to improve the ways these tests can benefit patients with cancer.

Please note that the treatment and follow-up for immunotherapy is not part of this study.

How many people will take part in the study?

Eighty (80) people are expected to be recruited for this particular study.

What happens during my involvement on this research study?

If you decide to take part in this study, you will be asked to sign this consent form. If you are a woman who is able to get pregnant, you will have a pregnancy test to confirm you are not pregnant. You will then receive an **18F-fluorocholine (FCH) PET/CT scan** at the hospital before you start your immunotherapy. A sample of your blood will also be collected. About 4 tablespoons of blood will be taken from the vein. However, if your cancer shows a certain appearance on the **18F-fluorocholine PET/CT scan**, you will be asked to also have another type of PET/CT called an **18F-fluorodeoxyglucose (FDG) PET/CT scan** before and after 8 weeks of immunotherapy treatment. The **18F-fluorodeoxyglucose (FDG)PET/CT scan** is the standard (FDA approved) type of PET/CT scan that patients with other types of cancer have. The research study will continue to collect information about your health and treatment until you stop treatment, or when the cancer stops responding to treatment.

When?	***What will take place?***	***How long will it take?***
Before treatment	An **18F-fluorocholine (FCH) PET/CT scan** will be performed and a blood sample will be taken.	Total appointment time is about 2 hours. You will be in the scanner for less than 30 minutes.
Before treatment	An **18F-fluorodeoxyglucose (FDG) PET/CT scan** might be performed (it will be explained if it is going to be done)	Appointment time is 2 to 3 hours. You will be in the scanner for less than 30 minutes.
After 8 weeks of treatment	An **18F-fluorodeoxyglucose (FDG) PET/CT scan** might be performed (it will be explained if it is going to be done)	Appointment time is 2 to 3 hours. You will be in the scanner for less than 30 minutes.
After 16 weeks of treatment	A CT or MRI scan will be done. This would typically be done even if you were not in the study.	An MRI scan may take 1 to 2 hours. A CT scan may take less than 30 minutes.

What happens during my visit for a PET/CT scan?

You will be asked to not eat anything for at least 2 hours before any PET imaging appointment. A small plastic tube (intravenous catheter) will be placed into your arm vein. The PET tracer will be given to you through the vein. The PET tracer will give off a small amount of radioactive energy that can be picked up by the PET/CT scanner to form pictures. The PET/CT scanner is a large donut shaped machine. You will lie on a bed as the PET/CT moves around your body to make the pictures. The intravenous catheter will be removed after the scan. Before you leave the PET center, you will be asked to void (urinate).

Routine (Usual) Care CT or MRI Examinations

As part of your standard care, you physician will be ordering CT or MRI scans of your cancer at regular intervals. The choice of CT or MRI imaging will be decided by your treating physician.

What will be done with my blood sample?

Your blood sample will have genetic testing to examine the DNA in your blood. This is called a liquid biopsy. While genes that determine your physical characteristics are made of DNA, only the DNA that is related to your cancer will be examined by this test. The name of the genetic blood test used in this research study is Foundation One CDX. This genetic blood test is FDA approved and is used to identify the genes from cancer that are mutated (abnormal). Because doctors may find this test useful for a patient with your condition, the results of this test will be shared with your doctor. Results that include your full name and other identifiers may also be placed in your medical record.

The blood sample is sent to a laboratory on the mainland for processing. As a backup in case these samples are lost or damaged, 2 extra tubes of blood will be taken and stored at the University of Hawaii Cancer Center (UHCC) Genomics Core laboratory. These samples will be labeled with an ID (identifier) code made just for the research study and the date that the samples were collected. No other identifying information about you will be attached to the blood samples that are sent to the mainland for the Foundation One CDX test and to UHCC.

Can my genetic information be used to discriminate against me?

A new federal law, called the Genetic Information Nondiscrimination Act (GINA), generally makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. This law will protect you in the following ways:

- Health insurance companies and group health plans may not request your genetic information collected from this research.
- Health insurance companies and group health plans may not use your genetic information when making decisions regarding your eligibility or premiums.
- Employers with 15 or more employees may not use your genetic information when making a decision to hire, promote, or fire you or when setting the terms of your employment.

This federal law does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance, nor does it protect you against genetic discrimination by all employers. For more information about this law and how your genetic information is used for research, you may ask the research staff or study investigators.

What happens after my research study appointments?

The research study will receive updates from your cancer doctor about your condition. It is important that you do not miss any appointments with your doctor. Your doctor may also order other X-ray or radiology imaging tests (e.g. CT or MRI) over the weeks or months that you are being treated. The PET/CT scans done as part of this research study cannot replace these other imaging tests. It is important that you do not miss any imaging test appointments.

What possible side effects or risks do I need to be aware of?

This research study will expose you to a small amount of radiation. The amount of radiation is about as much as that from a standard (diagnostic) X-ray CT (computed tomography) scan of the body. X-ray CT scans are common and widely used imaging tests. The total radiation exposure from receiving three PET/CT scans is below the limits set by the FDA for radiation exposure to medical workers and research volunteers. It is possible but not known for certain whether this amount of radiation exposure can increase the risk of developing cancer by a small amount.

As of this time, there are no known serious side effects related to 18F-fluorocholine. Like any drug, there may be unknown side effects. The PET/CT scanner never comes into contact with you directly. However, it is possible to feel claustrophobic (afraid of being in a small space) or uncomfortable during the scan. This does not happen very often. If it does happen, you can ask at any time to stop the scan. Like all medical imaging tests, PET/CT scans cannot detect all cancers, especially if the amount of cancer is small.

If something found on your PET scan is felt to be important for your medical care, your doctor will be notified. This is done out of concern for your well-being, but it may make you worried. It may also cause your doctor to recommend other tests to you. You or your insurance company will have to pay for tests not performed as part of this research study.

While strict procedures will be followed to protect your privacy, there is always a risk to privacy if your personal health information is shared with a research study. Your doctor will be asked to provide your personal health information. The researchers may provide information to your doctor.

Are there benefits to taking part in the research study?

This study is not part of your doctor's plan for treating you. You should not expect to directly benefit from taking part in this study. However, if something found on the PET/CT scan has a good chance of helping you, it will be shared with your doctor. Knowledge gained in this study may help other people with cancer in the future. While it is possible that some information from the genetic blood test, PET/CT scan, CT scan, or MRI scan performed with this study can help you, there is no guarantee that it will.

What other choices do I have if I do not take part in the research study?

You can receive treatment without taking part in a research study. Your decision to take part or not take part in this study will not make any difference in your treatment. You may choose to not take part in this study without it making a difference in the care you get now or in the future.

Will my medical information be kept private?

Federal Privacy Regulations provide safeguards for privacy, security, and authorized access to health information. Information gained during this study and information known about you will be confidential (private) to the extent permitted by state and federal law. The results of this research may be presented at meetings or in publications; however, your identity will never be disclosed (shared) in any research meeting or publication.

USE AND DISCLOSURE (RELEASE) OF YOUR HEALTH INFORMATION/ HIPAA AUTHORIZATION

By signing this consent form you are authorizing the collection, use and release of your personal health information in medical records and test reports and any health information gathered about you as part of this study. Your information will only be used/disclosed as described in this consent form and as permitted by state and federal laws. Your personal health information is health information about you that could be used to identify you. This information may include information about AIDS or HIV infection, treatment for alcohol and/or drug abuse, or mental health or psychiatric services.

What personal information will be obtained, used, or disclosed:

Your protected health information will be used to collect the data needed to complete the research, to properly monitor (watch) how the study is done, and to answer research questions related to this study. This health information may come from your medical records, procedure reports, diagnostic and imaging test results, findings found on physical exam, and any information disclosed by you or your caregivers. The study will collect the least amount of information needed to accomplish the purposes of the research.

There is no expiration date to this authorization.

Who may receive, use or release information:

Your medical records and any health information related to this study may be used or released in connection with this research study to the following:

- The study researchers listed on this consent form and their research staff and other research personnel at The University of Hawaii Cancer Center for the purposes of conducting this research study.
- The Research and Institutional Review Committee of The Queen's Medical Center and staff members of the Research Regulatory Office for purposes of overseeing the research study and making sure that your ethical rights are being protected.
- Providers and other healthcare staff affiliated with QMC who are involved in your care.

Who may receive the information from the above groups:

The individuals or groups named above may release your medical records, this consent form and the information about you created by this study to:

- The sponsor of this study (the National Cancer Institute) and their designees,
- Federal, state and local agencies having oversight over this research, such as The Office for Human Research Protections in the U.S. Department of Health and Human Services, Food and Drug Administration, the National Institutes of Health,
- Representatives of outside groups hired by the hospital research department for audits to make sure studies are done as required,
- Providers and other healthcare staff involved in your care,
- Providers of radiology imaging services as well as other diagnostic service providers such as Foundation Medicine, Inc., the company that will be performing the genetic blood test.
- Staff in medical billing-related departments or insurance companies

There is a possibility that your information may be released again by the sponsor of the study or governmental agencies described above and no longer covered by federal privacy rules.

Right to Withdraw or Not Take Part in the Study

You may refuse to sign this authorization. If you refuse to sign this authorization, you will not be able to take part in this study. If you choose not to be in the study, or choose to withdraw from the study, or if you refuse to sign the authorization, it will not make a difference in your usual treatment, or your payment, and it will not change your eligibility for any health plan or health plan benefits that you are allowed.

If you decide to end your part in the study or are removed from the study, you may revoke (take away) your authorization. In order to take away this authorization, you must send a letter/notice to the researcher and address listed on the first page of this consent form.

If you take away your authorization, your part in the study will end and the study staff will stop collecting medical information from you and about you. The researchers and sponsor will continue to use information that has already been collected, but no new information about you will be collected unless the information is about an adverse event (a bad side effect) related to the study or to keep the scientific integrity of the study. If an adverse event happens, the investigators, federal agencies, and hospital Research and Institutional Review Committee may need to review your entire medical record.

Access to Your Information

You may see information from this study in your medical record; however, information related only to the study is kept separately and will not be available to you until the study is finished. This is designed to maintain the validity (integrity) of the study. If you wish to review your study records after the completion of the study, you should request this from the research doctor.

END OF HIPAA AUTHORIZATION SECTION

Information available on Clinicaltrials.gov

Information about this research study will be available on http://www.clinicaltrials.gov, as required by law. This website will not include information that can identify you. It will include a summary of the results after the research study is completed. You can search this website at any time for more information about this research study.

What happens if I am injured because I took part in this study?

If you are injured as a result of being in this study, you will get immediate medical care and treatment including hospitalization, if needed. The sponsor of the study and the study doctor do not have any funding (money) to pay for treating any injury or illness. If your insurance company does not pay for some (or all) of the treatment of your injury, you may be responsible for payment. You have legal rights if you feel you have been wrongfully injured.

Can I be removed from the research study?

You take part in this study of your own free will. You may be taken off the study without your consent if you do not keep your study visit or follow study directions or become pregnant.

What are the costs of taking part in this study?

The immunotherapy drugs used to treat your cancer are not part of this research study. You or your insurance company will still need to pay for your cancer treatment. Medical tests that are part of the ordinary care for someone with cancer will also have to be paid by you or your insurance company.

This research study will pay for the Foundation One CDX blood test, one CT (computed tomography X-ray) or MRI (magnetic resonance imaging) scan of your liver, and up to 2 standard 18F-fluorodeoxyglucose PET/CT scans. You will not have to pay for the research 18F-fluorocholine PET/CT scan.

If you belong to a Medicare Advantage Plan, the bills for your tests and services that are not paid for by the research study will be billed to regular Medicare first and the difference then billed to Medicare Advantage. Although Medicare Advantage will eventually reimburse the difference, this may result in higher copayment for you while you are on the study.

Will I be paid for taking part in this study?

You will receive $50 to cover the costs of transportation and time needed for 18F-fluorocholine PET/CT. If you have 18F-fluorodeoxyglucose PET/CT, you will receive $50 for additional time and transportation costs. You will not have to pay for parking at The Queen's Medical Center.

Since you are receiving compensation (payment of any kind) in this study, QMC is required to collect your name, address, and social security number through an Internal Revenue Service (IRS) Form W-9. If you receive more than $600 per year for taking part in one or more research studies, you may be required to pay taxes on that money. This does not include any payments you receive to pay you back for expenses like parking fees. You may receive an Internal Revenue Service (IRS) Form 1099 if you receive more than $600 in one year for taking part in one or more QMC research studies. Form W-9 will be shared with the QMC Finance office in order to keep track of this.

Will I be notified of any new findings?

Any important new information learned during this study will be given to you if that information will make a difference to your willingness to continue in this study.

CERTIFICATE OF CONFIDENTIALITY

This research study is covered under a Certificate of Confidentiality given by the Department of Health and Human Services. The Certificate protects the researchers (study doctors, and staff) from being forced to release any research information (data) in which you are identified, even under court order or subpoena, for criminal (related to a crime), administrative, or legislative proceedings. The information can be released if you or your guardian requests it in writing. This protection is not absolute. It does not, for example, apply to any state requirements to report certain communicable diseases, or to release information in cases of medical necessity. The researcher(s) must report cases of suspected child or elder abuse to the appropriate authorities.

Will I allow my blood samples to be used for other research in the future?

Your blood will only be used for research and will not be sold. There may be some samples of your blood left over at the end of the study. Your name or other personal information will not be on these blood samples. Will you allow this blood to be used for other research studies?

____ No. I ask that any unused samples of my blood be destroyed at the end of the study.

____ Yes, I will allow my blood to be used anonymously for research studies at The University of Hawaii Cancer Center (UHCC) in the future. These studies may include genetic tests on the blood.

____ Yes, I will allow my blood to be used anonymously for research studies at The University of Hawaii Cancer Center, but only if they are related to liver cancer or liver disease. These studies may include genetic tests on the blood.

Who can I contact for questions or concerns?

If you have any questions or concerns about any matter relating to this research, you may call Dr. Sandi Kwee at (808) 691-5466. If you cannot get satisfactory answers to your questions or you have comments or complaints about your treatment in this research study, you may contact:

Research & Institutional Review Committee, The Queen's Medical Center
1301 Punchbowl Street
Honolulu, HI 96813
Phone: (808) 691-4512

YOUR CHOICE TO SHARE GENETIC DATA WITH THE NATIONAL CANCER INSTITUTE

What is the purpose of sharing genetic data with the National Cancer Institute?

The National Cancer Institute (NCI) is a federal agency that receives its funds from Congress. The NCI is a part of the National Institutes of Health (NIH). The mission of the NCI is to lead, conduct, and support cancer research across the nation to advance scientific knowledge and help all people live longer, healthier lives. As part of this mission, the NCI created a national repository for cancer genetic information. This data repository can improve cancer research by allowing more researchers access to research data that has already been collected. The NCI has asked if you would allow your genetic information to be added to their national repository.

How will my genetic information and data be given to the NCI data repository?

The genetic information about your cancer is obtained from your blood sample. This genetic information along with information collected by the research study about your cancer (such as your risk factors and disease status) will be deposited into a NCI data repository with restricted access. Before sending this data to the NCI, all your personal identifying information such as your name, address, account and other identification numbers will be removed in accordance with government standards for privacy protection. All local and federal government regulations and standards will be followed to protect your confidentiality and the data collected from you.

What permissions will I be giving and how will my data be used?

Strict policies will make sure that data in the NCI repository is used according to the permissions you are giving when you sign this consent form. You are being asked to allow your samples, genetic and health information as described in the paragraph above to be stored in a NCI data repository and shared broadly with other scientists conducting health, medical, and

biomedical research only, and not any study of population origins or ancestry. These other scientists must have IRB approval before they can use the samples. The samples and information will be available for any future research question, such as research to understand what causes certain disease, or development of new scientific methods. This data can be used by either non-profit or for-profit organizations. Any results of research using this data may be shared publicly through scientific meetings and publications, however your identity will never be disclosed.

Are there any risks from sharing genetic data?

Some researchers believe that it may be possible to identify a person using only genetic data. However, identifying a person in this way would likely require a full copy of their DNA. This research study only collects information from a limited portion of DNA corresponding to a small number of genes related to cancer (usually less than 500). For reference, human beings have over 20,000 genes. We do not believe that it will be possible to identify you or your personal characteristics (such as race or ethnicity) based on the limited amount of genetic information that will be shared. However, it is possible that a method could be developed in the future to guess or predict your identity or personal characteristics using a small amount of genetic data. Because of this, we cannot guarantee that your genetic information will never be used to identify you or discriminate or harm the reputation of you or any group that you belong to.

Are there any benefits from sharing my data?

There is no benefit to you since you can no longer be identified as the source of this data.

Can I withdraw my consent for research use of my genetic information and data?

Yes, you can withdraw your consent at any time without penalty or loss of benefits to which you are entitled. However, NCI cannot take back any data already distributed to researchers.

PLEASE CHOOSE ONE OF THE FOLLOWING:

____ I give permission to allow my genetic information and data collected by this research study to be given to the NCI and shared with other researchers as described in this form.

____ I do not give permission for my information to be given to the NCI.

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AGREEMENT TO TAKE PART AND CERTIFICATION AND AUTHORIZATION OF PROTECTED HEALTH INFORMATION

I, or my legally authorize representative (the legal person who cares for me) have read and understand the description of this study such as the purpose and nature of this study, its expected length, the procedures to be done, reasonably known risks and discomforts, benefits to expect, other treatments I may have, release of my medical records, payment and medical treatment for injury, and removal without my consent for this research study.

I am taking part in this study of my own free will. I may withdraw (stop taking part) and/or withdraw my authorization for use and release of protected health information at any time after signing this consent form without it making a difference to my care now or in the future or any loss of benefits that I am allowed. My consent does not take away my legal rights in case of carelessness or negligence of anyone connected with this study. My signature means that I have read the information above or that it has been read to me, my questions have been satisfactorily answered, and at any time I have other questions, I can contact the researcher listed on the first page.

Specially Protected Health Information

I agree to the release of the following information should it be contained in my medical records: Acquired Immune Deficiency Syndrome (AIDS or HIV), alcohol and/or drug abuse treatment, or behavioral or mental health services.

cc: *Signed copy* of consent to patient

_____	_____	_____
Subject's Name (Print)	Subject's Signature	Date/ Time
_____	_____	_____
Witness' Name (Print)	Witness' Signature	Date/ Time

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In my judgment the subject is voluntarily and knowingly giving informed consent and has the legal capacity to give informed consent to take part in this research study.

_____	_____	_____
Individual Obtaining Consent (Print)	Consenter's Signature	Date/ Time

(Investigator: fax a copy of this signed page to Research Regulatory Office at 691-7897 within 24 hours of signing.)