IRB Use Only
Approval Date: April 17, 2024
Expiration Date: March 31, 2025

Title of Study: Liquid Biopsy for Hepatocellular Carcinoma Molecular Characterization and Assessment of Treatment Response After Y90 Radioembolization: A Pilot Study			
Title of Consent (if different from Study Title):			
Principal Investigator: **Sirish Kishore, MD**	VAMC:	VA Palo Alto HCS	IRB# 73453

Are you participating in any other research studies? _____ Yes _____No

CONCISE SUMMARY

- Liver cancer is a common problem in Veterans. We are investigating a new type of blood test that may be able to determine how aggressive your liver cancer is, and whether it can be used to help monitor the success of your treatment.
- Your participation in this study is **voluntary**.
- Participation in the study consists of obtaining **two additional vials of blood** when you come in for your lab draws right before your treatment, and at 1 month, 3 months and 6 months after treatment as part of your routine clinical care. There will be no separate needle sticks or invasive tests for the research protocol.
- This study may be inconvenient for you, as you will need to travel to the Palo Alto VA for the lab draws, but these can be done during scheduled visits for your treatment day, or follow up CT/MRI scans which are part of the normal follow up of liver cancer after treatment to minimize the inconvenience.
- Nobody will profit from your participation in this study. The purpose of this study is to learn more about the subtypes of liver cancer that can be identified by this test, and whether the test can be used to help monitor your treatment response either alone or in combination with your imaging tests.
- You will still get all of the standard of care follow up procedures as part of this study.
- You may stop participating in this study at any time.

PURPOSE OF RESEARCH

You are invited to participate in a study to determine if liquid biopsy, a method of detecting cancer from a blood draw, can be used to sub-classify your liver cancer before treatment, as well as evaluate whether this blood test can be used to monitor your response to a radiation treatment called Y-90 radioembolization, which is commonly used to treat liver cancer. Currently, the only way to detect this cancer and monitor treatment involves looking at changes in imaging over time. This is often combined with a blood test known as alpha-fetoprotein (AFP) which is not produced in many liver cancers. In this study, we plan to determine how this liquid biopsy technique and standard imaging tools, either alone, or in combination, are able to predict and monitor response to the radioembolization treatment.

The VA Palo Alto expects to enroll 12 total participants in this research study.

VOLUNTARY PARTICIPATION

Your participation in this study is entirely voluntary. Your decision not to participate will not have any negative effect on you or your medical care. You can decide to participate now but withdraw your consent later and stop being in the study without any loss of benefits or medical care you are entitled to.

DURATION OF STUDY INVOLVEMENT

This research study is expected to take 2 years to complete. Your involvement would be for 6 months beginning prior to your Y90 treatment and then 6 months following the treatment. The time for the blood draws will be about 20 minutes, therefore an estimated total for the 6 draws would be about 1.5 hours over the 6 month study period.

PROCEDURES

If you choose to participate, Dr. Sirish Kishore and his research staff will arrange to have you scheduled for your procedures and scans.

Blood Draws:
Blood draws will be collected during the following periods throughout the study and will be obtained at the time of the lab draws that are ordered as part of your clinical care: once at baseline, on the same day of Y-90 treatment just prior to therapy; 4-6 weeks post Y-90 treatment; 3 months post Y-90 treatment; and 6 months post Y-90 treatment. During your standard of care blood draws, two additional tubes of blood will be obtained and sent to the Sponsor, OneCellDx, for the liquid biopsy analyses. The additional tubes will equal 20 ml of blood (or approximately 4 teaspoons).

Imaging Data:
Information about your CT or MRI scan will be obtained from your medical record for each of your follow up visits.

The results of the study of your specimens will be used for research purposes only and you will not be told the results of the tests.

The process of determining all or nearly all of your DNA sequence is called whole genome sequencing. It is different from genetic testing that does not involve whole genome sequencing because it provides a much more detailed snapshot of your genome. This research will not include whole genome sequencing.

PARTICIPANT RESPONSIBILITIES

As a participant, your responsibilities include:

- Follow the instructions of the investigators and study staff.
- Keep your study appointments. If it is necessary to miss an appointment, please contact the investigators or research study staff to reschedule as soon as you know you will miss the appointment.
- Tell the investigators or research staff if you believe you might be pregnant.
- Ask questions as you think of them.
- Tell the investigators or research staff if you change your mind about staying in the study.

WITHDRAWAL FROM STUDY

If you first agree to participate and then you change your mind, you are free to withdraw your consent and stop your participation at any time. If you decide to withdraw from the study, you will not lose any benefits to which you would otherwise be entitled and your decision will not affect your ability to receive medical care for your condition.

If you want to stop being in the study you should tell the investigators or study staff. You can do this by contacting Luisa Manfredi, Study Coordinator at luisa.manfredi1@va.gov or 650-493-5000 x61706.

Data collected on you to the point of withdrawal remains part of the study database and may not be removed per the Food and Drug Administration.

The investigators may also withdraw you from the study for one or more of the following reasons:

- Failure to follow the instructions of the investigators and/or study staff.
- The investigators decide that continuing your participation could be harmful to you.
- The study is cancelled.
- Other administrative reasons.
- Unanticipated circumstances.

POSSIBLE RISKS, DISCOMFORTS, AND INCONVENIENCES

There are minimal risks associated with this study, as all of the imaging and procedures (phlebotomy) will be performed as part of your routine care. You may experience discomfort from the blood draw, such as slight pain, bruising, or bleeding. Other possible risks include fainting from a drop in blood pressure, muscle weakness, or numbness or pain from nerve issues, but would not be any different than what is seen in standard of care blood draws.

POTENTIAL BENEFITS

We cannot and do not guarantee or promise that you will receive any benefits from this study. There are no direct benefits from participating in this study. We hope this research will benefit future patients through early cancer detection. If a signal is detected on liquid biopsy, this information could be used to further classify your tumor, where biopsy would not normally be part of initial care.

ALTERNATIVES

As this is not a treatment study there are no alternatives to the study. You may choose to not participate.

PARTICIPANT'S RIGHTS

You should not feel obligated to agree to participate. Your questions should be answered clearly and to your satisfaction.

You will be told of any important new information that is learned during the course of this research study, which might affect your condition or your willingness to continue participation in this study.

ClinicalTrials.gov

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.

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CONFIDENTIALITY

A confidential participant identification number will be used to ensure that information cannot be linked or traced to any person or family. Identifiers might be removed from identifiable private information and/or identifiable specimens and, after such removal, the information and/or specimens could be used for future research studies or distributed to another investigator for future research studies without additional informed consent from you.

Patient information may be provided to Federal and other regulatory agencies as required. The Food and Drug Administration (FDA), for example, may inspect research records and learn your identity if this study falls within its jurisdiction. The purpose of this research study is to obtain information on the safety and effectiveness of insert name of the liquid biopsy assays; the results will be provided to the sponsor, the Food and Drug Administration and other federal and regulatory agencies as required.

The purpose of the data collected for this project is for scientific research only and there will be no attempt to identify directly or indirectly any subjects in the research data. We will keep your name and all the information you tell us in this study confidential as possible. We may publish the results of this study for others to read about, but you will not be identified in any articles about the study by name, social security number, address, telephone number, or any other direct personal identifier. Also, other federal agencies as required, such as the VA Office of Research Oversight and the VA Office of the Inspector General may have access to your information.

Information about you participating in this research study may be added to your VA Medical Records.

We will keep your name and all the information you tell us in this study confidential as possible. We may publish the results of this study for others to read about, but you will not be identified in any articles about the study by name, social security number, address, telephone number, or any other direct personal identifier. Also, other federal agencies as required, such as the VA Office of Research Oversight and the VA Office of the Inspector General may have access to your information.

Any of your specimens which are used in research may result in new products, tests or discoveries. In some instances, these may have potential commercial value and may be developed and owned by the Investigators, Stanford University and/or others. However, donors of specimens do not retain any property rights to the materials. Therefore, you would not share in any financial benefits from these products, tests or discoveries.

FINANCIAL CONSIDERATIONS

Will I get paid?
There is no payment for participation in this study.

Will I have to pay anything?
There will be no costs to you for any of the treatment or testing done as part of this research study. However, medical care and services provided by the VA that are not part of this study (e.g., normal hospital and prescription expenses which are not part of the research study) may require co-payments if your VA-eligibility category requires co-payment for VA services.

COMPENSATION for Research Related Injury

If you are injured as a direct result of being in this study, medical treatment will be available. If you are eligible for veteran's benefits, the cost of such treatment will be covered by the VA. If not, the cost of such treatments may still be covered by the VA depending on a number of factors. In most circumstances, the treatment must be provided in a VA medical facility. No other form of compensation for injuries is available. However, by signing this form you have not released the VA from liability for negligence.

CONTACT INFORMATION

Questions, Concerns, or Complaints: If you have any questions, concerns or complaints about this research study, its procedures, risks and benefits, or alternative courses of treatment, you should contact the Study Coordinator, Luisa Manfredi, at luisa.manfredi1@va.gov or 650-493-5000 x61706. You should also contact the Study Coordinator at any time if you feel you have been hurt by being a part of this study.
Appointment Contact: If you need to change your appointment, please contact Luisa Manfredi, Study Coordinator at luisa.manfredi1@va.gov or 650-493-5000 x61706.

Independent Contact: If you are not satisfied with how this study is being conducted, or if you have any concerns, complaints, or general questions about the research or your rights as a participant, please contact the Stanford Institutional Review Board (IRB) to speak to someone independent of the research team at (650)-723-5244 or toll free at 1-866-680-2906. You can also write to the Stanford IRB, Stanford University, 1705 El Camino Real, Palo Alto, CA 94306.

Health Information Portability and Accountability Act (HIPAA)

There are rules to protect your private health information. Federal and state laws and the federal medical law, known as the HIPAA Privacy Rule, also protect your privacy. By signing this form, you provide your permission called your 'authorization,' for the use and disclosure of information protected by the HIPAA Privacy Rule.

How will my health information be used in the study?

Your health information will be de-identified prior to use in this study. Your pre-procedure and post-procedure liver imaging will be de-identified and entered into the study database for imaging assessments of the baseline tumor and response to treatment. Laboratory values will also be recorded to demonstrate biochemical changes that occur during the course of treatment. Operative reports and imaging reports will also be reviewed for information related to the tumor and the tumor treatment. The de-identified health information will be uploaded to the study database for analysis.

What Personal Health Information Will Be Used or Shared?

The following health information, linked to you by your name, telephone numbers, dates and SSN will be used for this research:

- Treatment dates
- Medical history and physical examination information
- Progress notes
- Laboratory Test Results on blood, tissue, urine
- Operative reports
- CT and MRI Scans
- Discharge Summaries

Who May Use or Share Your Health Information?

By signing this document, you allow the following individuals and entities to obtain, use and share your health information for this research study:

- The Principal Investigator Dr. Sirish Kishore and members of the VA research team.
- Departments within the VA Health Care System responsible for the oversight, administration, or conduct of research.
- The Stanford University Administrative Panel on Human Subjects in Medical Research and other Stanford University Officials responsible for the oversight, administration, or conduct of research.

Who May Receive and Use Your Health Information?

The investigators may share your health information with the following individuals as part of this research study.

- The Palo Alto Veterans Institute for Research (PAVIR), who administers the funding for this project, and any agents or outside entities hired by PAVIR to assist them in carrying out their responsibilities.
- OneCellDx (Sponsor)
- The Office for Human Research Protections in the U.S. Department of Health and Human Services
- Other outside individuals or entities hired by the VA Palo Alto Health Care System to do certain work in support of the VA Health Care System
- The Office for Human Research Protections in the U.S. Department of Health and Human Services
- The Food and Drug Administration (FDA)
- Other outside individuals or entities hired by the VA Palo Alto Health Care System to do certain work in support of the VA Health Care System

We will protect your health information as required by all laws, however health information shared with others may no longer be protected by Federal laws or regulations and might be shared by the parties above.

Do I have to sign this form?

No. Signing this form is voluntary. The VA may not condition treatment, payment, enrollment or eligibility for benefits based on signing this form. If you decide not to sign the form, you will not be able to take part in this study.

If I sign now, can I decide later not to continue in the study?

Yes. You are free to take back your permission and stop being in the study. The investigators will not collect any more information about you after you take back your permission, but they can continue to use your information that was collected before you took back your permission.

Your request to take back your permission must be done in writing. Either give your written request to the investigator or send it by mail to: Dr. Sirish Kishore, 3801 Miranda Ave MC114, Palo Alto, CA 94304

Does My Permission for the use my Personal Health Information Expire?

Yes. Your information cannot be used forever. Your permission related to the use and sharing of your health information expires when this research study is completed or on 4/1/2050

HIPAA regulations require you to give separate written permission (signature) for the use of your protected health information.

_____ _____

Signature of Participant Date

_____

Print Name of Participant

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EXPERIMENTAL SUBJECT'S BILL OF RIGHTS

As a research participant you have the following rights. These rights include but are not limited to the participant's right to:

- be informed of the nature and purpose of the experiment;
- be given an explanation of the procedures to be followed in the medical experiment, and any drug or device to be utilized;
- be given a description of any attendant discomforts and risks reasonably to be expected;
- be given an explanation of any benefits to the subject reasonably to be expected, if applicable;
- be given a disclosure of any appropriate alternatives, drugs or devices that might be advantageous to the subject, their relative risks and benefits;
- be informed of the avenues of medical treatment, if any available to the subject after the experiment if complications should arise;
- be given an opportunity to ask questions concerning the experiment or the procedures involved;
- be instructed that consent to participate in the medical experiment may be withdrawn at any time and the subject may discontinue participation without prejudice;
- be given a copy of the signed and dated consent form; and
- be given the opportunity to decide to consent or not to consent to a medical experiment without the intervention of any element of force, fraud, deceit, duress, coercion or undue influence on the subject's decision.

Signing your name means you agree to be in this study and that you will receive a copy of this signed and dated consent form.

_____ _____

Signature of Participant Date

_____

Print Name of Participant

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Person Obtaining Consent:

_____ _____
Signature of Person Obtaining Consent Date

_____
Print Name of Person Obtaining Consent

HIPAA regulations require the participant to give separate written permission (signature) for the use of their protected health information.

Person Obtaining Consent HIPAA Authorization confirmation:

☐ Confirm the participant signed the VA HIPAA Authorization section of this consent form