Protocol Title:

TUMOR MARKERS, LIQUID BIOPSIES, AND PATIENT REPORTED OUTCOMES IN METASTATIC COLORECTAL, PANCREAS, BILIARY, AND ESOPHAGOGASTRIC CANCERS

DF/HCC Principal Research Doctor / Institution: Aparna R. Parikh, MD
Massachusetts General Hospital

Main Consent

Introduction and key information

All research is voluntary. It is your choice whether you take part in this research or not.

The following is a short summary of this research study to help you decide whether you would like to be a part of this study. More detailed information is provided later in this form.

For purposes of this research, you will be referred to as a "participant."

1. Why am I being invited to take part in a research study?

You are invited to take part in in this research study, because you have cholangiocarcinoma, gastric, gastroesophageal, pancreatic or colorectal cancer and are receiving anti-cancer therapy at Massachusetts General Hospital.

2. Why is this research being done?

This research study is designed to help us evaluate how patient-reported outcomes (e.g. symptoms, quality of life) and biomarkers compare to standard of care clinical assessments such as imaging and tumor markers in predicting the clinical outcomes (e.g. disease progression and survival).

3. What does this research study involve and how long will it last?

Prior to starting anti-cancer therapy and at subsequent designated visits (every one month), we will obtain a blood sample (2-4 teaspoons) and ask you to answer a series of questionnaires to measure your quality of life, mood, and symptoms. Study staff will assist you as needed. This should take about 20-30 minutes. All information collected will be kept confidential.

You will be in this research study for as long as you are on anti-cancer therapy for your cancer.

You may be taken off the research study for reasons such as:

- It is considered to be in your best interest
- The study procedures are found to be unsafe or ineffective
- There is any problem with following study procedures
- There are any problems with research funding
- Or for any other reason

If you are removed from the research study, the research Investigator will explain to you why you were removed.

In addition, you can stop participating in the research study at any time.

It is expected that about 600 people will take part in this research study.

Information about you and your health is personal and private. Generally it cannot be obtained without your written permission. By signing this form, you are providing that permission and your information may be obtained and used in accordance with this informed consent and as required or allowed by law. This means that researchers may obtain information regarding your past medical history, as well as specimens and samples from previous health care providers such as hospitals and labs.

4. What are the risks to participating in this study?

There are risks to taking part in any research study.

However, in general since the collection of blood or tissue in this study will occur in the setting of previous or future procedures that are part of your routine care, no additional procedures are required and therefore the expected clinical risks to you are minimal.

Major known risks to participating in this research study include:

- Disclosure of sensitive personal information resulting in a loss of privacy
- Possible emotional distress due to personal questions
- Potential genetic discrimination related to test results

5. Will being in this study benefit me in any way?

Taking part in this research study may or may not benefit you. We hope the information learned from this research study will provide more information about more effective treatment programs for people with cholangiocarcinoma, pancreatic, esophagogastric or colorectal cancers in the future.

6. What are my options?

If you decide to participate, please sign and date at the end of this form.

We will give you a copy and you can refer to this consent form at any time during the research study.

If you choose not to participate in this research study, the research doctors will discuss other treatment options with you and/or refer you back to your primary doctor.

A. WHY IS THIS RESEARCH STUDY BEING DONE?

The purpose of this research study is to evaluate how patient-reported outcomes (e.g. symptoms, quality of life) and biomarkers compare to standard of care clinical assessments such as imaging and tumor markers in predicting the clinical outcomes (e.g. disease progression and survival).

B. WHAT OTHER OPTIONS ARE THERE?

Taking part in this research study is voluntary. Instead of being in this research study, you have the following options:

- Decide not to participate in this research study
- Participate in another research study.

If you choose not to participate, are not eligible to participate, or withdraw from this research study, this will not affect your present or future care and will not cause any penalty or loss of benefits to which you are otherwise entitled.

We encourage you to take some time to think this over, to discuss it with other people and your primary doctor, and to ask questions now and at any time in the future.

C. WHAT IS INVOLVED IN THE RESEARCH STUDY?

Before the research starts (screening): Prior to signing this consent form, our research team reviewed your medical record to determine that you were eligible to participate in this research study.

After you sign this consent form: Prior to starting anti-cancer therapy and at subsequent designated visits (every month), we will obtain a blood sample (2-4 teaspoons) and ask you to answer a series of questionnaires to measure your quality of life, mood, and symptoms. Study staff will assist you as needed. This should take about 20-30 minutes. All information collected will be kept confidential.
Additionally, if you agree to participate in this research study, the following items involving your tissue, blood and clinical information may occur. These items will not involve any additional activity on your part.

1) In the future, if you undergo a biopsy, surgery, or other clinical procedure instead of discarding your left over biological samples that are in excess of what is needed for routine clinical testing, we will save them in what is called a “Tissue Bank” for possible future research. These tissues may include tumor tissue or normal tissue. We may also collect any tissues remaining from previously performed biopsies, surgery, or other procedures.
2) If you have already had a procedure or care at another hospital, we may request and use part of any stored tissues which resulted from your care there. By signing this consent form you give us permission to contact the hospital where you had any previous procedure to request a small portion of the available tissues and the associated medical information such as a pathology report and treatment records. We will store these tissues and information in the same manner as the rest of the study and seek permission to perform the same range of testing as on your tissues stored here. Whether such a tissue is shared with us will be up to the institution that is storing the tissues according to their rules or regulations.
3) We will collect and save information from your medical history, which includes questions about your health, current medications and any allergies. Health questionnaires completed by you during your clinical visits, may be collected and saved as well.
4) Your tissue specimens may be used to create a living tissue sample (called a “cell line”) that can be grown in the laboratory. In some cases, these cell lines can be grown and propagated in the laboratory indefinitely. Any cell lines generated will be named with a code. Your name or directly identifiable information will not be associated with any cell lines generated.

5) Genetic testing may be performed on blood or tissue collected. None of your genetic information will be associated with any identifiers, such as name, date of birth, or medical record number.

National Institutes of Health (NIH) Genomic Data Sharing:

Rapid progress in understanding and treating cancer will occur when some of the genetic information derived from your tissues and blood can be shared with other researchers. In particular, the National Institutes of Health (NIH) and other organizations have developed special data (information) repositories that analyze data and collect the results of certain types of genetic studies. These central banks will store your genetic information and samples, and provide them to qualified researchers to do more research. Therefore, we are asking your permission to share your results with these public databases. Some of this information may be made available over the internet and will be freely available to anyone who is interested (an open access database). Other, more detailed information may only be accessed by scientists at other research centers who have received special permission to review your de-identified data (a controlled access database).

Your information or samples will be sent only with a code number attached. Your name or other directly identifiable information will not be shared with these repositories or with other investigators. There are many safeguards in place to protect your information and samples while they are stored in these repositories and used for research. There is a slight risk of loss of privacy when sharing this information with these banks but we have established procedures to encode your samples and information and to protect your data. The repositories also have robust procedures in place to protect the confidentiality of the stored data. We will do everything we can to protect your data but we cannot absolutely guarantee its privacy or predict how genetic information will be used in the future.

National Institutes of Health (NIH) Data Sharing Involving Germline Research:

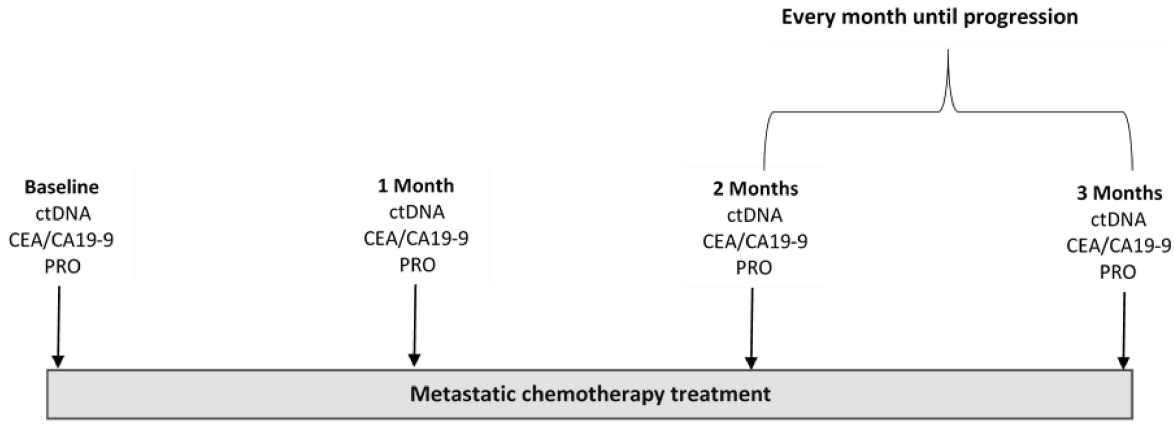
In order to allow the greatest amount of research to be performed on the tissue that you donate, researchers for this study may share results of sequencing your genes (which shows how your DNA is organized) with other scientists. In particular, the National Institutes of Health (NIH) and other organizations have developed special data (information) repositories that analyze data and collect the results of certain types of genetic studies. These central banks will store your genetic information and samples, and provide them to qualified researchers to do more research. Some of this information may be made available over the

internet and will be freely available to anyone who is interested (an open access database). Other, more detailed information may only be accessed by scientists at other research centers who have received special permission to review your de-identified data (a controlled access database). Neither type of database will contain information that is traditionally used to identify you, such as your name, address, medical record number, telephone number or social security number. However, people may develop ways in the future that would allow someone to link your genetic or medical information in our databases back to you. For example, someone could compare information in our databases with information from you (or a relative) in another database and be able to identify you (or a relative). Because the DNA sequence of each individual is unique (with the exception of identical twins), there is a very remote possibility that if a complete sequence determination of your DNA were publicly disclosed, it could be used by a researcher to determine your identity. It is also possible that there could be violations to the security of the computer systems used to share the codes linking your genetic and medical information to you. Patterns of genetic variation also can be used by law enforcement agencies to identify a person or his/her relatives.

Your privacy is very important to us and we will use many safety measures to protect your privacy. However, in spite of all the safety measures that we will use, we cannot guarantee that your identity will never become known. Although your genetic information is unique to you, you do share some genetic information with your children, parents, brothers, sisters and other relatives. Consequently, it may be possible that researchers looking at your genetic information could guess your identity based on other genetic information that they might know about your relatives. Similarly, it may be possible that genetic information from you could be used to help identify your relatives.

There may be other privacy risks that we have not foreseen. While we believe the risks to you and your family are very low, we are unable to tell you exactly what all the risks are.

Research Study Plan:



D. WHAT ARE THE RISKS OR DISCOMFORTS OF THE RESEARCH STUDY?

There are risks to taking part in any research study.

However, in general since the collection of blood or tissue in this study will occur in the setting of previous or future procedures that are part of your routine care, no additional procedures are required and therefore the expected risks to you are minimal.

There are small risks associated with obtaining blood samples. You may experience slight pain, swelling, bleeding bruising, or infection (not common) at the site of blood draw. Fainting or light-headedness can sometimes occur and last a few minutes. Whenever possible, and in almost all circumstances, blood samples will be obtained at the time of a scheduled routine blood draw, so that no additional needle stick will be involved. However, it is possible that researchers may request additional blood samples outside of your routine procedures.

Only tissues that are in excess of what is required for routine and expected clinical testing will be collected and used in this study. Molecular analyses will be performed on material only after all necessary clinical tests have been performed. If there is not enough tissue for clinical uses and for research, then the tissue will not be released for research purposes. Still, there is a small risk that if your samples are used for this research study, they might not be available for clinical use or testing in the future. However, we will make every effort to minimize this risk. Specifically, the designated committee of clinicians and scientists who oversee the repository will release your specimen only if they think the research to be performed justifies the use of your material. Most importantly, the material will not be released for research purposes unless the committee

believes that the material remaining after the research test is performed will be sufficient for any expected future clinical testing.

You may find some of the questions in the questionnaires to be emotionally upsetting. You may decline to answer questions which upset you. If you feel worried or upset at any time, a research assistant or a study investigator is available to talk with you about this and can be reached at the number below. You can also talk about these feelings at your oncology appointment. Investigators are ethically required to report to legal authorities in cases of child abuse, elder abuse, or if you intend to harm yourself or others. If these situations arise during the course of the study, appropriate clinical steps will be taken to protect you or whomever may be at risk. Any participants who become psychologically distressed during the course of the study may receive a referral for mental health treatment from the research Investigator.

One of the potential risks of this study is to your privacy. We take careful measures to protect your privacy and confidentiality. Methods used to strictly preserve your confidentiality include: using the special ID code, passwords, and restricting access to research databases. However, in spite of all of the safety measures that we use, we cannot guarantee that your identity will never become known.

Although your genetic information is unique to you, you do share some genetic information with your children, parents, siblings, and other blood relatives. Consequently, though highly unlikely, it may be possible that genetic information from them could be used to identify you. Similarly, it may be possible that genetic information from you could be used to help identify them.

Risks of Genetic Testing:
There is a risk that your test results could lead to genetic discrimination. A 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. However, this law does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance. There may be other unknown privacy risks.

During the research study, you will be provided with any new information that may affect your health or willingness to participate. You may be asked to sign a new consent form that shows that you have been informed of new information relating to this research study.

E. WHAT WILL HAPPEN IF I AM REMOVED FROM THE STUDY OR DECIDE TO END MY PARTICIPATION IN THE RESEARCH?

You will be in this research study for as long as you are on anti-cancer therapy for your cancer.

You may be taken off the research study for reasons such as:

- It is considered to be in your best interest
- The study procedures are found to be unsafe or ineffective
- There is any problem with following study procedures
- There are any problems with research funding
- Or for any other reason

You can stop being in the research study at any time. Tell the research doctor if you are thinking about stopping or decide to stop. Leaving the research study will not affect your medical care. You can still get your medical care from your hospital or Investigator.

If you choose to not participate, or if you are not eligible to participate, or if you withdraw from this research study, this will not affect your present or future care and will not cause any penalty or loss of benefits to which you are otherwise entitled.

If you decide to withdraw from a study that involves de-identified samples and data, it will not be possible to remove the samples that have already been processed or data that have already been recorded.

F. WILL I BE PAID TO TAKE PART IN THIS RESEARCH STUDY?

You will not be paid for participating in this study.

G. WHAT ARE YOUR COSTS?

Taking part in this research study will not lead to added costs to you or your insurance company.

You or your insurance company will be charged for other portions of your care during this research study that are considered standard care. You may be responsible for co-payments and deductibles that are standard for your insurance coverage.

If you have questions about your insurance coverage, or the items you might be required to pay for, please call financial services for information. The contact information for financial services:

- Massachusetts General Hospital: (617) 726-2191

The National Cancer Institute provides an online resource to help people participating in cancer clinical trials understand which services their insurance company is required by law to pay. This can be found at the website below.

http://www.cancer.gov or 1-800-4-CANCER (1-800-422-6237)

H. WHAT HAPPENS IF I AM INJURED OR BECOME SICK BECAUSE I TOOK PART IN THIS RESEARCH STUDY?

If you think you have been injured as a result of taking part in this research study, tell the person in charge of this research study as soon as possible. The research doctor's name and phone number are listed in this consent form.
The treating hospital will offer you the care needed to treat injuries directly resulting from taking part in this research. These treatments may be billed to you or your insurance company. You will be responsible for deductibles, co-payments and co-insurance. There are no plans to pay you or give you other compensation for the injury.

You do not give up your legal rights by signing this form.

We will need to collect certain personal information about you for insurance or payment reporting purposes, such as your name, date of birth, gender, social security number or Medicare identification number and information related to this research study. We may be required to report this information to the Centers for Medicare & Medicaid Services. We will not use this information for any other purpose.

If you go to the Emergency Room or to another hospital or doctor it is important that you tell them that you are in this research. If possible, you should give them a copy of this consent form.

I. WHOM DO I CONTACT IF I HAVE QUESTIONS ABOUT THE RESEARCH STUDY?

If you have questions about the study, please contact the research Investigator or study staff as listed below:

Massachusetts General Hospital

- Aparna R. Parikh, MD: (617) 724-4000

24 hour contact for questions about the study: call Massachusetts General Hospital at (617) 724-4000 and ask your doctor to be paged.

For questions about your rights as a research participant, please contact a representative of the Office for Human Research Studies at Dana-Farber Cancer Institute (617) 632-3029. This can include questions about your participation in the study, concerns about the study, a research related injury, or if you feel/felt under pressure to enroll in this research study or to continue to participate in this research study.

J. RETURN OF RESEARCH RESULTS

Most tests done on samples in research studies are only for research and have no clear meaning for health care. If the research with your identifiable information or samples gives results that do have meaning for your health, the researchers will contact you to let you know what they have found.

K. CLINICALTRIALS.GOV (CT.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.

L. FUTURE USE OF DATA AND SPECIMENS

Your personal information and/or biospecimens collected during this study may be stored and used for future research. Any personal identifiers will be removed so that the information or samples cannot be linked back to you. As a result, we will no longer be able to identify and destroy them.

Investigators, including investigators from collaborating institutions, can request this data and samples for new research. Samples and data may also be shared with outside non-profit academic investigators as well as with for-profit pharmaceutical investigators or commercial entities, with whom we collaborate.

You will not be asked to provide additional informed consent for the use of your de-identified information or samples in future research.

Future research studies may include genetic research. Your genes are unique to you. At this time, you cannot be identified through this research. There is a risk that you might be reidentified in the future as genetic research progresses

M. CONFIDENTIALITY

We will take measures to protect the privacy and security of all your personal information, but we cannot guarantee complete confidentiality of study data.

Medical information created by this research study may become part of your hospital medical record. Information that does not become part of your medical record will be stored in your study file. It may also become part of a DF/HCC research database called CORIS.

The study team plans to publish the results of this research study and when we do, we may be asked to make the data we collect available to other researchers. We will not include information that identifies you in any publications or to the researchers who request the data to do research.

The Genetic Information Nondiscrimination Act of 2008 (GINA) is a federal law that protects Americans from being treated unfairly because of differences in their DNA that may affect their health, and may prevent discrimination by health insurers and employers based on genetic information. GINA is intended to ease concerns about discrimination that might keep some people from getting genetic tests that could benefit their health, and enable people to take part in research studies such as this without fear that their DNA information might be used against them by health insurers or their workplace. This protection does not extend to disability or life insurance. Additional information can be found at http://www.genome.gov/10002328.

N. GENETIC RESEARCH

There is a risk that your test results could lead to genetic discrimination. A 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. However, this law does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance. There may be other unknown privacy risks.

During the research study, you will be provided with any new information that may affect your health or willingness to participate. You may be asked to sign a new consent form that shows that you have been informed of new information relating to this research study.

O. PRIVACY OF PROTECTED HEALTH INFORMATION (HIPAA AUTHORIZATION)

The Health Insurance Portability and Accountability Act (HIPAA) is a federal law that requires Dana-Farber/Harvard Cancer Center (DF/HCC) and its affiliated research doctors, health care providers, and physician network to protect the privacy of information that identifies you and relates to your past, present, and future physical and mental health conditions ("protected health information"). If you enroll in this research study, your "protected health information" will be used and shared with others as explained below.

1. What protected health information about me will be used or shared with others during this research?

- Existing medical records, including mental health records.
- New health information created from study-related tests, procedures, visits, and/or questionnaires

2. Why will protected information about me be used or shared with others?

The main reasons include the following:

- To conduct and oversee the research described earlier in this form;
- To ensure the research meets legal, institutional, and accreditation requirements;
- To conduct public health activities (including reporting of adverse events or situations where you or others may be at risk of harm); and
- To provide the study sponsor with information arising from an adverse event or other event that relates to the safety or toxicity of the drug(s) used in the study and for the purpose of this or other research relating the study drug(s) and their use in cancer;
- To better understand the diseases being studied and to improve the design of future studies; and,
- Other reasons may include for treatment, payment, or health care operations. For example, some medical information produced by this research study may become part of your hospital medical record because the information may be necessary for your medical care. (You will also be given a notice for use and sharing of protected health information.)

3. Who will use or share protected health information about me?

- DF/HCC and its affiliated research doctors and entities participating in the research will use and share your protected health information. In addition, other DF/HCC offices that deal with research oversight, billing or quality assurance will be able to use and share your protected health information.

4. With whom outside of DF/HCC may my protected health information be shared?

While all reasonable efforts will be made to protect the confidentiality of your protected health information, it may also be shared with the following entities:

- Outside individuals or entities that have a need to access this information to perform functions relating to the conduct of this research such as analysis by outside laboratories on behalf of DF/HCC and its affiliates (for example, data storage companies, insurers, or legal advisors).
- Other research doctors and medical centers participating in this research, if applicable
- Federal and state agencies (for example, the Department of Health and Human Services, the Food and Drug Administration, the National Institutes of Health, and/or the Office for Human Research Protections), or other domestic or foreign government bodies if required by law and/or necessary for oversight purposes. A qualified representative of the FDA and the National Cancer Institute may review your medical records.
- Hospital accrediting agencies
- A data safety monitoring board organized to oversee this research, if applicable

Some who may receive your protected health information may not have to satisfy the privacy rules and requirements. They, in fact, may share your information with others without your permission.

5. For how long will protected health information about me be used or shared with others?

- There is no scheduled date at which your protected health information that is being used or shared for this research will be destroyed, because research is an ongoing process.

6. Statement of privacy rights:

- You have the right to withdraw your permission for the research doctors and participating DF/HCC entities to use or share your protected health information. We will not be able to withdraw all the information that already has been used or shared with others to carry out related activities such as oversight, or that is needed to ensure quality of the study. To withdraw your permission, you must do so in writing by contacting the researcher listed above in the section: "Whom do I contact if I have questions about the research study?"
- You have the right to request access to your protected health information that is used or shared during this research and that is related to your treatment or payment for your treatment, but you may access this information only after the study is completed. To request this information, please contact the researcher listed above in the section: "Whom do I contact if I have questions about the research study?"

P. DOCUMENTATION OF CONSENT

My signature below indicates:

- I have had enough time to read the consent and think about participating in this study;
- I have had all of my questions answered to my satisfaction;
- I am willing to participate in this study;
- I have been told that my participation is voluntary and I can withdraw at any time

Signature of Participant
or Legally Authorized Representative

Date

Relationship of Legally Authorized Representative to Participant

DFCI Protocol Number: 18-380	Approved Date (DFCI IRB Approval): 06/10/2020
Date Posted for Use: 06/26/2020	

To be completed by person obtaining consent:

Adult Participant

The consent discussion was initiated on _____ (date).

Signature of individual obtaining consent: _____

Printed name of above: _____

Date: _____

☐ A copy of this signed consent form will be given to the participant or legally authorized representative.

☐ 1) The participant is an adult and provided consent to participate.

☐ 1a) Participant (or legally authorized representative) is a non-English speaker and signed the translated Short Form in lieu of English consent document:

As someone who understands both English and the language spoken by the participant, I interpreted and/or witnessed, in the participant's language, the researcher's presentation of the English consent form. The participant was given the opportunity to ask questions.

Signature of Interpreter/Witness: _____

Printed Name of Interpreter/Witness: _____

Date: _____

☐ 1b) Participant is physically unable to sign the consent form because:

☐ The participant is illiterate.

☐ The participant has a physical disability.

☐ Other (please describe): _____

The consent form was presented to the participant who was given the opportunity to ask questions and who communicated agreement to participate in the research.

Signature of Witness: _____

Printed Name of Witness: _____

Date: _____

☐ 2) The participant is an adult who lacks capacity to provide consent and his/her legally authorized representative:

☐ 2a) gave permission for the adult participant to participate

☐ 2b) did not give permission for the adult participant to participate