INFORMED CONSENT DOCUMENT

Project Title: **Immunotherapy combined with Yttrium-90 RadioEmbolization in the treatment of Colorectal Cancer with Liver Metastases**

Principal Investigator: Chandrikha Chandrasekharan, MD

IDE sponsor-Investigator: Parren McNeely, M.D.

Research Team Contact: Susan Butcher, RN 319- 467-5827
Research Team Members: Daniel Berg, MD; and Saima Sharif, MD,

This consent form describes the research study to help you decide if you want to participate. This form provides important information about what you will be asked to do during the study, about the risks and benefits of the study, and about your rights as a research subject.

- If you have any questions about or do not understand something in this form, you should ask the research team for more information.
- You should discuss your participation with anyone you choose such as family or friends.
- Do not agree to participate in this study unless the research team has answered your questions and you decide that you want to be part of this study.

WHAT IS THE PURPOSE OF THIS STUDY?

This is a research study. We are inviting you to participate in this research study because you have been diagnosed with metastatic colorectal cancer with liver metastases.

The purpose of this research study is to find out more about the side effects of **immunotherapy** with a form of **radiation** treatment for the cancer in the liver called **yttrium-90 radioembolization (Y90-RE)**. Radioembolization is a minimally invasive procedure where beads are filled with radioactive isotype Y-90 drug and then are injected in the blood vessels that feed the tumor. Y90-RE is one of the therapies used to treat patients with liver cancer. The immunotherapy drug is called durvalumab. You may receive 1-5 doses of the drug up to every 2 weeks to determine how many durvalumab infusions are tolerable.

We are trying to study what doses of durvalumab are safe for people in combination with this form of radiation treatment. Everyone in this study will receive durvalumab, which is still experimental and isn't approved by the U.S. Food and Drug Administration (FDA) for metastatic colorectal cancer. However, the FDA has allowed the use of this drug in this research study. Microscopic radioactive particles (TheraSphere®) will be used for radioembolization to deliver the Y90 drug to your liver. TheraSphere® is considered investigational, which means that it has not been approved by the U.S. Food and Drug Administration.

The immunotherapy drug is not new and has been approved for other cancers, e.g. bladder cancer and lung cancer. We don't know all the ways that this drug may affect people. The primary goal of this study is to assess safety. We also want to know if combining these two kinds of treatments will help

fight your cancer.

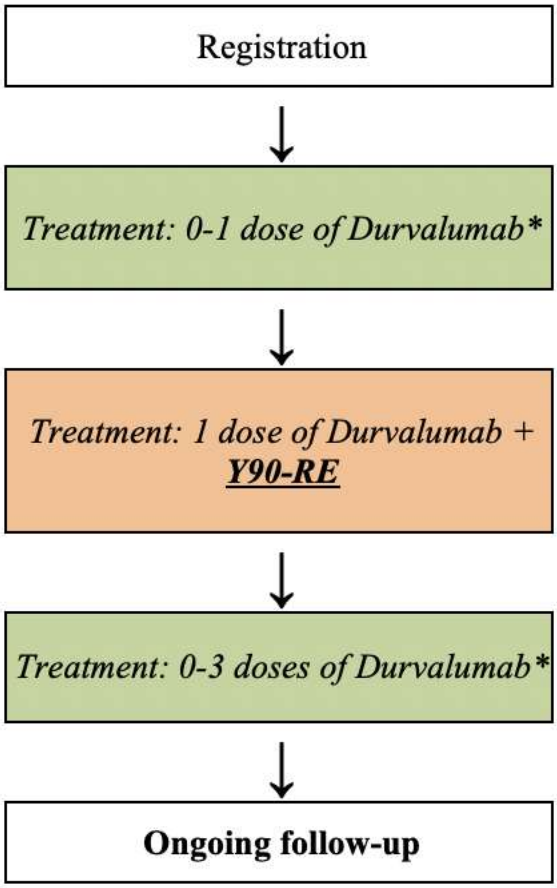
It is important to note that prior studies of immunotherapy treatments when given alone have not shown any benefit for patients with metastatic colorectal cancer. The immunotherapy drug durvalumab, therefore, is being combined with the Y90 radiation to see if these two treatments will help each other. We still don't know if the study is likely to help you, but we hope the information from this study will help us develop a better treatment for metastatic colorectal cancer with liver metastasis in the future.

HOW MANY PEOPLE WILL PARTICIPATE?

Approximately 18 people will take part in this study conducted by investigators at the University of Iowa.

HOW LONG WILL I BE IN THIS STUDY?

If you agree to take part in this study, your involvement will last for approximately 2 years from the time you enter the study until you begin follow-up. This includes the study treatment, radioembolization (Y90-RE) in combination with durvalumab, which may continue for up to 10 weeks. You will come for clinic visits and to receive study treatment 1-5 times, with each visit lasting between 4 and 6 hours. The illustration below summarizes the sequence of events:



* Your study team will let you know how many doses of immunotherapy drug durvalumab you will receive (1 to 5 times depending on the dose determined by the study protocol). Your detailed follow-up schedule will be provided to you by the study team. Duration between treatments is at least 2 weeks.

WHAT WILL HAPPEN DURING THIS STUDY?

If you agree to be in the study, you will be asked to participate in the following:

While on this study, you will receive radioembolization and durvalumab in combination. Radio-embolization will be given one time during the study treatment. Durvalumab is a drug given by IV infusion. Depending on assigned group, the number of infusions can range from 1 to 5 throughout the study treatment. Each treatment cycle is 14 days long. This means you will return to University of Iowa Hospitals and Clinics (UIHC) approximately every 14 days to evaluate your disease and whether or not the treatment is benefiting you. You will be asked by the study team to have a biopsy of your tumor at end of treatment (8 weeks after radioembolization). In addition, if you have a biopsy of your tumor for clinical reasons as requested by your doctor at the end of this study, the study team may request the excess tissue collected for this study and for future studies.

Screening Visit

Before you are enrolled onto the study, you will have what is called a Screening Visit. During this visit, we will do some tests and procedures to see if you are eligible to take part in this research study. The study doctor will review the results of these tests and procedures. If you aren't eligible, the study doctor

will tell you why. At this visit, we will:

- Ask you about your medical history
- Give you a physical exam, including height, weight, and vital signs (blood pressure, temperature, and heart rate)
- Review medications you are currently taking
- Draw a blood sample for standard CBC, chemistries, thyroid function tests, cholesterol, triglycerides, amylase, lipase, CEA, CA-19-9, and research
- Test your blood or urine for pregnancy if you are a female able to become pregnant
- Draw a blood sample for HIV, Hepatitis B, and Hepatitis C
- Perform an electrocardiogram (ECG) of your heart
- Measure your tumor using CT, MRI, and/or PET/CT imaging
- Request a piece of your tissue biopsy sample already stored within the clinical archive at UIHC or request that you have a biopsy to collect tissue for this study

If after your screening visit it is determined that you are eligible for the study, you will begin study treatment.

Study Treatment Visits:

Cycle 1, Day 1

At this visit, we will:

- Draw a blood sample for standard CBC, chemistries, CEA, CA-19-9, amylase, and, lipase
- Give you a physical exam, including weight, and vital signs (blood pressure, temperature, heart and breathing rates)
- Review medications you are currently taking
- Test your blood or urine for pregnancy if you are a female able to become pregnant
- Administer first dose of durvalumab. This will be given into a vein in your arm and will last approximately 60 minutes.
- Collect research blood and tissue
- Complete a Quality-of-Life questionnaire

  Radioembolization Mapping: You will undergo an outpatient procedure in the interventional radiology department with IV sedation or pain medication where an interventional radiologist will perform the first part of your radioembolization procedure. Access to your liver arterial blood supply will be obtained by placing a very small tube into your blood stream, usually from a skin puncture in the groin, and several pictures will be obtained of your tumor and normal liver blood supply using contrast, using a procedure called catheter directed angiography. Fluoroscopy will be used to position the tube for this procedure. The analysis can take between 1-2 hours in most cases. A radioembolization simulation will be performed by injecting radioactive dissolvable, microscopic, protein particle into your liver. Your groin puncture site will be sealed. You will then undergo a scan in the nuclear medicine department to identify if you are a good candidate for radioembolization. If the interventional radiologist feels you may proceed with radioembolization, a dose of Y90 will be ordered and TheraSphere® device will be used for the radioembolization procedure at another schedule date.

Cycle 2 and each additional Cycle (approximately every 14 days)

At this visit, we will:

- Give you a physical exam, including weight, and vital signs (blood pressure, temperature, heart and breathing rates)

- Review medications you are currently taking
- Ask you about side effects or health problems since your last visit
- Draw a blood sample for standard CBC, chemistries, amylase, lipase, CEA, CA-19-9, and research
- Measure your tumor using CT and/or MRI imaging (to be done every 3 months)
- Test your blood or urine for pregnancy if you are a female able to become pregnant (to be done every 4 weeks)
- Administer durvalumab (treatments after Cycle 2 are dependent on assigned group)
- Collect research tissue (Cycle 2 and 8 weeks after the radioembolization)
- Perform an electrocardiogram (ECG) of your heart at Cycle 2 and 4, and at the end of treatment visit.
- Complete a Quality-of-Life questionnaire
- **Radioembolization administration: (Cycle 2 only)** You will undergo a second outpatient procedure in the interventional radiology department with IV sedation or pain medication where an interventional radiologist will perform the second part of your radioembolization procedure. Access to your liver arterial blood supply will be obtained by again placing a very small tube into your blood stream, usually from a skin puncture in the groin, and angiography will be performed of your liver. Fluoroscopy will be used to position the tube for this procedure. The radioembolization particles (TheraSphere®) will be administered through your liver arteries, which may take 10-15 minutes per administration. Your groin puncture site will be sealed. You will then undergo a scan in the nuclear medicine department to identify deposition of your radioembolization.

End of Treatment: Tissue Biopsy

You will be asked by the study team to have a biopsy of your tumor at end of treatment (8 weeks after radioembolization). In addition, if you have a biopsy of your tumor for clinical reasons as requested by your doctor at the end of this study, the study team may request the excess tissue collected for this study and for future studies.

Tissue/Blood/Data Storage for Future Use

As part of this study, we are obtaining tissue and blood from you. We would like to study your tissue and blood in the future, after this study is over. Your sample, information, and/or data may be placed in a central repository or other national repositories sponsored by the National Institutes of Health or other Federal agencies. If this happens, it may be stripped of identifiers (such as name, date of birth, address, etc). Other qualified researchers who obtain proper permission may gain access to your sample and/or data for use in approved research studies that may or may not be related to in the purpose of this study.

Blood cells removed from the blood samples will be used to make a cell line and DNA or conduct whole genome sequencing. Cell lines are produced by growing blood cells in a laboratory and allow us to have a source of the DNA without having to redraw your blood. These blood cells can be stored for decades or more. The cell lines, DNA and genome sequencing results and data will be made available to researchers trying to learn more about the cause of diseases.

Each of the cells in your body contains DNA. DNA is the instruction manual that determines your appearance in things like eye color or how tall you can be. Your DNA may also lead to higher or lower risk of certain diseases. Your environment will also determine some of your disease risk.

Your DNA is a string of four building blocks, called "bases." These bases are represented by the letters G, A, T, and C. There are billions of these letters strung together in every human's DNA and they are arranged in packages like words. Each of these "words" have specific jobs in the body. Most of the time the letters are the same in everyone. But about 1% of the population might have an "A" where someone else has a "G." This difference can explain why some people have blue eyes and others brown eyes, or why some have a high risk for a certain cancer and others a low risk. All these letters come together to create your "genome sequence", a kind of book of your genetics. It now possible to read off each of these letters and read your complete genome sequence. Your DNA sequence is unique to you. You inherit your DNA in almost equal parts from each of your parents. In very rare cases, your genome can also change through "mutations." A mutation is like if you tried to copy a page from a book, but misspelled some words. Mutations usually result from copying errors that occur in certain letters when being passed from parent to child.

When we take a sample of your blood/tissue for this study, it will go to a lab to read off those letters and give us a report on the tumor genome. It is our hope this will help us to better understand how the tumor genetics works and/or what causes it to not work well, as when a mutation leads to tumor growth

The tests we might want to use to study your tissue and blood may not even exist at this time. Therefore, we are asking for your permission to store your tissue and blood so that we can study them in the future. These future studies may provide additional information that will be helpful in understanding metastatic colorectal cancer, but it is unlikely that what we learn from these studies will have a direct benefit to you. It is possible that your tissue and blood might be used to develop products tests, or discoveries that could be patented and licensed. In some instances, these may have potential commercial value and may be developed by the Investigators, University of Iowa, commercial companies, organizations funding this research, or others that may not be working directly with this research team. However, donors of tissue and blood do not retain any property rights to the materials. Therefore, there are no plans to provide financial compensation to you should this occur.

Your tissue, blood and data will be stored with a code which may be linked to your medical record number. If you agree now to future use of your tissue, blood and data but decide in the future that you would like to have it removed from future research, you should contact Chandrikha Chandrasekharan MD at (319) 356-2425. . However, if some research with your tissue, blood and data has already been completed, the information from that research may still be used

WILL I BE NOTIFIED IF MY DATA AND BIOSPECIMENS RESULT IN AN UNEXPECTED FINDING?

We may learn things about you from the study activities which could be important to your health or to your treatment. If this happens, you can decide whether you want this information to be provided to you. If you choose to have this shared, you will be informed of any unexpected findings of possible clinical significance that may be discovered during review of results from your data and biospecimens. The results from the data and biospecimens we collect in this research study are the same quality as what you would receive as part of your health care. There may be benefits to learning such results (for instance, we may learn that your tumor has a mutation that qualifies for a clinical trial, or is particularly suited to a certain treatment), but there are risks as well (such as feeling worried about a finding for which no treatment is available). Your treating oncologist will share the results of the DNA and genetic testing from your tumor.

The data and biospecimens will be reviewed by a physician who normally reads such results and they will inform us if there are any unexpected findings. We will provide you with this information so that you may discuss it with your primary care physician. However, if you believe you are having symptoms that may require care prior to receiving any information from this study, you should contact your primary care physician. The study team/study will not cover the costs of any follow-up consultations or actions.

Please initial one of the following options:
_____ Yes, I want to be provided with this information.
_____ No, I do NOT want to be provided with this information.

Genetic Research
One purpose of this study is to look at genes (DNA) and how they affect health and disease. Genes are the instruction manual for the body. The genes you get from your parents decide what you look like and how your body behaves. They can also tell us a person's risk for certain diseases and how they will respond to treatment. In this study, all genetic research conducted will be focused to genetics of the tumor.

Genetic Information Nondiscrimination Act (GINA)

A federal law called the Genetic Information Nondiscrimination Act (GINA) generally makes it illegal for health insurance companies, group health plans, and employers of 15 or more persons to discriminate against you based on your genetic information. Based on this new law, health insurance companies and group health plans are prohibited from requesting your genetic information that we get from this research. This means that they may not use your genetic information when making decisions regarding your eligibility for insurance coverage or the amount of your insurance premiums. Be aware that this new federal law will not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance. The law also does not prohibit discrimination if you are already known to have a genetic disease or disorder.

Birth control and pregnancy information:

You must not be pregnant or breastfeeding, and you should not become pregnant or breastfeed while you are taking the study drug and for 90 days after your last dose of durvalumab. You must use an adequate method(s) to avoid pregnancy for the duration of this study. If you are a man who is sexually active with a woman of child bearing potential you should also use an adequate method(s) of birth control to avoid pregnancy of your partner for the duration of this study and for 90 days after your last dose of durvalumab. You should immediately contact your study doctor if there is a change in your method(s) to avoid pregnancy. The study team will discuss this with you in more detail and offer additional guidance and help answer your questions

WHAT ARE THE RISKS OF THIS STUDY?

You may experience one or more of the risks indicated below from being in this study. In addition to these, there may be other unknown risks, or risks that we did not anticipate, associated with being in this study. Everyone taking part in the study will be watched carefully for any effects. Many side effects go away soon after you stop taking study drug. In some cases, side effects can be serious, long lasting, or may never go away. There also is a risk of death. However, doctors don't know all the side effects that may happen. Side effects may be mild or very serious. Your health care team may give you medicines to help lessen side effects.

The information below is based on data from subjects in other clinical trials with Durvalumab and Radioembolization. In addition, there may be side effects that are not yet known that may occur.

You should talk to your study doctor about any side effects that you have while taking part in the study.

Radioembolization (Yttrium-90; Y90-RE)
Radioembolization is a form of radiation treatment where microscopic radioactive particles are injected in your tumor's blood stream targeting the cancer directly in the liver. It is considered a minimally invasive procedure and done as an outpatient by interventional radiology experts. Because tumors tend to have increased blood supply when compared to the normal liver, this approach allows for much more targeted doses of radiation to tumor than traditional means of external beam radiotherapy. As with any procedure and radiation, there is the possibility of collateral damage to the liver and your doctors doing this procedure keep that in mind when deciding upon how much radiation to consider in each patient. The predominant risks of radioembolization are as follows:

- Nausea with or without vomiting (20%)
- Pain, including abdominal pain (20%)
- Abnormal buildup of fluid in the abdomen (ascites) (8%)
- Fatigue (50%)
- Liver failure, possibly fatal (about 2%)
- Inflammation of the lives also (hepatitis), possibly fatal (2%)
- Abnormal liver function, including abnormal liver tests
- Future liver cirrhosis with high blood pressure in the portal vein
- Radiation-induced liver disease
- Irritation of the gallbladder radiation induced (2%)
- Bile duct injury
- Gall bladder injury
- Radiation injury to the lungs
- Stomach or bowel ulceration
- Injury to blood vessels
- Radiation injury to the pancreas
- Radiation injury to the skin
- Decreased white blood cell count and increase changes for infections
- Decrease platelet count and bleeding complications
- injury to the kidneys due to contrast
- allergic reaction due to contrast

Potential Risks of TheraSphere® when combined with Durvalumab

- The addition of durvalumab may increase the risk of life-threatening liver toxicity.

Durvalumab

Frequently reported side effects for Durvalumab include fatigue, nausea and vomiting, and loss of appetite.

Likely risks of Durvalumab *(events seen in more than 1 in 10 people)*

- Loose stool (diarrhea)
- Cough
- Fever (pyrexia)

- Rash/Dry itchy skin
- Anemia (including hemolytic anemia)
- Stomach pain (abdominal pain)
- Upper respiratory infection
- Underactive thyroid gland that can cause tiredness or weight gain (hypothyroidism)
- Accumulation of fluid causing swelling in the legs
- Changes in lab tests related to liver function

Less likely risks of Durvalumab *(events seen in more than 1 in 100 people)*

- Inflammation in the lungs (pneumonitis)
- Inflammation of the intestines (colitis)
- Overactive thyroid gland that can cause fast heart rate or weight loss (hyperthyroidism)
- Abnormal kidney function tests
- Increased levels of pancreas enzymes
- Night sweats
- Infusion related reactions
- Pneumonia
- Inflammation of the liver (hepatitis)Pain in muscles and joints (myalgia)
- Fungal infection in the mouth (oral candidiasis)
- Decreased secretion of hormones produced by the adrenal glands(adrenal insufficiency)
- Changes on the voice such as coarse, rough, raspy, strained, weak, breathy, or gravely (dysphonia)
- Pain while urinating (dysuria)
- Night sweats
- Oral and dental soft tissue infection
- Influenza

Uncommon *(events seen in less than 1 in 100 people)*

- Inflammation of the kidney (nephritis)
- Inflammation of the skin (dermatitis)
- Underactive function of pituitary gland (hypophysitis/hypopituitarism)
- Inflammation of the thyroid gland (Thyroiditis) Scarring of lung tissue (interstitial lung disease)
- Tear in the intestines (Intestinal perforation)
- Blistering rash (Pemphigoid)
- Inflammation of the muscles (myositis)

Rare *(seen in less than 1 in 1,000 people)*

- Type 1 Diabetes Mellitus
- Inflammation of multiple muscles (polymyositis)
- Weakness of the muscles (myasthenia gravis)
- Inflammation of the heart (myocarditis)
- Imbalance in body fluids and electrolytes (Diabetes Insipidus)
- Decrease in cells that help your blood clot (immune thrombocytopenia)

Risks of Other Study Procedures

Electrocardiograms (ECG): This procedure requires you to lie still for a few minutes. The ECG records the rhythm and electrical activity of your heart. Small sticky patches called electrodes are placed on your arms, legs, and chest and connected by wires to an ECG recording machine to record the rhythm and electrical activity of your heart. The information is recorded and printed onto paper. There may be mild discomfort from the sticky pads and a possibility of the skin being irritated by the adhesive on the sticky pads. Chest hair may need to be shaved prior to the placement of the sticky pads.

Blood Draws: For most people, needle punctures for blood tests do not cause any serious problems. However, they may cause fainting, bleeding, bruising, discomfort, dizziness, infections and/or pain at the injection site.

Biopsy risks: The risks of a tissue biopsy include pain, bruising, infection and/or bleeding. In order to reduce the risk of bleeding, the coagulation status is assessed in all patients prior to a biopsy. If the prothrombin (coagulating) time is too slow or the platelet count is low, a standard biopsy is not recommended. To perform the biopsy, CT guidance might be necessary. This means you will be exposed to radiation. The amount of radiation you will receive has a low risk of harmful effects.

Radiation Risk

You will receive radiation treatments in the course of this study. The radiation treatments are considered standard care for your condition. You will receive experimental chemotherapy in addition to radiation, because it is thought that the combination may increase the effectiveness of the treatment. This experimental addition of the chemotherapy drug (durvalumab) may also intensify radiation effects on some normal tissues, and increase the risk of radiation-related side effects. Short-term risks include skin changes such as redness, hair loss, or delayed wound healing; and long-term risks include causing a new tumor. The extent to which the risks of radiation therapy will be boosted by chemotherapy is not known.

Genetic Research

One risk of giving samples for this research may be the release of your name that could link you to the stored samples and/or the results of the tests run on your samples. To prevent this, these samples will be given a code. Only the study staff will know the code. The name that belongs to the code will be kept in a locked file or in a computer with a password. Only approved members of the research team will have access to your name.

WHAT ARE THE BENEFITS OF THIS STUDY?

We don't know if you will benefit from being in this study. Prior clinical trials of checkpoint inhibitors (including durvalumab) have failed to demonstrate a benefit to patients with microsatellite stable colorectal cancer.

However, we hope that, in the future, other people might benefit from this study because the information from this study will help doctors learn more about radioembolization in combination with durvalumab as a treatment for metastatic colorectal cancer with metastasis to the liver in the future. This information could help future cancer patients.

WHAT OTHER TREATMENT OPTIONS ARE THERE?

Before you decide whether or not to be in this study, your doctor will discuss the other options that are available to you. Instead of being in this study, you could

- Receive treatment or care for your cancer, such as chemotherapy, without being in a study. This includes Stivarga and Lonsurf, which have demonstrated benefits for this cancer
- Receive the same radioembolization without any immunotherapy
- Take part in another study
- Receive no treatment
- Receive comfort care, also called palliative care. This type of care helps reduce pain, tiredness, appetite problems and other problems caused by the cancer. It does not treat the cancer directly, but instead tries to improve how you feel. Comfort care tries to keep you as active and comfortable as possible.

WILL IT COST ME ANYTHING TO BE IN THIS STUDY?

You may have additional costs for being 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:

- Durvalumab – the investigational drug
- TheraSphere® - the investigational device
- Research bloods and research biopsies

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. These tests and procedures are:

- Y-90 radioembolization mapping at screening
- The embolization process, including any required labs and hospitalizations
- History and Physical Exams
- Complete Blood Count and Blood Chemistries
- Amylase and Lipase blood tests
- CEA and CA-19-9
- Triglycerides and cholesterol blood tests
- Creatinine clearance
- Thyroid function tests
- ECGs
- Urinalysis
- CT scan for tumor measurement at screening, cycle 6, and every 3 months thereafter
- MRI scans for tumor measurement at screening, cycle 6, and every 3 months thereafter
- Pregnancy tests, if applicable

You will also be responsible for any co-payments and deductibles.

You and/or your medical/hospital insurance carrier will remain responsible for your regular medical care expenses.

WILL I BE PAID FOR PARTICIPATING?

You will not be paid for being in this research study.

WHO IS FUNDING THIS STUDY?

Biocompatibles UK Ltd, a BTG International Group Company will pay the institution to cover costs related to the running of the study for the microscopic radioactive particles (TheraSphere®) that will be used for radioembolization. Astra Zeneca Pharmaceuticals will be providing the durvalumab free of cost to the patient.

WHAT IF I AM INJURED AS A RESULT OF THIS STUDY?

- If you are injured or become ill from taking part in this study, medical treatment is available at the University of Iowa Hospitals and Clinics.
- The University of Iowa does not plan to provide free medical care or payment for treatment of any illness or injury resulting from this study unless it is the direct result of proven negligence by a University employee.
- If you experience a research-related illness or injury, you and/or your medical or hospital insurance carrier will be responsible for the cost of treatment.

WHAT ABOUT CONFIDENTIALITY?

We will keep your participation in this research study confidential to the extent permitted by law. However, it is possible that other people such as those indicated below may become aware of your participation in this study and may inspect and copy records pertaining to this research. Some of these records could contain information that personally identifies you.

- federal government regulatory agencies,
- the U.S. Food and Drug Administration
- Biocompatibles UK Ltd, a BTG International Group Company
- AstraZeneca, the company providing durvalumab
- auditing departments of the University of Iowa, and
- the University of Iowa Institutional Review Board (a committee that reviews and approves research studies)

To help protect your confidentiality, we will keep study documents and binders in locked offices. Electronic information will be stored n password-protected computers. Where feasible, we will use a research ID to minimize using your name. All printed documents are stored in a locked office at the hospital. Any blood samples that we take for research testing are dated and named using your research ID. They are also stored at the University in a locked room. If we write a report or article about this study or share the study data set with others, we will do so in such a way that you cannot be directly identified.

The University of Iowa Hospitals and Clinics generally requires that we document your participation in research occurring in a University of Iowa Health Care facility. This documentation will be in either your medical record or a database maintained on behalf of the institution reflecting that you are

participating in this study. The information included will provide contact information for the research team as well as information about the risks associated with this study. We will keep this Informed Consent Document in our research files; it will not be placed in your medical record chart.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. A copy of the informed consent document will be available on this website. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.

A version of the informed consent document will be available on the website, Regulations.gov (Docket ID: HHS-OPHS-2018-0021), as required by U.S. Law. The informed consent document will not include information that can identify you. You can search this website at any time.

WILL MY HEALTH INFORMATION BE USED DURING THIS STUDY?

The Federal Health Insurance Portability and Accountability Act (HIPAA) requires University of Iowa Health Care to obtain your permission for the research team to access or create "protected health information" about you for purposes of this research study. Protected health information is information that personally identifies you and relates to your past, present, or future physical or mental health condition or care. We will access or create health information about you, as described in this document, for purposes of this research study and for your treatment. Once University of Iowa Health Care has disclosed your protected health information to us, it may no longer be protected by the Federal HIPAA privacy regulations, but we will continue to protect your confidentiality as described under "Confidentiality."

We may share your health information related to this study with other parties including federal government regulatory agencies, the University of Iowa Institutional Review Boards and support staff, Biocompatibles UK Ltd, a BTG International Group Company (the company providing the TheraSphere® used for radioembolization and sponsoring this study), AstraZeneca Pharmaceuticals LP and its Affiliates who are located around the world as well as companies who work for AstraZeneca who also may be located around the world.. Biocompatibles UK Ltd and AstraZeneca Pharmaceuticals may also inspect any part of your medical record for the purposes of auditing the conduct of the study.

You cannot participate in this study unless you permit us to use your protected health information. If you choose *not* to allow us to use your protected health information, we will discuss any non-research alternatives available to you. Your decision will not affect your right to medical care that is not research-related. Your signature on this Consent Document authorizes University of Iowa Health Care to give us permission to use or create health information about you.

Although you may not be allowed to see study information until after this study is over, you may be given access to your health care records by contacting your health care provider. Your permission for us to access or create protected health information about you for purposes of this study has no expiration date. You may withdraw your permission for us to use your health information for this research study by sending a written notice to Dr. Chandrasekharan located at 200 Hawkins Drive, Iowa City, IA 52242. However, we may still use your health information that was collected before withdrawing your permission. Also, if we have sent your health information to a third party, such as the study sponsor, or we have removed your identifying information, it may not be possible to prevent its future use. You will receive a copy of this signed document.

IS BEING IN THIS STUDY VOLUNTARY?

Taking part in this research study is completely voluntary. You may choose not to take part at all. If you decide to be in this study, you may stop participating at any time. If you decide not to be in this study, or if you stop participating at any time, you won't be penalized or lose any benefits for which you otherwise qualify.

What if I Decide to Drop Out of the Study?

If you decide to leave the study early, we will ask you to discuss your cancer treatment plans with your doctors so that you continue to receive clinical treatment for your cancer.

Will I Receive New Information About the Study while Participating?

If we obtain any new information during this study that might affect your willingness to continue participating in the study, we'll promptly provide you with that information.

Can Someone Else End my Participation in this Study?

Under certain circumstances, the researchers might decide to end your participation in this research study earlier than planned. This might happen because you had a bad reaction to the study drug or because in our judgment it would not be safe for you to continue.

WHAT IF I HAVE QUESTIONS?

We encourage you to ask questions. If you have any questions about the research study itself, please contact: Dr. Chandrikha Chandrasekharan at (319) 356-2425. If you experience a research-related injury, please contact: Dr. Chandrikha Chandrasekharan at (319) 356-2425. If you are calling after hours or on the weekend, please call 319-356-1600 and ask for the hematology oncology fellow on call. Tell the operator that you are a research subject of Dr. Chandrasekharan's.

If you have questions, concerns, or complaints about your rights as a research subject or about research related injury, please contact the Human Subjects Office, 105 Hardin Library for the Health Sciences, 600 Newton Rd, The University of Iowa, Iowa City, IA 52242-1098, (319) 335-6564, or e-mail irb@uiowa.edu. General information about being a research subject can be found by clicking "Info for Public" on the Human Subjects Office web site, http://hso.research.uiowa.edu/. To offer input about your experiences as a research subject or to speak to someone other than the research staff, call the Human Subjects Office at the number above.

This Informed Consent Document is not a contract. It is a written explanation of what will happen during the study if you decide to participate. You are not waiving any legal rights by signing this Informed Consent Document. Your signature indicates that this research study has been explained to you, that your questions have been answered, and that you agree to take part in this study. You will receive a copy of this form.

Subject's Name (printed): _____

_____ _____
(Signature of Subject) (Date)

Statement of Person Who Obtained Consent

I have discussed the above points with the subject or, where appropriate, with the subject's legally

authorized representative. It is my opinion that the subject understands the risks, benefits, and procedures involved with participation in this research study.

_____ _____

(Signature of Person who Obtained Consent) (Date)