

<b>MEDICAL RECORD</b>	<b>CONSENT TO PARTICIPATE IN A CLINICAL RESEARCH STUDY</b> <ul style="list-style-type: none"> <li>• Adult Patient or</li> <li>• Parent, for Minor Patient</li> </ul>
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INSTITUTE: National Cancer Institute

STUDY NUMBER: 15-C-0021 PRINCIPAL INVESTIGATOR: Tim Greten, M.D.

STUDY TITLE: A Pilot Study of AMP-224, a PD-1 Inhibitor, in Combination with Stereotactic Body Radiation Therapy (SBRT) in Patients with Metastatic Colorectal Cancer

Continuing Review Approved by the IRB on 08/24/16

Amendment Approved by the IRB on 08/27/16 (B)

Date posted to web: 09/02/16

Standard

## INTRODUCTION

We invite you to take part in a research study at the National Institutes of Health (NIH).

First, we want you to know that:

Taking part in NIH research is entirely voluntary.

You may choose not to take part, or you may withdraw from the study at any time. In either case, you will not lose any benefits to which you are otherwise entitled. However, to receive care at the NIH, you must be taking part in a study or be under evaluation for study participation.

You may receive no benefit from taking part. The research may give us knowledge that may help people in the future.

Second, some people have personal, religious or ethical beliefs that may limit the kinds of medical or research treatments they would want to receive (such as blood transfusions). If you have such beliefs, please discuss them with your NIH doctors or research team before you agree to the study.

Now we will describe this research study. Before you decide to take part, please take as much time as you need to ask any questions and discuss this study with anyone at NIH, or with family, friends or your personal physician or other health professional.

### Why is this study being done?

Our immune system helps to protect us from germs and can also fight against cancer. T-cells are a type of white blood cell that can find and kill germs and tumors. T-cells are often present inside tumors, but cancers block the activity of these T-cells in many different ways. In tumors, some T-cells become dysfunctional, meaning that they are not able to kill tumor cells. These dysfunctional T-cells in the tumor make a protein called “PD-1” which they express on their surface. Some functional T-cells may also be present, but they are usually outnumbered.

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AMP-224 is an investigational drug that binds to the PD-1 on the surface of the T-cells. AMP-224 therefore blocks the dysfunctional cells so that the functional cells can fight the tumor. "Investigational" means that AMP-224 has not been approved by the Food and Drug Administration (FDA) as either a prescription or over-the-counter drug. It has not been tested in combination with stereotactic body radiation therapy (SBRT), which is the main goal of this study.

Stereotactic radiation treatment is a type of radiation therapy in which a few very high doses of radiation are delivered to small, well-defined tumors. The goal is to deliver a radiation dose that is high enough to kill the cancer while minimizing exposure to surrounding healthy organs. In this protocol SBRT is being used for research to see if tumor antigens will be released. This research is being done to study if the safety and effectiveness of the investigational drug AMP-224 together with either 1 or 3 days of SBRT directed to the liver.

This is the first study in which AMP-224 will be tested in combination with SBRT.

In addition to the AMP-224 and radiation treatment you will also receive an additional small dose of chemotherapy drug called cyclophosphamide. Cyclophosphamide is a chemotherapy drug that has been shown to also have some immune effects at lower doses.

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

You have been invited to take part in this research study because you have been diagnosed with metastatic colorectal cancer that has spread to the liver and that has either not responded to prior treatment, or there are no curative treatment options available.

### **How many people will take part in this study?**

Approximately 25 people will take part in this study.

### **Description of Research Study**

#### **What will happen if you take part in this research study?**

##### **Before you begin the study**

Before you begin this study you will have several exams and tests to make sure you are eligible for this study. The exams and tests are part of regular cancer care and may be done even if you do not join the study. If you recently had some of the tests, they may not need to be repeated. The research team will explain these exams and tests to you. You will have:

- History and physical exam
- Review of current medications and past treatments
- Routine blood work
- Viral blood tests

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<ul style="list-style-type: none"> <li>• Routine urine tests</li> <li>• Tumor measurements using special x-rays called computerized tomography (CT or CAT scans) or magnetic resonance imaging (MRI) of your chest, stomach, and pelvis areas</li> <li>• A heart test called an electrocardiogram or ECG to check your heart</li> <li>• Urine or blood pregnancy test</li> </ul>	
<b>During the study</b>	
<p>If the exams, tests and procedures show that you can be in the study, and you choose to take part, then you will begin treatment.</p>	
<p>Before you begin treatment you will have a mandatory biopsy of your tumor using a needle. You will have another mandatory biopsy of your tumor around day 29 after you start treatment unless you were unable to tolerate the first biopsy.</p>	
<p>Treatment involves receiving Cyclophosphamide (CTX) through your vein (IV) and SBRT on day 0 and AMP-224 through an IV once every 2 weeks for 6 doses. After you have completed the first two doses of AMP-224, you will have another biopsy of your tumor. If your disease is responding and you are tolerating the treatment well you will have the option of continuing the same every two week dose schedule until your disease shows clear evidence of growth.</p>	
<p>SBRT begins with a treatment planning session, which involves using imaging (4D computerized tomography) to precisely map the exact position of the tumor to be treated. These images are then used to create customized treatment plans in which sophisticated computerized devices direct several radiation beams of different intensities at different angles, so that the radiation is directed precisely to the tumor.</p>	
<p>The dose of AMP-224 is 10 milligrams per kilogram (a unit of body weight equal to about 2.2 pounds). AMP-224 will be administered over a minimum of 2 hours in the first treatment cycle. For subsequent treatment cycles, AMP-224 will be administered over a minimum of 1 hour. The AMP-224 infusion duration may be increased for patient safety at any time at the Investigator's discretion. CTX and AMP-224 will be administered on different days as an intravenous (injected into a blood vessel through a plastic tube or needle) injection.</p>	
<p>There are two groups of patients on the study. The first group of patients will receive one dose of radiation treatment (the SBRT). We plan to treat approximately 6 patients like this and this will be the first part of the study.</p>	
<p>Once the first part of the study is complete we will enroll new patients to the second part of the study. In this part of the study patients will receive 3 doses of the SBRT. In other words the main difference between the first and second parts of the study will be the length of time you receive the radiation – either one or three doses.</p>	
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### When you are finished taking the drugs (treatment)

You will be seen weekly for three weeks, then every two weeks for one month, then month two, and month five after that after completion of the study treatment to assess for possible delayed or ongoing side effects and overall clinical status. At these visit, you will have basic blood tests as well as blood collected for research purposes.

### Study Chart

<b>Day 0</b>	<ul style="list-style-type: none"> <li>• History and physical exam</li> <li>• Review of current medications and treatments</li> <li>• Routine blood tests</li> <li>• Stereotactic body radiation therapy</li> <li>• CTX infusion</li> </ul>
<b>Day 1</b>	<ul style="list-style-type: none"> <li>• Physical exam</li> <li>• Vital Signs</li> <li>• Review of current medications and treatments</li> <li>• Routine and research blood tests</li> <li>• Routine urine tests</li> <li>• ECG</li> <li>• Report any side effects</li> <li>• Pre-medications</li> <li>• AMP-224 Infusion</li> </ul>
<b>Day 8</b>	<ul style="list-style-type: none"> <li>• Physical exam</li> <li>• ECG</li> <li>• Report any side effects</li> <li>• Review of current medications and treatments</li> <li>• Routine and research blood tests</li> </ul>
<b>Day 15</b>	<ul style="list-style-type: none"> <li>• Physical exam</li> <li>• Vital Signs</li> <li>• Review of current medications and treatments</li> <li>• Routine and research blood tests</li> <li>• Routine urine tests</li> <li>• Report any side effects</li> <li>• Pre-medications</li> <li>• AMP-224 Infusion</li> </ul>
<b>Day 29</b>	<ul style="list-style-type: none"> <li>• Physical exam</li> <li>• Vital Signs</li> <li>• Review of current medications and treatments</li> <li>• Routine and research blood tests</li> <li>• Routine urine tests</li> </ul>

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	<ul style="list-style-type: none"> <li>• Tumor Biopsy</li> <li>• Report any side effects</li> <li>• Pre-medications</li> <li>• AMP-224 Infusion</li> </ul>
<b>Day 43</b>	<ul style="list-style-type: none"> <li>• Physical exam</li> <li>• Vital Signs</li> <li>• Review of current medications and treatments</li> <li>• Routine and research blood tests</li> <li>• Routine urine tests</li> <li>• Report any side effects</li> <li>• Pre-medications</li> <li>• AMP-224 Infusion</li> </ul>
<b>Day 57</b>	<ul style="list-style-type: none"> <li>• Physical exam</li> <li>• CT Scan or MRI</li> <li>• Vital Signs</li> <li>• Review of current medications and treatments</li> <li>• Routine and research blood tests</li> <li>• Routine urine tests</li> <li>• Report any side effects</li> <li>• Pre-medications</li> <li>• AMP-224 Infusion</li> </ul>
<b>Day 71</b>	<ul style="list-style-type: none"> <li>• Physical exam</li> <li>• Vital Signs</li> <li>• Review of current medications and treatments</li> <li>• Routine and research blood tests.</li> <li>• Routine urine tests</li> <li>• Report any side effects</li> <li>• Pre-medications</li> <li>• AMP-224 Infusion</li> </ul>

## Birth Control

If you are a woman who is breast feeding or pregnant, you may not take part in the study because we don't know how this medicine would affect your baby or your unborn child. If you are a woman who can become pregnant, or are the partner of a woman who can become pregnant, you will need to practice an effective form of birth control before starting study treatment, during study treatment, and for 3 months after you finish study treatment. If you think that you or your partner is pregnant, you should tell your study doctor or nurse at once.

Effective forms of birth control include:

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<ul style="list-style-type: none"> <li>• abstinence</li> <li>• intrauterine device (IUD)</li> <li>• hormonal [birth control pills, injections, or implants]</li> <li>• tubal ligation</li> <li>• vasectomy</li> </ul>	
<b>Risks or Discomforts of Participation</b>	
<b>Cyclophosphamide (CTX)</b> Specific symptoms that have been associated with cyclophosphamide as listed below. However, we will be using cyclophosphamide at a much lower doses at which the side effects listed are unlikely: <ul style="list-style-type: none"> <li>• Changes in blood counts including: low red cell count (causing fatigue and shortness of breath), low platelet count (increasing the risk of bleeding and bruising), decrease in white blood cells (increasing the risk of infection and the need for treatment with antibiotics or other treatment)</li> <li>• Loss of appetite, nausea, vomiting</li> <li>• Diarrhea, stomach pain</li> <li>• Mouth sores</li> <li>• Hair loss</li> <li>• Fatigue</li> <li>• Muscle or joint aches</li> <li>• Bladder damage which can cause blood in your urine</li> </ul>	
<b>Stereotactic body radiation therapy (SBRT)</b> In general, radiation can cause the following side effects regardless of the site that is being treated. <ul style="list-style-type: none"> <li>• Tiredness</li> <li>• Lowered blood counts</li> <li>• Skin reddening</li> <li>• Mild ache at the site that received radiation</li> </ul>	
These side effects tend to go away after the radiation therapy is completed. However, there are some long-term or chronic side effects that primarily affect the small bowel, liver, kidneys, and spinal cord. Many of these side effects take months to years to develop. Rarely, treatment with	
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radiation may also lead to developing other types of cancer, usually years after receiving the treatment. It is possible that you may experience some, all, or none of the side effects described above. It is also possible that your specific treatment may cause some side effects that we cannot anticipate. For that reason, you will be watched closely while you are receiving treatment for any signs that might signal the earliest stage of toxicity so that we can treat them early.

Specific symptoms that have been associated with SBRT to the liver area are the following:

- Nausea, vomiting
- Diarrhea
- Abdominal pain
- Feelings of claustrophobia
- Skin irritation
- Fatigue
- Sore throat and trouble swallowing
- Late or delayed side effects (the side effects noted above but they occur after the radiation has completed)

#### **AMP-224**

While you are taking part in this study, you are at risk for side effects. You should talk to your doctor about possible side effects. Other drugs (pre-medications) will be given to make side effects less serious and less uncomfortable. Many side effects may go away shortly after AMP-224 is stopped, but in some cases side effects can be serious and long lasting. It is not known how long the side effects may last. The unforeseen side effects may range from mild to life-threatening. During and after your participation in the study, it will be very important for you to report any possible side effects or symptoms you develop to your study doctor.

Certain side effects can follow the administration of any protein such as AMP-224; these include:

- fever (high body temperature)
- chills (shaking)
- skin rash (redness or bumps on the skin)
- itching
- joint pain
- swelling

If any of these side effects appear, it is anticipated that they will be mild and easy to control. There is also a possibility that a more severe response may occur, resulting in a fall in blood pressure (causing dizziness, light-headedness and fainting), shortness of breath, and pain in the

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chest, low back and side. Some side effects may be serious and may even result in death. You will be closely observed for all of these symptoms. Should side effects occur, appropriate treatment will be started as determined by your study doctor.

AMP-224 is developed to play a role in immune function. There is a risk that AMP-224 could affect this function. There are cases where patients who received other drugs that affect the immune system developed illnesses such as dermatitis (inflammation of the skin), enterocolitis (inflammation of the bowel), autoimmune hepatitis (inflammation of the liver), lymphopenia (low white blood cells that fight infection), fatigue (tiredness), and hypophysitis (inflammation of the pituitary gland). Patients receiving AMP-224 will be carefully monitored for diarrhea, abdominal cramping (pain in the abdomen), fatigue (tiredness), headaches, arthralgias (joint pain), changes in sight, and any skin changes such as rash (redness or bumps on the skin), itching, or discoloration. If any of these symptoms appear, you should notify your study doctor right away. In addition, blood tests will be done at regular interval to look for changes in liver function, thyroid function (a gland important in regulating metabolism), and adrenal gland function (a gland important in responding to stress and regulating salt and water levels).

Side effects associated with other drugs that affect the immune system occurred anywhere from 1 week to a few months after starting the drug.

Your body may react to AMP-224 by thinking that the drug is a foreign substance and does not belong to your body. If this happens, your body will develop specific proteins (antibodies [substances in the body that normally fight infection]) that block AMP-224. The effects of developing these proteins are not known. However, if your body makes these proteins, it could limit your ability to respond to AMP-224 or related drugs if you were to receive these drugs in the future. There is also the possibility of developing an allergic reaction.

Because AMP-224 study drug is investigational, its use may involve other risks that are not known or cannot be predicted at the present time. These risks may affect you during the study and/or at some point in the future. During the study, it is important that you report any new or unusual symptoms to your doctor immediately.

To date, AMP-224 has been tested in 44 patients; 6 at 0.3 mg/kg, 4 at 1 mg/kg and 4 at 3 mg/kg, 24 at 10 mg/kg, and 6 at 30 mg/kg. Patients enrolled in that study have received between 1 and 42 doses of AMP-224. Side effects considered related to AMP-224 have been generally mild to moderate in intensity. Side effects that have occurred in  $\geq 10\%$  of patients that were considered at least possibly related to AMP-224 are: chills (shivers), rigors (muscle spasms), fatigue (feeling tired), decreased appetite, facial redness, nausea, back pain, diarrhea, and fever.

One patient who was not pre-medicated had a severe infusion reaction to AMP-224 which included chills (shivers), rigors (muscle spasms), and elevated blood pressure. The patient recovered after the infusion was stopped and after receiving treatment medications.

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## Tumor Biopsy

Before you begin treatment on this protocol we will obtain a piece of your tumor (biopsy) using a needle with minimal risk to you. You will have this biopsy again on day 29. You will be given local anesthesia (numbing medicine) and a sedative prior to the biopsy. The biopsy will be taken through a needle put through the skin into your tumor. After the procedure the nurses will watch your blood pressure and other vital signs. This biopsy is not optional and you cannot participate in this study if you do not agree to the biopsies. If the first biopsy is too difficult or if you experience too much discomfort as a result of it you will be able to continue on the protocol without undergoing the second biopsy. However, an attempt at the first biopsy is needed to enter this study. There are other studies at NIH which may also be options for you and which do not involve biopsies.

## Risk of Radiation

This research study involves exposure to radiation from stereotactic body radiation therapy and the CT used during your biopsies. Please note that this radiation exposure is not necessary for your medical care and is for research purposes only. The total amount of radiation you will receive in this study is from up to 3 treatments of stereotactic body radiation therapy and 2 CT guided biopsies. The NIH Radiation Safety Committee has reviewed the use of radiation in this research study and has approved this use as involving acceptable risk and necessary to obtain the research information desired.

Using the standard way of describing radiation dose, from participating in this study, you will receive a total of 2400 rem to your gallbladder wall and liver and 600 rem to your adrenals. The total effective dose will be 309 rem. All other organs will receive smaller amounts of radiation. The amount of radiation received in this study exceeds the dose guideline established by the NIH Radiation Safety Committee for research subjects. The guideline is an effective dose of 5 rem (or 5,000 mrem) received per year.

The specific side effects related to the effects of stereotactic body radiation therapy are described above.

If you would like more information about radiation and examples of exposure levels from other sources, please ask the investigator for a copy of the pamphlet called, *An Introduction to Radiation for NIH Research Subjects*.

Please tell your doctor if you have taken part in other research studies or received any medical care at the NIH or other places/hospitals that used radiation. This way we can make sure that you will not receive too much radiation. Consider x-rays taken in radiology departments, cardiac catheterization, and fluoroscopy as well as nuclear medicine scans in which radioactive materials were injected into your body.

*If you are pregnant, you will not be permitted to participate in this research study.* It is best to avoid radiation exposure to unborn or nursing children since they are more sensitive to radiation than adults.

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### **Blood Sampling**

Risks of blood sampling include bruising or bleeding at the needle site; rarely infection. This is treated with bandages, pressure and, if infection, antibiotic medicines. For more information about risks and side effects, ask your study team.

### **Potential Benefits of Participation**

#### **Are there benefits to taking part in this study?**

We hope that you will get personal medical benefit from taking part in this study, but we cannot be certain. These potential benefits could include shrinking of your tumor or lessening of your symptoms, such as pain, that are caused by the cancer. Because there is not much information about the drug's effect on your cancer, we do not know if you will benefit from taking part in this study, although the knowledge gained from this study may help others in the future who have cancer.

### **Alternative Approaches or Treatments**

#### **What other choices do I have if I do not take part in this study?**

Instead of being in this study, you have these options:

- Getting treatment or care for your cancer without being in a study
- Taking part in another study
- Getting 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. Instead, it tries to improve how you feel. Comfort care tries to keep you as active and comfortable as possible.

Please talk to your doctor about these and other options.

### **Research Subject's Rights**

#### **What are the costs of taking part in this study?**

If you choose to take part in the study, the following will apply, in keeping with the NIH policy:

- You will receive study treatment at no charge to you. This may include surgery, medicines, laboratory testing, x-rays or scans done at the Clinical Center, National Institutes of Health (NIH), or arranged for you by the research team to be done outside the Clinical Center, NIH if the study related treatment is not available at the NIH.

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- There are limited funds available to cover the cost of some tests and procedures performed outside the Clinical Center, NIH. You may have to pay for these costs if they are not covered by your insurance company.
- Medicines that are not part of the study treatment will not be provided or paid for by the Clinical Center, NIH.
- Once you have completed taking part in the study, medical care will no longer be provided by the Clinical Center, NIH.

### **Will your medical information be kept private?**

We will do our best to make sure that the personal information in your medical record will be kept private. However, we cannot guarantee total privacy. Organizations that may look at and/or copy your medical records for research, quality assurance, and data analysis include:

- The National Cancer Institute (NCI) and other government agencies, like the Food and Drug Administration (FDA), which are involved in keeping research safe for people.
- National Cancer Institute Institutional Review Board
- The study Sponsor, Center for Cancer Research or their agent(s).
- Qualified representatives from Amplimmune, Inc, the pharmaceutical company who produces AMP-224.

### **Stopping Therapy**

Your doctor may decide to stop your therapy for the following reasons:

- if he/she believes that it is in your best interest
- if your disease comes back during treatment
- if you have side effects from the treatment that your doctor thinks are too severe
- if new information shows that another treatment would be better for you

In this case, you will be informed of the reason therapy is being stopped.

You can stop taking part in the study at any time. However, if you decide to stop taking part in the study, we would like you to talk to the study doctor and your regular doctor first.

If you decide at any time to withdraw your consent to participate in the trial, we will not collect any additional medical information about you. However, according to FDA guidelines, information collected on you up to that point may still be provided to The Center for Cancer Research, Amplimmune, Inc. or designated representatives. If you withdraw your consent and leave the trial, any samples of yours that have been obtained for the study and stored at the NCI can be destroyed upon request. However, any samples and data generated from the samples

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that have already been distributed to other researchers or placed in the research databases **cannot** be recalled and destroyed.

### **Conflict of Interest**

The National Institutes of Health (NIH) reviews NIH staff researchers at least yearly for conflicts of interest. This process is detailed in a Protocol Review Guide. You may ask your research team for a copy of the Protocol Review Guide or for more information. Members of the research team who do not work for NIH are expected to follow these guidelines but they do not need to report their personal finances to the NIH.

Members of the research team working on this study may have up to \$15,000 of stock in the companies that make products used in this study. This is allowed under federal rules and is not a conflict of interest.

The National Institutes of Health and the research team for this study are using AMP-224 developed by Amplimmune, Inc. through a joint study with your researchers and the company. The company also provides financial support for this study.

### **Optional Biopsy**

If you have a tumor outside of the radiation area that shrinks, we may ask you if you will undergo a needle biopsy of that particular tumor. The biopsy to be performed is exclusively for research purposes and will not benefit you. It might help other people in the future. Even if you sign "yes" to have the biopsy you can change your mind at any time. Please read the sentence below and think about your choice. After reading the sentence, circle and initial the answer that is right for you. The decision to participate in this part of the research is optional, and no matter what you decide to do, it will not affect your care.

I agree to have the tumor biopsy for the research tests in this study.

Yes            No            Initials \_\_\_\_\_

### **Use of Specimens and Data for Future Research**

To advance science, it is helpful for researchers to share information they get from studying human samples. They do this by putting it into one or more scientific databases, where it is stored along with information from other studies. A researcher who wants to study the information must apply to the database and be approved. Researchers use specimens and data stored in scientific databases to advance science and learn about health and disease.

PATIENT IDENTIFICATION	<b>CONTINUATION SHEET for either:</b> NIH-2514-1 (07-09) NIH-2514-2 (10-84) P.A.: 09-25-0099 File in Section 4: Protocol Consent
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MEDICAL RECORD	<b>CONTINUATION SHEET for either:</b> NIH 2514-1, Consent to Participate in A Clinical Research Study NIH 2514-2, Minor Patient's Assent to Participate In A Clinical Research Study
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We plan to keep some of your specimens and data that we collect and use them for future research and share them with other researchers. We will not contact you to ask about each of these future uses. These specimens and data will be stripped of identifiers such as name, address or account number, so that they may be used for future research on any topic and shared broadly for research purposes. Your specimens and data will be used for research purposes only and will not benefit you. It is also possible that the stored specimens and data may never be used. Results of research done on your specimens and data will not be available to you or your doctor. It might help people who have cancer and other diseases in the future.

If you do not want your stored specimens and data used for future research, please contact us in writing and let us know that you do not want us to use your specimens and/or data. Then any specimens that have not already been used or shared will be destroyed and your data will not be used for future research. However, it may not be possible to withdraw or delete materials or data once they have been shared with other researchers.

PATIENT IDENTIFICATION	<b>CONTINUATION SHEET for either:</b> NIH-2514-1 (07-09) NIH-2514-2 (10-84) P.A.: 09-25-0099 File in Section 4: Protocol Consent
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MEDICAL RECORD	<b>CONSENT TO PARTICIPATE IN A CLINICAL RESEARCH STUDY</b> <ul style="list-style-type: none"> <li>• Adult Patient or</li> <li>• Parent, for Minor Patient</li> </ul>
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### OTHER PERTINENT INFORMATION

**1. Confidentiality.** When results of an NIH research study are reported in medical journals or at scientific meetings, the people who take part are not named and identified. In most cases, the NIH will not release any information about your research involvement without your written permission. However, if you sign a release of information form, for example, for an insurance company, the NIH will give the insurance company information from your medical record. This information might affect (either favorably or unfavorably) the willingness of the insurance company to sell you insurance.

The Federal Privacy Act protects the confidentiality of your NIH medical records. However, you should know that the Act allows release of some information from your medical record without your permission, for example, if it is required by the Food and Drug Administration (FDA), members of Congress, law enforcement officials, or authorized hospital accreditation organizations.

**2. Policy Regarding Research-Related Injuries.** The Clinical Center will provide short-term medical care for any injury resulting from your participation in research here. In general, no long-term medical care or financial compensation for research-related injuries will be provided by the National Institutes of Health, the Clinical Center, or the Federal Government. However, you have the right to pursue legal remedy if you believe that your injury justifies such action.

**3. Payments.** The amount of payment to research volunteers is guided by the National Institutes of Health policies. In general, patients are not paid for taking part in research studies at the National Institutes of Health. Reimbursement of travel and subsistence will be offered consistent with NIH guidelines.

**4. Problems or Questions.** If you have any problems or questions about this study, or about your rights as a research participant, or about any research-related injury, contact the Principal Investigator, Tim Greten, M.D., Building 10, Room 3B43, Telephone: 301-451-4723. You may also call the Clinical Center Patient Representative at 301-496-2626. If you have any questions about the use of your specimens or data for future research studies, you may also contact the Office of the Clinical Director, Telephone: 301-496-4251.

**5. Consent Document.** Please keep a copy of this document in case you want to read it again.

PATIENT IDENTIFICATION	<b>CONSENT TO PARTICIPATE IN A CLINICAL RESEARCH STUDY (Continuation Sheet)</b> <ul style="list-style-type: none"> <li>• Adult Patient or</li> <li>• Parent, for Minor Patient</li> </ul> NIH-2514-1 (07-09) P.A.: 09-25-0099 File in Section 4: Protocol Consent
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MEDICAL RECORD	<b>CONSENT TO PARTICIPATE IN A CLINICAL RESEARCH STUDY</b> • Adult Patient or                      • Parent, for Minor Patient
STUDY NUMBER: 15-C-0021	
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COMPLETE APPROPRIATE ITEM(S) BELOW:			
<b>A. Adult Patient's Consent</b> I have read the explanation about this study and have been given the opportunity to discuss it and to ask questions. I hereby consent to take part in this study.		<b>B. Parent's Permission for Minor Patient.</b> I have read the explanation about this study and have been given the opportunity to discuss it and to ask questions. I hereby give permission for my child to take part in this study. (Attach NIH 2514-2, Minor's Assent, if applicable.)	
_____ Signature of Adult Patient/ Legal Representative		_____ Signature of Parent(s)/ Guardian	
_____ Date		_____ Date	
_____ Print Name		_____ Print Name	
<b>C. Child's Verbal Assent (If Applicable)</b> The information in the above consent was described to my child and my child agrees to participate in the study.			
_____ Signature of Parent(s)/Guardian		_____ Date	_____ Print Name
<b>THIS CONSENT DOCUMENT HAS BEEN APPROVED FOR USE          FROM AUGUST 24, 2016 THROUGH AUGUST 23, 2017.</b>			
_____ Signature of Investigator		_____ Date	_____ Signature of Witness
_____ Date		_____ Date	
_____ Print Name		_____ Print Name	

PATIENT IDENTIFICATION	<b>CONSENT TO PARTICIPATE IN A CLINICAL RESEARCH STUDY (Continuation Sheet)</b> • Adult Patient or                      • Parent, for Minor Patient NIH-2514-1 (07-09) P.A.: 09-25-0099 File in Section 4: Protocol Consent
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