INSTITUTE: National Cancer Institute

STUDY NUMBER: 18-C-0061 PRINCIPAL INVESTIGATOR: Udo Rudloff, M.D.

STUDY TITLE: A Phase IB/II Single-arm Study of M7824 (MSB0011359C) in Combination with Gemcitabine in Adults with Previously Treated Advanced Adenocarcinoma of the Pancreas.

Continuing Review Approved by the IRB on 02/12/19

Amendment Approved by the IRB on 04/18/19 (C) Date posted to web: 04/24/19

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?

In this study we will investigate safety of using M7824 given in combination with gemcitabine and whether this combined treatment will cause your tumors to shrink.

M7824 is an investigational (has not been approved by the FDA) agent that targets and blocks a pathway that prevents your immune system from effectively fighting your cancer.

Gemcitabine is an FDA approved standard treatment recommended for pancreatic cancer.

REVISION COPY

Different people have different sensitivity to gemcitabine. In this study we are planning to evaluate your sensitivity to gemcitabine first and assign you to a dosage of gemcitabine according to your sensitivity. Some people are at higher risk to side effects of gemcitabine. Pharmacogenomic blood tests can determine if you are in the low risk or high-risk category. If you are in the high-risk category you will receive the reduced dose of gemcitabine instead of the standard dose.

This study has two parts: safety and efficacy.

First, we are going to evaluate the safety of using M7824 in combination with gemcitabine. Decreasing doses of M7824 will be given to participants in the study to find the tolerated dose of M7824 when given in combination with gemcitabine.

Secondly, we will compare how well the recommended dose of M7824 in combination with gemcitabine works in making your tumors shrink.

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

You are being asked to take part in this study because you have been diagnosed with pancreatic cancer already treated with standard therapies.

How many people will take part in this study?

Up to 41 subjects will take part in this study. Approximately 18 participants will be enrolled in the safety part and approximately 23 participants will be enrolled in the efficacy part.

Description of Research Study

For your safety, some medications and therapies are not allowed during the study. You should tell the study doctor before you take any new medications (includes prescription, herbal, and over-the-counter remedies) or start a new therapy during the study.

Before you begin the study

Before you begin this study, you will need to have the following exams and tests to make sure you are eligible for this study. The exams and tests are part of regular cancer care. These tests will be done under a separate consent.

- A review of any past or current medical conditions, medicines you are taking and cancer history.
- Physical examination, including height, weight, and vital signs.
- Electrocardiogram (EKG – a record of your heartbeat) to evaluate your heart.
- Review of your symptoms and your ability to perform your normal activities.
- Imaging Assessments – a computed tomographic scan (CT) that produces a picture of your body using a small amount of radiation or magnetic resonance imaging (MRI) that uses a magnetic field to produce an image of your body. These will be used to examine your chest, abdomen, pelvis, and brain (if your doctor thinks this is needed).

- You will have blood drawn for:
  - routine blood tests to find out if you are anemic, have low blood counts, and if your liver, kidneys, and other organs are working well,
  - TB testing if your doctor thinks this is needed
- Pregnancy test if you are a woman who can have children
- You will be asked to provide confirmation of your diagnosis. If a pathology report or tumor sample from a previous surgery/biopsy is not available, we will perform a biopsy (collect a sample of your tumor) to confirm your diagnosis.

During the study

M7824 will be administered to you through an IV (intravenous catheter, a small plastic tube that is put into a vein, usually in your arm) once every 2 weeks (2 weeks = 1 Cycle).

Gemcitabine will be administered to you through an IV once weekly for seven weeks. After a rest of one week, it will be given once a week for three weeks followed by a rest of one week. The three weeks on and one week off schedule may continue until you have received gemcitabine for no more than 6 months.

You will continue treatment with M7824 alone unless your disease gets worse or you have unacceptable side effects.

Ongoing Procedures before treatment on the first day of each cycle

- Physical exam and vital signs measured
- Review of your symptoms and your ability to perform your normal activities
- Routine blood tests to find out if you are anemic, have low blood counts, , and if your liver, kidneys, and other organs are working well

Additional Procedures before treatment on first day of cycles:

- Blood tests to evaluate:
  - the gemcitabine dose for first 4 gemcitabine infusions
  - if your blood is clotting normally – on cycle 1
  - if your thyroid and pancreas are working well – on cycles 1, 2, 4, 7, every 6 weeks after that
  - tumor markers – on cycles 1, 3, 5, 7, every 6 weeks after that for up to one year, then every 12 weeks
- Pregnancy test – on cycles 1, 2, 4, 6, every 4 weeks after that
- Routine urine tests – on cycles 1, 2, 4, 7, every 6 weeks after that

- Electrocardiogram (EKG) to evaluate your heart – on Day 1 of Cycle 1 before and after the M7824 infusion.
- Imaging Assessments – a CT scan or MRI of chest, abdomen and pelvis – every 6 weeks for up to one year, then every 12 weeks. If a scan identifies objective response, a confirmatory clinical PET or CT or MRI will be obtained 4 weeks following initial documentation of objective response.

Research tests

In addition to the tests that we will conduct to determine whether you are having side effects or if you are responding to the study therapy, we will also collect samples from you for purposes of research only. These studies include:

- Blood samples to study
  - the effects of therapy on your immune system will be collected on Day 1 of cycles 1, 2, 3, 5, 6, 7 and after discontinuation of treatment;
  - drugs levels in your blood on Day 1 of cycles 1, 2, 3, 4, 5, 6, and after discontinuation of treatment;
  - markers of tumor activity including collecting and testing tumor DNA that we find in your bloodstream on Day 1 of cycles 1, 2, 3, 5, 7 and after discontinuation of treatment
- Two optional tumor biopsies might be collected before and after you have completed 3 cycles of therapy. Please see page 9 for the risks of biopsy. You will be asked to sign a separate consent each time you agree to have an optional biopsy. You can participate in the study even if you decide not to undergo the biopsy procedures. Although it is not clinically needed, samples will be used for disease evaluation first; leftover samples will be used to study the response of your immune system and do genetic testing.
- MRI to evaluate how well the drugs circulate in your tumor before start of treatment, on Day 1 of cycles 2, 4, 10 and after discontinuation of treatment.
- You will be asked to complete questionnaires to determine you general well-being and function - before start of treatment on cycles 4, 8, every 12 weeks after that. It will take you about 20 minutes and will only be done if you can complete the surveys in English.
- Genetic testing – Your tissue samples contain genes, which are made up of DNA (**d**eoxyribo**n**ucleic **a**cid) which serves as the "instruction book" for the cells that make up our bodies. We will use the tissue samples and blood you provided to learn about how the genes in your tumor compare to genes in normal tissue. Your tissue will help us study how genes might play a role in pancreatic cancer and other diseases. We will not share the results of these research tests with you.

When we are conducting the above genetic tests, it is possible that we could identify changes in other parts of your DNA that are not related to this research. These are known as "incidental medical findings".

However, the analyses that we perform in our laboratory are for research purposes only; they are not nearly as sensitive as the tests that are performed in a laboratory that is certified to perform genetic testing. Changes that we observe unrelated to our research may or may not be valid. Therefore, we do not plan to inform you of the results of testing on your tissue and blood that is performed in our research lab. However, in the unlikely event that we discover a finding that is believed to be clinically important based on medical standards at the time that we first analyze your results, we will contact you. This could be many years in the future. We will ask you to have an additional tube of blood drawn to verify the findings we have seen in our lab. If the results are verified, you will be re-contacted and offered a referral to a genetic healthcare provider to discuss the results.

When you are finished taking the drugs

About 4 – 5 weeks after you have finished taking the study drugs, you will be asked to return for a safety follow up visit. At this visit, your will be asked questions about your health, get a physical exam, undergo blood and urine tests and might have a CT scan. If you are unable to return for this visit, we will obtain the information from you by telephone or e-mail.

If your disease did not get worse, but you finished taking M7824, we will invite you for imaging studies every 12 weeks. Also, if in the opinion of the investigator you can get benefit from more treatment, we might re-start treatment with M7824, but not gemcitabine.

If your disease got worse, after the safety visit, we will call or e-mail you or your physician approximately once every 3 months for 1 year and once every 6 months after that to ask about your health and about any other medications you may have taken for your cancer. If you still have unresolved health issues, caused by study drug, you will be invited to NIH for additional tests and treatment.

Birth Control

If you are a woman who is breast feeding or pregnant, you will 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 at least 28 days before starting study treatment, during study treatment, and for 4 months after the last drug infusion. 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:

- abstinence
- intrauterine device (IUD)
- hormonal [birth control pills, injections, or implants]

- tubal ligation
- vasectomy

Risks or Discomforts of Participation

If you choose to take part in this study, there is a risk that:

- You may lose time at work or home and spend more time in the hospital or doctor's office than usual
- You may be asked sensitive or private questions which you normally do not discuss
- If test shows you are more sensitive to gemcitabine, you will receive less than the approved weekly dose of gemcitabine.
- Because of combined therapy used on this study, you also might receive less than the approved weekly dose of gemcitabine.

The M7824 and chemotherapy used in this study may affect how different parts of your body work such as your liver, kidneys, heart, and blood. The study doctor will be testing your blood and will let you know if changes occur that may affect your health.

There is also a risk that you could have side effects from the study drug(s).

Here are important points about side effects:

- The study doctors do not know who will or will not have side effects.
- Some side effects may go away soon, some may last a long time, or some may never go away.
- Some side effects may interfere with your ability to have children.
- Some side effects may be serious and may even result in death.

Here are important points about how you and the study doctor can make side effects less of a problem:

- Tell the study doctor if you notice or feel anything different so they can see if you are having any symptoms.
- The study doctor may be able to treat some side effects.
- The study doctor may adjust the study drugs to try to reduce side effects.

Late side effects of the investigational agents may affect your ability to tolerate subsequent regimens of standard of care chemotherapy.

Below we show the most common and the most serious side effects that researchers know about. There might be other side effects that researchers do not yet know about. If important new side effects are found, the study doctor will discuss these with you.

Risks from study therapy

M7824

Common (occurring in more than 5 % of patients)

- Fatigue (tiredness)
- Nausea
- Diarrhea
- Decreased appetite
- Infusion-related reaction
- Chills (feeling cold)

Occasional (occurring in less than 5% of patients)

- Shortness of breath
- Rash
- Abdominal pain
- Non-cardiac chest pain

Allergic reactions or reactions in the context with the infusions might occur during treatment. Although M7824 is a fully human protein the risk cannot be completely excluded. In general, these reactions are mild to moderate and can be handled with appropriate drugs, but in very rare cases severe to life-threatening and even fatal reactions might occur, which require advanced cardiac life support.

For the prevention of infusion-related adverse effects and possible allergic reactions you will receive a premedication of an antihistamine drug (so-called H1 blocker) and acetaminophen 60 to 120 minutes before the 1st and 2d infusion.

In addition, immune-mediated side effects might be possible. These are:

- joint pain
- arthritis (inflammatory disease of the joint)
- pneumonitis (inflammatory disease of the lung)
- hypothyroidism (decreased function of the thyroid gland)
- hyperthyroidism (increased function of thyroid gland)
- thyroiditis (inflammatory disease of the thyroid gland)
- autoimmune hepatitis (inflammatory disease of the liver caused by the body's immune system)

- thrombocytopenia (decrease of the blood platelets)
- dry eyes
- inflammatory eye disease
- diabetes mellitus (high blood sugar levels)
- decreased function of the adrenal glands
- inflammatory disease of muscles characterized by pain and tenderness
- colitis (inflammatory disease of the large intestine)
- impairment of the brain function
- psoriasis
- nerve irritation
- autoimmune disorder (body's immune system approaches own cells)
- myocarditis

There is a risk of tumor lysis syndrome due to tumor shrinkage. This complication is caused by the breakdown products of dying cells and includes elevated blood potassium, elevated blood phosphorus, elevated blood uric acid and elevated urine uric acid, low blood calcium, and consequent acute kidney failure.

Risk of increased bleeding with M7824 administration.

Bleeding has been frequently observed in patients receiving the drug M7824. Patients may experience bleeding including, but not limited to: gum bleeding, nose bleeds, blood in their urine, blood in their stool, or coughing up blood. Occasionally, this bleeding can be serious and potentially life threatening. If you experience any bleeding on this trial, please tell the study team immediately.

Tell your doctor if you've had a life-long problem of frequent or excessive bleeding or bruising, or if you take aspirin or prescription medication to thin your blood.

If any of these side effects occur, you must inform your study doctor immediately.

Gemcitabine

Common (occurring in more than 20% of patients)

- Diarrhea, loss of appetite, nausea, vomiting
- Liver enzymes increase
- Fever
- Rash

Occasional (occurring in 4-20% of patients)

- Anemia which may require blood transfusions
- Low blood counts
- Blood loss from any cause
- Difficulty breathing
- Swelling of the body
- Flu-like Symptoms
- Infection, especially when white blood cell count is low
- Hair loss
- Feeling of "pins and needles" in arms and legs

Rare and serious (occurring in fewer than 4% of patients)

- Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat
- Damage to the heart
- Blood infection (sepsis)
- Damage to the liver
- Damage to the kidney

Risks from Blood Collection

Side effects of blood draws include pain and bruising in the area where the needle was placed, lightheadedness, and rarely, fainting. When large amounts of blood are collected, low red blood cell count (anemia) can develop.

Risks from Biopsy

This procedure usually causes only brief discomfort at the site from which the biopsy is taken. Rarely, infection or bleeding may occur at the needle site.

Tumor biopsies may be done by a specialist using the CT scanner or ultrasound machine to guide the biopsy needle into the tumor to ensure accuracy. To collect the optional research biopsies, you may be exposed to 2 CT scans. This radiation exposure is not required for your medical care and is for research purposes only. The amount of radiation you might receive in these procedures is 1.6 rem which is below the guideline of 5 rem per year allowed for research subjects by the NIH Radiation Safety Committee. The average person in the United States receives a radiation exposure of 0.3 rem per year from natural sources, such as the sun, outer space, and the earth's

air and soil. If you would like more information about radiation, please ask the investigator for a copy of the pamphlet, An Introduction to Radiation for NIH Research Subjects.

Privacy Risks:

The following general points are indirectly related to your participation in the research study.

1. Unanticipated medical information: During the course of this investigation, it is possible (although not likely) that we will obtain unanticipated information about your health or genetic background.

2. Release of medical records. In the course of applying for certain types of insurance (e.g., medical insurance, life insurance, or disability insurance), people are often asked to sign forms that authorize insurance companies to obtain their medical records. If you sign such a release form at some point in the future, it is possible that the insurance company would present this signed release form to the Clinical Center of the National Institutes of Health. In that event, the National Institutes of Health would comply with your request to provide the insurance company with your medical record. It is possible that information contained in your medical record might affect (either favorably or unfavorably) the willingness of the insurance company to sell you insurance. Your employability may also be affected.

3. Release of genetic information:

- Your privacy is very important to us and we will use many safety measures to protect your privacy. However, in spite of all of 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 blood relatives. Consequently, it may be possible that genetic information from them could be used to help identify you. Similarly, it may be possible that genetic information from you could be used to help identify them.

- While the controlled-access databases developed for this project will not contain information that is traditionally used to identify you, such as your name, address, telephone number, or social security number, 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 blood relative) in another database and be able to identify you (or your blood relative). It also is possible that there could be violations to the security of the computer systems used to store the codes linking your genetic and medical information to you.

- Since some genetic variations can help to predict the future health problems of you and your relatives, this information might be of interest to health providers, life insurance companies, and others. Patterns of genetic variation also can be used by law enforcement agencies to identify a person or his/her blood relatives. Therefore, your genetic information potentially could be used in ways that could cause you or your family distress, such as by revealing that you (or a blood relative) carry a genetic disease.

- There also may be other privacy risks that we have not foreseen.

There are state and federal laws that protect against genetic discrimination. There is also a federal law called the Genetic Information Nondiscrimination Act (GINA). In general, this law makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. However, it does not protect you against discrimination by companies that sell life insurance, disability insurance, or long-term care insurance. GINA also does not apply to members of the United States military, to veterans obtaining health care through the Veteran's Administration or the Indian Health Service. Lastly, GINA does not forbid insurance medical underwriting based on your current health status.

Potential Benefits of Participation

Are there benefits to taking part in this study?

The aim of this study is to find out whether the experimental treatment will cause your tumors to shrink. We do not know if you will receive personal, medical benefit from taking part in this study. 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

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

- Getting standard FDA approved 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.

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 need to take medication that is not allowed on the study
- if you become pregnant
- 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
- if the investigator decides to end the study

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

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.
- 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 Institutes of Health Intramural Institutional Review Board

- Qualified representatives from EMD Serono, the pharmaceutical company who produces M7824.

Portions of your samples, genomic data, and health information will be stored for an unlimited period of time to be used in future research. Your individual genomic data and health information will be put in a controlled-access database. This means that only researchers who apply for and get permission to use the information for a specific research project will be able to access the information. Your genomic data and health information will not be labeled with your name or other information that could be used to identify you. Researchers approved to access information in the database have agreed not to attempt to identify you.

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.

Certificate of Confidentiality

To help us protect your privacy, we have obtained a Certificate of Confidentiality. The researchers can use this Certificate to legally refuse to disclose information that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings, for example, if there is a court subpoena. The researchers will use the Certificate to resist any demands for information that would identify you, except as explained below.

You should also know that there are several circumstances in which the Certificate does not provide coverage. These include when information:

- will be used for auditing or program evaluation internally by the NIH; or
- must be disclosed to meet the legal requirements of the federal Food and Drug Administration (FDA).
- is necessary for your medical treatment and you have consented to this disclosure;
- is for other research.

In addition, identifiable, sensitive information protected by this Certificate cannot be admissible as evidence or used for any purpose in any action, suit, or proceeding without your consent.

You should understand that a Certificate of Confidentiality does not prevent you or a member of your family from voluntarily releasing information about yourself or your involvement in this research. If an insurer, employer, or other person obtains your written consent to receive research information, then the researchers will not use the Certificate to withhold that information.

The Certificate of Confidentiality will not protect against the required reporting by hospital staff of information on suspected child abuse, reportable communicable diseases, and/or possible threat of harm to self or others.

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 therapies developed by EMD Serono through a joint study with your researchers and the companies. The company also provide financial support for this study.

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.

These specimens and data will be used for future research and shared 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.

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, Udo Rudloff, M.D., Building 10, Room 2B38D, phone 240-760-6238. 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: 240-760-6187.

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

COMPLETE APPROPRIATE ITEM(S) BELOW:

A. Adult Patient's Consent

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.

_____ _____
Signature of Adult Patient/ Legal Representative — Date

_____
Print Name

B. Parent's Permission for Minor Patient.

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 Parent(s)/ Guardian — Date

_____
Print Name

C. Child's Verbal Assent (If Applicable)

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

THIS CONSENT DOCUMENT HAS BEEN APPROVED FOR USE FROM FEBRUARY 12, 2019 THROUGH FEBRUARY 15, 2020.

_____ _____ _____ _____
Signature of Investigator — Date — Signature of Witness — Date

_____ _____
Print Name — Print Name