INSTITUTE/CENTER: National Cancer Institute

PRINCIPAL INVESTIGATOR: Christian Hinrichs, MD

STUDY NUMBER: 19-C-0002

STUDY TITLE: A Phase II Study of M7824 in Subjects with Recurrent Respiratory Papillomatosis

IRB Approval Date: 09/20/2019

Cohort: *Treatment*

Consent Version: *7/24/2019*

WHO DO YOU CONTACT ABOUT THIS STUDY?

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This consent form describes a research study and is designed to help you decide if you would like to be a part of the research study.

You are being asked to take part in a research study at the National Institutes of Health (NIH). Members of the study team will talk with you about the information described in this document. 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). Take the time needed to ask any questions and discuss this study with NIH staff, and with your family, friends, and personal health care providers. Taking part in research at the NIH is your choice.

If the individual being asked to participate in this research study is not able to give consent to be in this study, you are being asked to give permission for this person as their decision-maker. The term "you" refers to you as the decision-maker and/or the individual being asked to participate in this research, throughout the remainder of this document.

IT IS YOUR CHOICE TO TAKE PART IN THE STUDY

You may choose not to take part in this study for any reason. If you join this study, you may change your mind and stop participating in the study at any time and for any reason. In either case, you will not lose any benefits to which you are otherwise entitled. However, to be seen at the NIH, you must be taking part in a study or are being considered for a study. If you do choose to leave the study, please inform your study team to ensure a safe withdrawal from the research.

WHY IS THIS STUDY BEING DONE?

The main purpose of this study is to see if M7824 works in treating recurrent respiratory papillomatosis (RRP).

M7824 is an investigational drug, which means that the Food and Drug Administration (FDA) has not approved it for sale or for marketing for recurrent respiratory papillomatosis. This study is a Phase 2 clinical trial. Phase 2 trials test the effectiveness (if the drug works) and safety of an investigational drug.

M7824 belongs to a family of molecules called anti-PD-L1 antibodies. PD-L1 is a protein on the surface of cells that regulates whether that cell can be killed by immune system cells. PD-L1 is thought to be able to stop or decrease the response of the immune system to different kinds of diseased cells, such as cancer cells or cells infected with a virus. M7824 interferes with the activity of PD-L1 and is thought to have an effect on the immune system (in particular white blood cells) that may cause an immune response or increase the effectiveness of the response.

M7824 has been tested at different dose levels to see which dose is safe and well tolerated when given once every two weeks. Based on this information it was determined that 1200 mg drug strength would be used in this research trial.

Another purpose of the trial is to find out whether M7824 can reduce papillomas. Another goal of the study is to learn more about your disease and your response to this investigational drug. To do this, we will draw blood and collect tissue to measure certain "biomarkers". "Biomarkers" refer to different types of markers found in the blood and tissue that are associated with the disease and/or your response to the investigational drug. For this, samples of your blood and papilloma may be collected. The purpose of this research is to find out if there are any disease-related markers which may help in predicting how subjects respond to M7824. This is described in more detail below.

WHY ARE YOU BEING ASKED TO TAKE PART IN THIS STUDY?

You are being asked to take part in this trial because you have aggressive recurrent respiratory papillomatosis that has not yet been treated, or your disease may not have responded adequately to available treatments.

HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?

Up to 26 patients will be enrolled on this trial.

WHAT WILL HAPPEN IF YOU TAKE PART IN THIS RESEARCH STUDY?

Before you begin the study

Before receiving the investigational drug, you will have several tests performed to check whether the trial is suitable for you. Your doctor will review your medical history and the drugs that you are currently taking as well as the previous treatments of your disease to determine whether you can participate in this trial. A small part of tumor tissue that was previously collected from you may be used to confirm the diagnosis of recurrent respiratory papillomatosis. Some of these tests or procedures are part of regular care and may be done even if you are not being considered to join

the study. If you have had some of these tests or procedures recently, they may or may not have to be repeated. The following tests and procedures will be performed prior to starting treatment:

1. Complete history and physical examination.
2. Routine blood tests and viral studies
3. For females of child-bearing potential, a pregnancy test will be done. You will not be able to participate if you are pregnant.
4. CT scan of chest (if necessary) to evaluate any papillomas in your lungs
5. An endoscopy procedure in the clinic called flexible nasopharyngolaryngoscopy. For this procedure, the doctor uses a flexible endoscope (a small tube with a built-in camera) to look at the structures inside the nose, throat, larynx (voice box) and upper windpipe. This is a procedure to assess your throat and larynx; you will likely have already had this procedure before.
6. Evaluation of the veins in your arms to determine if your veins are large enough to allow your blood to be collected during an apheresis procedure (see #4 under "Before Treatment" for a description of procedure).

During the study

Before Treatment

If you are determined eligible to be in the study, you will have the following additional tests that will be performed for research purposes only:

1. Endoscopy procedure under anesthesia (sedation or general anesthesia). This procedure allows us to make sure we know where all of your papilloma disease is located, to make sure that your airway will be open enough to undergo the experimental treatments and to get biopsies of your papilloma. If we are concerned that your papilloma may cause breathing issues while you receive the experimental treatment, we may remove some of the papilloma to make your breathing safer. This pre-treatment biopsy is required because it will confirm the diagnosis and provide information that is critical to the goals of this study.

   The biopsy will be studied in the research laboratory to evaluate additional proteins and characteristics in your papilloma. You will not receive results of the research testing because they are being conducted in a research lab and are not valid for treatment purposes. The research testing on the biopsy may include growing cell lines (cells which keep dividing and growing in the laboratory, sometimes for years allowing us to continually study those cells). In addition, a portion of the biopsy will be reviewed by the pathologist at your study site to confirm your diagnosis of benign papilloma. You will receive the results of this review.
2. You will have blood collected (approximately 7.5 tablespoons for research testing). You will not receive results of the research testing. One of the laboratory tests help us determine certain immune elements present in your blood.
3. You will be asked to complete the Voice Handicap Index-10 assessment questionnaire. This will tell us the extent to which RRP is affecting your voice. We will have you complete the same questionnaire later on in the study to see if this changes.

4. You may have an apheresis procedure for research. The apheresis procedure involves inserting a catheter (tube) into your vein to allow your blood to be collected. White blood cells will be separated from the rest of your blood and stored until the time they are used for research and the rest of the blood will be returned to you through the same catheter it came out of or through second needle in your other arm. We will try to use IV catheters already in place, but may need to give you an additional IV catheter. You will be asked to sign a separate consent for this procedure, and may decline to have this procedure. If you decide not to have the apheresis, it will not affect your participation in this study.

After the research samples have been collected, you will begin treatment. Your participation in the Study Treatment Period may continue for as long as you are receiving benefit and you do not meet any of the withdrawal criteria.

During treatment

M7824 will be administered at a dose of 1200 mg every other week (Day 1 of a 14-day cycle (weeks 1, 3, 5, 7, 9 and 11)) for up to 12 weeks total (6 cycles), which are broken down into two courses. Each course has three cycles. You will only proceed to course 2 if you have had a partial response to M7824. If you have a partial response after course 2, you can choose to receive up to 2 more courses of therapy. M7824 will be given as an infusion through a vein (IV) over approximately a 60-minute period.

You will be monitored closely while you are participating in this trial. You will need to inform your study doctor about any prescription and non-prescription medications you are taking. Your doctor will help determine whether you should continue these drugs, whether you need to change the way you are taking these drugs, or whether you need to switch to another medication.

Some of the tests done before starting treatment will be repeated 6 and 12 weeks after starting treatment to check on how the treatment is working.

Every 2 weeks while receiving study treatment:

- Physical examination which may include flexible nasopharyngolaryngoscopy in the clinic.
- Vital signs and weight.
- Pregnancy test in women of childbearing potential.
- Routine blood tests
- Blood collection (approx. 3-4 tablespoons) for research testing.
- Review of side effects that you have experienced and medications that you are taking.
- Voice Handicap Index-10 assessment questionnaire.
- Infusion of M7824.

Additional studies at a single time point two weeks after the initial dose

- Endoscopy procedure under anesthesia (sedation or general anesthesia) to see if there are clinical signs of inflammation in your airway or if there is blockage of your airway and to

obtain biopsies which will be used for research purposes to evaluate how your disease is responding to the treatment.

- Optional apheresis procedure to collect white blood cells (also called leukocytes) which will be used for research.

Every 6 weeks while receiving study treatment:

- Physical examination.
- Flexible nasopharyngolaryngoscopy in the clinic.
- Voice Handicap Index-10 assessment questionnaire.
- CT scan of chest (if used for response assessment) to evaluate your RRP status.

When you are finished taking the study treatment:

- Endoscopy procedure under anesthesia (sedation or general anesthesia) to either perform a biopsy to verify that your papilloma is gone if you had a complete response to the treatment, or to remove all visible papilloma with normal surgery techniques if you do not have a complete response to the treatment.
- If you respond to the treatment, you will be evaluated every 6 weeks (3 times), then every 12 weeks (3 times), then every 26 weeks (two times) or until you experience disease progression.
- You will be evaluated 42 days after the last dose of M7824 if you do not experience a response to treatment.
- If you do not experience a response to treatment you will be contacted annually to document additional disease recurrence and treatments that you have received.
- Evaluations will include:
    - Physical Exam
    - Pregnancy test in women of childbearing potential
    - Vital signs.
    - Flexible nasopharyngolaryngoscopy in the clinic.
    - Blood tests (about 1 tablespoon) to check your blood counts, blood chemistries and other tests to monitor your health.
    - Blood collection (approx. 3-4 tablespoons) for research testing.
    - Review of side effects that you have experienced and medications that you are taking.
    - Voice Handicap Index-10 assessment questionnaire.

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 if your partner is capable of becoming pregnant and you wish to participate in this study, and you have not had your prostate or testicles removed, or you are not receiving continuous hormone therapy, then you must use a medically acceptable method of birth control and refrain from donating sperm while you are receiving the study drug and for a period of at least 4 months after your last dose of the study drug.

If your partner becomes pregnant during the course of treatment, you must inform your doctor immediately. Your doctor will ensure that you and your partner receive information about options available to you in relation to pregnancy and that you and your partner are fully supported in whichever option you chose. Acceptable birth control options for you and your partner include:

- Intrauterine device (IUD)
- Approved hormonal contraceptives or therapies (birth control pills, Depo-Provera, or Lupron Depot)
- Surgical Sterilization (you and/or your partner)
- Barrier methods (such as a condom or diaphragm) used with a spermicide

Embryofetal toxicity

Based on how the study drug works, there is also a risk of embryofetal toxicity (risks to your unborn baby).

Risks to an Unborn Child and Sexual Partner

Your study doctor will discuss the risks to unborn children for drugs used in this study. The effects of the study drugs, if any, on unborn children are unknown.

RISKS OR DISCOMFORTS OF PARTICIPATION

What side effects or risks can I expect from being in this study?

What could be the side effects of the study drug?

In a clinical study like this one, every risk or side effect cannot be predicted. Each person's reaction to a study drug, device or procedure may be different. You may have a side effect or be at risk for symptoms, illnesses and/or complications that could not be predicted by your study doctor or the sponsor of this clinical study. If such side effects occur, you must inform your study doctor immediately.

Based on animal studies and previous studies in humans, the following possible side effects could occur:

Infusion-related reactions including hypersensitivity (allergic reactions to the drug infusion)

Allergic reactions or reactions in the context with the infusions might occur during treatment. Although the study drug is a fully human protein the risk cannot be completely excluded. Infusion-related reactions have already been observed under treatment with a similar drug which is currently in the clinical development at the Sponsor. Infusion-related reactions may

be mild to moderate such as nausea, vomiting or dizziness, but could also be severe to life-threatening (anaphylactic reaction) and even fatal reactions might occur, which require advanced cardiac life support. Severe to life-threatening symptoms could be bronchospasm, dyspnea (difficulty in breathing), low blood pressure, irregular heart or cardio-vascular collapse/cardio-respiratory arrest.

For the prevention of infusion-related adverse effects and possible allergic reactions you may receive a premedication of an antihistamine drug (Benadryl® or similar) and acetaminophen (Tylenol®) 30 to 60 minutes before every infusion. In addition, as a preventive measure, you will undergo an overnight stay at the hospital for observation after the first two infusions of the study drug. For other doses, you will be asked to remain in the study center for at least 2 hours after the end of the infusion.

Immune-related Adverse Events (irAEs)/Autoimmune Disorders

Immune-related adverse events (irAEs)/autoimmune disorders (illnesses caused by an over activity of your body's immune-system that normally protects you from infections). Immune-mediated side effects have been observed with other drugs which are similar to one component of the study drug. These similar drugs comprise a drug which is currently in the clinical development at the Sponsor and other drugs which are already on the market. Symptoms/illnesses such as arthralgia (joint/joints pain), arthritis (inflammatory disease of the joint), pneumonitis (inflammation of the lung tissue), hypothyroidism (decreased function of the thyroid gland), hyperthyroidism (increased function of thyroid gland), autoimmune hepatitis (inflammation of the liver caused by the body's immune system), iritis (inflammatory eye disease), diabetes mellitus (high blood sugar levels), adrenal insufficiency (decreased function of the adrenal glands), myositis (inflammation of a muscle characterized by pain and tenderness), myocarditis (inflammation of muscle of the heart) or inflammation of other organs and autoimmune disorder (body's immune system approaches its own cells and causing destruction) might occur. The potential side effects listed above may be temporary, long term, permanent or result in death. However, based on the experience with the other drugs most of these potential side effects are usually manageable and reversible. That means they will stop once the drug is discontinued. One immune-related adverse event of colitis (inflammation of the bowel tissue) with subsequent bleeding and anemia has been observed with the use of this drug. The colitis might present with no or limited symptoms. It is important that you notify your treating physician immediately if you experience mild abdominal pain, blood in your stools, or mild diarrhea. Rarely nerve inflammation may also be seen leading to temporary or in extremely rare cases permanent nerve damage. This may present in a number of ways including localized weakness, changes in vision or hearing and nausea and vomiting.

Anemia

Anemia, a reduction of your red blood cell number is considered a potential risk as it has been observed in animal studies with the study drug. During the study, your red blood cell count will be closely monitored. In case of a significant decrease, your study doctor will stop treatment with the study drug as appropriate and apply adequate medicinal treatment which may include blood transfusions.

Alterations in wound healing or repair of tissue damage

This is a potential risk considering how the drug works. If you have a wound or tissue damage, there may be a delay/alteration in the healing of that wound. Please make your doctor aware if you plan to undergo any kind of surgery while you are participating in this study.

Rash

You may experience a rash that appears as a red flat area on the skin with small raised bumps.

Rash with skin thickening/keratoacanthoma/skin cancer

Taking into account experience with other investigational drugs, which are similar to one component of the study drug, additional possible side effects include skin rash with excessive skin thickening, a certain type of a benign skin tumor that can form a dome-shaped lump (keratoacanthoma) and a certain type of skin cancer. Your study doctor will carefully monitor your skin for any of these changes. If a suspicious skin rash or lesion is detected, your study doctor may take a skin biopsy (small piece of tissue) for analysis in a laboratory. You may also be asked to see a skin specialist (dermatologist) for further assessment and testing. The skin lesion may need to be surgically removed. We recommend limiting your sun exposure during treatment due to the known association between TGF-β inhibitors and skin tumors.

Bleeding

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.

Less common side effects:

- Inflammation in the lungs (pneumonitis that can be fatal)
- Inflammation of the colon (colitis) which can lead to abdominal pain and diarrhea with or without blood. If left untreated, this may lead to a tear in the wall of the intestine which can be serious and life threatening.
- Inflammation of the liver called hepatitis, that can cause liver failure and death
- Inflammation of the thyroid (thyroiditis)
- Feeling faint, joint and abdominal pain, salt craving, skin darkening like a suntan
- Weight gain
- Anxious, angry
- Can't sleep
- Increased sweating

- Hair loss
- Muscle pain, tenderness and/or weakness
- Inflammation of the heart (myocarditis) (May cause your heart to have difficulty pumping blood throughout your body, which can cause chest pain, difficulty breathing, swelling in your legs. You may also experience a fast or irregular heartbeat that can cause dizziness or fainting. Sometimes this condition can lead to death.)
- Skin changes (rash, itchiness, redness)
- Allergic reactions, causing:
    - swelling of the face, lips and throat
    - breathing difficulties which might be serious
    - hives or nettle-like rash
    - change in blood pressure

The side effects listed above may or may not be caused by problems with your lungs, colon, liver, thyroid, adrenal gland, muscles, heart, and skin. They may be temporary, long term, permanent or result in death. However, most of these side effects are reversible. That means they will stop once the drug is discontinued.

Other immune-related events were observed with similar drugs in this class, such as type I diabetes mellitus, pituitary dysfunction, inflammation of the kidney, inflammation of the eyes, inflammation of the joint, inflammation of the brain, inflammation of the pancreas and inflammation of the nervous system.

Allergic reactions or reactions in the context with the infusions might occur during treatment. Infusion related reactions have been observed under treatment with the study drug, as seen for other similar drugs. In general, these reactions are mild to moderate and can be handled with appropriate drugs, but in rare cases, 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 and paracetamol (acetaminophen) before every infusion.

There is a chance the study drug could lead to Tumor Lysis Syndrome (TLS) due to tumor shrinkage. TLS is when cancer cells break down and the body has to get rid of the broken-up cell parts. Sometimes your body can't remove the cell parts quickly enough and the levels of some products in your blood, such as salts and acids, can rise. This can happen especially in participants with large tumors or a high number of white cells in the blood. TLS can lead to serious problems, such as effects on your kidney and heart (including abnormal heart rhythms) or seizures. These side effects can result in needing kidney dialysis (a special machine to remove toxins from the blood) or be fatal. Your study doctor knows to watch out for signs of this condition and how to treat this condition should it occur.

Any side effects or other health issues occurring during the study will be followed up by the study doctor.

Other side effects linked to medical procedures during the trial

Blood samples

Each time a blood sample is needed, a needle will be put into a vein in your arm (or into your central venous catheter, if you have one). You may feel pain when the needle goes through the skin. Other side effects associated with drawing your blood for blood tests may include infection, bruising, redness, discomfort or bleeding at the site of the needle stick, and possible lightheadedness and fainting.

Electrocardiogram (ECG)

An electrocardiogram or ECG is a test that records the electrical activity of the heart. It is used to measure the rate and regularity of heartbeats as well as the size and position of the heart chambers, and the presence of any damage to the heart. For this test, you will be asked to lie down, and small patches that have an adhesive edge with a gel in the middle, called electrodes, will be placed on your arms, legs, and chest. The areas where the electrodes are placed will be cleaned and, if needed, some hair may be shaved or clipped to allow for better attachment of the electrodes. The adhesive from the patches may irritate your skin.

CT scan

During a CT scan, you're briefly exposed to much more radiation than you would be during a plain X-ray. Radiation exposure potentially increases your risk of developing cancer. Although rare, the intravenous (IV) contrast material involved in some CT scans causes medical problems or allergic reactions in some people. Most reactions are mild and result in hives or itchiness. In rare instances, an allergic reaction can be serious and potentially life threatening. Make sure to tell your study doctor if you've ever had a prior reaction to contrast material during medical tests.

Papilloma biopsy under anesthesia

You are required to have general anesthesia three times for this protocol – before treatment starts, two weeks after treatment has started, and after completing treatment. Although rare, serious risks associated with general anesthesia include an adverse drug reaction, stroke, heart attack or death. You will be asked to sign a separate consent prior to each procedure involving anesthesia. Aside from the risk of anesthesia, this procedure carries a risk of post-operative tongue or throat discomfort that may last for several days and a very small risk of a chipped tooth from the instruments in your mouth. We use special tooth guards to prevent this from happening.

Flexible nasopharyngolaryngoscopy

Complications are very uncommon; but may include tearing, gagging, coughing, and, less frequently, nose bleeding due to the scope being passed through the nose.

Apheresis

The most common side effects from this procedure are pain and bruising at the catheter site. You may also experience tingling of the lips and fingers due to the medicine used to keep blood from

clotting. You may feel faint or light-headed during or after the procedure. Rarely this procedure may cause bleeding or infection at the catheter site.

Other

It is possible that other side-effects could occur which are not described in this consent form. It is also possible that you could have a side effect that has not occurred before.

POTENTIAL BENEFITS OF PARTICIPATION

Are there benefits to taking part in this study?

The aim of this study is to see if this experimental treatment will cause your papilloma to shrink. We do not know if you will receive personal, medical benefit from taking part in this study. These potential benefits could include shrinking of your papilloma or lessening of your papilloma-associated symptoms. Because there is not much information about the drug's effect on your disease, 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 papilloma and other types of growths caused by viruses or cancers.

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 papilloma without being in a study
- Taking part in another study

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 papilloma progresses
- if you need to use medication that is not allowed on the study
- 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 sponsor, the FDA, the Institutional Review Board or your doctor decides to stop or interrupt the study
- If you become pregnant
- If you cannot or do not come to your clinic visits or do not follow the study procedures

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 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 a drug, developed by EMD Serono through a joint study with your researchers and the company. The company also provides 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.

We plan to keep some of your specimens and data that we collect, 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.

COMPENSATION, REIMBURSEMENT, AND PAYMENT

Will you receive compensation for participation in the study?

Some NIH Clinical Center studies offer compensation for participation in research. The amount of compensation, if any, is guided by NIH policies and guidelines.

You will not receive compensation for participation in this study.

Will you receive reimbursement or direct payment by NIH as part of your participation?

Some NIH Clinical Center studies offer reimbursement or payment for travel, lodging or meals while participating in the research. The amount, if any, is guided by NIH policies and guidelines.

On this study, the NCI will cover the cost for some of your expenses. Some of these costs may be paid directly by the NIH and some may be reimbursed after you have paid. Someone will work with you to provide more information.

Will taking part in this research study cost you anything?

NIH does not bill health insurance companies or participants for any research or related clinical care that you receive at the NIH Clinical Center.

- If some tests and procedures performed outside the NIH Clinical Center, 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 NIH Clinical Center.
- Once you have completed taking part in the study, medical care will no longer be provided by the NIH Clinical Center.

CLINICAL TRIAL REGISTRATION AND RESULTS REPORTING

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.

CONFIDENTIALITY PROTECTIONS PROVIDED IN THIS STUDY

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 NIH 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
- The study Sponsor (Center for Clinical Research) or their agent(s)

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

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.

If we share your specimens or data with other researchers, in most circumstances we will remove your identifiers before sharing your specimens or data. You should be aware that there is a slight possibility that someone could figure out the information is about you.

Further, the information collected for this study is protected by NIH under a Certificate of Confidentiality and the Privacy Act.

Certificate of Confidentiality

To help us protect your privacy, the NIH Intramural Program has received a Certificate of Confidentiality (Certificate). With this certificate, researchers may not release or use data or information about you except in certain circumstances.

NIH researchers must not share information that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings, for example, if requested by a court.

The Certificate does not protect your information when it:

1. is disclosed to people connected with the research, for example, information may be used for auditing or program evaluation internally by the NIH; or
2. is required to be disclosed by Federal, State, or local laws, for example, when information must be disclosed to meet the legal requirements of the federal Food and Drug Administration (FDA);
3. is for other research;
4. is disclosed with your consent.

The Certificate does not prevent you from voluntarily releasing information about yourself or your involvement in this research.

The Certificate will not be used to prevent disclosure to state or local authorities of harm to self or others including, for example, child abuse and neglect, and by signing below you consent to those disclosures. Other permissions for release may be made by signing NIH forms, such as the Notice and Acknowledgement of Information Practices consent.

Privacy Act

The Federal Privacy Act generally protects the confidentiality of your NIH medical records we collect under the authority of the Public Health Service Act. In some cases, the Privacy Act protections differ from the Certificate of Confidentiality. For example, sometimes the Privacy Act

allows release of information from your medical record without your permission, for example, if it is requested by Congress. Information may also be released for certain research purposes with due consideration and protection, to those engaged by the agency for research purposes, to certain federal and state agencies, for HIV partner notification, for infectious disease or abuse or neglect reporting, to tumor registries, for quality assessment and medical audits, or when the NIH is involved in a lawsuit. However, NIH will only release information from your medical record if it is permitted by both the Certificate of Confidentiality and the Privacy Act.

POLICY REGARDING RESEARCH-RELATED INJURIES

The NIH 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 NIH, the NIH Clinical Center, or the Federal Government. However, you have the right to pursue legal remedy if you believe that your injury justifies such action.

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, Christian Hinrichs, MD, hinrichs@nih.gov, 240-764-6059. *Other researchers you may call are:* Erin Ferraro, RN, at 240-760-6163 or Scott Norberg, DO, at 240-858-3303. You may also call the NIH Clinical Center Patient Representative at 301-496-2626, or the NIH Office of IRB Operations at 301-402-3713, if you have a research-related complaint or concern.

CONSENT DOCUMENT

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

Adult Research Participant: I have read the explanation about this study and have been given the opportunity to discuss it and to ask questions. I consent to participate in this study.

Signature of Research Participant	Print Name of Research Participant	Date

Legally Authorized Representative (LAR) for an Adult Unable to Consent: I have read the explanation about this study and have been given the opportunity to discuss it and to ask questions. I am legally authorized to make research decisions on behalf of the adult participant unable to consent and have the authority to provide consent to this study. As applicable, the information in the above consent was described to the adult participant unable to consent who agrees to participate in the study.

Signature of LAR	Print Name of LAR	Date

Investigator:

Signature of Investigator	Print Name of Investigator	Date

Witness to the oral short-form consent process only: This section is only required if you are doing the oral short-consent process and this English consent form has been approved by the IRB for use as the basis of translation.

Witness:

Signature of Witness*	Print Name of Witness	Date

***NIH ADMINISTRATIVE SECTION TO BE COMPLETED REGARDING THE USE OF AN INTERPRETER:**

____ An interpreter, or other individual, who speaks English and the participant's preferred language facilitated the administration of informed consent and served as a witness. The investigator obtaining consent may not also serve as the witness.

____ An interpreter, or other individual, who speaks English and the participant's preferred language facilitated the administration of informed consent but did not serve as a witness. The name or ID code of the person providing interpretive support is: _____.