PRINCIPAL INVESTIGATOR: Julius Strauss, MD

STUDY TITLE: Phase II Trial of M7824 in Subjects with HPV Associated Malignancies

STUDY SITE: NIH Clinical Center

Cohort: Affected Patient

Consent Version: 11/19/2021

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.

The remaining document will now describe the research study in more detail. This information should be considered before you make your choice. Members of the study team will talk with you about the information in this document. Some people have personal, religious, or ethical beliefs that may limit the kinds of medical or research interventions in which they would want to participate. Take the time you need to ask any questions and discuss this study with NIH staff, and with your family, friends, and personal health care providers.

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?

In this study, we will investigate if treatment with M7824 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.

M7824 has been tried in other types cancers. Recently, the manufacturer of the drug closed 3 large studies because the drug was not shown to help those patients more than standard therapies. In addition, in some cases it seemed like the drug might make the cancer grow faster. However, the type of cancer treated in those studies was not the same as your cancer.

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 cancer associated with human papillomavirus (HPV) infection.

HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?

Up to 120 subjects will take part in this study.

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. You will be removed from the study if you are not eligible.

- A review of any past or current medical conditions, medicines you are taking and cancer history.
- Physical examination, including height, weight, and vital signs.
- 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 and pelvis. If your doctor thinks this is needed, you might have additional imaging of your bones or brain.
- 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.
    - tests for HIV, Hepatitis B and Hepatitis C. (If you are infected with HIV, Hepatitis B or C you will be able to participate in this study, with some caveats. We will tell you what the results mean, how to find care, how to avoid infecting others, how we report these infections, and the importance of informing your partners at possible risk because of your infection).
- Routine urinalysis.
- Pregnancy test if you are a woman who is able to become pregnant.
- 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).

You will be treated with 26 doses (1 course) of M7824 and at this point the drug will be withheld (approximately 1 year after start of the treatment). We will follow you after that and if your disease gets worse we will repeat treatment with another 26 doses of M7824 followed by withholding of the drug. You will have as many courses of M7824 as you need.

The treatment might be interrupted prematurely if you have unacceptable side effects or in the opinion of Investigator your disease worsened to the point when this drug does not help you anymore.

Before start of the treatment we will do:

- Electrocardiogram (EKG – a record of your heartbeat) to evaluate your heart.
- Routine urinalysis.
- Blood test to check if your blood is clotting normally.

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, the status of your immune system and if your liver, thyroid, kidneys, and other organs are working well
- Pregnancy test

Additional Procedures before treatment on first day of certain cycles:

- Imaging Assessments – a CT scan or MRI of chest, abdomen and pelvis – every 6 to 12 weeks depending on your response to the treatment.

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 might also collect samples from you for purposes of research only. Some of your samples will be sent outside of the NIH for testing, but any information that can be used to identify you will be removed before we send them. These samples and studies include:

- Blood samples collected on Day 1 of cycles 1, 2, 4, and every 6 weeks after that to study
  - the effects of therapy on your immune system
  - markers of tumor activity including collecting and testing tumor DNA that we find in your bloodstream.

  No more than 7 tablespoons of blood will be taken at a time.

- Two optional tumor biopsies might be collected before and at the time you have the first imaging study after you started therapy. Please see page 8 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 for research, such as evaluation of your immune system response, detection of HPV and genetic testing.
- 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 cancer and other diseases. We will not share the results of these research tests with you.

When you are finished taking the drugs

About 4 – 5 weeks after you have finished taking the study drug, 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, and undergo blood tests.

After the safety follow up visit, we will call you or your physician approximately once every 3 months for a year and every 6 months after that. We will 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.

If your disease did not get worse, but you finished taking M7824, we will invite you for imaging studies every 3 months for a year and every 6 months after that.

If your treatment is interrupted prematurely before you finish 26 doses of the M7824, you will be asked to come for additional end of treatment visit during the week of discontinuation of the drug. At this visit, you will be asked questions about your health, get a physical exam, undergo blood tests and might have a CT scan.

If you are unable to return for these visits, we will call you to ask about your health and any side effects you have.

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 able to 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 2 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:

- total 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

The M7824 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.

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.

M7824

Common (occurring in more than 5 % of patients)

- Fatigue (tiredness and lack of energy)
- Nausea

- Diarrhea
- Constipation
- Vomiting
- Swelling of your lower legs or hands
- Fever
- Decreased appetite
- Loss of body fluids (dehydration)
- Skin growths called keratoacanthomas that resemble skin cancer. These usually go away after treatment and can leave a scar.
- Rash, blisters, skin discoloration and other skin abnormalities
- Bleeding has been frequently observed in patients receiving M7824. Patients may experience bleeding in different organs such as gums, nose, ears, eyes, vagina, breast, blood in the urine, stool, or bleeding in the internal organs or skull, coughing up or vomiting blood. Occasionally, this bleeding can be serious and potentially life threatening and require you to receive a blood transfusion. 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.
- Shortness of breath
- Cough
- Anemia: low number of red blood cells that can cause tiredness and shortness of breath. May require a transfusion.
- Abdominal pain
- Headache
- Itching

Occasional (occurring in less than 5% of patients)

- Chills (feeling cold)
- Blood clots that form throughout the body, blocking small blood vessels. Symptoms may include chest pain, shortness of breath, leg pain, problems speaking, or problems moving parts of the body
- Easy bruising
- Reaction to other drugs such as rash, anaphylaxis, and changes in blood

- Infusion-related reaction, including dizziness or fainting (low blood pressure), flushing, rash, fever, shortness of breath or sick to your stomach, or pain at the site of infusion. Although usually reversible with treatment, it can be severe or life threatening.
- Back pain
- Cancerous growth on the skin that can be removed
- Stroke
- Slow wound healing
- Thickening of the skin, nails

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.

In addition to the above, we have seen a few cases of nodular regenerative hyperplasia. This is when small growths, or nodules, occur in the liver. These usually do not cause symptoms, but can occasionally be associated with high blood pressure in the vein to the liver which could over time lead to liver damage.

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 side effects are caused by over activity of your body's immune system. The immune system normally works to protect you from things that are harmful such as infections, foreign substances, and sometimes from cancer. If the immune system is overactive, it can attack normal parts of the body because it mistakenly recognizes them as foreign/harmful.

Examples of these side effects are listed below. In rare cases, immune-related side effects can be life-threatening or fatal.

Types of immune-related side effects:

- Inflammation in the lungs (pneumonitis: symptoms may include but are not limited to a new or worsening cough, shortness of breath possibly with fever. Preliminary data suggested that there may be the tendency of higher frequency and severity in Japanese patients compared with non-Japanese patients: tell your study doctor right away if you have any of these symptoms as it may need to be treated urgently.
- Hypothyroidism (decreased function of the thyroid gland)

- Hyperthyroidism (increased function of thyroid gland)
- Thyroiditis (inflammatory disease of the thyroid gland)
- You may develop inflammation of the liver called hepatitis. Signs and symptoms of this include yellowing of the skin or whites of the eyes, dark urine, severe nausea and vomiting, pain in the upper right side of your abdomen, skin itchiness, not feeling hungry and bleeding or bruising more easily than normal.
- Thrombocytopenia (decrease of the blood platelets)
- Uveitis (inflammation in the eyes)
- Diabetes mellitus (high blood sugar levels)
- Problems with your adrenal glands (Adrenal Insufficiency): may cause stomach pains, vomiting, muscle weakness and fatigue, depression, low blood pressure, weight loss, kidney problems, and changes in mood and personality. These complications may be permanent and may require hormone replacement.
- Myositis (inflammation of the muscles characterized by pain and tenderness)
- Inflammation of the intestine (colitis). It may cause abdominal pain and diarrhea with or without blood. Fever may be present. It may require you to receive additional fluids. If left untreated, in rare occasions this may lead to a tear in the wall of the intestine which can be serious and life threatening.
- Autoimmune encephalitis is a type of brain inflammation where the body's immune system attacks healthy cells and tissues in the brain or spinal cord
- Myocarditis (inflammation of the heart muscle)
- Pemphigoid (fluid-filled blisters that can be itchy)
- Kidney problems: you may have an increase of creatinine levels in a blood test (creatinine is a protein marker that measures kidney function) but not have any symptoms or feel unwell. Uncommonly a patient may experience nephritis which is an inflammation of the kidneys that stops the kidneys from working properly
- Problems with the pituitary gland (hypopituitarism): Hypopituitarism refers to decreased output of hormones from the pituitary gland in the brain and may be caused by inflammation of the pituitary gland (hypophysitis). Symptoms may include headaches, thirstiness, and trouble seeing or double vision, leakage of breast milk or irregular periods in women. These complications may be permanent and may require hormone replacement
- Pancreatitis (inflammation of the pancreas)
- Liver problems: Increases in the blood level of substances called enzymes found within your liver cells. The enzyme changes are unlikely to make you feel unwell, however, if these blood enzyme levels become very high, your study doctor may need to stop the study medication

- Nervous system problems: symptoms can include unusual weakness of legs, arms, or face, numbness, or tingling in hands or feet. In rare situations, there is the potential for the inflammation of the nervous system to be severe.

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

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. No more than 7 tablespoons of blood will be taken at a time during this study.

Risk from Electrocardiogram

Other than possibly experiencing some minor skin irritation from the electrodes, there are no anticipated risks related to the echocardiogram.

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 will 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. Your radiation exposure from this procedure is below the guidelines allowed for research subjects at the NIH. See **What are the risks of radiation from being in the study?** below for more details.

Risks Due to Contrast Agents for CT

You may receive a contrast agent as part of your CT scan. Contrast agents can cause allergic reactions and kidney damage. Allergic reactions can include mild itching associated with hives but can also result in a serious life-threatening emergency from difficulty breathing. If this occurs, it is treatable.

Structural MRI

Magnetic resonance imaging (MRI) uses a strong magnetic field and radio waves to take pictures of the body. If you have a history of metastases to your brain or if we are concerned that you may have metastases to your brain, we will obtain pictures of your brain for this study. The MRI scanner is a metal cylinder surrounded by a strong magnetic field. During the MRI, you will lie on a table that can slide in and out of the cylinder. We will place soft padding or a coil around your head. You will be in the scanner about 30 minutes. You may be asked to lie still for up to 30 minutes at a time. While in the scanner you will hear loud knocking noises, and you will be fitted with earplugs or earmuffs to muffle the sound. You will be able to communicate with the MRI staff at all times during your scan, and you may ask to be moved out of the machine at anytime.

It is very important for the experiment that you do not move your head or body inside the scanner. We will use padding around your head to help keep it in place.

We may place a bar in your mouth to help keep your head still.

Risks for MRI

People are at risk for injury from the MRI magnet if they have some kinds of metal in their body. It may be unsafe for you to have an MRI scan if you have pacemakers or other implanted electrical devices, brain stimulators, some types of dental implants, aneurysm clips (metal clips on the wall of a large artery), metal prostheses (including metal pins and rods, heart valves, and cochlear implants), permanent eyeliner, tattoos, an implanted delivery pump, or shrapnel fragments. Welders and metal workers may have small metal fragments in the eye. You will be screened for these conditions before having any MRI scan. If you have a question about metal in your body, you should inform the staff. You will be asked to complete an MRI screening form before each MRI scan you have.

In addition, all magnetic objects (like watches, coins, jewelry, and credit cards) must be removed before entering the MRI scan room.

People with fear of confined spaces may become anxious during an MRI. Those with back problems may have back pain or discomfort from lying in the scanner. The noise from the scanner is loud enough to damage hearing, especially in people who already have hearing loss. Everyone having a research MRI scan will be fitted with hearing protection. If the hearing protection comes loose during the scan, you should let us know right away.

There are no known long-term risks of MRI scans.

Risks of Gadolinium enhanced MRI

During part of the MRI you will receive gadolinium, a contrast agent, through an intravenous (iv) catheter. It will be done for research and medical purposes.

It is not known if MRI with contrast is completely safe for a developing fetus. Therefore, all women of childbearing potential will have a pregnancy test performed no more than 24 hours before each MRI scan with contrast. The scan will not be done if the pregnancy test is positive.

The risks of an IV catheter include bleeding, infection, or inflammation of the skin and vein with pain and swelling.

Mild symptoms from gadolinium infusion occur in fewer than 1% of those who receive it and usually go away quickly. Mild symptoms may include coldness in the arm during the injection, a metallic taste, headache, and nausea. In an extremely small number, fewer than one in 300,000 people, more severe symptoms have been reported including shortness of breath, wheezing, hives, and lowering of blood pressure. You should not receive gadolinium if you previously had an allergic reaction to it. You will be asked about such allergic reactions before gadolinium is given.

People with kidney disease are at risk for a serious reaction to gadolinium contrast called “nephrogenic systemic fibrosis (NSF)”. This condition always involves the skin and can also involve the muscles, joints and internal organs. NSF has resulted in a very small number of deaths. A blood test of your kidney function may be done within the month before an MRI scan with gadolinium contrast. You will not receive gadolinium for a research MRI scan if your kidney function is below the safe level.

Most of the gadolinium contrast leaves the body in the urine. However, the FDA has issued a safety alert that indicates small amounts of gadolinium may remain in the body for months to years. The

effects of the retained gadolinium are not clear. At this time, retained gadolinium has not been linked to health risks in people whose kidneys work well. Some types of gadolinium contrast drugs are less likely to remain in the body than others. In this study, we will use the gadolinium contrast drugs that are less likely to remain in the body. We will also give you additional information called a "Medication Guide." Upon request, we will give you individual information about retained gadolinium we see on your studies.

What are the risks of radiation from being in the study?

During your participation in this research study, you will be exposed to radiation from CT scans and CT guided biopsies (optional). The amount of radiation exposure you will receive from these procedures is equal to approximately 10.4 rem. A rem is a unit of absorbed radiation.

Note: The 2 CT guided biopsies are optional and depend on your decision to agree to the biopsies and their location with your study doctor. Of the 10.4 rem, you will receive around 1.6 rems from the optional CT guided biopsies.

Every day, people are exposed to low levels of radiation that come from the sun and the environment around them. The average person in the United States receives a radiation exposure of 0.3 rem per year from these sources. This type of radiation is called "background radiation." This study will expose you to more radiation than you get from everyday background radiation. No one knows for sure whether exposure to these low amounts of radiation is harmful to your body.

The CT scans and CT guided biopsies that you get in this study will expose you to the roughly the same amount of radiation as 34.7 years' worth of background radiation. Being exposed to too much radiation can cause harmful side effects such as an increase in the risk of cancer. The risk depends on how much radiation you are exposed to. Please be aware that about 40 out of 100 people (40%) will get cancer during their lifetime, and 20 out of 100 (20%) will die from cancer. The risk of getting cancer from the radiation exposure in this study is 1.0 out of 100 (1.0%) and of getting a fatal cancer is 0.5 out of 100 (0.5%).

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 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.

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 have developed a method of using drugs such as M7824 to treat cancer that will be evaluated in this study. This means it is possible that the results of this study could lead to payments to NIH scientists and to the NIH. By

law, government scientists are required to receive such payments for their inventions. You will not receive any money from the development of this method of M7824 use.

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.

Genomic Data Sharing

As part of this research study, we will put your genomic data in a large database for broad sharing with the research community. These databases are commonly called data repositories. The information in this database will include but is not limited to genetic information, race and ethnicity, and sex. If your individual data are placed in one of these repositories, they will be labeled with a code and not with your name or other information that could be used to easily identify you, and only qualified researchers will be able to access them. These researchers must receive prior approval from individuals or committees with authority to determine whether these researchers can access the data.

Summary information about all of the participants included in this study (including you) is being placed in a database and will be available through open access. That means that researchers and non-researchers will be able to access summary information about all the participants included in the study, or summary information combined from multiple studies, without applying for permission. The risk of anyone identifying you with this information is very low.

NIH policies require that genomic data be placed in a repository for sharing. Therefore, we cannot offer you a choice of whether your data will be shared. If you do not wish to have your data placed in a repository, you should not enroll in this study.

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 are 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
- 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, Julius Strauss, MD, Phone: 301-480-0202, Email: julius.strauss@nih.gov. 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 should sign below if either:

1. **A short form consent process has been used to enroll a non-English speaking subject or**
2. **An oral presentation of the full consent has been used to enroll a blind or illiterate subject**

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: _____.