PRINCIPAL INVESTIGATOR: Julius Strauss, MD

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

STUDY SITE: NIH Clinical Center

Cohort: Screening

Consent Version: November 1, 2019

WHO DO YOU CONTACT ABOUT THIS STUDY?

Julius Strauss, MD
Phone: 301-480-0202
Email: julius.strauss@nih.gov

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?

You have come to the NIH in order to participate in a research study that is being conducted by the National Cancer Institute (NCI). For every research study, patients must fulfill a list of criteria, which are based primarily on their medical condition, in order to determine their suitability to participate in the research study. These eligibility criteria are necessary to ensure the integrity of the research study as well as make the study as safe as possible for the patients participating in the research study. In order to determine whether you meet these eligibility criteria for this protocol, we must perform a series of medical tests or procedures, such as blood tests, scans, and evaluation of your tissue or tumor specimens. These tests and procedures are designed to evaluate your disease

and to evaluate your general medical condition and the function of certain organs, such as the liver and kidneys.

The tests and procedures required for determining eligibility for this research study are described below. Your doctor or nurse will provide a description of these procedures or tests, the purpose of the procedures or tests and their risks.

Your doctor will explain the results of the screening procedures and tests once they are available. If the results of the testing indicate that you are eligible to participate in this research study, the research study will be discussed with you, and you will have the opportunity to decide whether you will participate in the research study. It is possible you may not be eligible for any research study based on the results of the procedures and tests. Under these circumstances, alternate therapies will be discussed or you will return to the care of your physician at home.

DESCRIPTION OF PROCEDURES AND TESTS

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.

History and Physical Examination: A summary of your medical record will be requested from your physician when you are initially referred to the NIH. In addition, a physician or nurse practitioner at the NIH will review your medical history with you, and you will have a detailed physical examination.

Blood Tests: Blood will be drawn from either an arm vein or a central venous access device, if you have one. This will be used for measurements of your blood counts, liver and kidney function, serum chemistries and other routine tests that determine whether you meet the requirements for participating in this protocol. Some of the blood may also be used for research tests that may not be available in other hospital clinical labs. These research tests may also be used to determine your eligibility for this study or they may be measured as a baseline for comparison changes in the test result after treatment. For women of childbearing potential this will include a pregnancy test. You will not be able to participate in this study if you are pregnant.

HIV, Hepatitis B, and Hepatitis C Testing: As part of this study, we will test you for infection with the human immunodeficiency virus (HIV; the virus that causes AIDS), Hepatitis B, and Hepatitis C. 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. If you are infected with HIV, Hepatitis B or C you will be able to participate in this study, with some caveats.

Urine Tests: Urine tests may include a routine urinalysis, pregnancy test, or a 24-hour urine collection to measure kidney function.

Quality of Life Assessment: You will be asked to answer questions about the effect of your illness on your behavior and everyday activities. This usually takes less than 30 minutes for you to complete.

MRI Scan: Magnetic Resonance Imaging or MRI is a scan that provides your doctor with multiple detailed pictures of the inside of the body. MRI does not use radiation. In order to visualize some

structures in the body, including tumors, a special dye or contrast agent may have to be injected into you intravenously. This test takes between 35-120 minutes to complete depending on the area of the body being scanned. You will lie on a stretcher with your head in a head rest to prevent movement during the scan. The stretcher will be placed in a strong magnetic field, but you should not feel anything from the magnet. You must remove anything that is metal before having this test. You will hear a loud, repetitive, thumping noise. Younger patients and patient who have difficulty holding still or tolerating being placed in a scanner, can receive medications to make them sleep through the procedure by a doctor called an anesthesiologist. If you are awake for the procedure, you will be able to communicate with a technician at all times and can request to be removed from the scanner at any time. MRI scans will only be used for select patients as necessary.

CT Scan: A Computerized Tomography or CT scan provides multiple detailed pictures of the inside of the body, like an MRI scan, but the CT scan uses radiation, similar to an X-ray. CT scans may be done with or without oral or intravenous contrast. The scan may take between 30-90 minutes to complete depending on the areas of the body being scanned and the type of scanner.

Biopsies: In order to establish or confirm your tumor(s) are HPV positive, we will need to sample a piece of tissue or tumor. Biopsies for HPV testing will only be taken if your previous tissue or pathology specimens cannot be obtained. Biopsies may be performed with a needle or surgery. The procedure is similar for each of these types of biopsies. After the skin is cleaned thoroughly, a small amount of numbing medicine is given as a shot into the skin over the biopsy site. If a needle biopsy is being done, a needle is put through the skin into the tumor, tissue or bone marrow to pull out a small piece that is trapped in the needle. If a surgical biopsy is required, depending on the location to be biopsied, this may be done in the operating room, clinic, or your room. The tissue or tumor is removed by cutting a small piece of it with a sharp knife or scalpel. This procedure will require stitches or staples to close the skin. For each of these biopsies, a bandage is placed over the biopsy site; the bandage should be changed daily for up to 7 days, when the doctor will remove the stitches.

RISKS OR DISCOMFORTS OF PARTICIPATION

The primary risks or discomforts of participating in this protocol are from complications caused by the screening tests and procedures. The following describes the most common risks of these tests and procedures. Your doctor or nurse will also discuss with you in detail any risks or discomforts of the procedures or test(s) you will be scheduled to undergo.

Blood tests: If blood needs to be drawn from a vein in your arm, this will cause some pain and may result in bruising at the site of the needle stick. If a bruise does form at the end of the needle puncture site, it will generally go away on its own without any treatment. If you have a central venous catheter, drawing blood from this line is associated with a small chance of infection, which could require treatment with antibiotics or, rarely, removal of the line. Side effects of blood draws may also include lightheadedness, and rarely, fainting. When large amounts of blood are collected, low red blood cell count (anemia) can develop.

Radiographic Tests: MRI and CT scans are common standard imaging tests used in the diagnosis and monitoring of many diseases and will only be used as necessary. Although these tests have been in use for many years, their potential long-term effects on the body are still being learned. The most common discomfort is the length of time a patient must lay still or flat while a scan is

being performed. Occasionally, a patient may become uncomfortable within the closed space of the scanners (claustrophobia), particularly during an MRI. If this occurs, cool air can be blown over you by a fan if desired or your doctor can order a medicine for you to help you relax during this scan. Keeping the room well lit can also reduce this claustrophobic feeling. If a contrast agent (the special dye) is given with the scan there is a small risk of having a reaction to the contrast. In the small group of patients who have a reaction, the most common symptoms are nausea, pain in the vein where the contrast was given, headache, a metallic or bitter taste in the mouth, and a warm or flushing feeling that lasts from 1-3 minutes. Rarely, these symptoms may require treatment. In very rare cases, people have had more severe allergic reactions that result in skin rashes, shortness of breath, wheezing, or lowering of the blood pressure. If you have had a reaction in the past, be sure to tell your doctor or nurse about it. The radiation dose you receive, if your scan includes the use of X-rays or radioactive chemicals, is within the safe limits defined by the NIH Radiation Safety Guidelines, and is considered essential for your medical care.

In some cases, you may require medicines to make you sleep so you can be still during the procedure. The risks from this sedation or anesthesia are dependent on the types of medication used. These risks will be fully explained to you prior to the procedure and a separate informed consent will be obtained for anesthesia.

An IV line may need to be inserted for administration of the contrast agent or anesthetic. This can cause pain at the site where the IV is placed and carries a small risk of bruising or infection.

Patients with a cardiac pacemaker, neural pacemaker, some types of surgical clips, cochlear implants, foreign metal objects, permanent retainers, or any iron-containing material within the body should not undergo MRI, because of the effect of the strong magnet on these objects.

Biopsy: Pain or discomfort may occur during and after the biopsy, even with the use of local anesthetics. There may be some mild burning sensation when the numbing medicine is injected into the skin. There may be bleeding from the biopsy site, which requires putting pressure on it to stop the bleeding. Rarely infections can occur at the biopsy site. This can be treated with antibiotics.

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. The amount of radiation you will receive in this procedure 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.

Blood and Tissue Samples: Specimens may be collected from you during the screening process, treatment, or follow-up and saved for the future to study scientific questions related to the research study that you are being evaluated for. If there are any risks to you or your family associated with these scientific studies, which are not covered in this consent form, your consent will be obtained before such studies are performed.

Unforeseeable and/or unknown risks/discomforts may occur.

POTENTIAL BENEFITS OF PARTICIPATION

Are there benefits to taking part in this study?

Although there may be no direct benefit to you for participating in the screening portion of the research study, it will determine whether you are eligible to participate in the experimental treatment portion of this research study. You will also have the benefit of a consultation with one of the NIH doctors to discuss your treatment, and, if you so desire, the results of these screening tests and procedures will be communicated to your personal physician.

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 PARTICIPATION

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

- if he/she believes that it is in your best interest
- 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. 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.

RESEARCH SUBJECT'S RIGHTS

Joining this research study is voluntary. You may ask the doctors and nurses any questions about your evaluation for eligibility. If you decide at any time that you do not want undergo screening any more, then tell us and we will stop.

USE OF SPECIMENS AND DATA FOR FUTURE RESEARCH

Specimens and data that we collect during the screening process may be saved for specific research studies for the research protocol that you are being evaluated for in order to prevent us from having to put you through another procedure in the future. These specimens and data will only be used for this purpose if you agree to participate in the primary research study. The consent for the primary research study will explain the studies that will be performed with the extra tissue or tumor.

We would not normally put patients through a potentially risky procedure for the sole purpose of obtaining samples for research. However, if you are having a procedure or test that is necessary to make a diagnosis, assess the extent of a tumor, or to treat the tumor, we would like to store left over specimens 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.

Some of 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.

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.

The NCI generally does not cover expenses during screening. If you are scheduled for and begin treatment, the NCI will cover the cost for some of your expenses. 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 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: _____.