THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center

Informed Consent

INFORMED CONSENT/AUTHORIZATION FOR PARTICIPATION IN RESEARCH WITH OPTIONAL PROCEDURES

Phase I/II Study of M7824 plus curative intent re-irradiation with Stereotactic Body Radiation Therapy (SBRT) in patients with local-regionally recurrent head and neck squamous cell carcinoma 2019-0608

Subtitle: Re-irradiation 2019-0608

Study Chair: Renata Ferrarotto

_____ _____
Participant's Name Medical Record Number

This is an informed consent and authorization form for a research study. It includes a summary about the study. A more detailed description of procedures and risks is provided after the summary.

STUDY SUMMARY

The goal of this clinical research study is to learn if the combination of M7824 with stereotactic body radiation therapy (SBRT) can help to control head and neck squamous cell carcinoma (HNSCC) that is recurrent (has come back). The safety of the study drug will also be studied

This is an investigational study. M7824 is not FDA approved or commercially available. It is currently being used for research purposes only. The study doctor can describe how the study drug is designed to work. SBRT is delivered using FDA-approved and commercially available methods. It is considered investigational to use M7824 in combination with SBRT to treat HNSCC.

The study drug(s) may help to control the disease. Future patients may benefit from what is learned. There may be no benefits for you in this study.

Your participation is completely voluntary. Before choosing to take part in this study, you should discuss with the study team any concerns you may have, including side effects, potential expenses, and time commitment. If you take part in this study, you may experience side effects, some of which may be severe or fatal.

You can read a list of potential side effects below in the Possible Risks section of this consent.

You may receive the study drug for up to 1 year.

M7824 will be provided at no cost to you while you are on study. You and/or your insurance provider will be responsible for the costs of radiation therapy.

You may choose not to take part in this study. Instead of taking part in this study, you may choose to receive chemotherapy, radiation, surgery, and/or a combination of these approaches. You may choose to receive other investigational therapy, if available. You may choose not to have treatment for cancer at all. In all cases, you will receive appropriate medical care, including treatment for pain and other symptoms of cancer.

1. STUDY DETAILS

Screening Tests

Signing this consent form does not mean that you will be able to take part in this study. The following screening tests will help the doctor decide if you are eligible:

- You will have a physical exam, including a skin exam by a dermatologist. During the physical exam, the full range of motion of your neck will be checked.
- You will have a CT or MRI scan of the neck to check the status of the disease. If the doctor thinks it is needed, you may also have a CT scan of the abdomen and pelvis and/or an MRI scan of the brain.
- Blood (about 4-6 teaspoons) will be drawn for routine tests.
- You will have an EKG to check your heart function.
- You will have a tumor biopsy for biomarker testing. Your doctor will tell you what kind of biopsy you will have. Biomarkers are found in the blood/tissue and may be related to your reaction to the study drug.
- You will have your photo taken for identification. This photo will not be provided to the study sponsor.
- Your swallowing function will be tested with a special type of x-ray called a modified barium swallow (MBS). During the test, you will eat and drink foods and liquids mixed with a "contrast" chemical called barium that will make your throat more visible in the x-rays. A special x-ray tube will be connected to a television screen to allow the doctor to watch the foods and liquids pass from your mouth and down your throat.
- You will have a video-strobe procedure to check your vocal cords. To perform a video-strobe procedure, a small camera will be inserted into your throat through your nose or mouth. You will be awake for this procedure, and the study staff will give you the option of receiving a numbing spray for your nose and/or throat.
- You will have swallowing therapy. You will learn swallowing exercises that will help with possible swallowing problems during and after the study.
- You will complete questionnaires about your swallowing capacity, symptoms, and quality of life. These should take about 20 minutes to complete.

The study doctor will discuss the screening test results with you. If the screening tests show that you are not eligible to take part in the study, you will not be enrolled. Other treatment options will be discussed with you.

Up to 21 people will be enrolled in this study. All will take part at MD Anderson.

Study Drug Administration

Each study cycle will be 28 days long. There are 12 cycles in total. If you are found to be eligible to take part in this study, you will receive M7824 by vein over about 1 hour on Days 1 and 15 of every cycle.

You will receive radiation therapy for 2 weeks in a row (Monday, Wednesday, and Friday) starting on Day 15 of Cycle 1.

During Cycle 1, you will be given standard drugs to help decrease the risk of side effects. If your doctor thinks they are needed, you may also receive them during Cycle 2 and beyond. You may ask the study staff for information about how the drugs are given and their risks.

You will no longer be able to take the study drug(s) if the disease gets worse, if intolerable side effects occur, or if you are unable to follow study directions.

Your participation on the study will be over after the follow-up visits.

Study Visits

At each study visit:

- You will have a physical exam.
- Blood (about 4-6 teaspoons) will be drawn for routine tests. If you can become pregnant, blood (about ½ teaspoon) will be drawn for a pregnancy test. This test will be repeated every 3 months.

On **Day 1 of Cycle 1:**

- Blood (about 1-2 teaspoons) will be drawn before and after your dose of study drug for pharmacokinetic (PK) testing. PK testing measures the amount of study drug in the body at different time points.
- Blood (about 6-8 teaspoons) will be drawn for immune system and biomarker tests.

On **Day 15 of Cycles 1 and beyond:**

- You will have a skin exam done by a dermatologist. This exam will be repeated every 3 months.
- During Cycles 1 and 2 only, blood (about 5-6 teaspoons) will be drawn for biomarker testing.

At Some Point During Cycles 3-6:

- You will have a modified barium swallow.
- You will have the full range of motion of your neck checked.

- You will have a video-strobe procedure to check the status of the disease.
- You will complete questionnaires about your symptoms. These should take about 10-15 minutes to complete.

You will also have study visits on **Day 1 of Cycles 2, 3, 6, and 12**.

- Blood (about 5-6 teaspoons) will be drawn on Day 1 of Cycles 2, 3, 6, and 12 for biomarker testing.
- On Day 1 of Cycle 3, blood (about 1-2 teaspoon) will be drawn before and after your dose of study drug for PK testing. On Day 1 of Cycle 2 and either Day 1 of Cycle 6 or at the End of Treatment Visit (whichever comes first), PK blood samples will only be drawn before your dose.
- On either Day 1 of Cycle 6 or at the End of Treatment Visit (whichever comes first), blood (about 1-2 teaspoons) will be drawn for immune system testing.

You will have an MRI or CT scan of your chest or neck to check the status of the disease. If the doctor thinks it is needed, you may also have a CT scan of the abdomen and pelvis and/or an MRI scan of the brain. These scans will be repeated on Months 3, 6, 9, and 12 only.

If the disease gets worse at any time, you will have a tumor biopsy for biomarker testing.

Follow-Up

About 90 days after your last dose of M7824:

- You will have a physical exam. This will include a skin exam done by a dermatologist.
- Blood (about 4-6 teaspoons) will be drawn for routine tests.

If the disease got worse, blood (about 5-6 teaspoons) will be drawn for biomarker testing.

Long-term Follow-Up

About 18 and 24 months after your last dose of study drug:

- You will have a physical exam. This will include a skin exam done by a dermatologist.
- You will have an MRI or CT scan of your chest or neck to check the status of the disease. If the doctor thinks it is needed, you may also have a CT scan of the abdomen and pelvis and/or an MRI scan of the brain.
- You will have a video-strobe procedure to check your vocal cords.
- You will have your medical photo taken for identification.
- You will complete questionnaires about your symptoms and quality of life. These should take about 10-15 minutes to complete.
- If the disease got worse, blood (about 6-7 teaspoons) will be drawn for biomarker and immune testing.

2. POSSIBLE RISKS

While on this study, you are at risk for side effects. You should discuss these with the study doctor. The more commonly occurring side effects are listed in this form, as are rare but serious side effects. You may also want to ask about uncommon side effects that have been observed in small numbers of patients but are not listed in this form. Many side effects go away shortly after treatment is stopped, but in some cases side effects may be serious, long-lasting or permanent, and may even result in hospitalization and/or death.

Side effects will vary from person to person, and some may occur after you have stopped receiving treatment. Tell the study staff about any side effects you may have, even if you do not think they are related to the study drugs/procedures.

M7824 Side Effects

Occurring in more than 10% of patients

• fever • swelling • fatigue • headache • itching • skin rash	• abdominal pain • loss of appetite • constipation • nausea/vomiting • diarrhea	• nosebleed • abnormal liver test (possible liver damage) • decreased strength • difficulty breathing • cough

ML824 may cause low red blood cell counts. A low red blood cell count (anemia) may cause difficulty breathing and/or fatigue. You may need a blood transfusion.

Frequency Unknown

• wound healing problems • skin thickening • pre-cancerous skin lesions	• bleeding from mucous membranes (possible bleeding gums, blood in the urine, and/or blood in a cough)	• bleeding in or from the tumor

M7824 may cause you to develop another type of cancer (such as squamous cell carcinoma, a type of skin cancer).

M7824 may also cause infusion reactions. Symptoms may include chills, shaking, fever, flushing, back pain, abdominal pain, difficulty breathing, wheezing, low blood pressure, and/or hives. In general, these reactions are mild to moderate and generally resolve after either slowing or stopping the infusion and/or by treatment with other drugs. In rare cases, infusion-related reactions might be severe and life-threatening, and require advanced cardiac life support and could be fatal. You may be given drugs to help prevent infusion reactions.

Based on how the study drug is designed, it may also cause serious side effects that affect your immune system. Some of these side effects start as inflammation in different areas of the body like the skin, hormone glands, pancreas, or appendix. Tell the study staff right away if you have diarrhea, nausea, vomiting, blurred vision, dizziness, fainting, or you are feeling cold all the time.

Radiation Therapy Side Effects

It is not known how often the side effects of radiation therapy may occur.

• swelling • swelling of the arms or torso • skin changes (possible dryness, itching, peeling, and/or blistering)	• hair loss at the treatment site • mouth problems • trouble swallowing • nausea • vomiting • diarrhea	• urinary and/or bladder changes • sexual changes • inability to produce children • joint problems • secondary cancers

Radiation therapy may cause you to develop another type of cancer. Side effects may not occur for up to 6 months after radiation therapy is over. Side effects will vary depending on what part of the body is receiving radiation therapy.

Blood draws may cause pain, bleeding, and/or bruising. You may faint and/or develop an infection with redness and irritation of the vein at the site where blood is drawn. Frequent blood collection may cause anemia (low red blood cell count), which may create a need for blood transfusions.

Having **biopsies** performed may cause pain, bruising, bleeding, redness, low blood pressure, swelling, and/or infection at the site of the biopsies. An allergic reaction to the anesthetic may occur. A scar may form at the biopsy site.

Drinking the contrast agent for the **modified barium swallow** may cause constipation. You can avoid constipation by drinking plenty of water (or putting water through your feeding tube if you cannot drink by mouth) after the procedure. The **x-rays** taken during the modified barium swallow send a small amount of radiation though the body. All radiation adds up over a lifetime and may increase the risk of a new cancer forming.

Questionnaires may contain questions that are sensitive in nature. You may refuse to answer any question that makes you feel uncomfortable. If you have concerns about completing the questionnaire, you are encouraged to contact your doctor or the study chair.

CT scans send x-rays through the body at many different angles. You will be exposed to a small dose of radiation. All radiation adds up over a lifetime and may increase the risk of new cancer forming. Some people may feel “closed in” while lying in the scanner. However, the scanner is open at both ends, and an intercom allows you to

talk with doctors and staff. If you feel ill or anxious during scanning, doctors and/or radiology technicians will give comfort, or the scanning will be stopped. When a CT scan of the abdominal area is taken, material may be inserted into the rectum to better define the bowel. You will usually drink liquid to help define various abdominal organs. This may cause nausea and/or vomiting. Solution may also be given by vein to make the x-ray pictures more accurate. This may cause an uncomfortable feeling of warmth, nausea, and/or severe allergic reactions. The solution injection may also cause pain, bleeding, bruising, hives, and/or itching.

During the **MRI**, you may feel mild vibrations throughout your body. The machine will produce a loud knocking noise. This is normal. You will be given earplugs to protect your ears. Some people, especially those who tend to feel uncomfortable in small or closed spaces, may feel “closed in” and become anxious while in the scanner. The scanner has an intercom, which will allow you to speak to the staff during the procedure. If you feel ill or anxious during scanning, tell the MRI staff and the scanning will be stopped if you wish. The MRI will require a catheter to be inserted into one of your veins in order to inject the MRI contrast agent. This may cause skin irritation, bleeding, and/or infection. You may have an allergic reaction to the contrast agent.

The magnetic field used in MRI scanning may harm you if you have certain types of metal in your body (as might be found in pacemakers, neurostimulators, or certain clips). It may cause problems with devices, such as pacemakers. If you have metal in your body or devices such as a pacemaker, you should discuss this with the study doctor.

EKGs may cause discomfort while lying on the exam table, and the tape on the EKG pads may cause skin irritation.

This study may involve unpredictable risks to the participants.

Pregnancy Related Risks
Taking part in this study can result in risks to an unborn or breastfeeding baby, so you should not become pregnant, breastfeed a baby, or father a child while on this study. You must use birth control during the study if you are sexually active.

Birth Control Specifications: If you can become pregnant, you must use appropriate birth control methods. Your doctor will talk with you about appropriate birth control methods.

Males: Tell the doctor right away if your partner becomes pregnant or suspects pregnancy.

Females: If you are pregnant, you will not be enrolled on this study. If you become pregnant or suspect that you are pregnant, you must tell your doctor right away.

Getting pregnant will result in your removal from this study.

3. COSTS AND COMPENSATION

If you suffer injury as a direct result of taking part in this study, MD Anderson health providers will provide medical care. However, this medical care will be billed to your insurance provider or you in the ordinary manner. You will not be reimbursed for expenses or compensated financially by MD Anderson or EMD Serono for this injury. You may also contact the Chair of MD Anderson's IRB at 713-792-6477 with questions about study-related injuries. By signing this consent form, you are not giving up any of your legal rights.

Certain tests, procedures, and/or drugs that you may receive as part of this study may be without cost to you because they are for research purposes only. However, your insurance provider and/or you may be financially responsible for the cost of care and treatment of any complications resulting from the research tests, procedures, and/or drugs. Standard medical care that you receive under this research study will be billed to your insurance provider and/or you in the ordinary manner. Before taking part in this study, you may ask about which parts of the research-related care may be provided without charge, which costs your insurance provider may pay for, and which costs may be your responsibility. You may ask that a financial counselor be made available to you to talk about the costs of this study.

Samples that are collected from you in this study may be used for the development of treatments, devices, new drugs, or patentable procedures that may result in commercial profit.

There are no plans to compensate you for any patents or discoveries that may result from your participation in this research.

You will receive no compensation for taking part in this study.

Additional Information

4. You may ask the study chair (Dr. Renata Ferrarotto, at 713-792-6363) any questions you have about this study. You may also contact the Chair of MD Anderson's Institutional Review Board (IRB - a committee that reviews research studies) at 713-792-6477 with any questions that have to do with this study or your rights as a study participant.

5. You may choose not to take part in this study without any penalty or loss of benefits to which you are otherwise entitled. You may also withdraw from participation in this study at any time without any penalty or loss of benefits. If you decide you want to stop taking part in the study, it is recommended for your safety that you first talk to your doctor. If you withdraw from this study, you can still choose to be treated at MD Anderson.

6. This study or your participation in it may be changed or stopped without your consent at any time by the study chair, EMD Serono, the U.S. Food and Drug Administration (FDA), the Office for Human Research Protections (OHRP), or the IRB of MD Anderson.

7. You will be informed of any new findings or information that might affect your willingness to continue taking part in the study, including the results of all of your standard tests performed as part of this research, and you may be asked to sign another informed consent and authorization form stating your continued willingness to participate in this study.

8. MD Anderson may benefit from your participation and/or what is learned in this study.

9. This study is sponsored and/or supported by: EMD Serono.

10. In a medical emergency, you may be cared for by someone who has a financial interest with the study sponsor(s)/supporter. If you have any questions about this, you may call the IRB at 713-792-6477.

Future Research

Data

Your personal information is being collected as part of this study. These data may be used by researchers at MD Anderson and EMD Serono and/or shared with other researchers and/or institutions for use in future research.

Samples

Samples (such as blood and/or tissue) are being collected from you as part of this study. Researchers at MD Anderson may use any leftover samples that are stored at MD Anderson in future research. Leftover samples stored by EMD Serono may be used in future research.

Before being used or shared for future research, every effort will be made to remove your identifying information from any data and/or research samples. If all identifying information is removed, you will not be asked for additional permission before future research is performed.

In some cases, all of your identifying information may not be removed before your data or research samples are used for future research. If future research is performed at MD Anderson, the researchers must get approval from the Institutional Review Board (IRB) of MD Anderson before your data and/or research samples can be used. At that time, the IRB will decide whether or not further permission from you is required. The IRB is a committee of doctors, researchers, and community members that is responsible for protecting study participants and making sure all research is safe and ethical.

If this research is not performed at MD Anderson, MD Anderson will not have oversight of any data and/or samples.

Genetic Research

Research samples collected from you as part of this study may be used for genetic research, which may include whole genome sequencing. Whole genome sequencing is a type of testing in which researchers study your entire genetic makeup (DNA).

This may help researchers learn how changes in the ordering of genes may affect a disease or response to treatment.

Authorization for Use and Disclosure of Protected Health Information (PHI):

A. During the course of this study, MD Anderson will be collecting and using your PHI, including identifying information, information from your medical record, and study results. For legal, ethical, research, and safety-related reasons, your doctor and the research team may share your PHI with:

- Federal agencies that require reporting of clinical study data (such as the FDA, National Cancer Institute [NCI], and OHRP)
- The IRB and officials of MD Anderson
- EMD Serono, who is a sponsor or supporter of this study, and/or any future sponsors/supporters of the study
- Any future licensees of the study technology
- Study monitors and auditors who verify the accuracy of the information
- Individuals who put all the study information together in report form

Study sponsors and/or supporters receive limited amounts of PHI. They may also view additional PHI in study records during the monitoring process. MD Anderson's contracts require sponsors/supporters to protect this information and limit how they may use it.

B. Signing this consent and authorization form is optional but you cannot take part in this study or receive study-related treatment if you do not agree and sign.

C. MD Anderson will keep your PHI confidential when possible (according to state and federal law). However, in some situations, the FDA could be required to reveal the names of participants.

Once disclosed outside of MD Anderson, federal privacy laws may no longer protect your PHI.

D. The permission to use your PHI will continue indefinitely unless you withdraw your authorization in writing. Instructions on how to do this can be found in the MD Anderson Notice of Privacy Practices (NPP) or you may contact the Chief Privacy Officer at 713-745-6636. If you withdraw your authorization, you will be removed from the study and the data collected about you up to that point can be used and included in data analysis. However, no further information about you will be collected.

E. 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.

CONSENT/AUTHORIZATION

I understand the information in this consent form. I have had a chance to read the consent form for this study, or have had it read to me. I have had a chance to think about it, ask questions, and talk about it with others as needed. I give the study chair permission to enroll me on this study. By signing this consent form, I am not giving up any of my legal rights. I will be given a signed copy of this consent document.

SIGNATURE OF PARTICIPANT DATE

PRINTED NAME OF PARTICIPANT

LEGALLY AUTHORIZED REPRESENTATIVE (LAR)

The following signature line should only be filled out when the participant does not have the capacity to legally consent to take part in the study and/or sign this document on his or her own behalf.

SIGNATURE OF LAR DATE

PRINTED NAME and RELATIONSHIP TO PARTICIPANT

WITNESS TO CONSENT

I was present during the explanation of the research to be performed under Protocol **2019-0608**.

SIGNATURE OF WITNESS TO THE VERBAL CONSENT PRESENTATION (OTHER THAN PHYSICIAN OR STUDY CHAIR) DATE

A witness signature is only required for vulnerable adult participants. If witnessing the assent of a pediatric participant, leave this line blank and sign on the witness to assent page instead.

PRINTED NAME OF WITNESS TO THE VERBAL CONSENT

PERSON OBTAINING CONSENT

I have discussed this research study with the participant and/or his or her authorized representative, using language that is understandable and appropriate. I believe that I have fully informed this participant of the nature of this study and its possible benefits and risks and that the participant understood this explanation.

PERSON OBTAINING CONSENT DATE

PRINTED NAME OF PERSON OBTAINING CONSENT

TRANSLATOR

I have translated the above informed consent as written (without additions or subtractions) into_____and assisted the people
(Name of Language)
obtaining and providing consent by translating all questions and responses during the consent process for this participant.

_____ _____
NAME OF TRANSLATOR SIGNATURE OF TRANSLATOR DATE

☐ Please check here if the translator was a member of the research team. (If checked, a witness, other than the translator, must sign the witness line below.)

_____ _____
SIGNATURE OF WITNESS TO THE VERBAL TRANSLATION DATE
(OTHER THAN TRANSLATOR, PARENT/GUARDIAN,
OR STUDY CHAIR)

_____
PRINTED NAME OF WITNESS TO THE VERBAL TRANSLATION