MC1973 / 19-011871

A Phase II Study of Hypofractionated Pre-Operative Radiation Therapy for Localized, Resectable Soft Tissue Sarcoma of the Extremity or Superficial Trunk

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RESEARCH PARTICIPANT CONSENT AND PRIVACY AUTHORIZATION FORM

Study Title: MC1973: A Phase II Study of Hypofractionated Pre-Operative Radiation Therapy for Localized, Resectable Soft Tissue Sarcoma of the Extremity or Superficial Trunk

IRB#: 19-011871

Principal Investigator: Safia Ahmed, M.D. and Colleagues

Key Study Information

This section provides a brief summary of the study. It is important for you to understand why the research is being done and what it will involve before you decide. **Please take the time to read the entire consent form carefully and talk to a member of the research team before making your decision.** You should not sign this form if you have any questions that have not been answered.	
It's Your Choice	This is a research study. Being in this research study is your choice; you do not have to participate. If you decide to join, you can still stop at any time. You should only participate if you want to do so. You will not lose any services, benefits or rights you would normally have if you choose not to take part.
Research Purpose	The purpose of this research study is to find out what effects, good and/or bad, preoperative "hypofractionated" radiation therapy (RT) has, as compared to preoperative "conventional" fractionated radiation therapy, has on wound complications associated with surgery. Hypofractionated is a shorter radiation therapy treatment length (fewer radiation treatment days) and administers the total radiation dose as larger daily doses, compared to conventionally fractionated therapy, for your soft tissue sarcoma of the extremity or superficial trunk. You are being asked to take part in this research study because you have a soft tissue sarcoma of the extremity or superficial trunk. Your doctor has recommended that you receive radiation therapy and surgery to treat the sarcoma.

What's Involved	Study participation involves radiation treatment, surgery of your sarcoma, CT or MRI scans, pregnancy testing if you are a woman of childbearing potential and quality of life questionnaires. Your participation in this study will last approximately 5 years. During the 5 years, we will follow you and your health to gather information on any short or long-term side effects, good and/or bad, that may have occurred from the radiation treatment or from the surgery.
Key Information	The purpose of this study is to evaluate the safety and effects of receiving pre-operative hypofractionated radiation therapy course of 15 treatment days compared to 25 conventional fractionation treatment days, for soft tissue sarcomas. We will also be looking at how the different RT treatments affect acute wound complication rates after surgery. While you are participating in this study, you have the following tests and procedures. If you have any of these tests or procedures in the allowable time-frame, you may not need to repeat them. Tests and procedures you will have done are: • History and physical exam • Hypofractionated Radiation Treatment • MRI or CT • Review scans for staging and treatment plan • Surgery • Pregnancy testing – if you are woman of childbearing potential • Assessment of your health and wellbeing • Patient reported outcomes questionnaire Possible risks and discomforts associated with radiation are divided into early side effects (those happening during or shortly after RT), and late side effects (those happening well after the completion of RT). All risks and discomforts are listed in detail below. We would like to follow your health and wellbeing for up to 5 years total. This study may not make your health better. However, with your help, researchers will better understand the side effects from each treatment and possibly lessen those side effects for future treatments.

	You do not have to be in this study to receive treatment for your sarcoma.
Learn More	If you are interested in learning more about this study, read the rest of this form carefully. The information in this form will help you decide if you want to participate in this research or not. A member of our research team will talk with you about taking part in this study before you sign this form. If you have questions at any time, please ask us.

Making Your Decision

Taking part in research is your decision. Take your time to decide. Feel free to discuss the study with your family, friends, and healthcare provider before you make your decision. Taking part in this study is completely voluntary and you do not have to participate.

If you decide to take part in this research study, you will sign this consent form to show that you want to take part. We will give you either a printed or electronic copy of this form to keep. A copy of this form will be put in your medical record.

For purposes of this form, Mayo Clinic refers to Mayo Clinic in Arizona, Florida and Rochester, Minnesota; Mayo Clinic Health System; and all owned and affiliated clinics, hospitals, and entities.

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Contact Information

If you have questions about …	You can contact …
▪ Study tests and procedures ▪ Materials you receive ▪ Research-related appointments ▪ Research-related concern or complaint ▪ Research-related injuries or emergencies ▪ Withdrawing from the research study	**Principal Investigator:** Meng Welliver, M.D. (Rochester) **Phone:** (507) 284-2669 Mayo Clinic Rochester 200 First Street SW Rochester, MN 55905 **Principal Investigator:** Safia Ahmed, M.D. (Arizona) **Phone:** (480) 342-2000 5777 E. Mayo Blvd Phoenix, AZ 85054 **Principal Investigator** Michael Rutenberg, M.D., Ph.D. (Florida) **Phone:** (904) 953-1003 4500 San Pablo Road Jacksonville, FL 32224 Study Team Contact: RSTRADONCRES@mayo.edu
▪ Rights of a research participant	**Mayo Clinic Institutional Review Board (IRB)** **Phone:** (507) 266-4000 **Toll-Free:** (866) 273-4681
▪ Rights of a research participant ▪ Any research-related concern or complaint ▪ Use of your Protected Health Information ▪ Stopping your authorization to use your Protected Health Information ▪ Withdrawing from the research study	**Research Participant Advocate (RPA)** **(The RPA is independent of the Study Team)** **Phone:** (507) 266-9372 **Toll-Free:** (866) 273-4681 **E-mail:** researchparticipantadvocate@mayo.edu
▪ Billing or insurance related to this research study	**Patient Account Services** **Toll-Free:** (844) 217-9591

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Other Information:
A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law, and is also available on http://mayo.edu/research/clinical-trials. 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.

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

You are being asked to take part in this research study because you have soft tissue sarcoma of the extremity (arms, hands, legs or feet) or superficial trunk. Your doctor has recommended that you receive radiation therapy and surgery to treat the sarcoma.

The plan is to have about 120 people take part in this study at Mayo Clinic.

Why is this research study being done?

The purpose of this research study is to find out what effects, good and/or bad, preoperative hypofractionated radiation therapy has on wound complications after surgery as compared to preoperative conventional fractionated radiation therapy.

Information you should know

Who is Funding the Study?
The Department of Radiation Oncology is funding this study.

Information Regarding Conflict of Interest:
Your healthcare provider may be referring you to this research study. If your healthcare provider is also an investigator on this study, there is the chance that his or her responsibilities for the study could influence his or her recommendation for your participation.

If you prefer, your healthcare provider will be happy to refer you to another investigator on the research study team for you to decide if you want to participate in the study and to see you for the research study activities while you are in the study.

How long will you be in this research study?

You will be in the study throughout the course of your radiation treatments, surgery and for approximately 5 years after your surgery.

What will happen to you while you are in this research study?

You will need to have the following exams, tests or procedures to find out if you can be in the study.

These exams, tests or procedures are part of regular clinical care and may be done even if you do not join the study. If you have had some of them recently, they may not need to be repeated. This will be up to the Principal Investigator. The visits, tests and procedures will be discussed below, in detail.

The **Pre-treatment/Baseline Visit** will take about 1 -2 days. During this visit, we will do some tests and procedures to see if you are eligible to take part in this research study.
The Principal Investigator will review the results of these tests and procedures. If you are not eligible, the Principal Investigator will tell you why.

Tests and procedures being done:

- Ask you about your medical history
- Give you a physical exam, including height, weight, and "vital signs" (blood pressure, temperature, heart and breathing rates)
- MRI or CT scan
- Chest CT
- Pregnancy Testing (serum) for pregnancy, if you are a female able to become pregnant
- Symptom Assessment
- PROMIS & TESS QOLs - Give you a questionnaire to fill out about your general health, well-being and quality of life

Hypofractionated Radiation Treatment

- You will be receiving pre-operative hypofractionated radiation therapy course of 15 treatment days, rather than 25 treatment days that conventional fractionation treatment would be, for soft tissue sarcomas.

The **Pre-Operative/Post RT Assessment** Visit will take about 1 -2 days. During this visit, we will

- Ask you about your medical history
- Give you a physical exam, including height, weight, and "vital signs" (blood pressure, temperature, heart and breathing rates)
- MRI or CT scan
- Chest CT
- Symptom Assessment
- PROMIS & TESS QOLs - Give you a questionnaire to fill out about your general health, well-being and quality of life

The **Post-Operative Assessment** will occur 4-8 weeks after surgery.

- Pathology review
- Wound Complication Assessment

The **1 & 2 Year Post Surgery Assessments** (6 Months Post-Surgery) visit will take about 1 -2 days. During this visit, we will

- Ask you about your medical history
- Give you a physical exam, including height, weight, and "vital signs" (blood pressure, temperature, heart and breathing rates)
- MRI or CT scan
- Chest CT
- Symptom Assessment
- PROMIS & TESS QOLs - Give you a questionnaire to fill out about your general health, well-being and quality of life

The **3, 4 & 5 Year Post Surgery Assessments** (Annually Post Surgery) visit will take about 1 -2 days. During this visit, we will

- Ask you about your medical history
- Give you a physical exam, including height, weight, and "vital signs" (blood pressure, temperature, heart and breathing rates)
- MRI or CT scan
- Chest CT
- Symptom Assessment
- PROMIS & TESS QOLs - Give you a questionnaire to fill out about your general health, well-being and quality of life

<u>If your disease gets worse, you will not need to complete any more research study visits and we will just ask to collect health information about you for up to five years.</u>

Questionnaires
During this study, we will ask you to fill out questionnaires. We hope that you will answer all of the questions, but you can skip any questions you don't want to answer. The questionnaires will take about 15-20 minutes to complete.

Tests done only for research purposes are not meant to provide clinical information or help care for you. The results are only important for research. Therefore, the results of tests done with your information and samples will not be provided to you. In the rare event that a finding might affect the health of you or your family, we will contact you and you can choose whether to receive or refuse the information. If you decide to follow up and further medical testing or care is needed, the costs will be billed to you or your insurance.

What are the possible risks or discomforts from being in this research study?

You will be exposed to radiation from your radiation treatment plan. The amount of radiation has a low risk of harmful effects.

Radiation Risks

Early side effects – Likely:

- Mild (slight redness) to severe (painful skin blistering) skin reactions
- Tiredness
- Reduction in blood counts, which may result in bleeding or infection
- Diarrhea (if the pelvis is treated)
- Wound healing delay after surgery

Late Side Effects – Likely:

- Skin in the treated area may appear tanned and may stay this way for a number of years after radiation.
- Tissues in the treated area may feel hard and woody: If this occurs, it is likely to be permanent.
- Skin in the treated area, especially over the shin and elbow, may heal more slowly if injured or bruised.
- Pain in a treated limb, which may occur one to several years after completion of treatment and may last for many years.
- Swelling, which may occur in the first year after treatment; in many patients the swelling will go away.

- Some patients will have temporary swelling after they exercise. Some patients will have continual swelling and will need to use elastic stockings. If this swelling is severe, it may require the use of a pump that pushes swelling out of the arm or leg.
- Bones are more likely to break.

L*ess Common*:
- Bowel (intestine) injury
- Osteoradionecrosis (bone death)
- Bony fracture in the radiation field

Less Likely:
- Injury to the bowel (if abdominal wall is treated), such as a narrowing of the bowel or hole in the bowel and which may require surgery
- If the heart, lung, liver, or stomach is in the treatment area, these organs could be damaged, which may result in:
    - Heart: dizziness, weakness, shortness of breath, chest pressure and/or pain, and/or irregular heart beat
    - Lung: Inflammation of the lungs, cough, shortness of breath
    - Liver and stomach: Tiredness, digestion problems, pain in the upper abdomen, bloating, constipation, nausea and/or vomiting

Rare but serious:
- Injury to the spinal cord (if the back area is treated), which may result in weakness, muscle contraction, and/or loss of muscle function,
- Radiation can cause tumors in the tissues that were treated. This is rare (1 in 2,000) in adults but can occur many years after treatment.

Surgery Risks

Complications may occur when tumors are removed from the legs or arms whether or not radiation is given. If you have other health problems such as heart disease, lung disease, or diabetes at the time of surgery, you may have an increased risk for having heart or lung problems during surgery. Rarely, these complications may result in death.

With surgery alone, some patients also will have problems with the healing of their wound after removal of the tumor. However, the addition of radiation may increase the risk of wound healing problems. However, most patients will heal satisfactorily.

Likely:

- Decreased function of the arm or leg because of muscle, nerve, or skin damage

Less Likely:

- Treatment of large tumors with radiation and surgery may result in infection or lack of healing, which could lead to a longer time in the hospital and rarely, to surgically removing the arm or leg.

Early: Wound complications are expected to develop in about one third of patients. Other common radiation adverse events include:

- Fatigue
- Regional alopecia (hair loss)
- Diarrhea
- Skin erythema (skin redness, blistering and/or peeling)
- Desquamation within the treatment fields
- Reduction in blood counts

Long-term: Common long-term treatment adverse events include:

- Lymphedema of the extremity receiving radiation and surgery (tissue swelling)
- Subcutaneous fibrosis (skin thickening/scarring)
- Joint stiffness

There also is a risk of cancer occurring in a previously irradiated field.

Birth Control (Male & Female)

If you are sexually active and able to become pregnant or father a child, you must use birth control while undergoing radiation and you must agree to use one of the birth control methods listed below, prior to starting any radiation therapy:

- Hormonal methods, such as birth control pills, patches, injections, vaginal ring, or implants
- Barrier methods (such as a condom or diaphragm) used with a spermicide (a foam, cream, or gel that kills sperm)
- Intrauterine device (IUD)
- Abstinence (no sex)

If you are a female of childbearing potential, you must have a negative pregnancy test in order to participate in this study unless you cannot become pregnant. You should not become pregnant while undergoing radiotherapy on this study because the radiation therapy can affect an unborn baby. If you are pregnant, you will not be allowed to participate.

You should not become pregnant while on this study, but if you should become pregnant while you are on this study, you must tell your study doctor immediately.

Standard of Care Risks
Your doctor will discuss the risks of tests and procedures that are part of your standard clinical care including imaging and blood draws.

Loss of Confidentiality Risks
As with all research, there is a chance that confidentiality could be compromised; however, we take precautions to minimize this risk.

Are there reasons you might leave this research study early?

You may decide to stop at any time. You should tell the Principal Investigator if you decide to stop and you will be advised whether any additional tests may need to be done for your safety.

In addition, the Principal Investigator or Mayo Clinic may stop you from taking part in this study at any time:

- if it is in your best interest,
- if you don't follow the study procedures,
- if the study is stopped.

If you leave this research study early, or are withdrawn from thestudy, we will ask your permission to still collect health information about you for up to five years after you receive study treatment. If you do not agree to allow us to collect health information, no additional information about you will be collected; however, information already collected about you in the study may continue to be used.

We will tell you about any new information that may affect your willingness to stay in the research study.

What if you are injured from your participation in this research study?

Where to get help:
If you think you have suffered a research-related injury, you should promptly notify the Principal Investigator listed in the Contact Information at the beginning of this form. Mayo Clinic will

offer care for research-related injuries, including first aid, emergency treatment and follow-up care as needed.

Who will pay for the treatment of research related injuries?
Care for such research-related injuries will be billed in the ordinary manner, to you or your insurance. You will be responsible for all treatment costs not covered by your insurance, including deductibles, co-payments and coinsurance.

What are the possible benefits from being in this research study?

This study may not make your health better. However, the information collected may help in determining better treatment plans for soft tissue sarcomas.

What alternative do you have if you choose not to participate in this research study?

You don't have to be in this study to receive treatment for your sarcoma. Your other choices may include receiving the same standard treatment and not be in the study. Talk to the Principal Investigator or your doctor if you have any questions about any of these treatments or procedures.

What tests or procedures will you need to pay for if you take part in this research study?

You won't need to pay for tests and procedures which are done just for this research study. These tests and procedures are:

- Toxicity assessments
- PROMIS QOL (Mayo Patient Survey)
- TESS QOL (Toronto Extremity Salvage Score)

However, you and/or your insurance will need to pay for all other tests and procedures that you would have as part of your clinical care, including co-payments and deductibles.

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If you have billing or insurance questions call Patient Account Services at the telephone number provided in the Contact Information section of this form.

Will you be paid for taking part in this research study?

You won't be paid for taking part in this study.

Will your information or samples be used for future research?

Your information or samples collected for this study will not be used or shared for future research studies even if the identifiable information such as your name, Mayo Clinic number or date of birth is removed.

How will your privacy and the confidentiality of your records be protected?

Mayo Clinic is committed to protecting the confidentiality of information obtained about you in connection with this research study. We will store research materials in a secure location and data will be stored on a password-protected computer. If the results of the research are made public, information that identifies you will not be used.

Representatives from the Mayo Clinic Institutional Review Board (the committee that reviews, approves, and monitors research on human subjects) may inspect study records during internal auditing procedures. However, these individuals are required to keep all information confidential.

During this research, information about your health will be collected. Under Federal law called the Privacy Rule, health information is private. However, there are exceptions to this rule, and you should know who may be able to see, use and share your health information for research and why they may need to do so. Information about you and your health cannot be used in this research study without your written permission. If you sign this form, it will provide that permission (or "authorization") to Mayo Clinic.

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Your health information may be collected from:

- Past, present and future medical records.
- Research procedures, including research office visits, tests, interviews and questionnaires.

Your health information will be used and/or given to others to:

- Do the research.
- Report the results.
- See if the research was conducted following the approved study plan, and applicable rules and regulations.

Your health information may be used and shared with:

- Mayo Clinic research staff involved in this study.
- Other Mayo Clinic staff involved in your clinical care.
- The Mayo Clinic Institutional Review Board that oversees the research.
- Federal and State agencies (such as the Food and Drug Administration, the Department of Health and Human Services, the National Institutes of Health and other United States agencies) or government agencies in other countries that oversee or review research.
- A group that oversees the data (study information) and safety of this research.

How your information may be shared with others:

While taking part in this study, you will be assigned a code that is unique to you, but does not include information that directly identifies you. This code will be used if your study information is sent outside of Mayo Clinic. The groups or individuals who receive your coded information will use it only for the purposes described in this consent form.

If the results of this study are made public (for example, through scientific meetings, reports or media), information that identifies you will not be used.

In addition, individuals involved in study oversight and not employed by Mayo Clinic may be allowed to review your health information included in past, present, and future medical and/or research records. This review may be done on-site at Mayo Clinic or remotely (from an off-site location). These records contain information that directly identifies you. However, the individuals will not be allowed to record, print, or copy (using paper, digital, photographic or other methods), or remove your identifying information from Mayo Clinic.

Is your health information protected after it has been shared with others?

Mayo Clinic asks anyone who receives your health information from us to protect your privacy; however, once your information is shared outside Mayo Clinic, we cannot promise that it will remain private and it may no longer be protected by the Privacy Rule.

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Your Rights and Permissions

Participation in this study is completely voluntary. You have the right not to participate at all. Even if you decide to be part of the study now, you may change your mind and stop at any time. You do not have to sign this form, but if you do not, you cannot take part in this research study.

Deciding not to participate or choosing to leave the study will not result in any penalty. Saying 'no' will not harm your relationship with your own doctors or with Mayo Clinic.

If you cancel your permission for Mayo Clinic to use or share your health information, your participation in this study will end and no more information about you will be collected; however, information already collected about you in the study may continue to be used.

You can cancel your permission for Mayo Clinic to use or share your health information at any time by sending a letter to the address below:

Mayo Clinic
Office for Human Research Protection
ATTN: Notice of Revocation of Authorization
201 Building 4-60
200 1st Street SW
Rochester, MN 55905

Alternatively, you may cancel your permission by emailing the Mayo Clinic Research Participant Advocate at: researchparticipantadvocate@mayo.edu.

Please be sure to include in your letter or email:

- The name of the Principal Investigator,
- The study IRB number and /or study name, and
- Your contact information.

Your permission for Mayo Clinic to use and share your health information lasts until the end of this study, unless you cancel it. The study does not end until all data has been collected, checked (or audited), analyzed, and reported. Because research is an ongoing process, we cannot give you an exact date when the study will end. Sometimes this can be years after your study visits and/or activities have ended.

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Enrollment and Permission Signatures

Your signature documents your permission to take part in this research.

Printed Name Date (mm/dd/yyyy) Time (hh:mm am/pm)

Signature

Person Obtaining Consent

- I have explained the research study to the participant.
- I have answered all questions about this research study to the best of my ability.

Printed Name Date (mm/dd/yyyy) Time (hh:mm am/pm)

Signature