MC200703

Radiation Therapy, Plasma Exchange, and Immunotherapy in Melanoma

NCT04581382

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MAYO CLINIC

Name and Clinic Number

Approval Date: **February 22, 2023**
Not to be used after: **August 25, 2023**

RESEARCH PARTICIPANT CONSENT AND PRIVACY AUTHORIZATION FORM

Study Title: MC200703: Radiation Therapy, Plasma Exchange, and Immunotherapy in Melanoma

IRB#: 20-003367

Principal Investigator: Dr. Jacob Orme 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 is to look at your blood samples and compare levels of metabolites (these are levels of vitamins, carbohydrates, proteins, etc., that are in your blood), before and after the plasma exchange (also known as "plasmapheresis" which is a way to "clean" or "flush out" your blood) that we hope will improve the effect of the standard immunotherapy treatment has on your cancer cells. You have been asked to take part in this research because you are an adult who is scheduled to receive immunotherapy for your melanoma.

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What's Involved	Study participation involves testing your blood before and after plasma exchange to help us see how well this procedure works to remove substances from your blood stream that affects how the immune system functions. You will only be in the study until you are finished receiving your plasma exchange procedure(s) and the study portion is completed. However, we will follow you during your treatment and follow-up visits, for up to 2 years.
Key Information	The risks of drawing blood include pain, bruising, lightheadedness, and/or fainting, and rarely infection at the site of the needle. The risks of plasma exchange are rare but may include hypotension, infection, and bleeding. You will be monitored throughout the entire procedure. Plasma exchange requires adequate vascular access. If your veins are not adequate for plasma exchange, we will place a temporary central venous access device (central line). The risks of central lines are rare but may include infection, thrombosis, and bleeding. You will be monitored throughout the procedure and the central line will be removed at the end of the third plasma exchange. As with all research, there is a chance that confidentiality could be compromised; however, we take precautions to minimize this risk. As a participant in this study, you will receive no direct benefit to your care. Your treatment will not be changed by the results of these tests. Results of these tests will not be available to you or your providers in your medical record or elsewhere.
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 Investigators:** Dr. Jacob Orme **Phone:** (507) 293-7683 Co-PI: Dr. Sean Park **Phone:** (507) 422-6666 **Study Team Contact:** RSTRADONCRES@mayo.edu **Institution Name and Address:** Mayo Clinic Department of Medical Oncology 200 First Street SW Rochester, MN 55905
▪ 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

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 are scheduled to receive immunotherapy for your melanoma. The goal of this study is to look at your blood samples and compare the before and aftereffects of plasmapheresis on your cancer.

Why is this research study being done?

The purpose of this research is to look at your blood samples and compare levels of metabolites (these are levels of vitamins, carbohydrates, proteins, etc., that are in your blood), before and after the plasma exchange (also known as “plasmapheresis” which is a way to "clean" or “flush out” your blood) that we hope will improve the effect of the standard immunotherapy treatment has on your cancer cells.

Information you should know

Who is Funding the Study?
Funding for this research comes from the Department of Medical Oncology and the National Institute of Health (NIH).

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 this study for up to 2 years.

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

If you agree to be in the study, you will be asked to participate in the following:

- Procedures such as: Vascular assessment, lab draws including research bloods, pregnancy test, Temporary line placement (in patients without adequate venous access)
- Therapeutic Plasma Exchange Routine Imaging
- Temporary Central line removal (in patients with line)

Some of 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.

Follow up visits that include the review of any side effects (good/bad), will be completed as per the Radiation Oncology clinician's discretion and will be assessed in Radiation Oncology by the Radiation Oncologist.

Screening Visit (≤30 days prior to registration):

- Pregnancy test (for women of childbearing potential)
- **#1 Research blood draw ** to determine eligibility (Pre-RT)**

If the levels of the research blood draw are **not** within the required limits for the study, you will not be able to participate in the research portion of your treatment plan. However, you will continue on with the treatment plan without being in this study.

If your blood test **is** within the required limits for the study you will continue on with line placement (if needed), the research blood draws, and the Therapeutic Plasma Exchange (TPE) as planned with your treating doctor.

Radiation Therapy (1 – 5 days of RT):

- Treatment will be delivered daily except on weekends and holidays, per the discretion of the radiation oncologist
- Treatment may not occur on consecutive days
- **#2 Research blood draw** (after the last RT day, just before starting the TPE procedure)

Therapeutic plasma exchange (TPE) procedure:

- After you finish the RT, you will start of the Therapeutic Plasma Exchange (TPE) in three sessions over a total of three (3) days in a row. One session per day.

Therapeutic plasma exchange (TPE) will take place in our outpatient Apheresis Clinic and take 1-2 hours for each session. In TPE, two peripheral IVs will be placed (one in each arm) or a temporary central access line will be placed for the procedure. Blood will be drawn out of IV or line port, filtered, and returned to the other IV or line port with albumin replacement fluid. The purpose of TPE is to measure the removal of substances from the blood we think may be stopping immunotherapy from working in some patients. Blood samples will be collected during TPE and so additional needle sticks will be needed. Blood product transfusion is *not* planned unless needed to prevent bleeding. If bleeding occurs or appears likely, human plasma will be given to prevent or stop this bleeding.

After the third and final Therapeutic Plasma Exchange procedure:

- **#3 Research blood draw** to be performed as part of TPE (no new needle stick) – Done after your last TPE procedure
- Removal of central line (if you have one) <u>after</u> blood draw
- Within 5 – 7 days after completion of the TPE, you will receive and start your planned immunotherapy (pembrolizumab or nivolumab) as scheduled by your oncologist.

2-3 weeks after Radiation Therapy <u>and</u> after the Therapeutic Plasma Exchange procedures:

- Toxicity assessment
- **#4 Research blood draw (**follow-up at standard clinical appointment prior to your next round of immunotherapy**)**

You will then continue with your therapy as planned by your oncologists.
Follow up as clinically indicated:

- Toxicity Assessment

Progression:

- **#5 Research blood draw** - If your disease progresses or comes back, we will collect one final research blood draw.

Overall, you will have five (5) blood samples, 36 ml at each collection, collected to help determine how well the plasmapheresis procedure removes substances from your blood stream that affect how the immune system functions in response to immunotherapy against your melanoma. We would also like to obtain waste product from the plasmapheresis procedure to measure this metabolite and treat other cells to see its effects.

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?

Blood Draw Risks
The risks of drawing blood include pain, bruising, lightheadedness, and/or fainting, and rarely infection at the site of the needle.

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

Therapeutic Plasma Exchange (TPE) Risks:
Complications with (TPE) that occasionally occur:

- Seepage of fluids at the needle site
- Bleeding
- Bruising (hematoma)
- Mild inflammation
- Infection
- Chills or feeling cold (can occur due to blood being removed temporarily)
- Allergic reactions caused by albumin and other procedure fluids used
- Hypocalcemia (low calcium levels)
- Hypokalemia (low potassium levels)
- Tingling in the lips, hands, and feet
- Feelings of anxiousness
- Feeling lightheaded for a short time due to the removal of blood.

- Embolism (air entering the veins)
- Fever
- Arrhythmias (abnormal heart rhythm)
- Drop in blood pressure.

We hope that the use of TPE may improve the cancer's response to the immunotherapy. Similarly, TPE may increase autoimmune side effects such as autoimmune colitis (inflammatory bowel disease). You will be monitored carefully throughout the procedure and every effort will be made to make you comfortable and to prevent and treat these complications. Treatments to help with side effects may include additional fluids, blood products, anti-inflammatory medications, and antibiotics. Should any adverse effect be noted, plasma exchange will be stopped, and safety will be reassessed.

Central Line Risks (only used in the event of inadequate venous access):
Complications with central lines that occasionally occur:

- Seepage of fluids at the line placement site
- Bleeding
- Bruising (hematoma)
- Thrombosis (clotting)
- Mild inflammation
- Infection
- Chills or feeling cold (can occur due to blood being removed temporarily)

In people without adequate peripheral veins, the use of a central line will allow therapeutic plasma exchange to take place. This line will be placed 48-72 hours before the plasma exchange to reduce the risk of bleeding. It will be removed immediately after the last session of TPE to reduce the risk of infection and thrombosis. Should any adverse effect be noted, line placement will be stopped and safety will be reassessed.

Unknown Risks:
During the course of procedure, unforeseen conditions may be revealed or occur.

Birth Control (Male & Female)
If you are sexually active and able to become pregnant or able to father a child, you must use birth control for the entire study and you must agree to use one of the birth control methods listed below, prior to starting any radiation therapy and after:

- 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)

You must use birth control for the entire study, up to 2 years. You must also use birth control for at least 5 months after your last dose of Pembrolizumab or Nivolumab.

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.

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.

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 the study, no more 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. Treatment costs for research-related injuries not covered by your insurance will be paid by Mayo Clinic.

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

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. Others with melanoma may benefit in the future from what we learn in this research study.

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 condition. Your other choices may include;

- Receiving treatment or care for your cancer without being in the study
- Taking part in another study
- Getting no treatment

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:

- Research Blood Draws

  - sPD-L1 – Screening
  - Research bloods (up to 5 time-points)
- Central line placement (if needed)
- Therapeutic Plasma Exchange (TPE)
  - Albumin (used with TPE procedure)

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.

These tests and procedures are:

- Routine Imaging
  - CT, MRI, etc., at the discretion of the treating physician
  - Pregnancy testing (if a woman of child-bearing potential)
  - Toxicity Assessments
- Pembrolizumab or nivolumab (Immunotherapy – Per physician preference)
- Radiation Therapy

You will also be responsible for any co-payments and deductibles.

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?

There is a very small chance that some commercial value may result from the use of your sample. This could include new products like a drug or a test to diagnose a disease. If that happens, you will not be offered a share in any profits.

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

Will your information or samples be used for future research?

We would like to keep your information and samples for future research. You can still take part in this current study even if you don't want your information or samples used for future research.

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Researchers at Mayo Clinic who aren't involved with this study may ask to use your information and/or samples for future research. Researchers at other institutions may also ask for a part of your information and/or samples for future studies. Unless you indicate otherwise, the future research may be on any topic. No direct benefits to you are expected from the future research. Your information and/or samples will only be shared consistent with your consent, and with all applicable laws and regulations.

If you approve release of your information and/or samples by checking 'yes' below, Mayo may send the information and/or samples to researchers who request them, but Mayo will not send your name, address, phone number, social security number, or any other identifying information with the information and/or samples. Your information and/or samples may be sent with a code, and only the researchers for this study at Mayo Clinic would be able to link the code to you.

Please read the following statements and mark your choices:

1. I permit my information and samples to be stored and used in future research of cancer at Mayo Clinic:

☐ Yes ☐ No Please initial here: _____Date: _____

2. I permit my information and samples to be stored and used in future research at Mayo Clinic to learn about, prevent, or treat any other health problems:

☐ Yes ☐ No Please initial here: _____Date: _____

3. I permit Mayo Clinic to give my information and samples to researchers at other institutions:

☐ Yes ☐ No Please initial here: _____Date: _____

You may withdraw your consent for future use of your information and/or samples at any time, by writing to the Principal Investigator at the address provided in the "Contact Information" section of this consent form.

Your information and/or samples would be removed from any repository where they are stored, if possible. Information and/or samples already distributed for research use will not be retrieved. When you die, your sample will be considered a gift to Mayo Clinic. That means that Mayo Clinic can use it for research forever. Since your sample has your genetic information in it, your family may want access to it after you die. They can use that information for many things, such as learning if you had a genetic disease or if you were related to someone.

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Read the following statement and mark your choice:

I permit Mayo Clinic to give my family access to my sample after I die:

☐ Yes ☐ No Please initial here: _____ Date: _____

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

Blood and waste samples are stored at Mayo Clinic in secured freezers. Research data is stored in files on computers which are password protected. If the results of the research are made public, information that identifies you will not be used.

Mayo Clinic is committed to protecting the confidentiality of information obtained about you in connection with this research study. Samples will be given research-specific identifiers that are separated from clinically identifiable information. These data will be stored in files on computers which are password protected.

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.

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.

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.

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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 forever, unless you cancel it.

Enrollment and Permission Signatures

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

	/ /	: AM/PM
Printed Name	Date	Time

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.

	/ /	: AM/PM
Printed Name	Date	Time

Signature