MC1771 / 17-001666

Phase Ib/II Study of Autologous Dendritic Cell Therapy Delivered Intratumorally After Cryoablation in Combination With Pembrolizumab for Patients With Metastatic or Unresectable Melanoma

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Name and Clinic Number
Protocol #: MC1771 **Version #: Mayo Addendum 2** **Version Date: 16Aug2019**

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RESEARCH PARTICIPANT CONSENT AND PRIVACY AUTHORIZATION FORM

Study Title: MC1771: Phase II study of Autologous Dendritic Cell Therapy Delivered Intratumorally after Cryoablation in Combination with Pembrolizumab for Patients with Metastatic or Unresectable Melanoma

IRB#: 17-001666

Principal Investigator: Matthew S. Block, M.D., Ph.D. and Colleagues

Please read this information carefully. It tells you important things about this research study. A member of our research team will talk to you about taking part in this research study. If you have questions at any time, please ask us.

Take your time to decide. Feel free to discuss the study with your family, friends, and healthcare provider before you make your decision.

To help you decide if you want to take part in this study, you should know:

- Taking part in this study is completely voluntary.
- You can choose not to participate.
- You are free to change your mind at any time if you choose to participate.
- Your decision won't cause any penalties or loss of benefits to which you're otherwise entitled.
- Your decision won't change the access to medical care you get at Mayo Clinic now or in the future if you choose not to participate or discontinue your participation.

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.

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 a copy of this form to keep. A copy of this form will be put in your medical record.

CONTACT INFORMATION

You can contact …	At …	If you have questions about …
Principal Investigator: Dr. Matthew Block	**Phone:** (507) 284-2511 **Institution Name and Address:** Mayo Clinic 200 First Street SW Rochester, MN 55905	▪ Study tests and procedures ▪ Research-related injuries or emergencies ▪ Any research-related concerns or complaints ▪ Withdrawing from the research study ▪ Materials you receive ▪ Research-related appointments
Mayo Clinic Institutional Review Board (IRB)	**Phone:** (507) 266-4000 **Toll-Free:** (866) 273-4681	▪ Rights of a research participant
Research Subject Advocate (The RSA is independent of the Study Team)	**Phone:** (507) 266-9372 **Toll-Free:** (866) 273-4681 **E-mail:** researchsubjectadvocate@mayo.edu	▪ Rights of a research participant ▪ Any research-related concerns or complaints ▪ Use of your Protected Health Information ▪ Stopping your authorization to use your Protected Health Information
Patient Account Services	**Toll Free:** (844) 217-9591	▪ Billing or insurance related to this research study

Other Information:
A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Website will not include information that can identify you. At most, the Website will include a summary of the results. You can search this Website at any time.

1. 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 been diagnosed with melanoma that is cannot be treated with local therapy. You also have at least 3 lesions visible on scans: Two lesions which can be used for cryoablation and vaccine injection and at least one additional lesion for measuring the progress of the cancer.

2. Why is this research study being done?

The purpose of this study is to test whether the combination of pembrolizumab with cryotherapy and a dendritic cell vaccine will stimulate your immune system and cause anti-tumor effects on the melanoma.

We will also determine the changes in your immune system during treatment and see if this treatment has any harmful side effects.

You will receive pembrolizumab which is approved by the U.S. Food and Drug Administration (FDA) for treatment of melanoma. The dendritic cell vaccine used in this study is considered investigational, which means it has not been approved the FDA for routine clinical use or for the use described in this study. However, the FDA has allowed the use of this vaccine in this research study.

You will undergo cryoablation on two of your tumors. Cryoablation is approved by the FDA to treat certain tumors. The use of cryoablation as a combination with pembrolizumab and dendritic vaccine has been allowed by the FDA for this study but is not approved for routine clinical use.

3. Information you should know

Who is Funding the Study?

The Mayo Clinic Transform the Practice initiative is funding the study.

4. How long will you be in this research study?

You will be in the study for up to 5 years. You will be able to receive study treatment for up to two years as long as your cancer is responding to the treatment and you are not having side effects that cannot be managed. After study treatment has stopped we will continue to follow you for long term effects up to 5 years after study entry.

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

Before beginning any research activities you will be asked to sign this informed consent form. If you agree to be in the study, you will be screened by your doctor to find out if you are eligible to enter the study. You will be asked to participate in the following:

Prior to Registration

- Physical exam including complete medical history, height, weight and vital signs
- ECOG performance status (assessment of your ability to carry out daily activities)
- Routine blood tests, including coagulation profile
- Pregnancy test if you are able to become pregnant
- PET/CT scan; CT scan of chest, abdomen and pelvis; or MRI

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 depending upon study requirements.

In addition, you will have the following exam which is not part of regular care:

Venous access assessment - This test will determine whether you are able to undergo apheresis through your veins. If your veins are not adequate, you will not be able to take part in the study. There is no charge for this test.

After registration but prior to start of treatment

You will also have the following which are not part of regular care:

- Research blood tests (required)

Cycle 1
Each 3-week (21 day) period in this study is called one cycle. During the first week, blood will be collected using a method called "apheresis" to isolate the cells that will be grown into dendritic cells. Dendritic cells are a powerful stimulator of immunity. Apheresis is a procedure where certain kinds of blood cells are separated from the rest of your blood. In this study, the cells to be separated are called white blood cells. The apheresis will be done at Mayo Clinic as an outpatient procedure and will take about 4 hours. You will need to be lying down while the apheresis is being done. An IV catheter (a small plastic tube) will be placed in a vein in your arm or in a vein under your collarbone. Blood will flow from your vein into a machine where certain types of blood cells will be separated from the other blood cells and saved. The rest of your blood will then flow back into your body. While the apheresis is being done you will be monitored by a health care professional trained to do apheresis. The cells separated from your blood during apheresis will be taken to a laboratory at the Mayo Clinic for processing.

If we are unable to obtain enough cells from the apheresis process, your doctor will decide whether another attempt to obtain the cells can be tried or you need to be taken off this study.

After the apheresis, you will receive a dose of the drug pembrolizumab. This drug will be given through your vein. After this dose, you will receive pembrolizumab every three weeks for up to two years.

Cycles 2 and 3
On the second and third cycles you will receive pembrolizumab on Day 1. On Day 1 or 2, you will have a tumor biopsy for research purposes. Immediately after the biopsy, you will have a procedure called cryoablation where one of your melanoma tumors (the one that was biopsied) will be frozen using a special probe to freeze it from the inside out. Then the dendritic cells will be injected in the space where the tumor was.

To help us monitor the effectiveness of the vaccine and improve your overall immunity, you will have an injection of Prevnar13® vaccine near the area of the dendritic cells injection. Prevnar13® is an FDA approved vaccine that has been used safely worldwide to prevent pneumococcal infections.

Depending on the location of the tumor, you may need to be observed in the hospital overnight following cryoablation. Research blood will be collected on Cycle 2, Days 2-5. The collection on Cycle 2, Day 2 will take place 2-4 hours after completion of cryoablation and dendritic cell therapy. A different tumor will be ablated for Cycle 3 than is ablated for Cycle 2.

Cycle 4 and subsequent cycles
On Day 1 of Cycle 4 and the subsequent cycles you will continue to receive pembrolizumab.

- CT scan, PET/CT, or MRI will be performed at the completion of Cycle 4 and then at the completion of every fourth cycle of treatment (i.e., after Cycle 8, 12, 16, etc.)
- We will routinely take blood to monitor your immune status prior to the start of Cycles 1 through 5 and prior to the start of each post-imaging cycle after that (prior to Cycle 9, 13, 17, etc.)
- A tumor biopsy will be performed at the end of Cycle 4 after radiologic evaluation

Tables of scheduled tests:

Prior to Registration

Timing	What will happen
Pre-study	• Physical exam including medical history, height, weight and vital signs • ECOG performance status • Routine blood tests including coagulation profile • Pregnancy test if you are able to become pregnant • Tumor imaging and measurement (CT scan, PET/CT or MRI)

Cycle 1 (21 day cycle)

Timing	What will happen
Day 1	• Physical exam and performance status • Apheresis • Pembrolizumab through a vein (IV) • Routine blood tests • Required research blood tests
End of Cycle 1	• Routine blood tests for coagulation profile

Cycles 2-3 (21 day cycle):

Timing	What will happen
Day 1 or 2	• Physical exam and performance status • Pembrolizumab through a vein (IV) • Tumor biopsy (a portion will be taken for research purposes) • Cryoablation (freezing) of tumor • Dendritic cells injected into tumor space • Prevnar®13 injection near dendritic cell injection • Routine blood tests

Timing	What will happen
	• Required research blood tests (Prior to start of Cycle 2 and 3, and Cycle 2, Days 1-5)
End of Cycle 2 only	• Routine blood tests for coagulation

Cycle 4 and subsequent cycles (21 day cycle):

Timing	What will happen
Day 1 (every 21 days)	• Physical exam and performance status • Routine blood tests • Pembrolizumab through a vein (IV) • Tumor imaging and measurement (CT scan, PET/CT or MRI) (end of Cycle 4 and then at the completion of every 4th cycle of treatment (end of Cycles 4, 8, 12, etc…)) until confirmed disease progression) • Mandatory research blood tests (prior to start of Cycles 4 and 5, and prior to the start of each post-imaging cycle thereafter (prior to Cycle 9, 13, 17, etc.))
End of Cycle 4 only	• Required research tumor biopsy (at the end of Cycle 4 only; after imaging)

End of treatment or progression of disease
You can receive treatment with pembrolizumab for up to two years. When your treatment is done or if your cancer has gotten worse, you will need to have the following tests done:

- Physical exam and performance status
- Routine blood tests
- Tumor imaging and measurement (CT scan, PET/CT or MRI)
- Research blood tests

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

Prevnar® Vaccine
The most common risks of this vaccine include fever and skin reaction at the site of injection. Less common risks include decreased appetite, diarrhea, vomiting, feeling irritable, and having difficulty with sleep. These reactions are usually short-lived.

Rare risks include severe allergic reaction and seizure from fever. You should not receive this vaccine if you have known severe allergic reaction to pneumococcal vaccine or any component of vaccine formula, including diphtheria toxoid.

Dendritic Cell Injection

Dendritic cell vaccine therapy in past clinical trials has demonstrated no significant side effects. The most common side effects were mild pain at the site of injection. These effects usually responded to treatment with acetaminophen as needed and resolved within 1 week. However, in this study we are testing the potential side-effects when this dendritic cell vaccine is combined with another immune therapy drug, pembrolizumab. Dendritic cells stimulate the immune system and may cause irritation, rash, nausea, flu-like symptoms, chills, swelling, or allergic type reactions. Extreme immune stimulation could result in severe allergic reaction and a condition called autoimmunity, where your immune system reacts strongly and starts to attack your own body. While these severe reactions have never happened before, one of the purposes of the current study is to see whether these reactions might occur.

Cryoablation

The most common side-effect of this procedure is pain at the site of cryoablation; an anesthesia team will provide necessary sedation during the treatment. Pain after cryoablation is typically very mild or nonexistent, and over the counter pain medications are usually enough. Less common risks include bleeding and infection at the site of cryoablation. In the past, with an older generation of equipment, cryoablation of large tumors in the liver resulted in widespread bleeding and failure of many organs. With our current equipment, patients who have had cryoablation of tumors have not experienced such severe reactions. One of the purposes of this study is to monitor for any potential side-effects of cryoablation and dendritic cell injection into the cryoablation site. If you undergo cryoablation of a tumor deep in the body, you may be monitored overnight in the hospital. If you undergo cryoablation of another site, you will be monitored as an outpatient. Additionally, the cryoablation procedure will be done using CT guidance. The amount of radiation you will receive has a very low risk of harmful effects.

There may be other side effects or risks that are not known at this time.

Apheresis

Common risks:

- Low blood pressure
- Light-headedness
- Paleness
- Sweating
- Bleeding/ bruising/ pain from the IV site

- Tingling or vibrating sensation in the hands, feet, and around the mouth due to low calcium
- Nausea or vomiting

These are mild, occur during the treatment, and resolve quickly with treatment or when the procedure is stopped.

Rare risks:

- Severe allergic reactions such as anaphylaxis
- Damage to your red blood cells (hemolysis)
- Failure of the instrument with inability to return your red blood cells
- Leakage of blood in the instrument
- Air embolism
- Tetany due to low calcium
- Abnormal heart rhythm due to low calcium
- In patients who have undergone an axillary (armpit) lymph node dissection (surgery to remove lymph nodes), there may be a slight increase in the risk of lymphedema (swelling of the arm) or infection.

These risks are rare. The apheresis instruments have safety systems to prevent many of these risks including detectors that sense air in the instrument, pressure sensors that would detect elevated pressures that could damage red blood cells, and sensors to detect blood leaks. You will be closely monitored by the nurse performing the procedure to detect any symptoms that could indicate low blood calcium levels that could cause some of these problems.

<u>Pembrolizumab</u>

Very common side effects (>10%) seen in people taking pembrolizumab include the following:

- Feeling tired
- Itching of the skin
- Rash
- Frequent or excessive bowel movements or diarrhea
- Fever
- Shortness of breath
- Decreased appetite
- Cough
- Nausea and vomiting
- Decrease in red blood cells that may result in patients feeling tired or short of breath

- Pain in joints
- Headache
- Back pain
- Swelling of the legs
- Muscle weakness or lack of energy
- Bowel movements occurring less often than usual (constipation)

Common side effects (1-10%) seen in people taking pembrolizumab include the following:

- Pain or cramping in a muscle or group of muscles
- Decreased release of thyroid hormone. Symptoms may include: feeling tired, weight gain, feeling cold easily, or bowel movements occurring less often than usual
- Abnormal laboratory result of liver test by blood that occasionally indicates liver failure, may have yellowing of the skin or whites of the eyes, fatigue, or leg swelling
- Feeling cold or sick
- Loss of skin color
- Pain or uncomfortable feeling in the belly
- Momentary feeling of whole body warmth possibly accompanied by sweating
- Sweating extensively while sleeping such that clothes and sheets are wet – "night sweats"
- Feeling dizzy or unsteady when walking or standing
- Loss of weight
- Pain in the back, arms, or legs
- Weakness
- Decreased platelets that may cause a tendency to bruise easily or bleed easily
- Dry eyes
- Blurred or changed vision
- Dry mouth
- Feeling of pain, pins & needles, or burning, usually in the fingers or toes
- Inflammation of the lungs (pneumonitis)
- Change of blood cholesterol or triglyceride level
- Change of blood sugar or albumin level
- Change of blood electrolytes, e.g. sodium, potassium, or magnesium
- Loss of body fluid - may feel tired, confused, have a dry mouth, or feel thirsty
- Lung infection
- Fluid around the lung
- Blood clot developed in lung
- Inflammation of the large intestine (colon) that may lead to frequent or excessive watery bowel movements

Serious Adverse Events (No Event Occurred in >2% of everyone treated)
Please note that some of these events have been previously stated above, so some have occurred more frequently but with less severity. Serious adverse events seen in people taking pembrolizumab include:

- Trouble thinking clearly or easily confused
- Decreased white blood cells, red blood cells, and platelets which may cause fever, feeling cold, infections, shortness of breath, feeling tired, a tendency to bruise easily, or a tendency to bleed easily
- Increased release of thyroid hormone which may cause anxiety, irritability, or trouble sleeping, weakness, trembling, sweating, feeling uncomfortable in warm weather, fast or uneven heartbeats, feeling tired, weight loss, and frequent or excessive bowel movements
- Infection throughout the body that may cause fever, feeling tired, feeling cold, and that does not respond to most antibiotics - this risk is serious and can be life threatening
- Inflammation of the lining around the heart which may feel like sharp chest pain and/or a fever
- Inflammation of the pancreas - symptoms may include: abdominal pain that radiates to the back, swollen or tender abdomen, fever, nausea and vomiting
- Inflammation of the muscles - symptoms may include weakness or pain in the muscles
- Inflammation of the kidneys causing them not to work as well, which may cause swelling of the legs and possibly need for dialysis
- Inflammation of the pituitary gland, which may cause headache, nausea, a sensation of the room spinning around you, blurred vision, double vision, extreme thirst, or weakness (hypophysitis)
- Change in blood pressure or body fluid level which may cause you to feel like you might pass out
- Failure of liver which may cause yellowing of the skin or eyes
- Decreased lung function which may cause difficulty breathing
- Damage to the peripheral nerves (hands and feet) causing weakness or numbness and tingling
- Cancer of the skin
- Inflammation of the heart muscle which can cause shortness of breath or heart rhythm problems which may be serious and require hospitalization, in rare cases can cause sudden death. (Immune-mediated myocarditis)
- Severe skin and digestive tract reaction that may include rash and shedding or breakdown of tissue - may have blisters, hives, and other lesions in various locations on the body including palms and soles, face and other extremities. This effect is serious and may be life threatening. [Stevens-Johnson Syndrome (SJS)]

- Toxic Epidermal Necrolysis Syndrome (TENS) is a rare, life-threatening skin condition that is usually caused by a reaction to a drug. The top layer of skin detaches from the lower layers of skin all over the body. This effect is similar to the skin damage from a severe burn and is serious and life threatening.
- Myasthenic Syndrome (muscle weakness)
- Guillain-Barre Syndrome (damage to the nervous system causing numbness and/or paralysis)
- In rare cases, adverse events from pembrolizumab can occur which may be life-threatening and may occur after patients have stopped taking drug.
- Vogt-Koyanagi-Harada syndrome – an autoimmune disorder that affects tissues containing melanin such as eyes and skin and is usually found based on eye problems such as dry eye, eye swelling, eye pain, eye infection, blurred vision, and more
- Hemophagocytic lymphohistiocytosis - an abnormal immune response with activation of certain types of white blood cells (lymphocytes and macrophages) and the release of inflammatory proteins which then cause a variety of symptoms such as fevers, rash, anemia, enlarged lymph nodes, enlarged liver, enlarged spleen, and more

Standard of Care Risks:
Your doctor will discuss the risks of pembrolizumab, other medications, imaging, and biopsies, as these tests and procedures are part of your standard clinical care.

Biopsy Risks:
Possible side effects include bleeding, bruising, infection, nausea, vomiting and pain. The research tumor biopsy will be performed using CT guidance. CT scans use X-rays to image the inside of your body. You will be exposed to radiation during the CT guided biopsy. The amount of radiation you will receive has a low risk of harmful effects.

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

Radiation Risks:
You will be exposed to radiation from the CT scans, PET/CT scans, or chest X-rays required for your care. You may also be exposed to radiation from CT guidance for cryoablation, biopsy, and dendritic cell injections. The amount of radiation has a low risk of harmful effects.

Pregnancy:
Because of the risks related to the study treatments, you will have to take precautions in order to prevent you or your partner from becoming pregnant in the course of the study.

All of the agents and procedures can cause harm to an unborn child if given to a pregnant person or to a person who fathers a child.

Because of the possible risks to an unborn child, if you are able to become pregnant, you will be asked to take a pregnancy test before starting this study. If you are pregnant, you will not be allowed to take part in this study

If you miss a period, or think you might be pregnant during the study, or your partner becomes pregnant while you are on the study, you must tell the Principal Investigator immediately. The Principal Investigator may ask for your permission to collect information about the outcome of the pregnancy and newborn child.

Other Risks:
Many side effects go away shortly after the study drug is stopped, but in some cases side effects can be serious, long lasting, or may never go away. There may be a risk of death. Some side effects may not be known. Side effects may range from mild to life- threatening. Other drugs may be given to make side effects less serious and less uncomfortable. As with any medication, allergic reactions are a possibility. Talk to the researcher and/or your healthcare provider about side effects and ask any other questions.

7. 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.

8. 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.

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

This study may not make your health better. However, the information learned from the results of this study may help benefit others.

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

You do not have to be in this study to receive treatment for your condition. Your other choices may include:

- Other standard medications for your cancer including pembrolizumab
- Enrollment in a study using other investigational drugs
- No treatment

You should talk to the researcher and your regular physician about each of your choices before you decide if you will take part in this study.

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

You will not need to pay for tests and procedures which are done just for this research study. These tests and procedures are:

- Apheresis
- Cryoablation
- Research tumor biopsy
- Prevnar13® and dendritic cell vaccines
- Research blood tests for immune monitoring

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

These tests and procedures include:

- Routine exams, blood tests, and scans (such as CTs, PET/CTs, MRIs)
- Pembrolizumab and administration
- Other drugs or treatments which are given to help you control side effects

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

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

You will not be paid for taking part in this study.

13. What will happen to your samples?

We would like to keep your samples for future research. You can still take part in this current study even if you don't want your samples used for future research. If you agree to give your samples, they will be the property of Mayo Clinic.

Other researchers at Mayo Clinic who aren't involved with this study may ask to use your sample for future research. Researchers at other institutions may also ask for a part of your sample for future studies. Your sample will be sent to researchers in a coded format, which protects your identity.

Some future studies may examine your DNA, which is the genetic information you inherited from your parents (genetic testing). The Principal Investigator may contact you if there are findings which may be useful for your health care. You would be given general information on the potential risks, benefits, and costs of choosing to learn about the findings.

Please read the following statements and mark your choices:

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

   ☐ Yes ☐ No Please initial here: _____Date: _____

2. I permit my sample 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 sample to researchers at other institutions:

   ☐ Yes ☐ No Please initial here: _____Date: _____

There is a very small chance that some commercial value may result from the use of your donated sample. If that happens, you won't be offered a share in any profits.

You may request to have your sample destroyed by writing to the Principal Investigator. The address is found in the "Contact Information" section of this consent form. Because we cannot predict how your sample will be used in the future, we cannot promise that samples can be retrieved and destroyed.

14. 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.

Various methods are used to safeguard confidentiality. Some or all of the following may be used in this study: assigning a specific code or registration number to each participant's data and samples, research materials stored in locked areas, password protected data stored on a computer.

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.

Health information may be collected about you from:

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

Why will this information be used and/or given to others?

- To do the research.
- To report the results.
- To see if the research was done correctly.

If the results of this study are made public, information that identifies you will not be used.

Who may use or share your health information?

- Mayo Clinic research staff involved in this study.

With whom may your health information be shared?

- The Mayo Clinic Institutional Review Board that oversees the research.
- Other Mayo Clinic physicians involved in your clinical care.
- Researchers involved in this study at other institutions.
- 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.
- The sponsor(s) of this study and the people or groups it hires to help perform this research.
- A group that oversees the data (study information) and safety of this research.

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 Privacy Rights

You do not have to sign this form, but if you do not, you cannot take part in this research study.

If you cancel your permission 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.

If you choose not to take part or if you withdraw from this study, it will not harm your relationship with your own doctors or with Mayo Clinic.

You can cancel your permission 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
200 1st Street SW
Rochester, MN 55905

Alternatively, you may cancel your permission by emailing the Mayo Clinic Research Subject Advocate at: researchsubjectadvocate@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 lasts forever, unless you cancel it.

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