MC1685 / 16-005856

Phase I/II Study of Dendritic Cell Therapy Delivered Intratumorally After Cryoablation and Anti-PD-1 Antibody (Pembrolizumab) for Patients With Non-Hodgkin Lymphoma

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MAYO CLINIC

Name and Clinic Number

Approval Date: **August 10, 2022**
Not to be used after: **November 23, 2022**

RESEARCH PARTICIPANT CONSENT AND PRIVACY AUTHORIZATION FORM

Study Title: MC1685: Phase I/II Study of Dendritic Cell Therapy Delivered Intratumorally after Cryoablation and Anti-PD-1 Antibody (Pembrolizumab) for Patients with Non-Hodgkin Lymphoma

IRB#: 16-005856

Principal Investigator: Dr. Yi Lin, 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.

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CONTACT INFORMATION

You can contact …	At …	If you have questions about …
Principal Investigator: Dr. Yi Lin	**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 Participant Advocate (The RPA is independent of the Study Team)	**Phone:** (507) 266-9372 **Toll-Free:** (866) 273-4681 **E-mail:** researchparticipantadvocate@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 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.

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 just been diagnosed with non-Hodgkin lymphoma (NHL) or have NHL that has either not responded to other treatment or has returned after treatment.

The plan is to have about 44 people take part in this study at Mayo Clinic.

2. Why is this research study being done?

This study is being done to:

- Determine if we can stimulate your immune system to fight your lymphoma
- Determine if blocking PD-1 signaling with pembrolizumab (MK-3475) can be used to stimulate your own immune system to fight your lymphoma
- Determine if freezing the tumor followed by injection of your dendritic cells can be used to vaccinate you against your lymphoma
- Determine how your immunity changes during treatment
- Determine if this treatment has any harmful side effects

The dendritic cell vaccine used in this study is considered investigational, which means it has not been approved by the Food and Drug Administration (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.

3. Information you should know

Who is Funding the Study?
The Shulze Family Foundation is funding the study with support from the Mayo Clinic and University of Iowa Lymphoma SPORE (The National Cancer Institute). The research funding will pay the institution to cover costs related to running this trial. Biocompatibles Inc., a BTG International group company, is also providing funding.

Merck, Inc. will provide the study drug, pembrolizumab (MK-3475).

Information Regarding Conflict of Interest:
This research has been reviewed by the Mayo Clinic Conflict of Interest Review Board and is being conducted in compliance with Mayo Clinic Conflict of Interest policies.

- Both the Mayo Clinic Conflict of Interest Review Board and the Institutional Review Board have reviewed the financial interest for one or more of the investigators and/or Mayo Clinic related to this research and they have determined that this financial interest poses no additional significant risk to the welfare of participants in this research project or to the integrity of the research.
- Additional information is available to any interested study participant regarding the details of this financial interest and how it is being managed by contacting the study coordinator or the Office of Conflict of Interest Review at 507-284-0075.
- One of the investigators associated with this project has received within the past 12 months consulting income from the company sponsoring this research, providing a product for the research or whose product is the subject of this research.

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

You will be in the study until 4 years after you were registered to this study.

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 asked to participate in the following tests and procedures, described in the tables below.

This study is being done to determine if your immune system can be stimulated to attack your tumor. We will stimulate your immune system in two ways. First, we will use a drug called pembrolizumab to reduce signals in your immune system. Second, we will collect white blood cells from your blood and grow these cells in a special lab to generate dendritic cells. Dendritic cells are a powerful stimulator of immunity. However, dendritic cells need to be educated in order to stimulate your immune system to destroy your lymphoma. We will educate these dendritic cells by killing a lymphoma tumor in your body by freezing it, called cryoablation, and then injecting the dendritic cells into the killed tumor.

The treatment portion of this study will take about one year. During the first week, blood will be collected using a method called leukapheresis to isolate the cells that will be grown into dendritic cells. Leukapheresis 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 leukapheresis 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 leukapheresis 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 leukapheresis is being done you will be monitored by a health care professional trained to do leukapheresis. The cells separated from your blood during leukapheresis will be taken right away to a laboratory at the Mayo Clinic for processing.

After the leukapheresis, you will receive your first dose of the drug pembrolizumab (MK-3475), a monoclonal antibody to PD-1. This drug will be given through your vein. After this dose, you will receive this drug every three weeks for one year. Each 3-week (21 day) period in this study is called one cycle.

The timing of cryoablation and dendritic cell vaccine will depend on the part or dose level of the study in which you are participating. You will participate in only one part or dose level of the study and will not be moved to another part or dose level within this study.

You will also be asked to complete a questionnaire booklet. This booklet contains questions about your health and well-being, and will be completed before you start treatment and before cycles 2, 4, 6, 8, 12 and 18. If you continue receiving pembrolizumab after cycle 18, we will ask you to complete the questionnaire booklet every 3 months while you receive treatment.

Phase II dose level 1 (Phase I is closed as of July 9, 2018)

On the second cycle of treatment in this dose level, you will receive pembrolizumab (MK-3475) on Day 1. On Day 2, you will have a procedure where one of your lymphoma tumors will be frozen using a special probe to freeze it from the inside out. Then in the space where the tumor was, the dendritic cells will be injected. To help us monitor the effectiveness of the vaccine and improve your overall immunity, you will have an injection of Prevnar® vaccine near the area of the dendritic cells injection. Prevnar® is an FDA approved vaccine that has been used safely worldwide to prevent pneumococcal infections.

After your first injection, you will receive two more dendritic cell vaccine injections on Days 8 and 15 within this 3-week cycle. These two dendritic cell injections will be in the same place where the tumor was frozen. You will also have a routine exam to check for any adverse events or symptoms.

On the third cycle of treatment in this cohort, you will receive pembrolizumab (MK-3475) on Day 1. On Days 2, 8, and 15, you will receive dendritic cell vaccine injections into the same place where the tumor was frozen. Prevnar® vaccine will be injected near the place of dendritic cell vaccine injection on Day 2. You will also have a routine exam to check for any adverse events or symptoms.

On the fourth and fifth cycles of treatment in this dose level, you will receive pembrolizumab (MK-3475) on Day 1. On Day 2, you will receive dendritic cell vaccine injection into the same place where the tumor was frozen. Prevnar® vaccine will be injected near the place of dendritic cell vaccine injection on Day 2.

On Cycles 6-18 in this dose level, you will receive pembrolizumab (MK-3475) on Day 1.

We will routinely take blood to monitor your immune status. We will biopsy one of your tumors on Cycles 1 and 6, and after you have completed treatment on this study.

While you are in this study you should not take any form of steroids unless instructed by your study doctor. This includes steroids that are given by IV (through a vein), inhaled, or taken by mouth. The goal of this study is to increase the production of certain blood immune cells in your body and using steroids may slow or stop the growth of those cells. You also should not donate blood for other people to use while you are on this study.

If the vaccine makes you ill, your physician may elect to delay or eliminate any or all the remaining doses.

During the monitoring period after active vaccine treatment, if you have lymphoma disease not requiring active chemotherapy, and you have unused dendritic cell vaccines in storage, you may be offered the option of repeating the vaccine treatments. If you agree to the repeat treatment, you will not undergo repeat leukapheresis procedure to make more vaccines. You will follow the same treatment schedule as before until all stored vaccines are used or the schedule is completed, whichever happens first. Vaccine treatment will also be stopped if you develop major side effect or progressive disease requiring active chemotherapy treatment.

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Table of scheduled tests:

Dose level 1

Timing	What will happen
Pre-Study	• Routine blood tests and exams • Routine pregnancy test for persons of childbearing potential • Routine whole body CT, PET, or MRI scans
Cycle 1 Day 1	• Limited CT or MRI scan of treatment and monitored lymphoma tumor, if needed • Research tumor biopsy (may be collected any time prior to the first vaccine injection) • Research blood collection for immune baseline (6 tablespoons) • Routine blood test (complete blood count) if the previous test was last collected more than 3 days before leukapheresis • Collect blood by leukapheresis • Make dendritic cell vaccine • Pembrolizumab (MK-3475) infusion by vein (IV)
Cycle 2 Day 1	• Routine exams, blood tests • Research blood collection (6 tablespoons) • Pembrolizumab (MK-3475) infused by IV
Cycle 2 Day 2	• Cryoablation (freezing) of a tumor • Dendritic cell vaccine injected into tumor space • Prevnar® injected near the dendritic cell vaccine injection
Cycle 2 Day 8	• Routine exam to check for adverse events • Dendritic cell vaccine injected into tumor space
Cycle 2 Day 15	• Routine exam to check for adverse events • Dendritic cell vaccine injected into tumor space
Cycle 3 Day 1	• Routine exams, blood tests • Pembrolizumab (MK-3475) infused by IV
Cycle 3 Day 2	• Dendritic cell vaccine injected into tumor space • Prevnar® injected near the dendritic cell vaccine injection
Cycle 3 Day 8	• Routine exam to check for adverse events • Dendritic cell vaccine injected into tumor space
Cycle 3 Day 15	• Routine exam to check for adverse events • Dendritic cell vaccine injected into tumor space

Timing	What will happen
Cycle 4 Day 1	• Routine exams, blood tests • Routine whole body CT, PET, or MRI scans • Research blood collection (6 tablespoons) • Pembrolizumab (MK-3475) infused by IV
Cycle 4 Day 2	• Dendritic cell vaccine injected into tumor space • Prevnar injected near the dendritic cell vaccine injection
Cycle 5 Day 1	• Routine exams, blood tests • Pembrolizumab (MK-3475) infused by IV
Cycle 5 Day 2	• Dendritic cell vaccine injected into tumor space • Prevnar® injected near the dendritic cell vaccine injection
Cycle 6 Day 1	• Routine exams and blood tests • Research blood collected (6 tablespoons) • Research tumor biopsy • Pembrolizumab (MK-3475) infused by IV
Cycle 7 through Cycle 18, every 3 weeks for each cycle, Day 1 of each cycle	• Routine exams and blood tests • Routine whole body CT, PET, or MRI scans (Cycles 8, 12, and 18 only) • Research blood collected (6 tablespoons) (Cycles 8, 12 and 18 only) • Pembrolizumab (MK-3475) infused by IV
Cycles 19 through Cycle 22, every 3 months for each cycle, starting at 8 weeks after last dose	• Routine exams, blood tests, and scans (whole body CT, PET, or MRI) • Research blood collection (6 tablespoons) • Research tumor biopsy (Cycle 19 only)
At the time of active disease progression requiring active retreatment or active treatment off of this study	• Routine exams, blood tests, and scans (whole body CT, PET, or MRI) • Research blood collection (6 tablespoons) • Research tumor biopsy

The blood collected for research will be about five tablespoons collected from your vein.

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 for lymphoma and other cancers have demonstrated no significant side effects. The dendritic cell vaccine used in this study has been tested in another clinical trial for lymphoma (LS1081/IRB 10-003023). No severe side-effects were seen in that study. 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 (MK-3475). Dendritic cells stimulate 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 hyper reacts 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 risk of this procedure is pain at the site of cryoablation. 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. We do not plan to cryoablate any tumors in the liver. With our current equipment, patients who have had cryoablation of lymphoma 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. Additionally, the cryoablation procedure will be conducted under x-ray guidance. The amount of radiation you will receive has a low risk of harmful effects.

Pembrolizumab (MK-3475)

Pembrolizumab works by helping your immune system to fight your cancer. However, pembrolizumab can also cause your immune system to attack normal organs and tissues in your body and can affect the way they work, which can result in side effects. These side effects may be serious (i.e., causing hospitalization or be life-threatening), may result in death, and/or may occur after you stop taking pembrolizumab. These side effects can affect more than one of your normal organs and tissues at the same time.

Very common side effects (greater than 10%) seen in people taking pembrolizumab (MK-3475) include the following:

- Itching of the skin
- Frequent or excessive bowel movements or diarrhea
- Cough

Common side effects (5-20%) seen in people taking pembrolizumab (MK-3475) include the following:

- Pain in joints, arthritis (arthralgia)
- Rash
- Fever
- Back pain
- Low levels of salt in the blood (hyponatremia) that may cause you to feel confused, have a headache, have pain or cramping in a muscle or group of muscles, or make you feel sick to your stomach
- Decreased release of thyroid hormone that may manifest as feeling tired, weight gain, feeling cold easily, or bowel movements occurring less often than usual
- Loss of skin color (vitiligo)
- Pain or uncomfortable feeling in the belly

Uncommon (less than 5%) side effects seen in people taking pembrolizumab include the following

- Inflammation of the lungs (pneumonitis) – you may feel short of breath and cough
- 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.
- Severe infusion reaction, which may be life-threatening - you may feel dizzy or faint, feel flushed, get a rash, have a fever, feel short of breath, experience a decrease in your blood pressure at the time of receiving your infusion (IV) or just after, or have pain at the site of infusion

- Inflammation of the bowels/gut, which may cause severe pain in your belly with loose or watery stools, and black, tarry, sticky stools or stools with blood or mucus (colitis)
- Inflammation of the skin so you may have peeling of the skin, itchiness, and/or skin redness. The skin inflammation (i.e., peeling, itching and redness) could also be widespread throughout your body. More severe skin reactions may involve the inside of your mouth, the surface of your eye and genital areas, and/or may cause the top layer of your skin to peel from all over your body which can cause severe infection (Severe skin reactions, including Stevens-Johnson syndrome or toxic epidermal necrolysis syndrome (TENS))

Rare (No event occurred in greater than 1% of everyone treated with pembrolizumab)

- Inflammation of the pancreas - symptoms may include abdominal pain that radiates to the back, swollen or tender abdomen, fever, nausea and vomiting (pancreatitis)
- Inflammation of the muscles that may have weakness or pain in the muscles (myositis)
- Inflammation of the eye - you may have eye redness, blurred vision, sensitivity to light, eye pain, see floaters, or have headaches (uveitis)
- Inflammation of the kidneys causing them not to work as well, you may pass less urine, cloudy or bloody urine, have swelling and low back pain (nephritis)
- Inflammation of the pituitary gland, which may cause headache, nausea, vomiting, a sensation of the room spinning around you (dizziness) changes in behavior, double vision, few to no menstrual cycles, or weakness (hypophysitis)
- Inflammation of the liver which may make you feel sick to your stomach and vomit, feel like not eating, feel tired, have a mild fever, a mild pain in the right side of your belly, cause yellowing of the skin or eyes and dark urine (hepatitis)
- Adrenal glands (glands on top of the kidneys) may not make enough hormone, which could cause tiredness, weight loss, muscle weakness, feeling faint, having joint, muscle, and bellyaches, nausea, vomiting, loose or watery stools, fever, salt craving, and sometimes darkening of the skin like a suntan (adrenal insufficiency)
- Type 1 diabetes, a condition that can cause too much sugar in your blood, feeling thirstier than usual, frequent urination, and weight loss – you may need to take insulin
- Inflammation of the heart muscle (middle layer of your heart) which can cause shortness of breath or heart rhythm problems or may be serious and require hospitalization. This may cause your heart to have difficulty pumping blood throughout your body, which can cause chest pain, shortness of breath, and swelling of the legs. You may experience a fast or irregular heartbeat that may cause dizziness or fainting, in rare cases can cause sudden death. (Immune-mediated myocarditis)
- Inflammation of the thyroid gland, an organ that makes and stores thyroid hormones. This condition may lead to change in your heart rate, blood pressure, body temperature, and the rate at which food is converted into energy (thyroiditis)

- Toxic Epidermal Necrolysis (TEN) 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 is similar to the skin damage from a severe burn and is serious and life threatening.
- Myasthenic Syndrome (muscle weakness), myasthenia gravis, or worsening of existing myasthenia gravis (nerve damage that causes muscle weakness and muscle fatigue) may make you feel weak and tired and may cause drooping of the eyelids, blurred or double vision, difficulty swallowing, slurred speech, weakness in your arms and legs, or difficulty breathing
- Guillain-Barre Inflammation of the nerves that may cause pain, weakness, or tingling in your hands and feet, and may spread to your legs, arms, and upper body, leading to severe muscle weakness and possible temporary paralysis
- Formation of small clusters of immune cells (called granulomas) in parts of your body such as your lymph nodes, eyes, skin, or lungs (sarcoidosis)
- Organ transplant rejection
- Inflammation of the spinal cord with pain, numbness, tingling, or weakness in the arms or legs, bladder or bowel problems including needing to urinate more frequently, urinary incontinence, difficulty urinating, and constipation (myelitis)
- Inflammation of the blood vessels (vasculitis) symptoms will depend on the blood vessels involved, for example, if it is your skin you may have a rash. If your nerves are not getting enough blood, you could have numbness or weakness, and may cause fever, weight loss, and fatigue.
- Inflammation of the brain with confusion and fever. This may also include disorientation, memory problems, seizures (fits), changes in personality and behavior, difficulty speaking, weakness or loss of movement in some parts of your body, and loss of consciousness (encephalitis)
- Inflammation of the spinal cord (with pain, numbness, tingling, or weakness in the arms or legs, bladder or bowel problems including needing to urinate more frequently, urinary incontinence, difficulty urinating, or constipation (myelitis)
- Low levels of parathyroid hormone (a hormone made by 4 tiny glands in your neck) which may result in low blood calcium and cause muscle cramps or spasms; fatigue or weakness; numbness, tingling, or burning in your fingertips, toes or lips (hypoparathyroidism)

Additionally, since pembrolizumab was approved in September 2014, the following side effects have been reported by people receiving pembrolizumab. These side effects were voluntarily reported from a group of people of unknown size. It is not possible to estimate the frequency of this side effect:

- Changes in eyesight, eye pain, whitish patches on the skin and hearing loss (Vogt-Koyanagi-Harada syndrome)
- Inflammation and scarring of the bile ducts (tubes that carry digestive fluid that is made in the liver). This can cause symptoms similar to those seen with inflammation of the liver (hepatitis) such as pain in the right side of your bellow, yellow eyes and skin, feeling tired, and itching (sclerosing cholangitis).
- Inflammation of the joints which may include joint pain, stiffness and/or swelling (arthritis)
- Severe responses of the immune system that cause the body to attack its own blood cells, spleen, liver, lymph nodes, skin and brain. This reaction may include fever, rash, inflammation of the liver, yellowing of the skin, an enlarged liver and spleen, low blood counts, and enlarged lymph nodes. The nervous system may also be affected and cause confusion, seizures, and even coma (hemophagocytic lymphohistiocytosis (HLH))

Please note: The side effects listed above can begin after treatment is completed.

Other less common side effects have been reported. The study doctor or staff can discuss these with you.

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

Data has emerged recently that patients treated with anti-PD-1 monoclonal antibodies, including pembrolizumab, have the potential for an increased risk of acute early GVHD and other severe complications when subsequently treated with allogeneic stem cell transplantation.

Tumor Biopsy
The risks of this procedure include pain, bleeding, or infection at the site of the biopsy. This may be performed under ultrasound or CT (x-ray) guidance. At the beginning of the study (Cycle 1) and at the time of disease progression, biopsy of a tumor biopsy may be done with complete surgical removal of one tumor by a surgeon under anesthesia. This biopsy will be performed as an outpatient procedure. The amount of radiation you will receive from the CT guidance has a low risk of harmful effects.

Other Risks
The risks of drawing blood include pain, bruising, or rarely, infection at the site of the needle stick.

You will be exposed to additional x-ray radiation during the research CT scans and during the research biopsies is x-ray guidance is necessary. The amount of radiation you will receive has a low risk of harmful effects.

Pregnancy and Birth Control:

The effect of Pembrolizumab and Dendritic Cells on a fetus (developing baby still in the womb), or on a breastfeeding infant, is unknown and may be harmful. Because of these risks, women cannot take part in this study if they are pregnant or breastfeeding.

If you are a female, you must have a negative pregnancy test in order to participate in this study unless you cannot become pregnant.

If you are sexually active and able to become pregnant, you must agree to use one of the birth control methods listed below:

- 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 and for at least 120 days after your last dose of study drug.

If you are sexually active, and able to father a child, you must agree to use one of the birth control methods listed below:

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

You must use birth control for the entire study and for at least 120 days after your last dose of study drug.

If your partner thinks she might have become pregnant while you are in the study or for 120 days afterwards, you must tell the Principal Investigator immediately. The Principal Investigator may ask for your partner's permission to collect information about the outcome of her pregnancy and her newborn. You won't have to stop taking the study drug or stop taking part in the study if your partner becomes pregnant.

Risk Summary:
Many side effects go away shortly after the study drug complex 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?

Taking part in this research study is voluntary. 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, the study sponsor or Mayo Clinic may stop you from taking part in this study at any time:

- If it is in your best clinical interest,
- If you do not 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. Treatment costs for research-related injuries not covered by your insurance will be paid by Mayo Clinic. 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. If you agree to take part in this study, there may or may not be direct medical benefit to you. We hope the information learned from this study will benefit other people with Non-Hodgkin Lymphoma in the future.

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 chemotherapy or participating in other research studies. You should talk to the Principal Investigator or your doctor if you have any questions about any of these treatments or procedures.

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:

- Research blood tests for immune monitoring
- Pembrolizumab MK-3475 (supplied by Merck)
- Cryoablation
- Research tumor biopsy
- Prevnar® and dendritic cell vaccines
- Leukapheresis

However, you and/or your health plan will need to pay for all other tests and procedures that you would normally have as part of your regular medical care. These tests and procedures include:

- Routine exams, blood tests, and scans (CTs, MRIs, or PETs)
- 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.

For more information on clinical trials and insurance coverage, you can visit the National Cancer Institute's Web site at http://cancer.gov/clinicaltrials/understanding/insurance-coverage. You can print a copy of the "Clinical Trials and Insurance Coverage" information from this Web site or you can call 1-800-4-CANCER (1-800-422-6237) and ask them to send you a free copy.

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 sample for future research. You can still take part in this current study even if you don't want your sample used for future research. If you agree to give your sample, it 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 Non-Hodgkin Lymphoma 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. If the results of the research are made public, information that identifies you will not be used.

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.
- Merck and Co., Inc.

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.
- Biocompatibles Inc., a BTG International group company

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 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 lasts forever, unless you cancel it.

MAYO CLINIC

Name and Clinic Number

Approval Date: **August 10, 2022**
Not to be used after: **November 23, 2022**

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