ID: UMCC 2017.056	Augmentation of the Graft vs. Leukemia Effect Via Checkpoint Blockade With Pembrolizumab	NCT03286114

UNIVERSITY OF MICHIGAN
CONSENT TO BE PART OF A RESEARCH STUDY

INFORMATION ABOUT THIS FORM

You may be eligible to take part in a research study. This form gives you important information about the study. It describes the purpose of the study, and the risks and possible benefits of participating in the study.

Please take time to review this information carefully. After you have finished, you should talk to the researchers about the study and ask them any questions you have. You may also wish to talk to others (for example, your friends, family, or other doctors) about your participation in this study. If you decide to take part in the study, you will be asked to sign this form. Before you sign this form, be sure you understand what the study is about, including the risks and possible benefits to you.

1. GENERAL INFORMATION ABOUT THIS STUDY AND THE RESEARCHERS

1.1 Study title: Augmentation of the Graft vs. Leukemia Effect via Checkpoint Blockade with Pembrolizumab for Relapse of Primary Malignancy after Allogeneic Hematopoietic Stem Cell Transplant: A Feasibility Study. (UMCC # 2017.056)

1.2 Company or agency sponsoring the study: University of Michigan

1.3 Names, degrees, and affiliations of the researchers conducting the study:

John Magenau, MD Division of Hematology/Oncology, Internal Medicine; University of Michigan

2. PURPOSE OF THIS STUDY

2.1 Study purpose:

Allogeneic stem cell transplantation, also known as bone marrow transplant or BMT, is an effective treatment of leukemia, even in advanced stages. Studies have shown, however, that in many patients their leukemia comes back after receiving a stem cell transplant.

This research study is designed to test the safety and effectiveness of increasing immune system responses using the drug, pembrolizumab, to see whether pembrolizumab, can help patients with Acute Myeloid Leukemia (AML), Acute Lymphoblastic Leukemia (ALL), or Myelodysplastic Syndrome (MDS) whose cancer has come back (relapsed) after allogeneic transplantation.

Pembrolizumab is also known as Keytruda®. It was developed by the pharmaceutical company, Merck & Co., Inc., and has been approved by the United States Food & Drug Administration (FDA) for treatment in patients with many types of cancer, including skin, lung cancer, bladder cancer, and lymphoma. Pembrolizumab has not been approved for use in people with your type of cancer. It is an experimental drug in this research study because this is one of the first studies to evaluate pembrolizomab in this setting.

3. INFORMATION ABOUT STUDY PARTICIPANTS (SUBJECTS)

Taking part in this study is completely **voluntary**. You do not have to participate if you don't want to. You may also leave the study at any time. If you leave the study before it is finished, there will be no penalty to you, and you will not lose any benefits to which you are otherwise entitled.

3.1 Who can take part in this study?

You are being asked to take part in this research study because you are at least 18 years of age and have Acute Myeloid Leukemia (AML), Acute Lymphoblastic Leukemia (ALL), or Myelodysplastic Syndrome (MDS) that has relapsed after you had a BMT.

3.2 How many people (subjects) are expected to take part in this study?
During this study, we expect to enroll about 20 people who will participate at the University of Michigan.

4. INFORMATION ABOUT STUDY PARTICIPATION

4.1 What will happen to me in this study?
The study team will explain the research study and answer any questions you have about the study. If you still want to participate in the study the study team will request you sign the consent form prior to any activities occurring that pertain to the study. Once your consent is obtained, the study team will look through your medical chart, ask you questions, and begin scheduling tests and procedures to determine if you are eligible for the study. The study team will inform you of the types of tests and procedures required before the study begins.

Once it is determined you are eligible to enter the study, tests and procedures done at your study visits as part of your regular cancer care will continue, but some may be done more often because you are participating in this research study. Also, some of the tests or procedures may have to be repeated if, for example, they were done too long ago or the results are not normal.

Some tests and procedures may be done that are not part of your regular cancer care and are being done only for this research study. Tests and procedures that are performed more often or are not part of your standard cancer care will be identified below as "Research".

Study Procedures
<u>Screening Phase</u>:
After you have signed this Informed Consent, you will have the following tests and procedures to determine whether you are eligible to take part in this research study. These tests can be done up to 2 weeks (14 days) before your first dose of pembrolizumab. These tests are routinely performed in individuals who have experienced relapse after BMT.

- **Review of Medical History:** You will be asked about previous diseases and surgeries that you have had and about your current disease and treatment.
- **Review of Prior and Current Medications:** You will be asked about medications you have taken or are currently taking including prescription and over the counter medication, vitamins, and herbal supplements.
- **Physical Examination**
- **Vital Signs:** Your temperature, pulse, respiratory rate, weight, blood pressure, and height will be measured.
- **Performance Status:** You will be asked about your ability to perform everyday tasks.
- **Pulse Oximetry:** Measuring the amount of oxygen in your blood by an easy and painless reading from your finger
- **Routine Blood Tests (approximately ½ tablespoon):**
    - Hematology: tests for blood cell count, coagulation studies

  - Chemistry: tests for kidney and liver function
  - Thyroid: tests for thyroid function
- **Routine Urinalysis**
- **Pregnancy Test (Women of child-bearing potential only):** A serum or urine pregnancy test will be performed within 72 hours before your first dose of pembrolizumab.
- **Bone Marrow:** A bone marrow biopsy and aspirate will be taken for disease assessment.
- **Research Blood Tests (approximately 1 tablespoon)**
  - Pharmacokinetics (PK): to see what your body does to pembrolizumab
  - Correlative studies: to check the status of you and your donor's immune system.
- **Research Buccal Swab:** Your cheek will be swabbed.

Study Drug Dosing
All subjects in this research study will begin by receiving Phase I which is 200 mg of pembrolizumab intravenously (directly into a vein) over 30 minutes every 3 weeks for up to 4 cycles (12 weeks). Each study cycle is 21 days.

Approximately 2 weeks after your 2nd dose (Day 35) of pembrolizumab, your response to the study drug will be assessed. If your disease is responding to the pembrolizumab, you will receive 2 more infusions. If your disease is not responding, you will not receive the two additional infusions of pembrolizumab in Phase I. Your doctor will discuss other treatment options at this time (e.g. chemotherapy).

About 2 weeks after your 4th dose or Day 77, your response to the study drug will be assessed. If you are tolerating the pembrolizumab and it is helping you by controlling your disease, you may continue to receive pembrolizumab every 3 weeks for up to an additional 13 doses (Phase II).

Phase I - Induction Phase
You will have the following tests and procedures on Day 1 of every study cycle performed during this phase of the study:

- **Review of Adverse Events**
- **Physical Examination**
- **Vital Signs:** Your temperature, pulse, respiratory rate, weight, and blood pressure will be measured.
- **Performance Status:** You will be asked about your ability to perform everyday tasks.
- **Routine Blood Tests (approximately ½ tablespoon)** for blood cell counts, coagulation studies, and to assess kidney, liver, and thyroid function.
- **Routine Urinalysis**
- **Serum or Urine Pregnancy Test (Women of child-bearing potential only)**
- **Bone Marrow Aspirate:** Approximately two weeks (Study Day 35) after your second infusion of pembrolizumab, you will have a bone marrow procedure to assess your disease.
- **Research Blood Tests (approximately 1 tablespoon):** Study Days 14, 35, and 56
  - Pharmacokinetics (PK)
  - Correlative studies
- **Pembrolizumab infusion:** You can receive up to 4 doses of pembrolizumab during the induction phase, depending on the results of the bone marrow on Day 35. If your disease is responding to the pembrolizumab, you will receive 2 more infusions. If your disease is not responding, you will not receive any additional doses of pembrolizumab during this phase.

Response after Phase I (Induction)

On Study Day 77, or about two weeks after Cycle 4 of Phase I, you will have the following tests and procedures performed:

- **Review of Current Medications and Adverse Events**
- **Physical Examination**
- **Vital Signs:** Your temperature, pulse, respiratory rate, weight, and blood pressure will be measured.
- **Performance Status:** You will be asked about your ability to perform everyday tasks.
- **Routine Blood Tests (approximately ⅓ tablespoon)** for blood cell counts and to assess kidney and liver function.
- **Pregnancy Test (Women of child-bearing potential only):** A serum or urine pregnancy test will be performed within 72 hours of your first dose of pembrolizumab.
- **Bone Marrow Aspirate:** for disease assessment
- **Research Blood Tests (approximately 1 tablespoon)**

If you are tolerating the pembrolizumab and your bone marrow assessment shows it is helping you, you may continue to receive pembrolizumab every 3 weeks for up to an additional 13 doses or until either your disease progresses, you have an unacceptable toxicity, or you are removed from the study for another reason.

If your bone marrow assessment shows that the pembrolizumab is not helping you, you will not receive any additional doses of pembrolizumab and will enter the **Follow-up Phase** of the study described below.

If you only received 2 infusions of pembrolizumab during the Induction Phase (Phase I) but your bone marrow assessment shows that the study drug was helping you, you may be considered for additional doses of pembrolizumab. Your study doctor will discuss this with you.

Phase II – Maintenance Phase

If your disease assessment on Day 77 shows a response, you may continue to receive pembrolizumab. This is the Phase II or Maintenance Phase of this research study. During the Maintenance Phase, you will have the following tests and procedures performed:

- **Review of Adverse Events**
- **Physical Examination**
- **Vital Signs and Weight**
- **Performance Status:** You will be asked about your ability to perform everyday tasks.
- **Routine Blood Tests (approximately ⅓ tablespoon)** for blood cell counts and to assess kidney, liver, and thyroid function.
- **Routine Urinalysis**
- **Research Blood Tests (approximately 1 tablespoon):** On Day 168 (Dose 9) and Day 252 (Dose 13)
    - Pharmacokinetics (PK)
    - Correlative studies
- **Pembrolizumab infusion:** You can receive up to 13 additional doses of pembrolizumab during the maintenance phase as long as you continue to tolerate the study drug and it continues to help you.

  ** You will not receive additional doses of pembrolizumab after you complete the Maintenance Phase.

Post-Maintenance

Approximately 2 weeks after your last dose of pembrolizumab, you will have the following tests and procedures:

- **Review of Adverse Events**
- **Physical Examination**

- **Vital Signs and Weight**
- **Routine Blood Tests (approximately ⅓ tablespoon)** for blood cell counts and to assess kidney and liver function.
- **Bone Marrow Aspirate:** for disease assessment
- **Research Blood Tests (approximately 1 tablespoon)**

Follow-Up Phase
You will return to the University of Michigan Cancer Center 30 days and and 90 days after your last infusion of pembrolizumab for the following tests and procedures:

- **Review of Adverse Events**
- **Physical Examination**
- **Vital Signs and Weight**
- **Routine Blood Tests (approximately ⅓ tablespoon** for blood cell counts and to assess kidney and liver function.
- **Research Blood Tests (approximately 1 tablespoon)**

Relapse
If your disease shows signs of progression any time while you are taking pembrolizumab or while you are in the follow-up phase, you will have a bone marrow aspirate and research blood samples (1 tablespoon) collected.

Research Studies
Tests will be performed on your blood and bone marrow samples to assess your disease and your immune response. Some of the testing may include genetic testing. Genes carry information about features found in you and people who are related to you, such as eye or hair color. The researchers are interested in the way that genes affect how your body responds to the therapy at different time points.

Your blood samples that are collected for correlative studies will be frozen and stored. All of the frozen samples will then be tested for the protocol specified testing at the same time at the end of the study. Samples will be identified with your subject study ID number. The University of Michigan study team will have access to the code linking your subject study ID number with your personal information. Your samples will not be shared with researchers outside of the University of Michigan.

Optional Studies
We would like your permission to store your blood and/or bone marrow samples leftover from the protocol specified testing noted above for future research. The future research may be similar to this study or may be completely different. You can take part in this study even if you do not agree to let us store your unused blood and/or bone marrow samples for future research.

If you give us your permission, we will store your unused blood and/or bone marrow samples in at the University of Michigan for 10 years. Even if you give us your permission now to keep your unused samples, you can change your mind later and ask us to destroy them by telling your study doctor or a member of the study team. Keep in mind, however, that all protocol specified testing must be completed on your samples before they are destroyed. Also, the results of any non-protocol specific testing that has already been completed or is in progress at the time of your request will still be used to preserve the integrity of the research.

Your unused blood and/or bone marrow samples will not be shared with researchers outside of the University of Michigan.

For an explanation of the risks associated with this future research, please refer to Genetic Information Nondiscrimination Act (GINA) and Privacy and confidentiality risks in Section 5.1 below.

You will not find out the results of future research on your unused blood and/or bone marrow specimens. Allowing us to store and use your samples for future research will not benefit you directly.

The University of Michigan may benefit financially from future research on your blood and/or bone marrow samples.

You will make your choice about giving your permission to store your unused blood and/or bone marrow samples in Section 12 of this Informed Consent.

The table on the next page shows another way of looking at the tests and procedures you will have at each study visit.

Study Period	Screening	Phase I: Induction				Response Post-Induction	Phase II: Maintenance[1]	Post-Maintenance[1]	Follow-Up	
Study Dose/Study Day (D)	Days -14 to -1	1 (D1)	2 (D21)	3 (D42)	4 (D63)	(D77)	Doses 5-17 (D84-D365)	End of dosing (D365)	30 and 90 Days after last dose	Relapse
Demographics and Medical History	X									
Prior and Concomitant Medication Review	X					X				
Review Adverse Events	X	X	X	X	X	X	X	X	X	
Physical Exam	X	X	X	X	X	X	X	X	X	
Vital Signs and Weight (Height measured at Screening only)	X	X	X	X	X	X	X	X	X	
Performance Status	X	X	X	X	X	X	X			
Pregnancy Test (urine or serum)	X	X	X	X	X	X				
Routine Hematology Blood Tests	X	X	X	X	X	X	X	X	X	
Routine Coagulation Blood Tests	X	X	X	X	X					
Routine Chemistry Blood Tests	X	X	X	X	X	X	X	X	X	
Routine Urinalysis	X	X	X	X	X		X			
Routine Thyroid Function Blood Tests	X	X	X	X	X		X			
Bone Marrow Biopsy and/or Aspirate	X		D35*			X*		X*		X
Research Blood Tests – PK and Correlative Studies	X		D35			X	D168[2] D252[3]	X	D425[4]	X
Research Buccal Swabs	X									
Study Drug Administration		X	X	X[5]	X[5]		X			
Post- Study Therapy Response Status								X		
Survival Status								X	X[6]	

1: For subjects showing a response after Day 77. Subjects not showing a response will proceed to the Post-Dosing (Follow-up Phase).
2: Dose 9
3: Dose 13
4: 60 days after last dose of pembrolizumab
5: Only if D35 bone marrow showed pembrolizumab was helping you
6: Will continue for every 8 or 12 weeks
*Bone Marrow Aspirate

Subject Responsibilities
As a subject participating in this research study, you have the following responsibilities. You should:

- Follow directions from the study staff.
- Make and keep study appointments.
- Give blood samples and urine samples.
- Tell the study staff about all of the medicines you take during the study.
- Tell the study staff about any changes to your health during the study.
- Not be part of any other research study while participating in this study.
- If you are female, you should not get pregnant or breastfeed a baby while in this study and for at least 120 days after your last dose of study drug.
- If you are a female of child bearing potential, you must agree to the use of two highly effective methods of contraception while in this study and for at least 120 days after your last dose of study drug. Your study doctor will discuss acceptable methods of contraception with you.
- If you are a male, you should not conceive a child with a female partner or donate sperm while in this study and for at least 120 days after your last dose of study drug.
- If you are a male capable of conceiving a child with a female partner, you must agree to the use of two highly effective methods of contraception while in this study and for at least 120 days after your last dose of study drug. Your study doctor will discuss acceptable methods of contraception with you.

4.2 How much of my time will be needed to take part in this study?

Visit	Number of Visits	Approximate Time of Visit
Screening	1	6 - 8 hours
Phase I: Induction Day 35 (bone marrow)	4 1	2 - 4 hours 1 - 3 hours
Response: Post-Induction	1	3 - 5 hours
Phase II: Maintenance	13	2 - 4 hours
Response: Post-Maintenance (End of Dosing)	1	3 - 5 hours
Follow-Up (30, 60, 90 days after last dose)	3	0.5 - 3 hours
Survival Follow-up clinic visit or Phone call	Every 8 weeks Every 12 weeks	1 - 3 hours 10 - 15 minutes

4.3 When will my participation in the study be over?
After you have completed the study procedures described in Section 4.1, you will be followed approximately every 8 weeks as part of your routine bone marrow transplant follow-up. If you are no longer able to come to the clinic for your follow-up visits, you will be contacted by phone every 12 weeks to check on your health status. We will check on the status of your health until death, withdrawal of consent, or the end of the study.

4.4 What will happen with my information and/or biospecimens used in this study?
Your collected information and biospecimens may be shared with others at Michigan Medicine.

Your collected information and biospecimens may also be shared with other researchers, both here or around the world, or with companies.

Additionally:

- With appropriate permissions, your identifiable collected information and biospecimens may be shared, and/or,
- Without your additional consent, your identifiable private information and identifiable biospecimens may be stripped of identifiers and used for future research studies or distributed to another researcher for future research studies

5. INFORMATION ABOUT RISKS AND BENEFITS

5.1 What risks will I face by taking part in the study? What will the researchers do to protect me against these risks?

Your study doctor and study staff will monitor you closely for side effects. Even with frequent blood tests and other examinations, taking the study drug involves risks, and some side effects cannot be predicted. Side effects can range from mild to severe and life-threatening. Many side effects will get better when you stop taking the study drug, but some may be long lasting or may never go away. Side effects may even cause death. You should tell your study doctor immediately about any side effects that you have or any change in how you feel while on this study. If you have side effects, your dose may have to be reduced, or you may have to stop taking the drugs and wait until you feel better before you start again. Your health care team may give you medicines or lower your dose of drugs to help lessen side effects. If any side effect is intolerable, you may have to permanently stop taking the drugs.

These risks will be minimized by:
We will minimize the risks by monitoring you carefully. We will provide the usual supportive care that would be routinely given to someone with your condition. If you have side effects from the investigational study treatment, we will make appropriate adjustments as defined by the study protocol. You may need to discontinue the investigational study treatment if the side effects are too serious. If you have signs of infection, you will receive appropriate antibiotics. If you have signs of bleeding you may need to receive transfusions of platelets, plasma, or red cells. If you start feeling sick to your stomach, you will be given medications to help reduce nausea. If you have vomiting, you may be given fluids through an IV.

Pembrolizumab:
Pembrolizumab/KEYTRUDA® is being studied by researchers and physicians at the University of Michigan to see if it is effective in treating various types of cancer, by itself or in combination with other therapies (e.g. chemotherapy) and to see what side effects are associated with its use.

As of 03–Sep-2016, pembrolizumab/KEYTRUDA® had been given to about 21,036 subjects with various cancers in clinical trials. Men and women with cancer were treated, some for up to approximately 2 years. Safety was studied across several cancers treated with different doses: 2 mg/kg every 3 weeks, 10 mg/kg every 2 or 3 weeks, and 200 mg fixed dose every 3 weeks Which is the FDA approved dosage. The side effects seen were similar.

Very Common side effects seen in ≥20% of subjects who received pembrolizumab:

- Itching of the skin
- Loose or watery stools
- Cough

Common side effects seen in ≥10% to 20% of subjects who received pembrolizumab:

- Joint pain
- Fever
- Back pain
- Rash

Common side effects seen in ≥1% to <10% of subjects who received pembrolizumab:

- Not enough thyroid hormone so you may feel tired, gain weight, feel cold, have infrequent or hard stools
- Too much thyroid hormone so you may feel anxious, angry, can't sleep, weak, tremble, sweat, tired, have loose and watery stools
- Inflammation of the lungs so you may feel short of breath and cough. Rarely this might lead to death.
- Inflammation of the bowels/gut that may cause pain in your belly with loose or watery stools
- Inflammation of the skin so you may have peeling of the skin, itching, skin redness
- Pain in your belly
- Loss of skin color
- Low level of salt in the blood that may cause you to feel tired, confused, headache, muscle cramps or sick to your stomach
- Dizziness or fainting (low blood pressure), flushing, rash, fever, shortness of breath or sick to your stomach at the time of receiving your infusion (IV) or just after, or pain at the site of infusion.

Common serious side effects seen in 1% to 4% of subjects who received pembrolizumab:

- Inflammation of the lungs so you may feel short of breath and cough. Rarely this might lead to death
- Inflammation of the bowels/gut that can cause pain in your belly with loose or watery stools
- Fever

Immune-mediated serious side effects seen in <1.0% of subjects who received pembrolizumab:

- Inflammation of the skin so you may have widespread peeling of the skin, itching, and skin redness. 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. Rarely these reactions lead to death.
- Inflammation of the liver that may cause a poor appetite, feeling tired, mild fever, muscle or joint aches, sick to your stomach and vomiting, pain in your belly, yellow eyes and skin, and dark urine
- Inflammation of the pituitary gland (a gland in the head), which may cause headaches, sick to your stomach, changes in behavior, double vision, few to no menstrual cycles, weakness, vomiting and dizziness or fainting.
- Adrenal glands (glands on top of the kidneys) may not make enough hormone causing tiredness, weight loss, muscle weakness, feeling faint, joint, muscle and abdominal aches, nausea, vomiting, loose or watery stools, fever, salt craving, and sometimes darkening of the skin like a suntan.
- Inflammation of the kidney so you may pass less urine or have cloudy or bloody urine, swelling and low back pain
- Inflammation of the muscles so you may feel weak or pain in the muscles
- Inflammation of the pancreas (a gland in your abdomen that controls sugar levels) so you may have severe pain in the top part of your belly that may move to the back, sick to your stomach, and vomiting that gets worse when you eat
- Inflammation of the eye so you may have redness of the eye, blurred vision, sensitive to light, have eye pain, see floaters or have headaches

- Too much sugar in your blood (diabetes), so you may feel thirsty, and are likely to need regular insulin shots
- Inflammation of the nerves that may cause pain, weakness or tingling in the hands and feet, and may spread to the legs, arms and upper body leading to severe muscle weakness and possible temporary paralysis.
- Inflammation of the middle layer of your heart wall (myocarditis) that 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. Sometimes this condition can lead to death

Additional serious side effects seen in <1.0% of subjects who received pembrolizumab:

- Dizziness or fainting (low blood pressure), flushing, rash, fever, shortness of breath or sick to your stomach at the time of receiving your infusion (IV) or just after, or pain at the site of infusion.

In addition to the above, the following side effect(s) have been seen in patients on pembrolizumab, but are still being evaluated to determine if they are related to the drug:

A condition where you will feel weakness and fatigue of your hip and thigh muscles and an aching back caused by your body's immune system attacking your healthy cells and tissues.

Additional Risk:
Some patients have experienced neutropenia, immune-mediated skin adverse reactions including, Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN).

Some of the symptoms listed in the sections above have been reported to occur simultaneously in patients treated with pembrolizumab. For example, Vogt-Koyanagi-Harada (VKH) syndrome is a grouping of symptoms including headache, loss of vision, eye pain, sensitivity to light, neck stiffness, hearing problems, and dizziness, that is caused by immune system activation against certain cells in the body. You should report any symptoms to the study team.

Potential Additional Risk
A potential added risk related to your transplant is the possibility that Pembrolizumab may increase your risk of graft-versus-host disease (GVHD) which could require treatment or be life threatening. You may develop GVHD anyway as a result of your transplant, as it is the most common, serious risk for your type of transplant. GVHD can occur in up to approximately 50% of patients after transplant and in severe cases that do not respond to treatment can result in death. GVHD has also been associated with less relapse of AML after transplant in some studies.

Risks of Study Procedures
Blood Draws
Collection of blood samples may cause pain, bleeding, bruising or infection. It is also possible that you may feel lightheaded or faint. Please tell your study doctor or the study nurse if you do not feel well after having your blood drawn at any time during your study participation.

Bone Marrow Aspiration
A bone marrow aspiration is a test involving a thin, hollow needle to withdraw a small amount of bone marrow, usually taken from the hip bone. Although the procedure includes the use of medications to decrease any pain

associated with the test, you may still experience some pain or discomfort. A potential but uncommon risk is the development of infection of the skin or underlying bone. You may also have some bleeding from the site.

Reproductive Risks

Women

If there is ANY chance that you can get pregnant, you must either agree to not have vaginal intercourse or you must use TWO types of birth control (one from each list below) AT THE SAME TIME. These birth control methods must be used from the time of enrollment, all during treatment including during temporary breaks from therapy, and for at least 120 days your last dose of study intervention. The following methods are considered acceptable birth control methods:

Primary forms

- tubal sterilization (tubes tied)
- partner's vasectomy
- intrauterine device
- hormonal contraceptives - (includes transdermal patch, injectables, implantables)

Secondary forms

- male latex condom with or without spermicide
- diaphragm with spermicide
- cervical cap with spermicide
- vaginal sponge (contains spermicide)

Any birth control method can fail. The reports of birth control failing are more frequent for female patients who use only a single form of birth control. Using two forms of birth control at the same time greatly reduces the chances of pregnancy.

If you become pregnant while taking pembrolizumab, you will be removed from the study. Your pregnancy will be monitored until your pregnancy has been completed or terminated. The outcome of your pregnancy will be reported to Merck, the supplier of pembrolizumab.

Men

Men must agree to either abstain from sexual activities that could result in pregnancy or use an acceptable form of birth control while taking part in the study and for at least 120 days your last dose of study intervention. Acceptable forms of birth control are male latex condom (with or without spermicide) or vasectomy. In addition, men should not donate sperm or semen while taking part in the study and for at least 120 days your last dose of study intervention.

If your partner becomes pregnant while you are taking pembrolizumab, you must notify the study doctor right away. The study doctor will request permission to follow the pregnancy to outcome. Your partner will be required to sign a separate pregnant partner consent before any information is collected.

Genetic Information Nondiscrimination Act (GINA)

The federal Genetic Information Nondiscrimination Act (GINA) generally makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. This law does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance. Under this law:

- Health insurance companies and group health plans may not request your genetic information that we obtain from this research
- Health insurance companies and group health plans may not use your genetic information when making decisions regarding your eligibility or premiums

- Employers with 15 or more employees may not use your genetic information that we obtain from this research when making a decision to hire, promote, or fire you or when setting the terms of your employment

GINA does not apply to the following groups, however these groups have policies in place that provide similar protections against discrimination:

- Members of the US Military receiving care through Tricare
- Veterans receiving care through the Veteran's Administration (VA)
- The Indian Health Service
- Federal employees receiving care through the Federal Employees Health Benefits Plans

Privacy and confidentiality risks

There are also non-physical risks associated with taking part in this study, such as the risks associated with a loss of privacy or confidentiality. For example, if your identity as a participant in this research or your identifiable genetic or health information were disclosed to unauthorized persons, there is the possible risk of discrimination by employers or insurance providers. The researchers believe that the risks of such improper disclosure are very small because strict privacy and confidentiality procedures for this research have been adopted.

As with any research study, there may be additional risks that are unknown or unexpected.

5.2 What happens if I get hurt, become sick, or have other problems as a result of this research?

The researchers have taken steps to minimize the risks of this study. Even so, you may still have problems or side effects, even when the researchers are careful to avoid them. Please tell the researchers listed in Section 10 "Contact Information" (below) about any injuries, side effects, or other problems that you have during this study. You should also tell your regular doctors.

If you think you have an injury or illness that is related to your participation in this clinical trial, it is important that you tell your study doctor immediately. If you have a clinical trial related injury or accident, the study staff will make sure that you get medical treatment.

You will receive appropriate medical care for any side affects you have while participating in this study. Your study doctor may also lower the drug dose or stop drug if you experience side effects.

You must inform your study doctor immediately if there are any changes in your health/condition, or if you have any concerns regarding the study. If for any reason you are seen by another healthcare provider or admitted to another hospital, you should make known your participation in this research study. These healthcare providers may wish to contact your study doctor to discuss your condition. Your study doctor may need to contact your other doctors if you develop any potentially significant, unexpected diseases or conditions that may have been caused by the study intervention or procedures or are discovered during the study.

5.3 If I take part in this study, can I also participate in other studies?

Being in more than one research study at the same time, or even at different times, may increase the risks to you. It may also affect the results of the studies. You should not take part in more than one study without approval from the researchers involved in each study.

5.4 How could I benefit if I take part in this study? How could others benefit?
You may not receive any direct personal benefits from being in this study. Taking part in this research study may not make your health better. Future AML, ALL, or MDS patients may benefit from knowledge obtained from the results of this research.

5.5 Will the researchers tell me if they learn of new information that could change my willingness to stay in this study?
Yes, the researchers will tell you if they learn of important new information that may change your willingness to stay in this study. If new information is provided to you after you have joined the study, it is possible that you may be asked to sign a new consent form that includes the new information.

6. OTHER OPTIONS

6.1 If I decide not to take part in this study, what other options do I have?
You may have standard chemotherapy agents (in consultation with your BMT physician or oncologist), palliative treatment (to relieve suffering and prolong quality of life, but not for sure), or no therapy at all. Your doctor can tell you more about these other treatments, their risks and their possible benefits. You should have this discussion about the risks and benefits or other alternatives prior to making your decision about whether or not you wish to take part in this research study.

7. ENDING THE STUDY

7.1 If I want to stop participating in the study, what should I do?
You are free to leave the study at any time. If you leave the study before it is finished, there will be no penalty to you. You will not lose any benefits to which you may otherwise be entitled and this will not affect your future medical care in any way. If you choose to tell the researchers why you are leaving the study, your reasons for leaving may be kept as part of the study record. If you decide to leave the study before it is finished, please tell your study doctor or one of the persons listed in Section 10 “Contact Information” (below).

You are free to partially or completely end your participation in the study. An example of partially ending your participation would be to discontinue receiving study intervention, while still allowing continuation of study follow-up procedures.

Please note that any information collected before you withdraw will be kept and used to complete the research.

Please note that even if you withdraw consent for further follow-up or contacts, if the study doctor becomes aware of additional safety information this will be reported to the sponsor in order to comply with legal or regulatory requirements.

7.2 Could there be any harm to me if I decide to leave the study before it is finished?
You are free to leave the study at any time. If you leave the study before it is finished, there will be no penalty to you. This will not affect your future medical care in any way and you will not lose any benefits to which you may otherwise be entitled. Tell the study doctor if you are thinking about stopping or decide to stop. It is important to tell the study doctor if you are thinking about stopping so any risks can be evaluated by your doctor. He or she will also tell you how to stop safely and discuss what follow-up care and testing could be most helpful for you. If you choose to tell the researchers why you are leaving the study, your reasons for leaving may be kept as part of the study record. If you decide to leave the study before it is finished, please tell your study doctor or one of the researchers listed in Section 10 “Contact Information” (below).

7.3 Could the researchers take me out of the study even if I want to continue to participate?
Yes. There are many reasons why the researchers may need to end your participation in the study. Some examples are:

- ✓ The researcher believes that it is not in your best interest to stay in the study.
- ✓ You become ineligible to participate.
- ✓ Your condition changes and you need treatment that is not allowed while you are taking part in the study.
- ✓ You do not follow instructions from the researchers.
- ✓ The study is suspended or canceled.

8. FINANCIAL INFORMATION

8.1 Who will pay for the costs of the study? Will I or my health plan be billed for any costs of the study?
The study will pay for research-related items or services that are provided only because you are in the study. Pembrolizumab will be provided at no cost to you. If you are not sure what these are, see Section 4.1 above or ask the researchers for a list. If you get a bill you think is wrong, call the researchers' number listed in section 10.1.

You or your health plan will pay for all the things you would have paid for even if you were not in the study, like:

- Health care given during the study as part of your regular care
- Items or services needed to give you study drugs or devices
- Chemotherapy
- Monitoring for side effects or other problems
- Deductibles or co-pays for these items or services.

If you do not have a health plan, or if you think your health plan may not cover these costs during the study, please talk to the researchers listed in Section 10 below or call your health plan's medical reviewer.

If you are injured or in the event of a medical emergency, dial 911 or visit your nearest Emergency Room. If you believe the study has made you sick or caused you injury, contact one of the people listed in section 10 of this document (Contact Information). If taking part in the study makes you sick or causes you injury, the study will not provide any compensation to you. You or your insurance provider will be billed for all costs of treatment for sickness or injury caused by the study. It is possible that your insurance will not cover these costs.
By signing this form, you do not give up your right to seek payment if you are harmed as a result of being in this study.

8.2 Will I be paid or given anything for taking part in this study?
No. You will not be paid for taking part in this study.

8.3 Who could profit or financially benefit from the study results?
The company whose product is being studied: Merck and Co., Inc.

The University of Michigan and the researchers performing this study will receive no financial interest in the outcome of this study. Research can lead to new discoveries, such as new tests, drugs, or devices. Researchers, their organizations, and other entities, including companies, may potentially benefit from the use of the data or discoveries. You will not have rights to these discoveries or any proceeds from them.

9. CONFIDENTIALITY OF SUBJECT RECORDS AND AUTHORIZATION TO RELEASE YOUR PROTECTED HEALTH INFORMATION

The information below describes how your privacy and the confidentiality of your research records will be protected in this study.

9.1 How will the researchers protect my privacy?
Your participation will occur at the University of Michigan medical center.

Your data will be kept confidential, to the extent permitted by applicable laws, in the following manner:
• Your name will not be used in any reports about the study
• You will be identified only by a study code: a subject ID number, and initials
• Your identifying information will be kept secure

We will assign a code number to the study data and biological samples and may use your initials. Some study data may contain information that could be used (perhaps in combination with other information) to identify you (e.g., initials, date of birth). Only the study team at the University of Michigan will have access to the code linking your subject ID number with your personal information.

Study data (that does not directly identify you) may be published in medical journals or shared with others as part of scientific discussions.

9.2 What information about me could be seen by the researchers or by other people? Why? Who might see it?
Signing this form gives the researchers your permission to obtain, use, and share information about you for this study, and is required in order for you to take part in the study. Information about you may be obtained from any hospital, doctor, and other health care provider involved in your care, including:

- Hospital/doctor's office records, including test results (X-rays, blood tests, urine tests, etc.)
- Mental health care records (except psychotherapy notes not kept with your medical records)
- Alcohol/substance abuse treatment records
- HIV/AIDS status
- Sexually transmitted disease and/or other communicable disease status
- Health plan/health insurance records
- All records relating to your cancer, the treatment you have received, and your response to the treatment
- Billing information
- Demographic information
- Personal identifiers

There are many reasons why information about you may be used or seen by the researchers or others during or after this study. Examples include:

- The researchers may need the information to make sure you can take part in the study.
- The researchers may need the information to check your test results or look for side effects.
- University, Food and Drug Administration (FDA) and/or other government officials, auditors, and/or the IRB may need the information to make sure that the study is done in a safe and proper manner.
- Study sponsors or funders, or safety monitors or committees, may need the information to:
    - Make sure the study is done safely and properly
    - Learn more about side effects
    - Analyze the results of the study

- Insurance companies or other organizations may need the information in order to pay your medical bills or other costs of your participation in the study.
- The researchers may need to use the information to create a databank of information about your condition or its treatment.
- Information about your study participation may be included in your regular UMHS medical record.
- Federal or State law may require the study team to give information to government agencies. For example, to prevent harm to you or others, or for public health reasons.

The results of this study could be published in an article, but would not include any information that would let others know who you are.

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.

9.3 What happens to information about me after the study is over or if I cancel my permission?
As a rule, the researchers will not continue to use or disclose information about you, but will keep it secure until it is destroyed. Sometimes, it may be necessary for information about you to continue to be used or disclosed, even after you have canceled your permission or the study is over.

Examples of reasons for this include:

- To avoid losing study results that have already included your information
- To provide limited information for research, education, or other activities (This information would not include your name, social security number, or anything else that could let others know who you are.)
- To help University and government officials make sure that the study was conducted properly

As long as your information is kept within the University of Michigan Health System, it is protected by the Health System's privacy policies. For more information about these policies, ask for a copy of the University of Michigan "Notice of Privacy Practices". This information is also available on the web at http://www.uofmhealth.org/patient+and+visitor+guide/hipaa. Note that once your information has been shared with others as described under Question 9.2, it may no longer be protected by the privacy regulations of the federal Health Insurance Portability and Accountability Act of 1996 (HIPAA).

9.4 When does my permission expire?
Your permission expires at the end of the study, unless you cancel it sooner. You may cancel your permission at any time by writing to the researchers listed in Section 10 "Contact Information" (below).

10. CONTACT INFORMATION

10.1 Who can I contact about this study?
Please contact the researchers listed below to:

- Obtain more information about the study
- Ask a question about the study procedures or treatments
- Talk about study-related costs to you or your health plan
- Report an illness, injury, or other problem (you may also need to tell your regular doctors)
- Leave the study before it is finished
- Express a concern about the study

Principal Investigator: John Magenau, MD
Mailing Address: University Hospital South, BMT Program
1500 E. Medical Center Drive
Ann Arbor MI 48109
Telephone: 734-615-5939

You may also express a concern about a study by contacting the Institutional Review Board listed below.

University of Michigan Medical School Institutional Review Board (IRBMED)
2800 Plymouth Road
Building 520, Room 3214
Ann Arbor, MI 48109-2800
Telephone: 734-763-4768 (For International Studies: US Country Code: 001)
Fax: 734-763-1234
e-mail: irbmed@umich.edu

If you are concerned about a possible violation of your privacy or concerned about a study you may contact the University of Michigan Health System Compliance Help Line at 1-866-990-0111.
When you call or write about a concern, please provide as much information as possible, including the name of the researcher, the IRBMED number (at the top of this form), and details about the problem. This will help University officials to look into your concern. When reporting a concern, you do not have to give your name unless you want to.

11. RECORD OF INFORMATION PROVIDED

11.1 What documents will be given to me?

Your signature in the next section means that you have received signed and dated copies of all of the following documents:

- This "Consent to be Part of a Research Study" document. (*Note: In addition to the copy you receive, copies of this document will be stored in a separate confidential research file and may be entered into your regular University of Michigan medical record.)*

12. SIGNATURES

Consent/Assent to Participate in the Research Study

I understand the information printed on this form. I have discussed this study, its risks and potential benefits, and my other choices with _____. My questions so far have been answered. I understand that if I have more questions or concerns about the study or my participation as a research subject, I may contact one of the people listed in Section 10 (above). I understand that I will receive a copy of this form at the time I sign it and later upon request. I understand that if my ability to consent or assent for myself changes, either I or my legal representative may be asked to re-consent prior to my continued participation in this study.

Legal Name: _____

Signature: _____

Date of Signature (mm/dd/yy): _____

For use only if required by sponsor:

Date of Birth (mm/dd/yy): _____

ID Number: _____

Consent/Assent for Participating in an Optional Sub-Study (Storage of unused blood/bone marrow samples for future research)

This project involves optional participation in a sub-study. I understand that it is my choice whether or not to take part in the sub-study. I understand that if my ability to consent or assent for myself changes, either I or my legal representative may be asked to re-consent prior to my continued participation in this study.

Please write your initials on the line next to the statement that reflects your choice.

_____ Yes, I agree to have my unused samples stored for future research.

_____ No, I do not agree to have my unused samples stored for future research.

Legal Name: _____

Signature: _____

Date of Signature (mm/dd/yy): _____

Principal Investigator or Designee

I have provided this participant and/or his/her legally authorized representative(s) with information about this study that I believe to be accurate and complete. The participant and/or his/her legally authorized representative(s) indicated that he or she understands the nature of the study, including risks and benefits of participating.

Legal Name: _____

Title: _____

Signature: _____

Date of Signature (mm/dd/yy): _____

PERSONAL CENSUS FORM

UMCC # 2017.056

Name _____ Date _____

The National Cancer Institute requires that The University of Michigan Comprehensive Cancer Center report race and ethnicity information about people who participate in clinical research to ensure that all populations are offered the opportunity to participate.

☐ Check here if you do not wish to provide some or all of the information below.

1. What race do you consider yourself to be? (Please select *one or more*)
   - ☐ American Indian/Alaska Native[a]
   - ☐ Asian[b]
   - ☐ Black or African American[c]
   - ☐ Native Hawaiian or Other Pacific Islander[d]
   - ☐ White[e]
   - ☐ More than one race[f]
2. Do you consider yourself to be Hispanic[g]? ☐ Yes ☐ No

---

[a] American Indian or Alaska Native- A person having origins in any of the original peoples of North, Central, or South America, and who maintains tribal affiliation or community attachment.

[b] Asian- A person having origins in any of the original peoples of the Far East, Southeast Asia, or the Indian subcontinent, including, for example, Cambodia, China, India, Japan, Korea, Malaysia, Pakistan, the Philippine Islands, Thailand and Vietnam.

[c] Black or African American- A person having origins in any of the black racial groups of Africa. (Terms such as “Haitian” or “Negro” are sometimes used in addition to “Black” or “African American.”)

[d] Native Hawaiian or Other Pacific Islander- A person having origins in any of the original peoples of Hawaii, Guam, Samoa, or other Pacific Islands.

[e] White- A person having origins in any of the original peoples of Europe, the Middle East, or North Africa.

[f] More than one race- (It is preferred that this be selected in addition to the selection of the specific races listed above, but this may also be solely selected.)

[g] Hispanic or Latino- A person of Mexican, Puerto Rican, Cuban, Central or South American, or other Spanish culture or origin, regardless of race. The term “Spanish origin” is sometimes used in addition to “Hispanic” or “Latino.”