



Consent of an Adult to Be in a Research Study

MAIN Consent Form

In this form "you" means a person 18 years of age or older who is being asked to volunteer to participate in this study.

Participant's Name _____ Medical Record # _____

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Sponsor: University of Virginia Health System

Funding Source: Merck, Sharp & Dohme
The University of Virginia Health System

What is the purpose of this form?

This form will provide you with information about this research study. You do not have to be in the study if you do not want to. You should have all your questions answered before you agree to be in this study.

Please read this form carefully. If you want to be in the study, you will need to sign this form. You will be given a signed copy of this form.

Who is funding this study?

This study is being funded with internal departmental funding from the University of Virginia Health System. The University of Virginia Health System is providing the study drug, HER2-BATs and funding procedures being done for research purposes. Merck is providing the study drug, pembrolizumab.

Is there a possible conflict of interest?

When a person or an organization has a financial or other interest large enough to seem as if it could affect their judgment, it is called a conflict of interest. Members of this study team have a conflict of interest with this study which is explained below.

One of the Study Investigators, Dr. Lawrence Lum, is the owner of the company which patented the study drug, HER2-BATs. Dr. Lum will oversee the manufacture of the drug and laboratory evaluations for this study; he will not be involved in recruitment, consenting, or any clinical evaluations. The Principal Investigator and others in charge of your clinical care do not have any ownership in the company, however, they could potentially profit from this study if the results are positive.



Why is this research being done?

The purpose of this study is to evaluate the safety and best dose level of an investigational treatment combination of 2 study drugs for people with metastatic breast cancer who have worsened after already receiving at least two lines of standard chemotherapy. **These 2 study drugs are called HER2-BATs and pembrolizumab.** We do not know whether HER2-BATs will work for your breast cancer. Previous clinical trials that were completed suggest that HER2-BATs may have clinical benefits to breast cancer patients but the number of patients in this clinical trial was small. Previous clinical trials also suggest that pembrolizumab may have clinical benefits to breast cancer patients.

HER2-BATs (bispecific antibody armed activated T cells) is an experimental anti-cancer drug. It is an anti-cancer agent created from your own immune cells (T cells) coated (“armed”) with an experimental drug made up of bispecific antibodies called Herceptin and OKT3. The HER2-BATs antibody is able to react against human breast cancer. An antibody is a type of protein that helps protect the body from bacteria and disease. HER2-BATs works by seeking out certain cancer cells like on breast tumor cells that have a molecule called Human Epidermal factor receptor 2 (HER2) on their surface. The HER2-BATs antibody targets the HER2 on the cancer cell and uses the body’s own immune system to destroy those cancer cells.

HER2-BATs is not approved by the Food and Drug Administration (FDA) for the treatment of breast cancer. As of May 2017, a total of 23 breast cancer patients have been treated with HER2-BATs on a previous completed phase I clinical trial. The drug was found to be active against breast cancer.

Pembrolizumab/KEYTRUDA is a drug that signals a protein called PD-L1 to recognize cancer cells. When PD-L1 recognizes cancer cells, it activates the immune system to destroy the cancer cells. Pembrolizumab is being studied to see if it is effective in treating over 30 types of cancer including breast cancer. Pembrolizumab is available by prescription to treat several different cancers, but not for breast cancer so it is considered an investigational drug in this study.

You are being asked to take part in this study because you have metastatic breast cancer and already had second line chemotherapy. All participants in this study will be treated with HER2-BATs and pembrolizumab.

Up to 37 people will be in this study at UVA.

How long will this study take?

Your participation in this study will require 17 study visits over 8 months. Each visit will last between 4 and 8 hours. If you live over 40 minutes away then you will be asked to stay in the area for 2 nights so the doctor can monitor your condition after you receive treatment. You will be treated with a 7-8 week course of investigational therapy and then you will have scans and other tests to see how you are responding to therapy.



What will happen if you are in the study?

Visit #1 SCREENING (will take up to 8 hours to complete):

If you agree to participate, you will sign this consent form before any study related procedures take place. Before you can start in the study, there will be a screening period. You will have tests and procedures during this time to make sure you are eligible and it is safe for you to participate.

The following tests will be performed as part of your routine clinical care and the results will be recorded for research purposes:

- Your **medical history and medication list** will be reviewed.
- A **physical exam** will be performed and your **vital signs** will be observed. Vital signs include checking your blood pressure, heart rate, temperature, height, and weight.
- You will be asked questions about your ability to complete daily activities and how you are feeling. This is your **daily activity assessment**.
- You may have a **MRI, CT, or PET/CT scan** (a special kind of x-ray) of the chest, abdomen, pelvis, or the whole body to evaluate your disease.
- Up to **1 tablespoon of blood will be drawn** to assess blood cell counts, blood clotting function, liver and kidney function, check certain salts, sugars and minerals.

The following tests are not part of routine cancer care and will be performed for research purposes:

- A Stem Cell Transplant specialist will determine your **eligibility for leukapheresis**. You may need to come in for a separate visit to complete leukapheresis eligibility.
- An electrocardiogram (**EKG**) will be performed to measure the electrical activity of your heart. If this test is not done for clinical care, we will perform it for research purposes.
- You will have a **MUGA or echocardiogram scan** (an ultrasound of your heart) to check your heart function. These scans create video images to check how your heart is pumping. If one of these tests is not done for clinical care, we will perform one of these tests for research purposes.
- If you have not recently completed a **MRI, CT, or PET/CT scan** of the chest, abdomen, pelvis, or the whole body, you will have one or more of these scans for research purposes.
- Up to **less than 1 tablespoon of blood will be drawn** or you will provide a **urine sample** for a **pregnancy test** if you are capable of becoming pregnant. This test must be negative in order to continue study participation. The results of the pregnancy test will be provided to you.
- Up to **less than 1 tablespoon of blood will be drawn** to check your thyroid function.
- You will provide a **urine sample** to check if there is blood or sugar in your urine.
- Up to **3 tablespoons of blood will be drawn** to test for HIV, hepatitis B, and C if one was not done for clinical purposes. These tests must be negative for you to participate in this study. If the Hepatitis C antibody test is positive, a second blood sample (**up to ½ teaspoon of blood will be drawn**) may need to be collected to determine if the disease is active. Positive Viral Hepatitis test results may be reportable to local health authorities according to local laws.



- You will be asked if any of your **leftover blood samples** can be banked for unspecified, future research. **This is optional.** See the *Collection of Samples and Health Information for Genetic Research and Specimen Banking* section below.
- **Archival (leftover) tissue** will be obtained from your previous biopsy, if available, to examine your tumor characteristics as they may relate to your response to treatment.

If these tests show you are eligible, you will return to the clinic (within 4 weeks) to begin study treatment.

STUDY TREATMENT ASSIGNMENTS

Within a week before your first study treatment visit, you will be placed into 1 of 3 study schedules described below. The study schedule group will be assigned based on the data collected in the study so far. **All participants will receive HER2-BATs.** The study groups will differ from one another by how often you receive the study drug, pembrolizumab. The first group of participants will start with schedule A.

Schedule	Treatment
A	• Pembrolizumab: 200mg at Visit 13
B	• Pembrolizumab: 200mg at Visit 8 and 13
C	• Pembrolizumab: 200mg at Visit 3, 8, and 13

Catheter Placement: You will need to have a special central venous catheter placed to administer the study drug. This catheter, called an infusa-port, will be placed before your first study drug infusion. The catheter will stay in place for the duration of your treatment(s) and will be removed when your doctor determines the catheter is no longer needed for any therapy(s).

STUDY VISITS:

BATs infusion treatment visits will take about 8 hours to complete.

Treatment visits without BATs infusion will take about 4-6 hours to complete.

If your disease gets worse, the study team will not collect blood samples from you to evaluate your immune system.

Visit #2 Leukapheresis Visit

We will collect your white blood cells (lymphocytes) using a procedure called **leukapheresis**. In this procedure, your blood is passed through a machine that removes lymphocytes and returns the rest of the blood cells and plasma back into your bloodstream.

You will have an IV catheter placed in each of your arms. One of the IV catheters will be used to remove your blood. The other IV catheter will return your cells back into your body after it goes through the leukapheresis device. If the veins in your arm are not suitable for the IV catheters, you will have a temporary central venous catheter placed to collect lymphocytes. The catheter will be placed



on the day of your leukapheresis procedure. This catheter will be removed following your leukapheresis procedure.

This procedure is being done for research purposes only. You will have blood tests performed before, during, and upon completion of the leukapheresis procedure to protect your health.

The lymphocytes will be taken to a laboratory at UVA and mixed with two proteins called OKT3 and IL-2. OKT3 will activate your T cells to multiply, at which point they are called “activated T cells” (ATC). IL-2 is a “nutrient” required by ATC. After 14 days in culture, the ATC will be coated with the bispecific antibody to produce bispecific antibody armed T cells (BATs), and then frozen and stored until they are scheduled to be infused.

You will have the leukapheresis once prior to study treatment. This visit will occur about 3 to 4 weeks before you begin your study treatment. If we are unable to collect enough cells or we are unable to make the BATs study drug, we may ask that you come in to complete the leukapheresis procedure again. If you need to come in a second time for your leukapheresis procedure, your doctor will discuss when you will need to come in.

The following tests will be performed as part of your routine clinical care and the results will be recorded for research purposes:

- Your **vital signs** will be observed. Vital signs include checking your blood pressure, heart rate, and temperature.
- **Less than 1 tablespoon of blood will be drawn and** you will provide a **urine sample** for a **pregnancy test** if you are capable of becoming pregnant. This pregnancy test must be negative in order to continue study participation. The results of the pregnancy test will be provided to you. This test must be done within 7 days prior to your leukapheresis procedure. If you have completed the pregnancy test as a part of your screening visit and it is within 7 days prior to your leukapheresis visit, you do not need to repeat this pregnancy test.

The following tests are not part of routine cancer care and will be performed for research purposes:

- At this visit up to **5 tablespoon of blood will be drawn** to check your blood cell counts, certain salts, sugars, and minerals, evaluate your immune system prior to treatment.
- **Up to 1 tablespoon of blood will be drawn** to check your blood type.

Visit #3 Schedule C only (within 7 days before first dose of HER2–BATs)

The following tests will be performed as part of your routine clinical care and the results will be recorded for research purposes:

- A **physical exam** will be performed and your **vital signs** will be observed. Vital signs include checking your blood pressure, heart rate, temperature, and weight.
- Your **medication list** will be reviewed.
- You will be asked questions for your **daily activity assessment**.
- Up to **less than 1 tablespoon of blood will be drawn** to assess blood cell counts, liver and kidney function, check certain salts, sugars and minerals.



The following tests are not part of routine cancer care and will be performed for research purposes:

- You will be given **pembrolizumab** (Schedule C only) through an IV for about 30 minutes.

Visits #4-7 and Visits #9-12 Study Procedures (2 visits per week over 5-6 weeks)

The following tests will be performed as part of your routine clinical care and the results will be recorded for research purposes:

- A **physical exam** will be performed at Visits 4, 6, and 9.
- Your **vital signs** will be observed. Vital signs include checking your blood pressure, heart rate, temperature, and weight.
- Your **medication list** will be reviewed at Visits 4, 6 and 9.
- You will be asked questions for your **daily activity assessment** at Visits 4, 6, and 9.
- **Up to less than 1 tablespoon of blood will be drawn** at Visits 4 and 9 to check your blood cell counts, certain salts, sugars, and minerals.
- You will be asked to **maintain a diary** of your temperature, blood pressure, medications taken, and any symptoms you experience for up to 3 days after each BATs infusion. You will be given detailed instructions as to how to complete this diary and how to contact the study team.

The following tests are not part of routine cancer care and will be performed for research purposes:

HER2-BATs You will be given up to 1×10^{10} dose per infusion of HER2-BATs twice per week. This BATs study drug will be given intravenously (using a central venous catheter) over about a 30 minute time-period. You will be monitored for up to at least 6 hours after the infusion.

- Up to **4 tablespoons of blood will be drawn** at Visits 4 and 9 to evaluate your immune system and assess whether the immunotherapy is enhancing anti-tumor activity.
- Depending on your side effects, **less than 1 tablespoon of blood may be drawn** to assess your cytokine levels after each BATs infusion (up to 48-72 hours after your infusion). Cytokines are proteins that help your immune system function.

Visit 8 Schedules B and C only (before your 5th BATs infusion) and Visit 13 Schedule A, B and C (after your 8th BATs infusion)

The following tests will be performed as part of your routine clinical care and the results will be recorded for research purposes:

- A **physical exam** will be performed and your **vital signs** will be observed. Vital signs include checking your blood pressure, heart rate, temperature, and weight.
- Your **medication list** will be reviewed.
- You will be asked questions for your **daily activity assessment**.
- Up to **less than 1 tablespoon of blood will be drawn** to assess blood cell counts, liver and kidney function, check certain salts, sugars and minerals.

The following tests are not part of routine cancer care and will be performed for research purposes:

- You will be given **pembrolizumab** through an IV for about 30 minutes at Visit 8 if you are in Schedules B and C. All Schedule Groups, A, B, and C will receive Pembrolizumab for Visit 13.



- Up to **less than 1 tablespoon of blood will be drawn** to check your thyroid function on Visit 13 if you are in Schedule C.

Visits #14-17

FOLLOW UP:

If you complete the course of experimental treatments, you will enter a follow-up period. Visit 14 will be 2 weeks after Visit 13 (Week 10). Visit 15 is 1 month after Visit 13. Visit 16 is 3 months after Visit 13. Visit 17 is 6 months after Visit 13.

Long Term Follow-up: After these visits, the study team may call to check in with you about every 3 months to see how you are doing, including what additional treatment you have received and the status of your disease. The study team will try to collect this long-term follow-up information from your medical record. If the necessary information is available in your medical record, then the study team may not contact you.

The following tests will be performed as part of your routine clinical care and the results will be recorded for research purposes:

- A **physical exam** will be performed and your **vital signs** will be observed at Visits 14-15. Vital signs include checking your blood pressure, heart rate, temperature, and weight.
- Your **medication list** will be reviewed at Visits 14, 15, and 16.
- You will be asked questions for your **daily activity assessment** at Visits 14 and 15,.
- You may have a **MRI, CT, or PET/CT scan** of the chest, abdomen, pelvis, or the whole body to evaluate your disease at Visits 15, 16, and 17.
- **About 1 tablespoon of blood will be drawn** at Visits 14, 15, 16, and to assess blood cell counts, thyroid, liver, and kidney function, check certain salts, sugars and minerals.

The following tests are not part of routine cancer care and will be performed for research purposes:

- You will have a **MUGA or echocardiogram scan** (an ultrasound of your heart) to check your heart function. If one of these tests is not done for clinical care, we will perform one of these tests for research purposes at Visit 14.
- Up to **4 tablespoons of blood will be drawn** at each visit to evaluate your immune system and assess whether the immunotherapy is enhancing anti-tumor activity.



IRB-HSR#19406: A Phase I/II Study of Anti-CD3 x Anti-HER2/*neu* (HER2Bi) Armed Activated T Cells (ATC) and Pembrolizumab Combination Therapy in Women with Metastatic Breast Cancer

Study Schedule

	Visit 1: Screening	Visit 2: Pheresis	Study Visits 3-13											Follow-up Visits 14-17			
			Week 1 (Visit 3)	Week 2		Week 3		Within Weeks 4-5 (Visit 8)	Week 6		Week 7		Week 8 (Visit 13)	Week 10	1 month	3 month	6 month
				Visit 4	Visit 5	Visit 6	Visit 7		Visit 9	Visit 10	Visit 11	Visit 12					
Informed Consent	X																
Medical History	X																
Physical Exam	X		X	X		X		X	X				X	X	X		
Vital Signs	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X		
Medications List Review	X		X	X		X		X	X				X	X	X	X	
Daily Activity Assessment	X		X	X		X		X	X				X	X	X		
Leukapheresis		X															
Pembrolizumab			X ¹					X ²					X				
HER2-BATs cell Infusion				X	X	X	X		X	X	X	X	X				
Patient Diary				X	X	X	X		X	X	X	X					
Blood Draws for Research ³	X	X		X	X	X	X		X	X	X	X		X	X	X	X
Blood Draws for Clinical Care	X		X	X				X	X				X	X	X	X	
Pregnancy Test (blood or urine)	X	X															
Urine Test	X																
EKG	X																
Echocardiogram or MUGA ⁴	X													X			
Tumor Imaging	X ⁴														X	X	X
Archival Tissue collection (if available)	X																

*Gray highlighted boxes include tests/assessments done for research.

¹ Only for Schedule Group C

² Only for Schedule Groups B and C

³ If your disease gets worse, the study team will not collect blood from you to evaluate your immune system.

⁴ Procedure will be done for research purposes if not already done recently for your standard of care.



What are your responsibilities in the study?

You have certain responsibilities to help ensure your safety. These responsibilities are listed below:

- You must come to each study visit.
- You must be completely truthful about your health history.
- Follow all instructions given.
- You should tell the study doctor or study staff about any changes in your health or the way you feel.
- Answer all of the study-related questions completely.
- Inform the study doctor or study staff as soon as possible if you have to take any new medications, including anything prescribed by a doctor or those that you can buy without a prescription (over-the-counter), including herbal supplements and vitamins. The study doctor will let you know if you can take these medications.
- You must have a responsible adult with you for 48 hours following each BATs cell infusion to assure your safety.

Specimens: Blood Testing

We will draw the following amounts of blood:

- Up to 5 tablespoons will be drawn on your Screening Day Visit#1.
- Less than 6 tablespoons will be drawn on your Leukapheresis Visit #2.
- Up to 2 teaspoons will be drawn on Visits 3, and 8
- Up to 1 tablespoon may be drawn on Visit 13.
- Less than 6 tablespoons may be drawn on the day of your BATs infusions.
- Up to 5 tablespoons will be drawn on each of the Follow-up Treatment Visits.

The blood will be taken to determine your eligibility for this study, evaluate your immune system, and possibly your cytokine levels. The total amount of blood we will be taking for research may be up to 51 tablespoons.

Optional Collection of Samples and Health Information for Specimen Banking

What Sort of Research Will Be Done On Your Sample(s)?

You are being asked to provide samples of your blood to be used for future research. You are also providing some samples to learn more about how people respond to study drug. If you stop study treatment early, there may be some leftover study drug or other blood samples that could be useful for future research. Along with specimens, researchers may need to collect some health information about you. Combining information from the specimen with information from your health records may be useful for this research. For this research, the following types of information could be included: diagnosis, treatment, and medical history.

If you agree, specimens collected for research will be added to a research specimen bank. The purpose of a specimen bank is to process, and store samples until researchers need them for future research. Some of your samples will be stored for an unlimited amount of time, so that they might be used for future research. Leftover study drug will be stored for at most 5 years.

The long-term goals of the samples collected in this bank will be mainly used for research on the immune system and cancer. Is it not possible, however, to list every research project that will include the samples because we cannot predict all of the research questions that will be important over the coming years. As we learn more, new research questions and new types of research may be done.



What will you have to do to give samples for research?

Blood samples will be collected for you at screening assessments, several times during treatment, and at your follow-up visits.

After the tests for your medical care are completed, there may be samples left over. Normally, these leftover samples would be thrown away. We are asking you to allow us to collect this leftover material for specimen banking.

How Will Your Sample(s) Be Labeled?

This research specimen bank is located at the University of Virginia under the leadership of Dr. Lawrence Lum. There is no set limit to the number of people who will provide samples to this bank.

Your sample(s) will not be labeled with your name or other information that would identify you directly. Instead, it will have a unique code that allows for it to be linked to some of your health information. This link means that your specimen can be identified but only indirectly. We can find out if we need to know which sample is yours in the event you wish the sample to be removed at a later date.

Which researchers can use your samples and what information about you can they have?

Your sample may be shared with researchers at the University of Virginia and at other institutions. Dr. Patrick Dillon will not give your name to other researchers who want to use your sample, but will only give them information like your age and what disease/condition you have. Those who would see the information would include researchers and the others listed under “Who will see your private information?” section of this consent document.

Some of the people who receive your information may not have to follow the privacy laws and may share or release your information because they do not have to follow the privacy laws.

What Are the Benefits To Donating Your Sample(s) For Specimen Banking?

It is very unlikely that any future research (specimen banking) performed using your specimen(s) would benefit you directly, but it may provide important medical knowledge that could help other patients with your medical condition or other medical problems in the future.

What Are The Risks of Donating Your Sample(s) For This Study?

Risks to Privacy from Specimen Banking:

The main risk of allowing us to store and use your samples and certain limited health information for research is a potential loss of privacy. One of the risks to you is the release of information from your health records. The University of Virginia will do its best to protect your records so that facts about you and your health will be kept private. The chance that information identifying you will be given to someone else is very small. However, we cannot *guarantee* it will be safe. To further safeguard your privacy, information obtained from future research will not be placed in your medical record.

There are certain risks of having health information given to other people by mistake. In the unlikely event that this happens, it could cause discrimination or mental harm to you or your family members if others were to see this information. The results could be that you may not be able to get or keep certain kinds of insurance. It could also hurt family relationships.



Your doctor will explain the risks of the routine medical procedures you are having. In some cases, your doctor will ask you to sign a separate clinical consent form that explains the risks of the procedure. Allowing your samples to be placed in the bank for future research will not change the risks of the medical procedure itself.

Will You Find Out the Results of the Research on Your Sample(s) for Specimen Banking?

Neither you, your health care provider, nor anyone in your family, will receive the results of any research done on your sample(s). The results will not be put in your health records. Therefore, results from any research done on your sample(s) will not affect your medical care. This helps protect you and other members of your family from harm that might be caused by this information.

What If You Change Your Mind About Donating Your Sample(s) for Specimen Banking?

If you decide now that your sample(s) can be kept for or specimen banking, and later change your mind, you can simply withdraw the sample(s) at that time. To withdraw you will need to write to the Principal Investigator listed on the first page of this form. We will then destroy any of your samples that has not already been used. However, if your sample has been used in research, the information that we have learned will remain in the study, even if you withdraw. Unless you withdraw from the study, permission for researchers to use your samples and to use and share your private health information for this study will never end.

What are the Reasons Why the Study Team Would Discard your Leftover Samples Early?

Leftover study drug created from your blood samples may be stored for up to 5 years. However, the study team may discard your samples early for several reasons. If the study team plans to discard your samples, they will attempt to notify you. The reasons for discarding your samples are:

- If the study doctor feels you will no longer benefit from storing your samples.
- If you withdraw your consent for the study team to save the samples or ask that they be destroyed.
- If the study team finds study drug created from your blood samples are not safe to use or are damaged.
- If the study closes.

What if You Would Like to Transfer Leftover Study Drug Created from Your Blood Samples to Another Storage Facility?

You may decide you no longer want the University of Virginia to store your study drug created from your blood samples and want to transfer your samples to another storage facility. It may or may not be possible to transfer your specimens to another facility. If you decide to transfer your samples, you may discuss this further with the study team at that time.

Will You Be Paid For Donating Your Sample(s) for Specimen Banking?

You will not be paid to donate your sample(s) for specimen banking.

Will Donating Your Sample(s) Cost You Any Money?

There is no cost to you to have your samples collected or used for genetic research and/or specimen banking.

If you want to know about the results before the study is done:

During the study your study leader will let you know of any test results that may be important to your health. In addition, as the research moves forward, your study leader will keep you informed of any new



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What are the risks of being in this study?

Risks from HER2-BATs include:

Very common side effects in more than 20 out of every 100 people taking HER2-BATs may include the following:

- Chills
- Headache
- Fever
- Nausea
- Vomiting
- Backache
- Hypotension (low blood pressure)
- Hypertension (high blood pressure)
- Fatigue

Common Side effects occurring in 1-3 out of every 100 people taking HER2-BATs may include the following:

- Subdural hematoma (bleeding in the brain)
- Allergic reactions
- Difficulty breathing
- Shortness of breath
- Cardiopulmonary arrest
- Neurologic damage such as weakness, numbness, cognitive impairment, or coordination problems

Rare, but serious side effects occurring in people taking HER2-BATs may include the following:

- Death

Risks from Pembrolizumab include:

Pembrolizumab works by helping your immune system 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 (greater than 20 in of every 100) seen in people taking pembrolizumab include the following:

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

Common (between 5 and 20 in every 100) seen taking pembrolizumab may include the following:

- Joint pain
- Fever
- Pain in your belly
- Back pain
- Rash
- Loss of skin color
- Not enough thyroid hormone, which may cause you to feel tired, gain weight, feel cold, or have infrequent or hard stools (hypothyroidism)



- Low level of salt in the blood that may cause you to feel tired, feel confused, headache, have muscle cramps, or sick to your stomach (hyponatremia)

Uncommon side effects (between 1 and 5 in every 100) seen in people taking pembrolizumab include the following:

- Too much thyroid hormone so you may feel anxious, feel angry, have trouble sleeping, feel weak, tremble, feel tired, sweat, have loose and watery stools (hyperthyroidism)
- Inflammation of the bowels/gut that may cause 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, itching, 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)
- Infusion reaction, where you may feel dizzy or faint, feel flushed, get a rash, have a fever, 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 lungs so you may feel short of breath and cough (pneumonitis)

Rare side effects (1 out of 100 or less) seen in people taking pembrolizumab include the following:

- Inflammation of the liver that may cause you to feel tired, have a mild fever, feel sick to your stomach and vomit, feel like not eating, have pain in the right side of your belly, yellow eyes and skin, and dark urine.
- Inflammation of the pituitary gland (a gland in the head), which may cause headaches or you feel 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, and feeling faint, having joint, muscle, and belly aches, nausea, vomiting, loose or watery stools, fever, salt craving, and sometimes darkening of the skin like a suntan (adrenal insufficiency)
- Inflammation of the kidney, so you may pass less urine or have cloudy urine, or bloody urine, swelling, and low back pain (nephritis)
- Inflammation of the muscles, so you may feel weak or pain in the muscles (myositis)
- 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 your back, feel sick to your stomach, and experience vomiting that gets worse when you eat (pancreatitis)
- Inflammation of the eye so you may have eye redness, blurred vision, sensitivity to light, eye pain, have headaches, or see floaters (uveitis)
- Type 1 Diabetes, a condition that can cause too much sugar in your blood, so you may feel thirstier than usual, frequent urination, and weight loss. You 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 possibly temporary paralysis (Guillain-Barré syndrome).
- Inflammation of the middle layer of your heart 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 (myocarditis)
- Inflammation of the thyroid gland, an organ that makes and store thyroid hormones. This condition may lead to change in heart rate, blood pressure, body temperature, and the rate at which food is converted to energy (thyroiditis)
- A condition that 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 (myasthenic syndrome/myasthenia gravis including exacerbation)
- The formation of small clusters of immune cells (called granulomas) in parts of your body such as your lymph nodes, eyes, skin, or lungs (sarcoidosis)
- 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, and constipation (myelitis)
- Inflammation of the blood vessels (vasculitis). Symptoms will depend on the particular blood vessels that are involved in the inflammatory process, for example; if it is your skin, you may get a rash. If your nerves are not getting enough blood, you could have numbness and weakness. You may also experience fever, weight loss, and fatigue.
- 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)
- Inflammation of the stomach (gastritis). You may have pain in your belly, feel full, and/or sick to your stomach. You may also experience nausea, vomiting and/or loss of appetite.
- Low number of red blood cells (cells that carry oxygen) due to destruction of red blood cells (hemolytic anemia). You may feel weak, tired, lightheaded, short of breath, and/or have a fast heartbeat. You may also experience difficulty with physical exercise, pale or yellow skin, dark urine, and/or fever.
- Not enough pancreatic enzymes (proteins that break down food) that leads to poor digestion of food (exocrine pancreatic insufficiency). You may have bloating, gas, discomfort in your belly, diarrhea, abnormal stool that is oily, and/or weight loss.

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:

- Inflammation of the joints which may include joint pain, stiffness and/or swelling (arthritis)



- Severe responses of the immune system that causes the body to attack its own blood cells, spleen, liver, lymph nodes, skin, and brain. This 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)
- 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 right side of your belly, yellow eyes and skin, feeling tired, and itching (sclerosing cholangitis).
- Inflammation or swelling of the nerve fibers of the eye which send visual information from your eye to your brain. When this health condition occurs, it often has a sudden onset of vision changes. These vision changes can include blurring of vision or complete loss of vision; loss of color vision in which colored objects appear grey; pain when moving your eyes, and/or loss of peripheral vision. It may affect one or both eyes at the same time (optic neuritis).

If you have had an allogeneic stem cell transplant (a procedure in which a person receives blood-forming stem cells from a donor), you may experience graft versus host disease (GvHD), which may include diarrhea, skin rashes, and liver damage, after receiving pembrolizumab. Sometimes this condition can lead to death.

Risk of Leukapheresis

The leukapheresis procedure has similar side effects that can happen when people donate blood. A small number of people can experience nausea, fainting, dizziness, blood loss, and infection. A temporary decrease in your platelet, red cell counts, and white blood cell count occurs with the procedure. Very rarely, there is a need to provide a transfusion if blood counts have fallen too low.

Pain, redness, bruising, infection, and blood clots can occur at the sites where the needles are placed. The anti-coagulant (citrate) used may cause muscle cramping, numbness, cold feeling, tingling sensations in the lips and fingers, and feeling anxious. Rarely, the anti-coagulant can cause seizures, abnormal heart rhythms or death in an allergic type reaction. Other side effects seen include mild tightness in the chest (sometimes), cough (sometimes), low and/or high blood pressure (sometimes), and slow pulse rate (sometimes) . There is also a risk of very rare or unknown side effects.

If there is a problem with the equipment or needle in your vein, the red blood cells and plasma may not be returned to you. This may cause a mild anemia.

If you have any side effects, unusual sensations or discomfort during leukapheresis, notify the nurse or doctor immediately.

Risk of Central Venous Catheter Placement:

If your veins cannot be used to collect lymphocytes during leukapheresis, you will have a temporary central venous catheter placed to collect lymphocytes and return your blood. This catheter is removed



immediately following the leukapheresis procedure. You will also be given the study drug through a different kind of central venous catheter, called an infusa-port. If this catheter is needed it may be placed at the same time as the temporary central venous catheter or it may be placed at a different visit. Having a central venous catheter inserted may cause:

- Local pain (common)
- Bleeding or blood loss (common)
- Infection (sometimes)
- Bleeding into or around your lungs (rare, but serious)
- Puncture of a lung leading to your lungs collapsing (rare, but serious)
- Cardiac arrest (rare, but serious)
- Death (rare, but serious)

Risks of Fluoroscopy (X-Ray):

You may also receive 1-2 minutes of fluoroscopy for the insertion of a catheter using X-rays. For this procedure, you could receive 1-2 mSv of effective radiation dose. The dose from this portion would be equivalent to several months of background radiation exposure. The precise risk from this dose is not known but is thought to be small. The above radiation dose is what you will receive from this study only and does not include any exposure you may have received or will receive from other tests. If you were to receive all of this imaging, the total effective radiation dose could be as high as 114 mSv. This radiation exposure is not necessary for your medical care but is necessary to obtain the research information desired. If you are pregnant, you may not participate in this research study. It is best to avoid radiation exposure to unborn children since they are more sensitive to radiation than adults.

Risks of having an MRI:

MRI scanning is a painless procedure that only requires that you lie quietly on a padded table that gently glides you into a cylindrical opening inside a large magnet.

While the scanner is performing your scan, you will hear some humming and thumping sounds. These are normal and should not worry you. Because of the magnetic field and radio frequencies people with any type of metal in their body should NOT have an MRI. This may include things like pacemakers, aneurysm clips or shrapnel. It is important that you inform the technologist if you have any of these metallic appliances. Please inform the technologist if you are pregnant or think that you may be pregnant.

There is a low risk of experiencing symptoms of anxiety or claustrophobia while lying in the scanner. Should you experience these symptoms or otherwise become uncomfortable you can voluntarily stop your participation in this study. There will be NO consequences to your clinical care or to your participation in the study should you choose to stop your participation.

Risk of using gadolinium:

You will receive or are scheduled to receive a contrast called Gadolinium for your MRI. This substance will help the tissues show up better.



The following risks are associated with gadolinium contrast:

- Allergic reaction. Some people experience temporary itching after receiving MRI contrast. Less than one person in 300,000 will experience severe allergic reaction which requires treatment. Severe allergic reaction may include difficulty breathing or wheezing, tightness in the throat, swelling of lips, tongue or throat, fast heartbeat.
- Contrast infiltration. Contrast that is injected outside the vein into other tissues can cause local pain and swelling at the injection site. Treatment generally consists of hot or cold packs and elevation of the affected arm. Infiltrations most often get better over time.
- Temporary metallic taste in the mouth, tingling in the arm, nausea, or headache occurs in less than 1 in 100 people.
- The FDA has received information about an extremely rare disease called Nephrogenic Systemic Fibrosis (NSF) is a rare disease that is linked with the use of Gadolinium in people with severe kidney disease.

NSF causes hardening and thickening (fibrosis) of the skin, connective tissues like muscles, tendons, ligaments, and blood vessels throughout the body. In addition, those who develop NSF may have scarring of their body organs. The signs of NSF also include:

- burning, itching, swelling, hardening and tightening of skin;
- red or dark patches on the skin;
- yellow spots on the whites of the eyes;
- stiffness in joints with trouble moving or straightening the arms, hands, legs or feet;
- pain deep in the hip bones or ribs;
- Muscle weakness.

In most of the cases reported to the FDA, symptoms of NSF started between 2 days to 18 months after a person received the Gadolinium-based contrast agent. NSF may get worse and may lead to death. There is no known treatment for NSF.

If you have any of the symptoms listed above after receiving Gadolinium-based contrast for a study MRI, please contact the study team immediately. The study team will review your symptoms and perhaps recommend a skin biopsy, which is the only way to determine if you actually have NSF.

The FDA has received information indicating that gadolinium may deposit in the brain and other organs of some people who have had four or more gadolinium contrast-enhanced MRI scans and it may remain for a long time. Although no signs or symptoms of negative health effects or changes to organs have been seen with these deposits to date, it is not known if these deposits may lead to negative health effects in the future.

Before you receive gadolinium/additional gadolinium for research:



- You will be screened by UVA Department of Radiology staff prior to getting gadolinium. If radiology screening shows that it might be unsafe for you to receive this contrast, then you will not be able to receive the contrast.

Risks Related to Radiation Exposure:

As a participant in this study you could receive radiation exposure from the following scans:

CT Scan: You may receive a Computed Tomography (CT) scan of your torso. Although each organ will receive a different dose, the total effective radiation dose you will receive from one of these scans is approximately 16 mSv. For comparison this dose is roughly 32% of the annual radiation dose safely allowed for a radiation worker such as the person performing your CT. The precise risk from this dose is not known but is thought to be small. You may have as many as two of these CT scans.

FDG PET/CT: You may receive a Positron Emission Tomography (PET) scan combined with a Computed Tomography (CT) scan using the radiopharmaceutical F-18 FDG. Using the standard way of describing radiation dose, your heart and pancreas will receive the most radiation from this study. All other organs will receive smaller amounts of radiation. Although each organ will receive a different dose, the total effective radiation dose you will receive from one of these PET/CT scans is approximately 27 mSv. For comparison, this dose is roughly 54% of the annual radiation dose safely allowed for a radiation worker such as the person performing your scan. The precise risk from this dose is not known but is thought to be moderate. You may have as many as two of these PET/CT scans.

MUGA Scan: You may receive a MUGA heart scan to image your heart chambers. This study requires the use of radioactive drugs to be injected into your body and then imaged with special cameras. While the nuclear medicine drugs are intended for your heart, other organs will receive some radiation dose. Although each organ will receive a different dose, the total effective radiation dose you will receive from just one of these scans is approximately 6.6 mSv. For comparison, this dose is 13% of the annual radiation dose safely allowed for a radiation worker such as the person performing your scans. The precise risk from this dose is not known but is thought to be small. You may have as many as two of these MUGA scans.

Blood Donation

If you participate in this study it may affect your ability to donate blood. If you have any questions call the organization where you donate blood and talk to one of their nurses.

Risks of having your blood drawn:

Having blood drawn may cause:

- ✓ pain (common),
- ✓ a bruise (sometimes),
- ✓ fainting or passing out (not very often), and
- ✓ infection (rare).

If the people doing the study are exposed to your blood or body fluids in a way that could give them a disease, your blood may be tested. The tests might check for:



- ✓ hepatitis,
- ✓ HIV (Human Immunodeficiency Virus), or
- ✓ other infections.

You and the person exposed would be told the test results. However, your name would be kept private. If your test is positive for hepatitis or HIV or any other infection that may affect your clinical care, we will tell you the results and help you understand what the results mean for you.

Risks of taking blood from an IV catheter:

Risk of Repeated Sticks

Sometimes the catheter stops working. In order to get the blood we need, we may have to stick you again with another needle.

Risks for women:

Pregnancy and Contraception

The drug(s) used in this study can harm an unborn or nursing baby. Therefore, you cannot be in this study if you are pregnant or nursing a baby. A pregnancy blood test will be done at your screening visit and within 7 days of your leukapheresis procedure before starting this study if you are a woman able to become pregnant. You MUST NOT become pregnant while on this study or for up to 4 months after your last dose of drug.

You and your partner must use an approved form of birth control during this study. Examples of birth control you may use are:

- IUD (intrauterine device)
- Vasectomy of a female subject's male partner
- Contraceptive rod implanted into skin

The birth control methods listed below are less effective. They may be used if combined with other birth control methods.

- Condoms
- Diaphragm with spermicide (cannot be used in conjunction with cervical cap/spermicide)
- Cervical cap with spermicide (nulliparous women only)
- Withdrawal
- Sponge (nulliparous women only)
- Oral contraceptive pill, contraceptive skin patch, vaginal contraceptive ring, vaginal contraceptive ring, or subcutaneous contraceptive injection

Ask your doctor for more details about the proper birth control method for you. If you become pregnant during this study, you must tell your doctor right away. Your doctor will discuss your treatment and the effect on the pregnancy.



Other unexpected risks:

You may have side effects that we do not expect or know to watch for now. Call the study coordinator or office nurse if you have any symptoms or problems.

Could you be helped by being in this study?

You may or may not benefit from being in this study. Possible benefits include: lessening symptoms from your disease, shrinking your tumor, and/or lengthening your survival; however, no guarantees can be made. In addition, information researchers get from this study may help others in the future.

What are your other choices if you do not join this study?

You do not have to be in this study to be treated for your illness or condition. You can get the usual treatment even if you choose not to be in this study. The usual treatment would include:

- Standard chemotherapy.
- You may be in another study if one is available to you.
- Your study doctor can provide information about your disease and the benefits and risks of other treatments.

If you are an employee of UVA your job will not be affected if you decide not to participate in this study. If you are a student at UVA, your grades will not be affected if you decide not to participate in this study.

Will you be paid for being in this study?

You will not get any money for being in this study.

You will be asked to stay locally and within 40 minutes of UVA for 48 hours after each of your BATs infusions if you live over 40 minutes away. Accommodations at the contracted hotel for the 2 nights following BATs infusion will be arranged by the study team and provided at no cost to you. The study team will pay the hotel directly.

If you choose a different hotel or accommodation source, you will need to make those arrangements. The study budget will reimburse up to the nightly rate agreed upon by contracted hotel for the 2 nights, up to \$54 per night (receipts will need to be provided). The study team will advise you on process for reimbursement or ability to pay hotel directly.

You should get your reimbursement about 4-6 weeks after you submit your receipts.

By agreeing to be in this study, you are donating your blood, samples for research, and giving up any property rights you may have in them. The results of this research using your donated materials may have commercial value. However, you will not receive any payments.

Will being in this study cost you any money?

The following procedures/tests, which are being done for research purposes, will be provided at no cost to you or your health insurance:



- Leukapheresis procedure
- Central venous catheter placement
- HER2-BATs production
- Pembrolizumab
- Blood draws to check your thyroid and immune system (including cytokine levels)
- Blood draw to detect HIV, Hep B, and Hep C
- Pregnancy test
- Urine test
- Tumor imaging at screening if it was not already done for standard of care purposes and/or it needs to be repeated
- Obtaining archival tissue

The following procedures/tests are being done for research purposes. These procedures are being done to support your care while you are in this study and will be charged to your health insurance. If your insurance company does not pay for these procedures, the study will pay:

- HER2-BATs drug and infusion procedure
- MUGA or echocardiogram
- EKG

You and/or your insurance company are responsible for costs of study visits, physical exams, labs for clinical care, drug administration charges (infusion/injection costs), nursing care and tumor imaging performed every 8-12 weeks.

You and/or your insurance company must pay for any tests or care given beyond what is required in this study. In addition, you and/or your health insurance may also have to pay for other drugs or treatments that are given to help you control any side effects. You will have to pay for any costs not covered by your health plan. You may be responsible for any co-payments or deductibles. You may wish to ask for an estimate of your financial costs. You may also wish to check with your insurance company before the study starts. Ask what they will cover and if they require you to get their permission before you decide to be in the study.

You will be responsible for the cost of travel to come to any study visit and for any parking costs.

What if you are hurt in this study?

If you are hurt as a result of being in this study, there are no plans to pay you for medical expenses, lost wages, disability, or discomfort. The charges for any medical treatment you receive will be billed to your insurance. You will be responsible for any amount your insurance does not cover. You do not give up any legal rights, such as seeking compensation for injury, by signing this form.

What happens if you leave the study early?

You can change your mind about being in the study any time. You can agree to be in the study now and change your mind later. If you decide to stop, please tell us right away. You do not have to be in this study to get services you can normally get at the University of Virginia.



Even if you do not change your mind, the study leader Dr. Patrick Dillon can take you out of the study. Some of the reasons for doing so may include:

- a) Your study physician is concerned about your health
- b) Your disease gets worse
- c) The side effects of the treatment are too dangerous for you
- d) New information shows the treatment will not work or is not safe for you
- e) You do not follow your doctor's instructions
- f) The study sponsor closes the study for safety, administrative or other reasons
- g) There is potential that your cells may not grow in culture or cannot be used for other reasons, for example, if the cells were no longer alive after processing, there was contamination in the processing of your cells, or if there was a bag breakage in the freezer. If there is any safety concern or if your cells are found to be non-viable (dead) you will not receive your armed activated T cells and you will be removed from the trial.

How will your personal information be shared?

The UVA researchers are asking for your permission to gather, use and share information about you for this study. If you decide not to give your permission, you cannot be in this study, but you can continue to receive regular medical care at UVA.

If you sign this form, we may collect any or all of the following information about you:

- Personal information such as name, address and date of birth
- Your health information if required for this study. This may include a review of your medical records and test results from before, during and after the study from any of your doctors or health care providers. This may include mental health care records, substance abuse records, and/or HIV/AIDS records.
- Blood samples if you agree to provide them for this study

Who will see your private information?

- The researchers to make sure they can conduct the study the right way, observe the effects of the study and understand its results
- People or groups that oversee the study to make sure it is done correctly
- The sponsor(s) of this study, and the people or groups it hires to help perform or review this research
- Insurance companies or other organizations that may need the information in order to pay your medical bills or other costs of your participation in the study
- Tax reporting offices (if you are paid for being in the study)
- People who evaluate study results, which can include sponsors and other companies that make the drug or device being studied, researchers at other sites conducting the same study, and government agencies that provide oversight such as the Food and Drug Administration (FDA) if the study is regulated by the FDA.
- If you tell us that someone is hurting you, or that you might hurt yourself or someone else, the law may require us to let people in authority know so they can protect you and others.



Some of the people outside of UVa who will see your information may not have to follow the same privacy laws that we follow. They may release your information to others, and it may no longer be protected by those laws.

The information collected from you might be published in a medical journal. This would be done in a way that protects your privacy. No one will be able to find out from the article that you were in the study.

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.

We have asked the federal government to issue a Certificate of Confidentiality, to help protect the privacy of your study records. If we receive a subpoena or court order demanding information from the study records that would identify you, we will use the Certificate to resist the demand. However, UVa will not use it in the following cases.

- You have agreed in writing to allow UVa to share the information with your employer, your insurance company for billing purposes, or someone else
- Reports to authorities where there is a danger that you may harm yourself or others, or if there is evidence of probable child or elder abuse or neglect.
- Reports to authorities if you have an infectious disease that health care providers are required to report by law.

In addition, the Certificate does not prevent government authorities who oversee research from reviewing this study. This Certificate does not mean that the government either approves or disapproves of this study. It just helps protect your privacy.

What if you sign the form but then decide you don't want your private information shared?

You can change your mind at any time. Your permission does not end unless you cancel it. To cancel it, please send a letter to the researchers listed on this form. Then you will no longer be in the study. The researchers will still use information about you that was collected before you ended your participation.

A copy of this consent form will be put in your medical record. (This is not the same as the record of this research study.) This means that everyone who is allowed to see your medical records will be able to find out that you are in this study. This is done so your regular doctors will know what you receive as part of this study. If you have other health problems during the study, they will be able to treat you properly.

We have asked the federal government to issue a Certificate of Confidentiality, to help protect the privacy of your study records. If we receive a subpoena or court order demanding information from the



study records that would identify you, we will use the Certificate to resist the demand. However, UVA will not use it in the following cases.

- You have agreed in writing to allow UVA to share the information with your employer, your insurance company for billing purposes, or someone else
- Reports to authorities where there is a danger that you may harm yourself or others, or if there is evidence of probable child or elder abuse or neglect.
- Reports to authorities if you have an infectious disease that health care providers are required to report by law.

In addition, the Certificate does not prevent government authorities who oversee research from reviewing this study. This Certificate does not mean that the government either approves or disapproves of this study. It just helps protect your privacy

Please contact the researchers listed below to:

- Obtain more information about the study
- Ask a question about the study procedures or treatments
- 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:

Patrick Dillon, MD

University of Virginia School of Medicine

Division of Hematology Oncology

PO Box 800716

Charlottesville, VA 22908 Telephone: 434-924-1495

What if you have a concern about this study?

You may also report a concern about this study or ask questions about your rights as a research subject by contacting the Institutional Review Board listed below.

University of Virginia Institutional Review Board for Health Sciences Research

PO Box 800483

Charlottesville, Virginia 22908 Telephone: 434-924-2620

When you call or write about a concern, please give as much information as you can. Include the name of the study leader, the IRB-HSR Number (at the top of this form), and details about the problem. This will help officials look into your concern. When reporting a concern, you do not have to give your name.



Specimen Banking Options:

You do not have to participate and agree for leftover blood specimens and/or leftover study drug created from your blood specimens to be collected for specimen banking in order to be in the main part of this study. No matter what you decide to do, your decision will not affect your medical care. You can tell us your choice by placing your initials in one of the options below:

BLOOD SAMPLE SPECIMEN BANKING:

Please indicate your choice by placing your initials below:

- ☐ YES Your blood sample(s) may be saved for future research and stored in a specimen bank.
- ☐ NO Your blood sample(s) may not be saved for future research and stored in a specimen bank.

STUDY DRUG CREATED FROM BLOOD SAMPLE SPECIMEN BANKING:

Please indicate your choice by placing your initials below:

- ☐ YES Study drug created from your blood samples may be saved for future research and stored in a specimen bank.
- ☐ NO Study drug created from your blood samples may not be saved for future research and stored in a specimen bank.

Signatures

What does your signature mean?

Before you sign this form, please ask questions about any part of this study that is not clear to you. Your signature below means that you have received this information and all your questions have been answered. If you sign the form it means that you agree to join the study. You will receive a copy of this signed document.

Consent From Adult

PARTICIPANT (SIGNATURE)

PARTICIPANT (PRINT)

DATE

To be completed by participant if 18 years of age or older.

If an interpreter is involved in the consent process because the potential subject does not speak English well or at all, the participant should NOT sign on the line above – leave this line blank. Instead, the participant should sign the Short Form or full consent written in the language they can understand.

Person Obtaining Consent

By signing below you confirm that you have fully explained this study to the potential subject, allowed them time to read the consent or have the consent read to them, and have answered all their questions.

PERSON OBTAINING CONSENT
(SIGNATURE)

PERSON OBTAINING
CONSENT (PRINT)

DATE



Interpreter

By signing below you confirm that the study has been fully explained to the potential subject in a language they understand and have answered all their questions.

_____ INTERPRETER(SIGNATURE)	_____ INTERPRETER (PRINT)	_____ DATE
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If an interpreter was used to explain this study to a potential subject, the interpreter must sign and date the line above.

Signature from Impartial Witness

If this consent form is read to the subject because the subject is blind or illiterate, an impartial witness not affiliated with the research or study doctor must be present for the consenting process and sign the following statement. The subject may place an X on the Participant Signature line above.

I agree the information in this informed consent form was presented orally in my presence to the **identified individual(s)** who has had the opportunity to ask any questions he/she had about the study. I also agree that the **identified individual(s)** freely gave their informed consent to participate in this trial.

Please indicate with check box the identified individual(s):

☐ Subject

_____ IMPARTIAL WITNESS (SIGNATURE)	_____ IMPARTIAL WITNESS (PRINT)	_____ DATE
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Leaving the Study Early

Signatures should be obtained in this section if the subject decides to leave the study early.

If you leave the study early the study leader will keep the data collected about you up until the time you leave the study to help determine the results of the study.

Check one option below:

____ I am withdrawing my consent from the intervention or treatment part of this study but agree to continue to have follow up information about me collected by the study team.

The follow up information will be collected by:

- Obtaining information from my medical records
- Phone call about every 3 months

____ I am withdrawing my consent for this study. No additional information may be collected about me including follow up information from my medical records.

Consent From Adult

PARTICIPANT

(SIGNATURE)

PARTICIPANT

(PRINT)

DATE

To be completed by participant if 18 years of age or older.

Person Obtaining Consent

By signing below you confirm that you have fully explained the implications of withdrawing from the study to the subject and have answered all their questions.

PERSON OBTAINING CONSENT

(SIGNATURE)

PERSON OBTAINING CONSENT

(PRINT)

DATE