UNIVERSITY of VIRGINIA

SCHOOL of MEDICINE

Official Title:

Novel immuno-epigenetic based platform for patients with peripheral T-cell lymphoma (PTCL) and cutaneous T-cell lymphoma (CTCL): an international phase Ib study of pembrolizumab combined with decitabine and/or pralatrexate

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Consent of an Adult to Be in a Research Study

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 # _____

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 copy of this form.

Who is funding this study?

The study is being supported by Merck & Co., Inc. Merck is providing the pembrolizumab study drug as well as study funding.

The Investigational New Drug (IND) Application for this drug combination is held by Dr. Owen O'Connor who is a physician and investigator at the University of Virginia. The University of Virginia Division of Hematology and Oncology is considered the sponsor of this study.

Key Information About This Research Study

Principal Investigator:	Enrica Marchi, MD Division of Hematology and Medical Oncology University of Virginia PO Box 800716 Charlottesville, VA 22908 Telephone: (434) 297-5529

You are being asked to take part in a research study. You do not have to take part in this study.
You should only agree to take part in this study after reading this consent form and discussing it with the study team. You may also discuss this with your family, friends, health care providers or others before you make a decision.

What problem is this study trying to solve?

The standard treatments used to treat lymphoma do not always work well or they may only work for a short period of time. This is why new treatments are always being developed and tested, to try to find something that will work better in fighting your disease.

This is a research study about the combination treatments of three drugs. The use of the combination study drugs is investigational and are not FDA approved.

You are being asked to participate in this study because you have peripheral T-cell Lymphoma (PTCL) or cutaneous T-cell lymphoma (CTCL) that has either relapsed (returned after initially responding to previous treatment), or is refractory (has not responded to previous treatment).

The purpose of this research study is to determine the maximum tolerated dose and safety of three drug combinations. Each combination is assigned to a different treatment arm. These treatment arms are as follows:

Arm A: pembrolizumab + pralatrexate
Arm B: pralatrexate + decitabine + pembrolizumab
Arm C: decitabine + pembrolizumab

You will be assigned to receive only one of these combinations that your doctor will discuss with you.

Decitabine is a type of drug called hypomethylating agent. It works by switching off a protein called DNA methyltransferase. This switches on genes that stop the cancer cells growing and dividing. Decitabine is currently approved by the US Food and Drug Administration (FDA) for treatment of myelodysplastic syndromes (MDS), however it is not approved for PTCL or CTCL.

Pembrolizumab is an antibody called a PD-1 receptor blocker that is a cancer immunotherapy called Keytruda. It works by blocking a protective mechanism on cancer cells. This allows your immune system to recognize and destroy cancer cells. Pembrolizumab has been FDA approved for certain cancers however it is not approved for PTCL or CTCL.

Pralatrexate is an anti-metabolite drug that works in a similar way to methotrexate, a chemotherapy drug used for many years to treat various types of cancer. Pralatrexate blocks how cells are made and therefore the growth of the tumor can be slowed, stopped, or the tumor size decreased. Pralatrexate alone is approved for marketing by the US FDA for patients with relapsed or refractory PTCL.

Why would you want to take part in this study?
You might like to take part in this study because the standard treatments used to treat lymphoma do not always work well or they may only work for a short period of time. This is why new treatments are always being developed and tested, to try to find something that will work better in fighting your disease.

Why would you NOT want to take part in this study?
You might not want to take part in this study because:

- You may not want to receive one of the experimental drug combinations.
- Neither you nor your doctor can choose which drug combination you will receive.
- There are health risks for the drugs used in this study, which are explained in detail later in this form.
- You may not want to have additional physical exams and blood drawn for safety lab tests.
- You may not want to have extra blood draws and give tissue for research purposes.

What will I have to do if I take part in this study?
Full details of all the procedures are found later in this form.

If you take part in this study you will:

- You will be asked to take an experimental drug combination.
- You will be asked to have extra physical exams and blood drawn for safety lab tests.
- You will be asked to have extra blood draws and give tissue for research analysis.

What is the difference between being in this study and getting usual care?
This is a research study about three different experimental drug combinations that have not been proven to be safe or helpful. This drug combination has not approved by the U.S. Food and Drug Administration (FDA). If you take part in this study, you are leaving the choice of treatment up to the study.

What other treatments may I receive if I decide to not take part in this study?
You may receive pralatrexate or another FDA approved drug as part of your regular clinical care if you decide not take part in this study. You may participate in a different clinical trial.

Up to 35 people may sign consent to participate in order to treat up to 26 participants at UVA. Up to 50 participants may sign consent to participate in this study at all sites in order to treat up to 38 participants at all sites.

How long will this study take?

Depending on which study drug you receive, your participation in this study may require up to 22 study visits every 3 months, with an expected treatment duration of about 6 months. Your treatment may be longer or shorter depending on your body responds to the treatment. Depending on which study drug you receive, each study visit may last 2-7 hours.

What will happen if you are in the study?

SCREENING (visit will last about 2-8 hours and may be completed over several visits)

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.

The study team may want to review results of tests and procedures that were done as part of your usual care before this study. The research team may ask you some questions and/or review your medical records for information and results, and may request copies of your medical records, which will become part of your study records, including the following:

- Your medical history
- Results from prior physical exams or laboratory tests
- Pathology reports
- Notes your clinicians may have made about your care

During screening, you will have tests and procedures to make sure you are eligible for the study and it is safe for you to participate.

Tests and procedures completed **as part of your clinical care** and recorded for research purposes may include the following

- Information such as your age, gender, and race.
- Review of your medical history, current medications and previous treatments.
- Physical exam, weight and vital signs (blood pressure, heart rate, etc.)
- You will have CT of neck, chest, abdomen, and pelvis (PET/CT is allowable, if available).
- Other imaging techniques documenting disease sites other than neck, chest, abdomen, and pelvis, if applicable
- Your health status and your well-being will be assessed. This is called ECOG performance status assessment.
- Approximately 2 tablespoons, or 30 mL, of blood will be collected to check your blood counts, certain levels of fats, salts, sugars, clotting, kidney, thyroid and liver.
- A urine test, called urinalysis, will be performed
- If you are a female of childbearing potential, a pregnancy test will be performed during screening within 7 days prior to cycle 1, dose 1 and again within 24 hours prior to first dose of the study drugs. The test must be negative for you to be in the study.
- If skin involvement is present, standardized photographs will be taken of lesions.
- If a biopsy of your tumor was not obtained recently, it will be performed at this time. This biopsy may be ***mandatory*** if needed to establish a diagnosis and is considered part of your standard clinical care. If you have recently had a biopsy performed or have one performed during screening for this study, leftover tissue will be collected for the study analyses.
- A bone marrow biopsy may be done if this is needed to establish a diagnosis and is considered part of your standard clinical care. Your doctor will discuss this in detail with you.

If these tests show you are eligible, you will return to the clinic to begin study treatment.

STUDY TREATMENT

Your visit schedule and the length of time each visit takes will depend on which drug combination you receive.

You will be assigned to 1 of 3 study treatment groups. Initially, participants will be assigned to either Arm A or Arm C. If both arms still need participants, then your study doctor will decide which treatment might be better for you. If either Arm A or Arm C is full (has all the participants needed), then you will automatically be assigned to the open Arm. Once both Arm A and Arm C are full, then participants will be assigned to Arm B.

Arm A: pembrolizumab + pralatrexate Arm B: pralatrexate + decitabine + pembrolizumab Arm C: decitabine + pembrolizumab

If you are assigned to Arm A or B you will be required to take leucovorin, folic acid, and vitamin B12 which is standard clinical practice for anyone taking pralatrexate to help control side effects. You will take leucovorin by mouth twice daily (except for the day before, the day of, and the day after pralatrexate treatment). You will take folic acid by mouth daily. Vitamin B12 will be given by intramuscular injection every 2 cycles (8 weeks).

Treatment Cycle 1

On days 1, 8, 15 & 22 you may come into the office for the following procedures:

- A review of any current medications will be performed.

- Physical exam, weight and vital signs.
- Your health status and your well-being will be assessed.
- If skin involvement is present, standardized photographs will be taken of lesions (day 1 only).
- Up to 3 tablespoons of blood will be collected for the following:
  - Up to 1 tablespoon (15 mL) to check your blood counts, certain levels of fats, salts, sugars, clotting, kidney, thyroid and liver,
  - Up to 1½ tablespoons (20 mL) in 1 day over a maximum of 8 blood draws for research tests to determine how long the study drugs stay in your body, and
  - 1 teaspoon (5mL) to examine the effect of the study drugs on your immune system.
- A review of any side effects (also known as 'toxicities') that you may be experiencing.
- Study drug administration and additional safety tests: The schedule will depend on the treatment Arm you are enrolled in, as described in the study calendar at the end of this section.

Treatment Cycle 2 and All Subsequent Cycles

In cycle 2 and each subsequent cycle (± 2 days), you may come into the office to meet with your study doctor. The following tests and procedures may occur:

- A review of any current medications will be performed.
- Physical exam, weight and vital signs.
- Your health status and your well-being will be assessed.
- If skin involvement is present, standardized photographs will be taken of lesions
- Approximately 2 ½ tablespoons of blood will be collected for the following:
  - Up to 2 tablespoons (30 mL) of blood will be collected to check your blood counts, certain levels of fats, salts, sugars, clotting, kidney, thyroid and liver
  - 1 teaspoon (5mL) to examine the effect of the study drug on your immune system (day 1 of each cycle).
- A review of any side effects (toxicities) that you may be experiencing.
- CT or PET/CT imaging will be performed at the end of cycle 2, then every 3-4 cycles and at the discretion of your study doctor as indicated for your clinical care.
- Study drug administration and additional safety tests: The schedule will depend on the treatment Arm you are enrolled in, as described in the study calendar at the end of this section.
- An optional biopsy may be performed for research purposes after cycle 3 or 4 if you agree to this. You will sign a separate consent addendum for the optional biopsy.

END OF TREATMENT:

If you stop the study treatment early, you will return for an End of Treatment visit within 1 week. The following tests and procedures will be performed as part of your clinical care and recorded for research purposes at the End of Treatment visit:

- Review of your current medications
- Physical exam and vital signs
- Performance Status (determining your ability to function and perform daily activities)
- About 2 tablespoons (30mL) of blood will be collected to check your blood counts, certain levels of fats, salts, sugars, kidney, thyroid and liver.

- About 1 teaspoon (5mL) of blood will be collected to examine the effect of the study drug on your immune system.
- Review any side-effects

END OF STUDY:

About 1 month after you last study drug treatment you will return for an End of Study visit. The following tests and procedures will be performed as part of your clinical care and recorded for research purposes at the End of Study visit:

- Review of your current medications
- Physical exam and vital signs
- Performance Status (determining your ability to function and perform daily activities)
- About 2 tablespoons (30mL) of blood will be collected to check your blood counts, certain levels of fats, salts, sugars, kidney, thyroid and liver
- Review any side-effects

FOLLOW UP:

When you stop and complete study treatments you will begin the last part of the study, the follow-up period. During this period, your study doctor will continue to assess your health condition. It is important to know, for example, if you have recovered, developed an illness or suffered an important adverse event. Depending on your response to treatment and how long you have been off treatment, you may have follow up visits about every 2 months for up to 1 year.

The following tests and procedures will be performed as part of your clinical care and recorded for research purposes at the follow up visits:

- A review of any current medications
- Review any side-effects
- Check on your disease status and whether you have received any additional disease treatment

STUDY FLOW CHART ARM A		**Treatment Cycles** Each cycle is 28 days										**Post-treatment**		
	Screen-ing	1, 4, 7, etc.				2, 5, 8, etc.			3, 6, 9, etc.			End of Treat-ment	End of Study	Follow-up Visits
		D1	D8	D15	D22	D1	D8	D15	D1	D8	D15	EOT	30 days after EOT	Every 8 weeks
Informed Consent	**X**													
Review study eligibility	**X**													
Demographics and Medical History	X													
Side effects and checking medications		X	X	X	X	X	X	X	X	X	X	X	X	X
Physical examination with performance status	X	X	**X C1 only**	**X C1 only**	**X C1 only**	X			X			X	X	
Vital Signs and Weight	X	X	X	X	X	X	X	X	X	X	X	X	X	
Pregnancy Test	X													
Clinical blood tests to check how your blood clots	X	X				X			X					
Clinical blood test: CBC with Differential	X	X	**X**	**X**	**X**	X	**X**	**X**	X	**X**	**X**	**X**	**X**	
Clinical Blood Testing: checking organ function	X	X	**X**	**X**	**X**	X	**X**	**X**	X	**X**	**X**	**X**	**X**	
Epstein Barr Virus testing	X													
Urine testing for organ function	X													
Clinical blood testing: thyroid function	X	X odd cycles				X odd cycles			X odd cycles			X	X	
CT or PET/CT with photographs	X					X[1]			X[1]					
Tissue Collection from New/Previous Biopsy	X[2]								**X[2]**					
Research Blood Collection[5]		**X[5]**	**X[4,5]**	**X[4,5]**		**X**			**X**			**X**		
Pralatrexate Infusion		**X**	**X**	**X**		**X**	**X**	**X**	**X**	**X**	**X**			
Pembrolizumab Infusion		**X[3]**			**X[3]**			**X[3]**		**X[3]**				

STUDY FLOW CHART ARM A		**Treatment Cycles** Each cycle is 28 days										**Post-treatment**		
	Screen-ing	1, 4, 7, etc.				2, 5, 8, etc.			3, 6, 9, etc.			End of Treat-ment	End of Study	Follow-up Visits
		D1	D8	D15	D22	D1	D8	D15	D1	D8	D15	EOT	30 days after EOT	Every 8 weeks
Status and disease treatments													**X**	**X**

Procedures that are not part of standard clinical care and are considered for research are marked with **bold "X"**.

1: CT or PET/CT will be done at screening, after cycle 2, and then when your clinician believes it is necessary (about every 3-4 cycles). The clinician may take photographs of any skin involved in your disease at the same time-points.

2: Tissue will be collected at screening from leftover tissue if possible, but a biopsy may be necessary as part of your clinical care. Tissue may also be collected for research purposes if you agree to an optional biopsy after cycle 3 or 4.

3: Pembrolizumab will be administered every 3 weeks, starting at Cycle 1, Day 1.

4: Cycle 1 only.

5: Blood draws may be at multiple timepoints after completing infusions during cycle 1

STUDY FLOW CHART ARM B		**Treatment Cycles** Each cycle is 28 days											**Post-treatment**		
	Screen-ing	1, 4, 7, etc.				2, 5, 8, etc.				3, 6, 9, etc.			End of Treat-ment	End of Study	Follow-up Visits
		D1	D8	D15	D22	D1	D8	D15	D22	D1	D8	D15	EOT	30 days after EOT	Every 8 weeks
Informed Consent	**X**														
Review study eligibility	**X**														
Demographics and Medical History	X														
Side effects and checking medications		X	X	X		X	X	X		X	X	X	X	X	X
Physical examination with performance status	X	X	**X C1 only**	**X C1 only**		X				X			X	X	
Vital Signs and Weight	X	X	X	X		X	X	X	X	X	X	X	X	X	
Pregnancy Test	X														
Clinical blood tests to check how your blood clots	X	X				X				X					
Clinical blood test: CBC with Differential	X	X	**X**	**X**	**X C1 only**	X	**X**	**X**	**X**	X	**X**	**X**	**X**	**X**	
Clinical Blood Testing: checking organ function	X	X	**X**	**X**		X	**X**	**X**	**X**	X	**X**	**X**	**X**	**X**	
Epstein Barr Virus testing	X														
Urine testing for organ function	X														
Clinical blood testing: thyroid function	X	X odd cycles				X odd cycles				X odd cycles			X	X	
CT or PET/CT with photographs	X					X[1]				X[1]					
Tissue Collection from New/Previous Biopsy	X[2]									**X[2]**					

STUDY FLOW CHART ARM B		**Treatment Cycles** Each cycle is 28 days											**Post-treatment**		
	Screen-ing	1, 4, 7, etc.				2, 5, 8, etc.				3, 6, 9, etc.			End of Treat-ment	End of Study	Follow-up Visits
		D1	D8	D15	D22	D1	D8	D15	D22	D1	D8	D15	EOT	30 days after EOT	Every 8 weeks
Research Blood Collection[5]		**X[5]**	**X[4,5]**	**X[4,5]**		**X**				**X**			**X**		
Pralatrexate Infusion		**X**	**X**	**X**		**X**	**X**	**X**		**X**	**X**	**X**			
Pembrolizumab Infusion			**X[3]**			**X[3]**			**X[3]**			**X[3]**			
Decitabine Infusion (Days 1-5 or 1-3 each cycle, depending on dose level)		**X**				**X**				**X**					
Status and disease treatments														**X**	**X**

Procedures that are not part of standard clinical care and are considered for research are marked with **bold "X"**.

1: CT or PET/CT will be done at screening, after cycle 2, and then when your clinician believes it is necessary (about every 3-4 cycles). The clinician may take photographs of any skin involved in your disease at the same time-points.

2: Tissue will be collected at screening from leftover tissue if possible, but a biopsy may be necessary as part of your clinical care. Tissue may also be collected for research purposes if you agree to an optional biopsy after cycle 3 or 4.

3: Pembrolizumab will be administered every 3 weeks, starting at Cycle 1, Day 8.

4: Cycle 1 only.

5: Blood draws may be at multiple timepoints after completing infusions during cycle 1, including timepoints after the last decitabine infusion for that cycle

STUDY FLOW CHART ARM C		**Treatment Cycles** Each cycle is 28 days											**Post-treatment**		
	Screen-ing	1, 4, 7, etc.				2, 5, 8, etc.				3, 6, 9, etc.			End of Treat-ment	End of Study	Follow-up Visits
		D1	D8	D15	D22	D1	D8	D15	D22	D1	D8	D15	EOT	30 days after EOT	Every 8 weeks
Informed Consent	**X**														
Review study eligibility	**X**														
Demographics and Medical History	X														
Side effects and checking medications		X	X	X		X	X	X		X	X	X	X	X	X
Physical examination with performance status	X	X	**X C1 only**			X				X			X	X	
Vital Signs and Weight	X	X	X	X C1 only		X			X	X		X	X	X	
Pregnancy Test	X														
Clinical blood tests to check how your blood clots	X	X				X				X					
Clinical blood test: CBC with Differential	X	X	**X**	**X C1 only**	**X C1 only**	X			**X**	X		**X**	**X**	**X**	
Clinical Blood Testing: checking organ function	X	X	**X**	**X C1 only**		X			**X**	X		**X**	**X**	**X**	
Epstein Barr Virus testing	X														
Urine testing for organ function	X														
Clinical blood testing: thyroid function	X	X odd cycles				X odd cycles				X odd cycles			X	X	
CT or PET/CT with photographs	X					X[1]				X[1]					
Tissue Collection from New/Previous Biopsy	X[2]									**X[2]**					
Research Blood Collection[5]		**X**[5]	**X**[4,5]	**X**[4,5]		**X**				**X**			**X**		

STUDY FLOW CHART ARM C		**Treatment Cycles** Each cycle is 28 days											**Post-treatment**		
	Screen-ing	1, 4, 7, etc.				2, 5, 8, etc.				3, 6, 9, etc.			End of Treat-ment	End of Study	Follow-up Visits
		D1	D8	D15	D22	D1	D8	D15	D22	D1	D8	D15	EOT	30 days after EOT	Every 8 weeks
Pembrolizumab Infusion			**X[3]**			**X[3]**			**X[3]**			**X[3]**			
Decitabine Infusion (Days 1-5 or 1-3 each cycle, depending on dose level)		**X**				**X**				**X**					
Status and disease treatments														**X**	**X**

Procedures that are not part of standard clinical care and are considered for research are marked with **bold "X"**.
1: CT or PET/CT will be done at screening, after cycle 2, and then when your clinician believes it is necessary (about every 3-4 cycles). The clinician may take photographs of any skin involved in your disease at the same time-points.
2: Tissue will be collected at screening from leftover tissue if possible, but a biopsy may be necessary as part of your clinical care. Tissue may also be collected for research purposes if you agree to an optional biopsy after cycle 3 or 4.
3: Pembrolizumab will be administered every 3 weeks, starting at Cycle 1, Day 8.
4: Cycle 1 only.
5: Blood draws may be at multiple timepoints after completing infusions during cycle 1, including timepoints after the last decitabine infusion for that cycle

What are your responsibilities in the study?

You have certain responsibilities to help ensure your safety.

- 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.
- Ensure that the study drug is taken as instructed, keep the study drug in a safe place away from other children, return any unused study drug at each visit, and report any lost or missed tablets.
- Ensure that the study drug is taken only by you, the person for whom it has been prescribed.
- 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.

Blood Testing

Depending on which study drug you receive, we may take (or "draw") up to 7 tablespoons of blood during the first cycle of study treatment. After the first month we may take up to 2½ tablespoons of blood per month,

depending on which drug you receive**.** The total amount of blood we will take will depend on which study drug you receive and how long you receive treatment.

Most of the blood we take will be tested to check your blood counts, certain levels of fats, salts, sugars, clotting, kidney, thyroid and liver function for your safety.

Up to 4½ tablespoons (65mL) of the blood we take will be tested to determine how long the study drugs stay in your body for research purposes.

If you receive treatment for 9 cycles, up to 4 tablespoons (60mL) of the blood we take will be tested to better understand how the immune system responds to the drug combinations for research purposes.

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 findings that may be important for your health or may help you decide if you want to continue in the study. The final results of the research will not be known until all the information from everyone is combined and reviewed. At that time you can ask for more information about the study results.

Collection of Samples and Health Information for Genetic Research and Optional Specimen Banking

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

You are being asked to provide samples of your blood and tissue to be used for 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
- age
- gender
- sample type

We plan to do genetic research on the DNA in your specimen sample. DNA is the material that makes up your genes. All living things are made of cells. Genes are the part of cells that contain the instructions which tell our bodies how to grow and work, and determine physical characteristics such as hair and eye color. Genes are passed from parent to child.

In addition, 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. The long term goals of the samples collected in this bank will be mainly used for research on lymphoma. It is not possible 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.

Your specimen sample may be used to create a living specimen sample (called a "cell line") that can be grown in the laboratory. This allows researchers to have an unlimited supply of your cells in the future without asking for more samples from you.

What will you have to do to give samples for research?
Your doctor will obtain blood and tissue from you for testing. This will be collected as part of the research study at the time points described above. These specimens may be used for genetic research and may also be banked and used in future research studies.

How Will Your Samples Be Labeled?
Enrica Marchi, MD will be responsible for storing your sample and for protecting your privacy.

Your samples 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 specimens can be identified but only indirectly. We can find out if we need to know which samples are yours in the event you wish the samples to be removed at a later date.

How Will Your Samples Be Stored and Labeled for Specimen Banking?
Craig Slingluff Jr., MD will be responsible for storing your samples for specimen banking and for protecting your privacy

This research specimen bank is located at the University of Virginia under the leadership of Craig Slingluff Jr., MD. There is no set limit to the number of people who will provide samples to this bank.

Your samples 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 specimens can be identified but only indirectly. We can find out if we need to know which samples are yours in the event you wish the samples to be removed from the bank later.

Which researchers can use your samples and what information about you can they have?
Your samples may be shared with researchers at the University of Virginia and at other institutions. Dr. Slingluff will not give your name to other researchers who want to use your samples, 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 Genetic Research and Specimen Banking?
The genetic research and specimen banking that is done with your samples is not meant to help you. But, doctors hope that in the future it will help people who have other diseases or conditions.

What Are The Risks of Donating Your Samples For This Study?

Risks to Privacy from Genetic Research and 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 procedure 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.

Because everyone has unique DNA, it is also possible, although very unlikely, that someone could identify you through your DNA if they have another sample of your DNA.

Information about your genetic make-up could mean that you and your family members could face problems that could lead to getting or keeping some kinds of insurance or affect your ability to get or keep a job. To keep this from happening, the results of these tests will not be given to anyone outside of the study staff. There is no way to predict all the possible risks of this research.

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

Neither you, your health care provider**,** nor anyone in your family, will receive the results of any research done on your samples. The results will not be put in your health records. Therefore, results from any research done on your samples 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 Samples for Specimen Banking?

If you decide now that your samples can be kept for specimen banking, and later change your mind, you can simply withdraw the samples 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 tissue that has not already been used. However, if your sample has been used in genetic 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 tissue and to use and share your private health information for this study will never end.

Will You Be Paid For Donating Your Samples for Genetic Research and Specimen Banking?

You will not be paid to donate your samples for genetic research and specimen banking.

Will Donating Your Samples Cost You Any Money?

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

Genetic Testing and Specimen Banking Options:

You have to participate and agree for specimens to be collected for **genetic research** in order to be in the main part of this study.

You do not have to agree for 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.

SPECIMEN BANKING:

Please indicate your choice by placing your initials below:

___ YES **Your sample(s) may be saved for future research and stored in a specimen bank.**

___ NO **Your sample(s) may not be saved for future research and stored in a specimen bank.**

Genome Wide Association Studies

Whole genome analysis may be performed on your DNA sample. Usually researchers study just a few areas of your genetic code that are linked to a disease or condition. In whole genome studies, all or most of your genes are analyzed and used by researchers to study links to many diseases or conditions.

In order to allow researchers to share test results, the National Institutes of Health (NIH) and other central repositories have developed special data (information) banks that collect the results of whole genome studies. The NIH or other data banks may store your genetic information and give it to other researchers to do more studies. We do not think that there will be further risks to your privacy and confidentiality by sharing your whole genome analysis with these databanks; however, we cannot predict how genetic information will be used in the future. The information will be sent with only a code number attached. Your name or other identifiable information will never be given to them. There are many safeguards in place to protect your information while it is stored in repositories and used for research.

There is a small chance that your genetic information could be shared with others by mistake. In the unlikely event that your information was mistakenly shared, and if it were linked to a medical condition, this could affect your ability to get or keep some kinds of insurance. If family members were to see the information it could also affect them. This could hurt family relationships. It is possible that you could be identified from the sample if someone has another sample from you. The two samples could be matched to then identify you from the sample given for this study.

Research using your whole genome information is important for the study of virtually all diseases and conditions. Therefore, the databank will provide study data for researchers working on any disease, which could include conditions such as HIV/AIDS, cancer, mental illness, and others.

What are the risks of being in this study?

Risks and side effects related to pembrolizumab:
Pembrolizumab, which is approved in the USA and some other countries, is available by prescription to treat several different cancers but may not be approved to treat your type of cancer.

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

Very common, some may be serious (i.e. causing hospitalization, life-threatening or where noted, may cause death) side effects (at least 20 out of 100 participants experienced)

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

Common, some may be serious (i.e. causing hospitalization, life-threatening or where noted, may cause death) side effects (5 to 20 out of 100 participants experienced)

- Joint pain
- Fever
- Back pain
- Rash
- Pain in your belly
- Loss of skin color
- Not enough thyroid hormone. So you may 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, have a headache, have muscle cramps, and/or sick to your stomach (hyponatremia)

Uncommon, some may be serious (i.e. causing hospitalization, life-threatening or where noted, may cause death) side effects (1 to 5 out of 100 participants experienced)

- Inflammation of the lungs, so you may feel short of breath and cough (pneumonitis). Sometimes this might lead to death.
- Too much thyroid hormone, so you may feel anxious, feel angry, have trouble sleeping, feel weak, tremble, sweat, feel tired, have loose and watery stools (hyperthyroidism)

- Infusion reaction, where you may feel dizzy or faint, feel flushed, get a rash, have a fever, feel short of breath, experience a decrease in your blood pressure at the time of receiving your infusion (IV) or just after, or have pain at the site of infusion
- Inflammation of the bowels/gut, which may cause severe pain in your belly with loose or watery stools, and black, tarry, sticky stools or stools with blood or mucus (colitis)
- Inflammation of the skin so you may have peeling of the skin, itchiness, and/or skin redness. The skin inflammation (i.e., peeling, itching, and redness) could also be widespread throughout your body. More severe skin reactions may involve the inside of your mouth, the surface of your eye, and genital areas, and/or may cause the top layer of your skin to peel from all over your body which can cause severe infection (Severe skin reactions, including Stevens-Johnson syndrome/or toxic epidermal necrolysis). These severe conditions can sometimes lead to death.

Rare, some may be serious (i.e. causing hospitalization, life-threatening or where noted, may cause death) side effects (less than 1 out of 100 participants experienced)

- Inflammation of the nerves that may cause pain, weakness or tingling in your hands and feet, and may spread to your legs, arms and upper body leading to severe muscle weakness and possible temporary paralysis (Guillain-Barré syndrome)
- Inflammation of the muscles so you may feel weakness or pain in the muscles (myositis)
- Inflammation of 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 have 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, see floaters, or have headaches (uveitis)
- Inflammation of the liver that may make you feel sick to your stomach and vomit, feel like not eating, feel tired, have a mild fever, a pain in the right side of your belly, yellow eyes and skin, and dark urine (hepatitis)
- Inflammation of the pituitary gland (a gland in the head), which may cause you to feel sick to your stomach or have headaches, changes in your behavior, double vision, few to no menstrual cycles, weakness, vomiting and dizziness, or fainting (hypophysitis)
- Adrenal glands (glands on top of the kidneys) that may not make enough hormone, which could cause tiredness, weight loss, muscle weakness, 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)
- Type 1 Diabetes, a condition that can cause too much sugar in your blood, feeling thirstier than usual, frequent urination, and weight loss. You are likely to need regular insulin shots.
- 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 middle layer of your heart wall 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). Sometimes this condition can lead to death
- Inflammation of the thyroid gland, an organ that makes and stores thyroid hormones. This condition may lead to change in your heart rate, blood pressure, body temperature, and the rate at which food is converted into energy (thyroiditis)

- A condition that may make you feel week 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 you 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.
- Inflammation of the protective sac surrounding your heart (pericarditis) which can cause sharp chest pain and shortness of breath (especially when lying flat), fever, and a fast or irregular heartbeat. In severe cases, your heart may have difficulty pumping blood throughout your body.

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 cause 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. This health condition often has a sudden onset of vision loss, loss of color vision, 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.

If you have had a solid organ transplant (for example, if you have received a kidney or heart transplant), you may experience rejection of the transplanted organ. Your doctor will monitor you and should tell you what signs and symptoms you should report depending on the type of organ transplant that you have had.

Patients treated with pembrolizumab BEFORE going on to receive an allogeneic stem cell transplant (a procedure in which a person receives blood-forming stem cells from a donor) should inform their transplant physicians that they have received pembrolizumab in the past. In patients with any hematologic malignancy (cancers of the blood like Hodgkin lymphoma, multiple myeloma): there is a potential for an increased risk of severe complications following allogeneic stem cell transplant in patients who previously received pembrolizumab BEFORE an allogeneic stem cell transplant. Reports of clotting of blood within the liver and severe graft versus host disease (which can include skin, liver, and gastrointestinal symptoms), including death, have been received for patients who received pembrolizumab BEFORE an allogeneic stem cell transplant.

Risks and side effects related to pralatrexate:

Likely (more than 20 out 100 participants experience these side effects):

- Stomatitis (pain, swelling, or sores on the inside of the mouth)
- Fatigue (feeling tired, weak or unwell)
- Nausea (feeling sick to your stomach)
- Epistaxis (nosebleeds)

Less Likely (10 to 20 out of 100 participants experience these side effects)

- Diarrhea
- Vomiting
- Fever
- Liver function test abnormal (ALT and AST)
- Dyspnea (shortness of Breath)
- Constipation
- Decreased blood cell counts
- Platelets (clot the blood to prevent bleeding)
- Neutrophils (fight infection)

- Red blood cells (carry oxygen)
- Alopecia (hair loss)

Rare but serious effects

- Approximately 2% of subjects were reported to have experienced severe skin reactions including severe shedding and loss of skin, ulcerations (sores) of the skin, and death of skin cells. Less than 2% of subjects have died as a consequence of these severe skin reactions.
- Less than 2% of subjects were reported to have experienced Tumor Lysis Syndrome (occurrence of blood electrolyte abnormalities, which may be caused by rapid killing of tumor cells). This may result in elevation of potassium in the blood which can cause heart arrhythmias (irregular heartbeat), and/or elevated phosphate or uric acid in the blood that can cause kidney malfunction. If you are at increased risk for this condition you may be admitted to the hospital for your first treatments so that you can receive treatment to avoid or decrease the effect of Tumor Lysis Syndrome.
- Less than 1% of subjects have died due to complications from stomatitis (sores in the mouth or throat) associated with low white blood cell counts (blood cells that fight infection) or poor appetite with inability to eat.
- Less than 1% of subjects have died due to complications from decreased blood cell counts (red blood cells that carry oxygen, white blood cells that fight infection, or platelets that clot blood and prevent bleeding).
- Less than 1% of subjects have or died due to sepsis (infection in the bloodstream) following dosing.
- Less than 1% of subjects have died due to cardiopulmonary arrest (heart stopped beating and breathing stopped).
- Less than1% of subjects have died due to bleeding from the lungs.
- Less than 1% of subjects have died due to respiratory failure (inability to breathe adequately.
- Other rare occurrences include: heart arrhythmias (abnormal heart beats), heart attack, heart failure (inadequate pumping of blood), stroke, infection or inflammation of the lungs, blood clots in the legs, blood clots going into the lung, viral infection of the colon, and kidney failure.

Certain medications should not be taken while you are receiving pralatrexate

- Antibiotics that are commonly called “sulfa” antibiotics should not be taken during study treatment because there is a possibility the medication could add to the side effects of Pralatrexate.
- Most pain medications can be taken while you are receiving Pralatrexate. A group of over the counter and prescription anti-inflammatory and pain medications called NSAIDs should be used with caution while you are on Pralatrexate. NSAIDs include common medications like aspirin, ibuprofen, and naproxen. If you are taking an NSAID, you must let your doctor know so he or she can closely monitor how well your kidneys are working.
- A medication that is used to treat gout, called Probalan (probenecid), should be used with caution while you are receiving Pralatrexate. Taking probenecid while on Pralatrexate may affect how well your kidneys work.

Risks and side effects related to decitabine

Decitabine has been studied in subjects with cancer of the blood and other organs of the body, as well as in subjects with other diseases. The following is a list of the most medically significant and/or most common side effects reported in prior studies. These side effects were previously attributed to treatment with decitabine. In some cases, side effects can be serious, long-lasting, or can cause death. Some side effects go away soon after

you stop the study drug and some may never go away. The study doctor may alter the dosage regimen of decitabine (if allowed by the study) or give you medicines to help lessen the side effects. This is not a complete list of all side effects that may occur. For more information about risks and side effects, please ask the study doctor.

Very common (more than 10 out 100 participants experience these side effects):

- anemia (a decrease in the number of red blood cells which may make you feel weak or tired)
- low number of white blood cells with or without fever
- decrease in the number of platelets, the cells that help your blood to clot
- infections, including pneumonia or of the lung, mouth, skin, or urinary tract (which may be bacterial, fungal or viral)
- nausea
- vomiting
- diarrhea
- stomach pain
- constipation
- feeling tired, unwell, or weak
- fever
- sore throat with swelling or pain of the nasal membranes or nose
- decreased appetite
- weight loss
- low blood levels of potassium
- pain (including muscle, joints, back, and chest pain)
- dizziness
- headache
- difficulty sleeping
- shortness of breath with or without exercise
- rash
- itchiness
- bruising, including tiny red or purple spots under the skin or other tissue
- nosebleed
- injection site reaction, including itching, pain, rash, redness, bleeding, bruising, swelling or damage where the injection/infusion was given**.**

Common (5 to 10 out of 100 participants experience these side effects):

- bone marrow failure which is a severe reduction of red and white blood cells and platelets (at nearly the same time) which can cause weakness, bruising, or make infections more likely
- a very severe infection of the blood which may include a decrease in blood pressure
- shivering (chills)
- upset stomach
- a disease affecting the gut which can result in fever, vomiting and stomach pain (diverticulitis)
- pain, swelling, or sores on the inside of the mouth
- runny nose or sinus infection

- bleeding including from the gums, eye, brain, stomach or rectum (hemorrhoids) or due to a catheter line
- muscle spasms
- anxiety
- sleepiness
- blood in the urine
- hair loss
- redness of the skin
- hives
- high blood pressure
- low blood pressure or dizziness upon standing
- fainting
- dehydration
- fluid around the lungs
- shortness of breath, dyspnea, sinusitis, post nasal drip, pulmonary signs and symptoms

Rare (less than 5 out of 100 participants experience these side effects):

- allergic reaction (may include skin inflammation, rash, trouble breathing; trouble speaking; fever, and/or diarrhea)
- pulmonary infection, and pulmonary embolism leading to difficulty breathing and possible cardio-respiratory complication
- renal failure with severe compromise of the organ function that can be fatal
- cardiac arrhythmia including atrial fibrillation

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 about 14 days before starting this study if you are a woman able to become pregnant. You MUST NOT become pregnant while on this study or for at least 4 months after your last dose of study drug.

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

- Norplant
- IUD (intrauterine device)
- Depo-Provera
- Birth Control Pills
- Birth Control Patch
- Sterilization

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

- Condoms
- Jellies or foam
- Withdrawal
- Sponge
- Diaphragm
- Rhythm
- Cervical cap

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.

Risks for men:

We also do not know the effects of these drugs on male sperm. If you are a male, you should not father a baby while you are in this study or for at least 4 months after your last dose of the study drug. You should also not donate to a sperm bank during this time. To do so may hurt your unborn baby. Use an effective method of birth control during this time. Effective forms of birth control are listed above).

If your partner becomes pregnant during this study or within 4 months after you took your last dose of study drug, you must tell your doctor right away.

Other unexpected risks:

You may have side effects that we do not expect or know to watch for now. Call the study leader 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 are that the study treatment may slow, stop, or decrease your cancer burden. 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 could include:

- Receiving pralatrexate without participating in the study
- Receiving a different agent, such as brentuximab vedotin, belinostat, romidepsin or gemcitabine, or vorinostat (for CTCL only)
- Radiation therapy
- Taking part in another research study
- Palliative care-care that will control your symptoms
- Getting no treatment

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.

By agreeing to be in this study, you are donating your blood and tissue 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:

- Research blood tests to determine how long the study drugs stay in your body
- Research blood tests to examine the effect of the study drugs on your immune system
- Collection and analysis of tissue for research from standard care biopsy
- Optional biopsy for research purposes
- Tissue banking
- If you receive pembrolizumab as part of the study, the pembrolizumab study drug will be provided by Merck & Co., Inc. at no cost. You or your insurance will be responsible for the costs associated with the study drug infusion.
- If you receive decitabine as part of this study, the decitabine study drug will be covered by study funding. You or your insurance will be responsible for the costs associated with the study drug infusion.

Pralatrexate which is an FDA approved treatment will not be provided. If you receive pralatrexate as part of the study, you or your insurance will be responsible for the cost of the drug and the costs associated with the study drug infusion.

You or your insurance will be responsible for the costs of additional safety labs and exams that are beyond the usual standard care.

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 your insurance company for an estimate of what these costs might be or if pre-approval is required.

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?

You do not give up any legal rights, such as seeking compensation for injury, by signing this form. If you feel you have been injured as a result of this study you may contact the Principal Investigator or the IRB (phone numbers are located near the end of this form). 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.

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 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 condition 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

If you decide to stop being in the study, we will ask you to tell your study doctor as soon as possible.

If study treatment is stopped, based on your or your study doctor's choice, you will be asked to continue to attend the post-treatment study visits or be otherwise contacted, unless you decide to withdraw completely from the study. If you stop taking part in the study completely, it is recommended that you go through the study withdrawal procedures that the study doctor considers necessary. After that, you will no longer be contacted about the study and no new information will be collected from you. However, information on your vital status may be collected from publicly available sources when the study is closed. If you have a side effect at your final study visit or withdrawal visit then your study doctor may wish to contact you and ask you about this, until it has completely resolved. The study drug suppliers may also ask the study doctor for this information.

Any data collected about you up until the time you leave the study must be kept in order to determine the results of the study.

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
- Social Security number ONLY IF you are being paid to be in this study
- 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.
- Tissue or blood samples if you agree to provide them for genetic testing 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.

Information about you and/or samples from you may be given to other researchers outside of the University of Virginia after all identifiers such as name, address, phone # have been removed.

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.

Information and samples obtained from you during this study may be used in future research. Your information and samples may be shared with other researchers inside or outside of the University of Virginia. They will not be sent with information that could identify you such as name, address or phone number.

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.

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 or complete the "Leaving the Study Early" part of this form and return it to the researchers. 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.

Please contact the Principal Investigator listed earlier in this form 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

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 22903 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.

You may also report a concern anonymously by calling the UVA Compliance Hotline phone number at 1-800-235-8700.

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

If an interpreter was used to explain this study to a potential subject, the interpreter must sign and date the line above.

Signature of 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

Notification of My Health Care Provider

Your health care provider will be notified of your participation in this study.

Leaving 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 up to every 2 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.

Signature From Adult

_____	_____	_____
PARTICIPANT (SIGNATURE)	PARTICIPANT (PRINT)	DATE

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

Person Obtaining Signature

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 SIGNATURE (SIGNATURE)	PERSON OBTAINING SIGNATURE (PRINT)	DATE

The study was explained to the following individuals in a language other than English.

☐ Subject

Interpreter

By signing below you confirm that the study has been fully explained in a language the person understood and that all of their questions have been answered.

_____	_____	_____
INTERPRETER (SIGNATURE)	INTERPRETER (PRINT)	DATE

If an interpreter was used via an outside phone service such as Cyracom, enter the interpreters ID# on the signature line above and document in the consenting process note that an outside interpreter via phone service was used to obtain consent.