RESEARCH PARTICIPANT CONSENT FORM

TITLE: A Multicenter, Open-Label Phase 2 Study to Evaluate the Safety and Efficacy of Lenvatinib in Combination with Pembrolizumab in Black Participants with Mismatch Repair-Proficient Recurrent Endometrial Cancer

PROTOCOL #: MCC-21-18659

IRB #: HM20023447

SPONSOR: VCU Massey Cancer Center

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OVERVIEW AND KEY INFORMATION

Taking part in this study is your choice.

We are asking you to take part in a research study. You should know that:

- Someone will explain this research to you.
- Taking part in this research is voluntary. Whether you take part is up to you.
- If you don't take part, you will not lose access to your medical care or any legal rights.
- You can take part now and later drop out, and it won't be held against you.
- You can have an unsigned copy of this consent form to review and think about.
- You can talk to your family and friends about your choice.
- If you don't understand, ask questions.
- Ask all the questions you want before you decide.

Why is this study being done?

The purpose of this study is to learn about two cancer drugs, lenvatinib and pembrolizumab. These drugs are used together to treat endometrial cancer. Most of the endometrial cancer patients in the first studies of these drugs were not Black.

We are doing this study because we want to find out if these drugs work as well in Black endometrial cancer patients as they did in the mostly non-Black patients who took part in previous studies.

Up to 100 people will take part in this study.

What are my other choices if I do not take part in this study?

If you decide not to take part in this study, you have other choices. For example:

- You may choose to have lenvatinib and pembrolizumab treatment without taking part in this study
- You may choose to have another type of treatment, if any are available
- You may choose to take part in a different study, if one is available
- Or you may choose not to be treated for cancer, and only receive comfort care to relieve symptoms caused by your cancer

What will happen if I decide to take part in this study?

During this study, you will take lenvatinib once a day by mouth every day. We will ask you to keep a diary and write down when you take your study drugs.

You will receive pembrolizumab through a needle or tube in a vein (intravenously, IV) every 3 weeks.

About 2 weeks after each time you receive pembrolizumab, you will have another study visit. At these visits we will give you surveys to fill out. These surveys will ask questions about your quality of life, how you're feeling, and the financial impact of your cancer treatment. These surveys will take about 30 minutes to fill out.

You may have up to 36 study visits each year that you are in the study.

We will ask to collect blood, vaginal, and urine samples for research purposes at the first study visit. We will collect blood samples for safety tests at all your study visits. We will also collect other information about you and your cancer treatment from your medical records.

How long will I be in this study?

If you do not have any serious side effects, you will continue to take the study drugs as long as they are keeping your cancer from growing.

After you stop taking the study drugs, your doctor and study team will continue to watch you for side effects for 30 days. They will follow your cancer status for as long as you agree. They will check in with you by phone or get records from your doctor's office every 3 months.

What are the risks and benefits of taking part in this study?

There are both risks and benefits to taking part in this study. It is important for you to think carefully about these as you make your decision.

Risks

We want you to know about a few key risks right now. We will give you more information in the "**WHAT POSSIBLE RISKS CAN I EXPECT FROM TAKING PART IN THIS STUDY?**" section.

If you choose to take part in this study, there is a risk that the study drugs may not be as good as other treatment approaches for treating your cancer.

There is also a risk that you could have side effects from the study drugs. These side effects may be worse and may be different than you would get with another approach.

Some of the most common side effects that the study doctors know about are:

- High blood pressure
- Diarrhea
- Tiredness
- Low appetite
- Low levels of thyroid hormones

There may be some risks the study doctors do not yet know about. Your study doctor or study team will let you know of any new findings.

Benefits

In previous studies of patients with your type of endometrial cancer, the combination of lenvatinib and pembrolizumab was better at treating their cancer than the previous standard treatment. The combination of lenvatinib and pembrolizumab is an approved treatment for your type of cancer. You do not need to take part in this study to receive this treatment.

Taking part in this study is not likely to benefit you directly. Patients in the future may benefit from the knowledge gained through your participation in the study.

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Now that you have a general overview of the study, we want to provide the details about what taking part would involve. Please read, or have someone read to you, the rest of this document. If there is anything you don't understand, be sure to ask your study doctor or study team.

WHAT WILL HAPPEN IF I TAKE PART IN THIS STUDY?

If you decide take part in the study, your cancer will be treated with lenvatinib and pembrolizumab.

You will be given a supply of lenvatinib to take home with you. You will take lenvatinib capsules every day by mouth and track it in your drug diary. You can take lenvatinib with or without food.

You will receive pembrolizumab IV every 3 weeks at the study site. It takes 30 minutes to give each dose of pembrolizumab.

About 2 weeks after each time you receive pembrolizumab, you will have another study visit. At these visits we will give you surveys to fill out. These surveys will ask questions about your quality of life, how you're feeling, and the financial impact of your cancer treatment.

WHAT TESTS AND PROCEDURES WILL I HAVE IF I TAKE PART IN THIS STUDY?

If you decide to take part in this study, most of the exams, tests, and procedures you will have are part of the usual approach when treating your type of endometrial cancer.

These usual procedures include:

- Physical exams
- Medical history
- Review of medicines you are taking
- CT or MRI scans every 6 to 9 weeks
- Blood samples for regular care

Your study doctor or study team can tell you more about these. The results of the usual exams, tests, and procedures may also be used for the research purposes of this study.

Surveys for Research Purposes

If you choose to take part in this study, we will ask you to fill out surveys. These surveys will ask questions about your quality of life, how you're feeling, and the financial impact of your cancer treatment.

Researchers will use this information to learn more about how cancer and cancer treatment affect people.

You will be asked to fill out these surveys every 3 weeks. The surveys will take about 30 minutes to complete. You don't have to answer any question that makes you feel uncomfortable.

Since these surveys are being used for research purposes, your study doctor might not see your responses. If you have any serious health issues or other concerns, please talk with your study doctor or a member of the study team right away.

Sample Collections for Research Purposes

This study also includes research using blood, vaginal, and urine samples. These samples are a required part of this study. When possible, we will try to collect your research samples at the same time as blood and urine samples for your regular care.

The samples will be used to learn more about how and why cancer cells respond to the study drugs.

This study may use your samples to sequence all or part of your DNA and your tumor DNA. Deoxyribonucleic acid (DNA) is the "blueprint" or "recipe" that gives the body's cells instructions

on how to do their jobs. Scientists can use a test called sequencing to determine the order of all or part of the molecules that make up DNA, like reading all the letters in a book.

The results of the research using your samples will not be provided to you. The samples are collected only for the research study. There will be no benefit to you. If any inventions or discoveries result from the use of your samples, there are no plans to share any money or profits with you. Samples will continue to be used until they are used up.

Blood Samples

Blood samples measuring 1 teaspoon will be collected at the first study visit and at 90 days during study treatment. These blood samples will be used for research purposes.

At each visit, a blood sample measuring 2-3 tablespoon will be collected to check on your health. These blood samples are a normal part of treating your cancer.

Urine Samples

You will be asked to collect a urine sample in a cup at your first study visit. This sample will be used for research purposes only.

Vaginal Samples

You or your doctor will be asked to collect a vaginal swab at your first study visit. This sample will be used for research purposes only.

Optional study you can choose to take part in

Genetic Testing

In addition to the main part of the research study, there is an optional part of the research. You can participate in the main part of the research without agreeing to take part in this optional part. This optional study will not benefit your health. The results will not be added to your medical records and you or your study doctor will not know the results.

Taking part in this optional study is your choice. You can still take part in the main study even if you say “no” to the optional study. There is no penalty for saying “no.” You and your insurance company will not be billed for these optional studies. If you sign up for, but cannot complete any of these studies for any reason, you can still take part in the main study.

What is involved in this optional sample collection?

If you agree to take part, here is what will happen next:

Your study doctor will obtain a blood sample of your during your first study visit and It will be tested for DNA ancestral analysis. This analysis is meant to see what part of your ancestry is of African descent. It does not tell us how genes affect health and disease or may look at how genes affect a person’s response to treatment.

Genetic Testing Risks

There are laws that protect your genetic information. However, there is a risk that someone could get access to your genetic information and identify you by name. In some cases, employers could use your genetic information to decide whether to hire or fire you. The study doctors believe the risk of this happening is very small. However, the risk may increase in the future as people find new ways of tracing information.

. WHAT ARE MY RESPONSIBILITIES IF I DECIDE TO TAKE PART IN THIS STUDY?

If you choose to take part in this study, you will need to:

- Keep your study appointments
- Tell your doctor about:
  - All medications and supplements you are taking
  - Any side effects
  - Any doctors' visits or hospital stays outside of this study
  - If you have been or are currently in another research study
- Take lenvatinib at the same time each day
- Write down in your drug diary when you take lenvatinib
- Bring all your remaining lenvatinib to each study visit
- Answer honestly when your doctor asks you questions
- Answer honestly when you fill out the study surveys

Do not get pregnant or breastfeed while taking part in this study. Do not father a baby while taking part in this study. Tell your study doctor right away if you think that you or your partner have become pregnant during the study or within 4 months after your last dose of study drug.

WHAT POSSIBLE RISKS CAN I EXPECT FROM TAKING PART IN THIS STUDY?

General Risks

If you choose to take part in this study, there is a risk that the study drugs may not be as good as another treatment at treating your cancer.

You also may have to do the following:

- Spend more time in the hospital or doctor's office.
- Be asked sensitive or private questions about things you normally do not discuss.
- May not be able to take part in future studies.

Participation in research might involve some loss of privacy. There is a small risk that someone outside the research study could see and misuse information about you.

Surveys may contain questions that are sensitive in nature. This study will ask you questions about personal topics, such as finances, that might be embarrassing to talk about. You may refuse to answer any question that makes you feel uncomfortable.

Reproductive Risks

The drugs used in this study could be very harmful to an unborn or newborn baby.If you are able to become pregnant, you will need to have a serum pregnancy test to find out if you can be in the study and each time you receive treatment. It is very important that you check with your study doctor about what types of birth control or pregnancy prevention to use during the study and for 4 months after you have completed the study.

Treatment with the study drugs involves risks that are currently unknown or unforeseeable. If you are or may become pregnant, treatment with the study drugs might involve risks to the embryo or fetus that are currently unforeseeable.

Side Effect Risks

The drugs used in this study may affect how different parts of your body work such as your liver, kidneys, heart, and blood. The study doctor will be testing your blood and will let you know if changes occur that may affect your health. Here are important points about side effects:

- Your study doctor does not know who will or will not have side effects
- Some side effects may go away soon, some may last a long time, or some may never go away
- Some side effects may interfere with your ability to have children
- Some side effects may be serious and may even result in death

Here are important points about how you and your study doctor can make side effects less of a problem:

- Tell your study doctor if you notice or feel anything different so they can see if you are having a side effect
- Your study doctor may be able to treat some side effects
- Your study doctor may adjust the study drugs to try to reduce side effects

The tables below show the most common and the most serious side effects that researchers know about. There may be other side effects of lenvatinib and pembrolizumab when given together that researchers do not yet know about. If important new side effects are found, your study doctor will discuss these with you.

Known Side Effects of the Combination of Lenvatinib and Pembrolizumab

COMMON, SOME MAY BE SERIOUS In 100 people treated with lenvatinib and pembrolizumab, more than 20 may have:
• High blood pressure • Diarrhea • Tiredness • Low appetite • Low levels of thyroid hormone • Nausea (feeling sick to the stomach) • Mouth sores • Pain, including joint pain • Voice changes • Hand-foot syndrome (palms of hands/soles of feet having pain, swelling, and blistering) • Severe skin reactions • Vomiting • Weight loss • Too much protein in the urine (possible fluid retention, possible sign of kidney damage) • Headache
OCCASIONAL, SOME MAY BE SERIOUS In 100 people treated with lenvatinib and pembrolizumab, from 4 to 20 may have:
• Muscle aches • Liver inflammation and damage • Low blood levels of magnesium (possible weakness, muscle cramps, irregular heartbeat) • Belly pain • Weakness • Bleeding • Abnormal digestive blood tests • Abnormal heart rhythm • Dehydration • Kidney inflammation and damage

• Difficulty breathing • Mouth pain • Confusion and delirium (loss of contact with reality) • Low blood levels of sodium (possible headache, confusion, seizures, coma) • Low blood levels of potassium (possible weakness) • Low levels of red blood cells (possible tiredness and shortness of breath)
RARE AND SERIOUS In 100 people treated with lenvatinib and pembrolizumab, 3 or fewer may have:
• Decreased production of adrenal hormones (possible weakness and/or low blood pressure) • Colon (large intestine/bowel) inflammation • Bleeding in the stomach, intestines • Seizure • Fainting • Temporary stroke symptoms • Brain damage that may be reversible (possible headache, confusion, seizures, vision loss)

Let your study doctor know of any questions you have about possible side effects. You can ask your study doctor questions about side effects at any time.

The researchers will let you know about any significant new findings (such as additional risks or discomforts) that might make you change your mind about participating in the study.

Interactions with Other Medications, Supplements, and Food

There are numerous medications, herbal products, vitamins, and dietary products that can interact with the study drugs. Interactions with medications and supplements may cause more side effects or decrease the effectiveness of the study drugs or other medications. Your study team will review your current medications and supplements to be sure that there are no concerns before you start taking the study drugs. You may be asked to stop taking certain supplements. You should not start taking any new over-the-counter or prescription medications or supplements without first checking with your study team about possible interactions.

You will be given a pocket card that identifies this research study. Carry this with you at all times. You should show it to your health care providers so that they can check with your study doctor or study team member about possible interactions that may occur with new medications added while you are participating in this study.

Imaging Risks

The imaging scans that you get in this study will expose you to low amounts of radiation. Every day, people are exposed to low levels of radiation that come from the sun and the environment around them. This type of radiation is called “background radiation.” No one knows for sure whether exposure to these low amounts of radiation is harmful to your body. The imaging scans you will get in this study are the same as you would get if you were getting other treatment for your cancer. You will not have extra scans just for this study.

As part of the scans that you get in this study, iodine may be injected into your vein. Some people are allergic to iodine. Let your study doctor know if you have an allergy to iodine or seafood or if you have kidney problems.

Sample Collection Risks

Common side effects of blood sample collection are brief pain and bleeding or bruising at the puncture site used to collect the blood sample. There is also a small risk of infection, light-headedness, and fainting.

Common side effects of vaginal swab collection are brief pressure and discomfort at the collection site.

CAN I STOP TAKING PART IN THIS STUDY?

Yes. You can decide to stop at any time. If you decide to stop for any reason, it is important to let the study doctor know as soon as possible so you can stop safely. If you stop, you can decide whether or not to let the study doctor continue to provide your medical information for the purpose of the study.

The study doctor will tell you about new information or changes in the study that may affect your health or your willingness to continue in the study. The study doctor may take you out of the study if:

- Your health changes and the study is no longer in your best interest
- You have serious side effects that require you to stop according to the rules of the study
- New information becomes available and the study is no longer in your best interest
- You do not follow the study rules
- The study is stopped by the sponsor, the Food and Drug Administration (FDA), or the institutional review board (IRB), which is a group of people who review the research with the goal of protecting the people who take part in the study

WHAT ARE THE COSTS OF TAKING PART IN THIS STUDY?

You and/or your health plan/insurance company will be billed for all standard costs of treating your cancer. This includes:

- the costs of lenvatinib and pembrolizumab
- the costs of getting pembrolizumab ready and giving it to you
- the costs of tests, procedures, medicines, or hospital admissions to manage any side effects
- your insurance co-pays and deductibles

You will not be charged for:

- any costs related to the blood and urine collections for research purposes
- any costs related to requesting stored tumor samples
- any costs related to surveys

These samples and surveys are not used for testing that affects your care.

Taking part in this study may mean that you need to make more visits to the clinic or hospital than if you were getting the usual approach to treat your cancer. You may:

- Have more travel costs.
- Need to take more time off work.
- Have other additional personal costs.

You will not be paid for taking part in this study. The research may lead to new tests, drugs, or other products for sale. If it does, you will not get any payment.

WHAT HAPPENS IF I AM INJURED OR HURT BECAUSE I TOOK PART IN THIS STUDY?

If you are injured or hurt as a result of taking part in this study and need medical treatment, please tell your study doctor. Your study doctor or study team will talk with you about your options for medical treatment.

Fees for such treatment will be billed to you or to your health plan/insurance company. Your health insurance company may or may not pay for treatment of injuries or illness as a result of your participation in this study. The study will not pay for medical treatment.

To help decrease the risk of injury or illness, it is very important to follow all directions provided by your study doctor or study team.

WHO WILL SEE MY MEDICAL INFORMATION?

Your privacy is very important to us. The researchers will make every effort to protect it, but your information may be given out if required by law. However, the researchers will do their best to make sure that any information that is released will not identify you.

Your research information and your personal identifying information will be kept private through the use of password-protected electronic files, locked research areas, and study identification numbers. Samples obtained for research purposes will be stored with the same safeguards. The results of this research may be presented at meetings or in publications, but you will not be identified by name.

There are organizations that may inspect your records. These organizations are required to make sure your information is kept private, unless required by law to provide information. Some of these organizations are:

- Virginia Commonwealth University (VCU)
- VCU Institutional Review Board (IRB)
- Food and Drug Administration (FDA)
- National Cancer Institute (NCI)

It will be noted in your protected electronic health record at VCU Health that you are in this study. Information about the study, including any medications you may receive, will be included in the record. This information is protected just as any of your other health records are protected.

In general, we will not give you any individual research results.

In the future, the identifiers (like your name and birthday) could be removed from the information and samples you provide for this study. After that removal, your information and samples could be used for new studies without asking for your consent again. Those possible new studies could be done by this study team or other researchers and might involve sequencing all or part of your DNA.

USE AND DISCLOSURE OF PROTECTED HEALTH INFORMATION

The Health Insurance Portability & Accountability Act (HIPAA) of 1996 provides for the protection of your health information from unauthorized use and disclosure. This section tells you what health information about you may be used and given out in the study and who may give and receive the information. By signing the consent form for this study, you agree that health information that identifies you may be used and disclosed as needed for this research.

Authority to Request Protected Health Information

The following people and/or groups may request your protected health information:

- Principal investigator and research staff
- Research collaborators
- VCU IRB
- Data and Safety Monitoring Committee
- Government/health agencies
- Others as required by law

Authority to Release Protected Health Information

The VCU Health System (VCUHS) may release the information identified in this authorization from your medical records and provide this information to:

- Health care providers at the VCUHS
- Principal investigator and research staff
- Research collaborators
- Data coordinators
- VCU IRB
- Data and Safety Monitoring Committee
- Government/health agencies
- Others as required by law

Once your health information has been disclosed to anyone outside of this study, the information may no longer be protected under this authorization.

Type of Information that may be Released

The following types of information may be used for the conduct of this research

- Complete health record
- Diagnosis and treatment codes
- Discharge summary
- History and physical exam
- Consultation reports
- Progress notes
- Laboratory test results
- Imaging reports (eg, X-ray reports)
- X-ray films/images
- Information about drug and alcohol abuse
- Information about Hepatitis B, Hepatitis C, and HIV tests
- Information about psychiatric care
- Complete billing record
- Itemized bill

Expiration of This Authorization

This authorization will expire (end) when the research study is closed, or when there is no need to review, analyze, and consider the data generated by the research study, whichever is later.

Right to Revoke Authorization and Re-disclosure

You may change your mind and revoke (take back) the right to use your protected health information at any time. Even if you revoke this authorization, the researchers may still use or disclose health information they have already collected about you for this study. If you revoke this authorization you may no longer be allowed to participate in the research study. To revoke this authorization, you must write to the principal investigator.

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WHERE CAN I GET MORE INFORMATION?

You may visit the NCI website at http://cancer.gov/ for more information about studies or general information about cancer. You may also call the NCI Cancer Information Service to get the same information at: 1-800-4-CANCER (1-800-422-6237).

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

WHO CAN ANSWER MY QUESTIONS ABOUT THIS STUDY?

You can talk to your study doctor about any questions or concerns you have about this study or to report side effects or injuries.

The investigator and study staff named below are the best person(s) to contact if you have any questions, complaints, or concerns about your participation in this research:

Chelsea Salyer, MD
Phone:804-628-7022
Email: chelsea.salyer@vcuhealth.org
Study Team
Email: MasseyGYN@vcu.edu

Evening/Weekend Doctor on Call at 804-828-0951; ask for the doctor carrying pager 9911

If you have general questions about your rights as a participant in this or any other research, or if you wish to discuss problems, concerns or questions, to obtain information, or to offer input about research, you may contact:

Virginia Commonwealth University Office of Research

800 East Leigh Street, Suite 3000, Box 980568, Richmond, VA 23298

(804) 827-2157; https://research.vcu.edu/human-research/

Do not sign this consent form unless you have had a chance to ask questions and have received satisfactory answers to all of your questions.

OPTIONAL STUDIES

Please circle your answer below to show if you would like to take part in the optional study:

Samples for Genetic Testing:

I agree that my blood sample and related health information may be used for the laboratory study described above.

YES NO

MY SIGNATURE AGREEING TO TAKE PART IN THE OPTIONAL STUDY

_____

Participant Name (*Printed*)

_____ _____

Participant Name (*Signature*) Date

MY SIGNATURE AGREEING TO TAKE PART IN THIS STUDY

I have been given the opportunity to carefully read this consent form. All of the questions that I wish to raise concerning this study have been answered.

By signing this consent form, I have not given up any of my legal rights or benefits. My signature indicates that I freely consent to participate in this research study. I will receive a copy of the signed consent form.

_____

Participant Name (*Printed*)

_____ _____

Participant Name (*Signature*) Date

_____

Person Conducting Informed Consent Discussion (*Printed Name*)

_____ _____

Person Conducting Informed Consent Discussion (*Signature*) Date