Title: Pembrolizumab and Chemoradiation Treatment for Advanced Cervical Cancer
NCT02635360
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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 # _____**

| | |
|---|---|
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| **Sponsor:** | The University of Virginia Cancer Center |
| **Funding Source:** | Merck Sharp & Dohme Corporation |

## What is the purpose of this form?

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

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

## Who is funding this study?

The University of Virginia Cancer Center. The study drug, Pembrolizumab, and some financial support is provided by Merck, the manufacturer of Pembrolizumab.

## Why is this research being done?

The purpose of this study is to test the safety and effectiveness of an investigational drug called pembrolizumab when added to chemoradiation, for treatment of advanced cervical cancer.

Pembrolizumab has not been approved for the treatment of cervical cancer and the combination of pembrolizumab and chemoradiation (CRT) is not approved for treatment of any cancers by the Food and Drug Administration (FDA).

The current standard treatment for advanced cervical cancer includes chemoradiation, which is administration of the drug cisplatin during several weeks of radiation treatments. Cisplatin is approved by the FDA for the treatment of advanced cervical cancer.

This study will help determine if adding pembrolizumab treatment to the standard treatment is safe and if providing this study drug at the same time will be more effective in treating advanced cervical cancer than providing pembrolizumab after chemoradiation.

You are being asked to participate in this research study because you have advanced cervical cancer.

Up to 25 patients will be in this study at UVA. Up to 88 patients will be in this study at other institutions in the United States.

## How long will this study take?

You will be required to make weekly office visits while you are receiving study treatment.

Your participation in this study will add about 30 minutes to each of your routine clinic visits and may require up to 3 study visits in addition to the visits for your routine clinical care assuming your tumor is not growing and you are not experiencing any unacceptable side effects. After you complete your study treatment, you will be followed for 5 years.

## What will happen if you are in the study?

### SCREENING (will take about 4-6 hours to complete):

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

**THE FOLLOWING TESTS WILL BE PERFORMED AS PART OF YOUR ROUTINE CLINICAL CARE AND THE RESULTS WILL BE RECORDED FOR RESEARCH PURPOSES:**

- **History and physical exam** which may include a **pelvic exam**. You will also have your heart rate, blood pressure and temperature taken.
- **Blood tests** to assess blood cell counts, liver and kidney function, blood mineral levels, blood clotting function and thyroid function. The amount of blood that will be drawn is approximately 2 tablespoons.
- A urine or serum **pregnancy test** if you are capable of becoming pregnant (this will be done within 72 hours of first dose of study treatment).
- **PET/CT scan** of the whole body to measure detectable tumor.
- **MRI** of the pelvis.
- **Review of medications and supplements** that you are currently taking.

**THE FOLLOWING TESTS ARE NOT PART OF ROUTINE CANCER CARE AND WILL BE PERFORMED FOR RESEARCH PURPOSES:**

- About 5 tablespoons of **blood will be drawn** for biomarker tests. Biomarkers such as DNA sequences, proteins, or cells are substances in your body that can be used to detect a disease or to find out if the cancer treatment is working.
- **Fresh tumor tissue** will be collected for screening purposes by biopsy, which is a procedure to remove a small sample of your cervix tissue. This procedure will likely be performed in your doctor's office, but

it could take place in a procedure room under anesthesia if another procedure requiring anesthesia is happening at the same time. Your study doctor will explain the details of the procedure to you. Archival tumor tissue from a previous biopsy or surgical procedure may also be collected in addition to the fresh tumor tissue.

- You will be asked about any previous **unpleasant symptoms or reactions** from previous procedures and biopsies.

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

## RANDOMIZATION

You will be randomly assigned (like the flip of a coin) to 1 of 2 study treatment groups. You have an equal chance of being assigned to any one of the groups. Neither you nor your doctor can choose which group you are assigned.

**Both GROUPS A and B will receive:**

- Cisplatin- the standard chemotherapy drug for treatment of advanced cervical cancer. This drug is administered into your vein (intravenously, IV) over 60 minutes for 5-6 weeks.
- Radiation treatments will occur for 5-6 weeks.
- Pembrolizumab- the study drug. You will receive this study drug intravenously over 30 minutes. This treatment will last for 3 cycles of 21 days each with the infusion occurring on the first day of each cycle.

**GROUP A: will receive the study drug <u>after</u> chemotherapy and radiation.**

**GROUP B: will receive the study drug <u>during</u> chemotherapy and radiation.**

**** For the purpose of this study we will refer to Pembrolizumab as the "study drug"****

## STUDY TREATMENT (will take about 4-6 hours to complete)

The study treatments and schedules below are separated for Groups A and B.

**<u>GROUP A:</u>**

**<u>THE FOLLOWING TESTS WILL BE PERFORMED AS PART OF YOUR ROUTINE CLINICAL CARE AND THE RESULTS WILL BE RECORDED FOR RESEARCH PURPOSES:</u>**

- **History and physical exam** which may include a **pelvic exam** will be performed at your physician's recommendation. You will also have your heart rate, blood pressure and temperature taken every week for Weeks 1-6 and then again at Weeks 9, 12, and 15.
- **Blood tests** to assess blood cell counts, liver and kidney function, blood mineral levels, blood clotting function. Every week during Weeks 1-6, the amount of blood that will be drawn is approximately 2 tablespoons.
- You will be asked questions about your **ability to complete daily activities** every week during Weeks 1-6 and then again at Weeks 9, 12, and 15.

- You will be given the standard **chemotherapy and radiation** every week during Weeks 1-6.

**THE FOLLOWING TESTS ARE NOT PART OF ROUTINE CANCER CARE AND WILL BE PERFORMED FOR RESEARCH PURPOSES:**

- You will be given the **study drug** every 3 weeks during Weeks 9-15.
- Up to 1 teaspoon of **blood will be drawn** to check your thyroid function on the day of study drug treatment during Weeks 9-15.
- Up to 2 teaspoons of **blood will be drawn** to check for certain minerals and proteins in your blood and your blood count every 3 weeks during Weeks 9-15.
- About 5 tablespoons of **blood will be drawn** for biomarker tests. Biomarkers such as DNA sequences, proteins, or cells are substances in your body that can be used to detect a disease or to find out if the cancer treatment is working. This will occur around the 5$^{th}$ week of your radiation treatment.
- **Fresh tumor tissue** will be collected around the 5$^{th}$ week of your radiation treatment by biopsy, which is a procedure to remove a small sample of your cervix tissue. This procedure will likely be performed in your doctor's office, but it could take place in a procedure room under anesthesia if another procedure requiring anesthesia is happening at the same time. Your study doctor will explain the details of the procedure to you.
- You will be asked about if you have had any **unpleasant symptoms or reactions** to the study drug at every visit during Weeks 1-15.

**GROUP B:**

**THE FOLLOWING TESTS WILL BE PERFORMED AS PART OF YOUR ROUTINE CLINICAL CARE AND THE RESULTS WILL BE RECORDED FOR RESEARCH PURPOSES:**

- **History and physical exam** which may include a **pelvic exam** will be performed at your physician's recommendation. You will also have your heart rate, blood pressure and temperature taken every week while you are receiving treatment.
- **Blood tests** to assess blood cell counts, liver and kidney function, blood mineral levels, and blood clotting function will be performed every week while you are receiving treatment. The amount of blood that will be drawn is approximately 2 tablespoons.
- You will be asked questions about your ability to complete daily activities weekly during treatment.
- You will be given the standard **chemotherapy and radiation** every week during Weeks 1-6.

**THE FOLLOWING TESTS ARE NOT PART OF ROUTINE CANCER CARE AND WILL BE PERFORMED FOR RESEARCH PURPOSES:**

- You will be given the **study drug** every 3 weeks at Week 1, Week 4, and Week 7.
- Up to 1 teaspoon of **blood will be drawn** to check your thyroid function prior to each treatment with the study drug.
- About 5 tablespoons of **blood will be drawn** for biomarker tests. Biomarkers such as DNA sequences, proteins, or cells are substances in your body that can be used to detect a disease or to find out if the cancer treatment is working. This will occur around the 5$^{th}$ week of your radiation treatment.
- **Fresh tumor tissue** will be collected through a biopsy around the 5$^{th}$ week of your radiation treatment by biopsy, which is a procedure to remove a small sample of your cervix tissue. This procedure will likely be performed in your doctor's office, but it could take place in a procedure room under

anesthesia if another procedure requiring anesthesia is happening at the same time. Your study doctor will explain the details of the procedure to you, depending on how the biopsy sample will be obtained.
- You will be asked about if you have had any **unpleasant symptoms or reactions** to the study drug every week.

## END OF STUDY VISIT (GROUPS A and B):

You will be asked to come to the clinic for an end of treatment visit 35 ± 5 days after you complete your study treatment, if your disease becomes worse, or if your study treatment has been stopped due to unpleasant symptoms and reactions to the study drug.

If you stop taking the study drug because your disease has progressed, your study physician will ask you to return to the clinic within 30 days after you stop the study drug.

**THE FOLLOWING TESTS WILL BE PERFORMED AS PART OF YOUR ROUTINE CLINICAL CARE AND THE RESULTS WILL BE RECORDED FOR RESEARCH PURPOSES:**

- **History and physical exam** which may include a **pelvic exam**. You will also have your heart rate, blood pressure and temperature taken.
- **Blood tests** to assess blood cell counts, liver and kidney function, blood mineral levels, blood clotting function. The amount of blood that will be drawn is approximately 2 tablespoons.
- You will be asked questions about your ability to complete daily activities.
- **PET/CT scan** of the whole body to measure detectable tumor 12 weeks after completion of treatment.

**THE FOLLOWING TESTS ARE NOT PART OF ROUTINE CANCER CARE AND WILL BE PERFORMED FOR RESEARCH PURPOSES:**

- Up to 1 teaspoon of **blood will be drawn** check your thyroid function 1 Month after your last study treatment.
- About 5 tablespoons of **blood will be drawn** for biomarker tests. Biomarkers such as DNA sequences, proteins, or cells are substances in your body that can be used to detect a disease or to find out if the cancer treatment is working. This will be collected 3 Months after your last radiation treatment.
- **Fresh tumor tissue** will be collected at about 3 Months after your last radiation treatment. This will procedure will be done the same as your previous tumor biopsies.
- You will be asked about if you have had any **unpleasant symptoms or reactions** to the study drug 1 Month after your last study treatment.

## FOLLOW UP (GROUPS A and B):

If you discontinue study treatment prior to your disease becoming worse, you will be followed every 3 months from the date of the last dose of study drug until your disease becomes worse or for up to 5 years whichever comes first.

**Study Schedule: GROUP A**

| | Screening Visit | Treatment Visits | | End of Treatment Visits | | Follow-up Visit |
|---|---|---|---|---|---|---|
| | | Weeks 1-6, Day 1 every week | Weeks 9-15, Day 1 every 3 weeks | Visit 1 (1 month post-treatment) | Visit 2 (3 months post-treatment) | |
| Informed Consent | X | | | | | |
| Medical History | X | | | | | |
| Physical Exam | X | X | X | X | X | |
| Vital signs | X | X | X | X | | |
| Medication Assessment | X | | | | | |
| Disease Assessment | X | X | X | X | X | X |
| Standard Cisplatin Chemotherapy | | X | | | | |
| Radiation | | X | | | | |
| Pembrolizumab Administration | | | X | | | |
| Tissue Collection | X | X[1] | | | X | |
| Blood Draws for Research | X | X | X | X | X | |
| Blood Draws for Clinical Care | X | X | X | X | | |
| Pregnancy Test (Urine or Serum) | X | | | | | |
| MRI Scan | X | | | | | |
| CT Scan | X | | | | X | |

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

**[1] Tissue collection will occur at Week 5 +/- 2 weeks**

**Study Schedule: GROUP B**

| | Screening Visit | Treatment Visits | End of Treatment Visits | | Follow-up Visits |
|---|---|---|---|---|---|
| | | Weeks 1-7, Day 1 every week | Visit 1 (1 month post-treatment) | Visit 2 (3 months post-treatment) | |
| Informed Consent | X | | | | |
| Medical History | X | | | | |
| Physical Exam | X | X | X | X | |
| Vital signs | X | X | X | | |
| Medication Assessment | X | | | | |
| Disease Assessment | X | X | X | X | X |
| Standard Cisplatin Chemotherapy | | X | | | |
| Radiation | | X | | | |
| Pembrolizumab Administration | | X[1] | | | |
| Tissue Collection | X | X[2] | | X | |
| Blood Draws for Research | X | X | X | X | |
| Blood Draws for Clinical Care | X | X | X | | |
| Pregnancy Test (Urine or Serum) | X | | | | |
| MRI Scan | X | | | | |
| CT Scan | X | | | X | |

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

**[1] Pembrolizumab infusions will occur on the first day of Weeks 1, 4, and 7**

**[2] Tissue collection will occur at Week 5 +/- 2 weeks**

## What are your responsibilities in the study?

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

- You must come to each study visit.
- You must be completely truthful about your health history.

- Follow all instructions given.
- You should tell the study doctor or study staff about any changes in your health or the way you feel.
- 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.
- You must not eat grapefruit or drink grapefruit juice during the course of your participation in this study.
- 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

We will take (or "draw") up to 2-3 tablespoons of blood per week, and up to 5 tablespoons of blood for research testing while you are receiving treatment.

The 2 tablespoons of blood per week will be used to measure how well your kidney and liver are doing, sugar and salts in your blood, and to measure the white and red blood cells. This is considered routine blood work for someone receiving chemotherapy. If you are in Group A, these blood draws will be collected for research purposes during Months 3-4.

1 tablespoon of blood will be drawn prior to your pembrolizumab treatment to check how well your thyroid functions. This will be done for research purposes.

5 tablespoons will be collected for research purposes during screening, around the 5$^{th}$ week of your radiation treatment, and about 3 months after your last radiation treatment. This blood is used for looking at things called biomarkers, a characteristic in your blood that would indicate if the study drug was having the desired effect on your body.

When these tests are done any left-over sample will be thrown away or they will be de-identified. This means there is no information that could be used by anyone to determine who the sample came from.

## 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.

# What are the risks of being in this study?

## Risks from Cisplatin include:

**Likely (equal to or more than 10 out of 100):**

- Fatigue
- Lowered white blood count may increase risk of infection
- Lowered red blood cells may lead to anemia, tiredness, or shortness of breath
- Decrease in kidney function
- Loss of appetite and weight loss
- Diarrhea, constipation, nausea, and vomiting, and abdominal pain
- Complete hair loss
- Numbness or tingling in fingers or toes
- Skin rash
- Changes in taste
- Ringing in the ears and hearing loss
- Changes in electrolytes in the blood such as magnesium and potassium or an increase in calcium

**Less Likely (equal to or greater than 1 but less than 10 out of 100):**

- Allergic reactions
- Chills and fever with aches and pains
- Lowered platelets may lead to an increase in bruising or bleeding
- Sores in mouth and throat (that can lead to difficulty swallowing and dehydration)
- Altered vision
- Skin irritation and swelling if the drug leaks from the vein into which it is being injected into the surrounding skin
- Changes in heart rhythm

**Rare but serious (less than 1 out of 100):**

- Seizures
- Secondary cancers such as acute leukemia
- Kidney failure requiring dialysis
- Deafness
- Hemolytic uremic syndrome (low red blood cell count, low platelet count and kidney damage)

## Risks from Pembrolizumab include:

**What is known about this study drug?**

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 (greater than 20 in every 100) seen in people taking Pembrolizumab include the following:**

- 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 (between 5 and 20 in every 100) seen in people taking Pembrolizumab include the following:**

- 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 feel sick to your stomach (hyponatremia)

**Uncommon, Some May be Serious (i.e. causing hospitalization, life-threatening or where noted, may cause death) Side Effects (between 1 and 5 in every 100) seen in people taking Pembrolizumab include the following:**

- 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. These severe conditions can sometimes lead to death. (Severe skin reactions, including Stevens-Johnson syndrome/or toxic epidermal necrolysis)

**Rare, Some May be Serious (i.e. causing hospitalization, life-threatening or where noted, may cause death) Side Effects (less than 1 in every 100) seen in people taking Pembrolizumab include the following:**

- 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-Barre 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. Sometimes this condition can lead to death (myocarditis)
- Inflammation of the thyroid gland, an organ that makes and stores thyroid hormones. This condition may lead to change in your heart rate, blood pressure, body temperature, and the rate at which food is converted into energy (thyroiditis)
- 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)

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 of the skin and hearing loss (Vogt-Koyanagi-Harada syndrome)

In addition to the above, **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.

**Risks from study procedures include:**

**Tumor Biopsy**: We will ask you to allow us to obtain tissue from a biopsy procedure. Having biopsies performed may cause pain, bruising, bleeding, redness, low blood pressure, swelling and/or infection at the site of the biopsy. Other potential risks will be described to you and discussed with you by physicians who conduct these biopsies.

**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 3 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 up to 120 days 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.

**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 include: lessen symptoms from your disease, shrink your tumor, and/or may lengthen your survival; however, no guarantees can be made. In addition, information researchers get from this study may help others in the future.

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

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

- Getting treatment or care for your cancer without being in a study which could include chemoradiation with cisplatin
- Taking part in another study
- Supportive comfort care (also called palliative care). This type of care helps reduce pain, tiredness, appetite problems, and other problems caused by the cancer. It does not treat the cancer directly, but instead tries to improve how you feel. Comfort care tries to keep you as active and comfortable as possible.
- 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, 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:

- Blood testing for the following:
    - The amount of biomarkers (body substances that detect disease or finds out if the cancer treatment is working)
    - To check your thyroid function
    - Certain blood tests (assessing blood cell counts, liver and kidney function, blood mineral levels, blood clotting function) if not already done as part of your standard of care
- Disease assessments to check for unpleasant symptoms or reactions from the study drug
- Any additional costs related to tissue biopsy collection
- The study drug pembrolizumab will be provided by the study at no cost to you. However, the cost of administering the drug will be billed to you and/or your insurance.

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

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

## What if you are hurt in this study?

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

## What happens if you leave the study early?

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

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

a) Your study physician is concerned about your health
b) Your disease gets worse
c) The side effects of the treatment are too dangerous for you
d) New information shows the treatment will not work or is not safe for you
e) You do not follow your doctor's instructions
f) The study sponsor closes the study for safety, administrative or other reasons

If you decide to stop being in the study, we will ask you to complete the End of Study procedures and follow the instructions of the study staff.

## 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.

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

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

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

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

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

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

## Please contact the researchers listed below to:

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

Linda Duska, MD
University of Virginia School of Medicine
Department of Obstetrics and Gynecology, Division of Gynecologic Oncology
PO Box 800712
Charlottesville, VA 22908 Telephone: (434) 924-1570

## What if you have a concern about this study?

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

University of Virginia Institutional Review Board for Health Sciences Research
PO Box 800483
Charlottesville, Virginia 22908
Telephone: 434-924-9634

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.

# 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.**

**Consent from Impartial Witness**

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

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

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

☐ Subject

| _____ | _____ | _____ |
|---|---|---|
| IMPARTIAL WITNESS (SIGNATURE) | IMPARTIAL WITNESS (PRINT) | DATE |