NCI Protocol #: 10496
Local Protocol #: PhII-216
Protocol Version Date: April 15, 2025

Protocol Title: A Phase 2 Study of Ipatasertib in Combination with Pembrolizumab for First Line Treatment of Recurrent or Metastatic Squamous Cell Cancer of the Head and Neck

Informed Consent Version Date: April 15, 2025

SUMMARY OF CHANGES – Consent

#	Section	Comments
1.	General	Updated version date.

2.	Possible Side Effects of pembrolizumab (MK-3475)	Updated the risk profile for Pembrolizumab to match the protocol CAEPR (Version 2.9, January 31, 2025):
		
		• Increase in Risk Attribution:
		  • Changed to Common from Occasional: Anemia which may require blood transfusion
		  • Changed to Occasional from Rare: Lung problems (pneumonitis and other conditions). Symptoms may include: new or worsening cough, chest pain, shortness of breath
		  • Changed to Occasional from Also Reported on Pembrolizumab (MK-3475) Trials But With Insufficient Evidence for Attribution (i.e., added to the Risk Profile): Constipation; Cough
		
		• Provided Further Clarification:
		  • Skin: itching; acne; rash (can be severe); blisters and peeling on the skin, mouth; skin changes; hives (under Occasional) is now reported as Skin: itching; acne; rash (can be severe); blisters and peeling on the skin; skin changes; hives (under Occasional).
		  • Damage to organs in the body when donor cells attack host organs which may cause yellowing of eyes and skin, itchy dry skin, diarrhea or muscle weakness (under Rare and Serious), should have been reported as Damage to organs in the body when donor cells attack host organs which may cause yellowing of eyes and skin, itchy dry skin (under Rare and Serious).

Research Study Informed Consent Document

Study Title for Participants: Testing the addition of an anti-cancer drug, ipatasertib, to the usual immunotherapy treatment (pembrolizumab) for recurrent or metastatic squamous cell cancer of the head and neck

Official Study Title for Internet Search on http://www.ClinicalTrials.gov: Protocol 10496, A Phase 2 Study of Ipatasertib in Combination with Pembrolizumab for First Line Treatment of Recurrent or Metastatic Squamous Cell Cancer of the Head and Neck (NCT #: TBD)

Overview and Key Information

What am I being asked to do?

We are asking you to take part in a research study. This study has public funding from the National Cancer Institute (NCI), part of the National Institutes of Health (NIH) in the United States Department of Health and Human Services. We do research studies to try to answer questions about how to prevent, diagnose, and treat diseases like cancer.

We are asking you to take part in this research study because you have advanced head and neck squamous cell cancer.

Taking part in this study is your choice.

You can choose to take part or you can choose not to take part in this study. You also can change your mind at any time. Whatever choice you make, you will not lose access to your medical care or give up any legal rights or benefits.

This document has important information to help you make your choice. Take time to read it. Talk to your doctor, family, or friends about the risks and benefits of taking part in the study. It's important that you have as much information as you need and that all your questions are answered. See the "Where can I get more information?" section for resources for more clinical trials and general cancer information.

Why is this study being done?

This study is being done to answer the following question:

Can we safely lower the chance of your head and neck squamous cell cancer growing or spreading by adding a drug to the usual combination of drugs?

We are doing this study because we want to find out if this approach is better or worse than the usual approach for your head and neck squamous cell cancer. The usual approach is defined as care most people get for first line relapsed/metastatic head and neck squamous cell cancer.

What is the usual approach to my relapsed/metastatic head and neck squamous cell cancer?

The usual approach for patients who are not in a study is treatment with immunotherapy using pembrolizumab. This drug has been approved by the Food and Drug Administration (FDA) for your cancer. There are no treatments that are proven to help patients with your health condition live longer compared to treatment with pembrolizumab.

What are my choices if I decide not to take part in this study?

- You may choose to have the usual approach described above.
- You may choose to take part in a different research study, if one is available.
- You may choose not to be treated for cancer.
- You may choose to only get comfort care to help relieve your symptoms and not get treated for your cancer.

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

If you decide to take part in this study, you will either get the study drugs pembrolizumab and ipatasertib on Days 1 through 14, or you will get pembrolizumab alone on Day 1, until your disease gets worse or the side effects become too severe, for a maximum treatment of 24 months.

After you finish your study treatment, your doctor will continue to follow your condition at least every three months and watch you for side effects. This may include clinic visits or phone calls, as deemed appropriate for your condition by your doctor. The follow-up with your doctor will continue until your disease gets worse, you begin a new therapy, or death.

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 to make sure you know about a few key risks right now. We give you more information in the "What 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 pembrolizumab and ipatasertib may not be as good as the usual approach for your cancer at shrinking or stabilizing 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 the usual approach for your cancer.

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

- Tiredness
- Rash
- Diarrhea, heartburn, nausea, vomiting
- Loss of appetite
- Headache

There may be some risks that the study doctors do not yet know about.

Benefits

There is evidence that adding ipatasertib to similar therapies is effective in improving some treatment outcomes for patients with cancer. It is not possible to know now if ipatasertib with pembrolizumab will extend your life compared to the usual approach. This study will help the study doctors learn things that will help people in the future.

If I decide to take part in this study, can I stop later?

Yes, you can decide to stop taking part in the study at any time.

If you decide to stop, let your study doctor know as soon as possible. It's important that you stop safely. This may mean you will have one last study visit to make sure there are no additional concerns before you stop participating in the study. If you stop, you can decide if you want to keep letting the study doctor know how you are doing.

Your 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.

Are there other reasons why I might stop being in the study?

Yes. The study doctor may take you off the study if:

- Your health changes and the study is no longer in your best interest.
- New information becomes available and the study is no longer in your best interest.
- You do not follow the study rules.
- For women: You become pregnant while on the study.
- The study is stopped by the Institutional Review Board (IRB), Food and Drug Administration (FDA), or study sponsor (NCI). The study sponsor is the organization who oversees the study.

It is important that you understand the information in the informed consent before making your decision. 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 nurse.

What is the purpose of this study?

The purpose of this study is to compare the usual treatment alone to using ipatasertib plus the usual treatment. The addition of ipatasertib to the usual treatment could help shrink or stabilize your cancer. But, it could also cause side effects, which are described in the risks section below.

This study will help the study doctors find out if this different approach is better, the same, or worse than the usual approach, and confirm if this approach is safe and tolerable. To decide if it is better, the study doctors will be looking to see if pembrolizumab plus ipatasertib increases the life of patients before the disease gets worse.

There will be about 48 people taking part in this study.

What are the study groups?

We will use a computer to assign you to one of the study groups. This process is called "randomization." It means that your doctor will not choose and you cannot choose which study group you are in. You will be put into a group by chance. You will have a 50 % chance of being in Group 1 or Group 2.

This study has 2 study groups.

- **Group 1**

  If you are in this group, you will get the usual drug used to treat this type of cancer, pembrolizumab, plus a study drug called ipatasertib. You will receive pembrolizumab through a vein in the arm on Day 1 and ipatasertib as a pill once a day for the first 14 days of each cycle. You will take both these drugs during every 21-day cycle, for a maximum treatment of 24 months. See the study calendar for more information.

  You will not be able to get additional doses of the drug ipatasertib. This drug is not approved by the FDA for treatment of your disease.

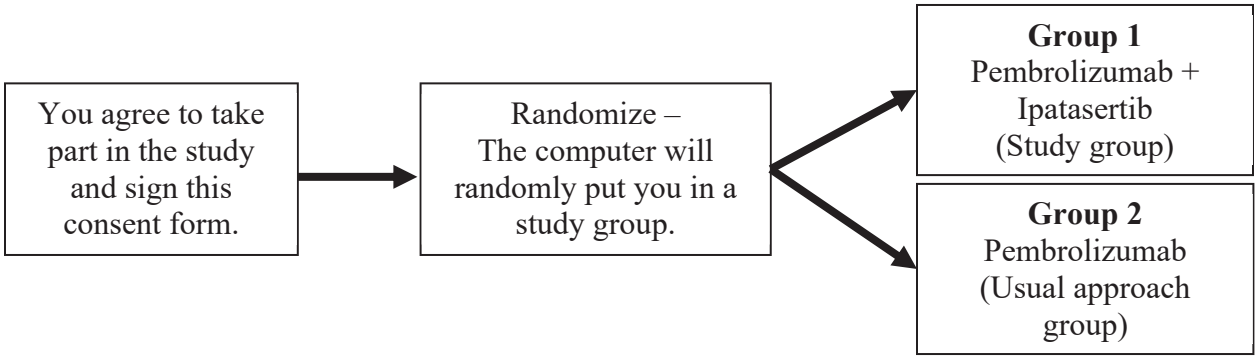
  There will be about 24 people in this group.

- **Group 2**

  If you are in this group, you will get the usual drug used to treat this type of cancer, pembrolizumab, through a vein in the arm on Day 1 of each 21-day cycle, for a maximum treatment of 24 months. See the study calendar for more information.

There will be about 24 people in this group.

Another way to find out what will happen to you during this study is to read the chart below. Start reading at the left side and read across to the right, following the lines and arrows.



What exams, tests, and procedures are involved in this study?

Before you begin the study, your doctor will review the results of your exams, tests, and procedures. This helps your doctor decide if it is safe for you to take part in the study. If you join the study, you will have more exams, tests, and procedures to closely monitor your safety and health. Most of these are included in the usual care you would get even if you were not in a study.

Listed below are exams, tests, and procedures that need to be done as part of this study to monitor your safety and health, but may not be included in the usual care. We will use them to carefully follow the effects of the study treatment, including preventing and managing side effects.

These exams, tests, and procedures to monitor your safety and health include:

- Blood counts done weekly during the first cycle of treatment.
- Physical exams done weekly during the first cycle.

The study will use genetic tests that may identify changes in the genes in your tumor DNA. Your genes carry information about you and your family, from the color of your eyes to health conditions for which you may be at risk, such as certain kinds of cancer.

Finding these changes would not affect your treatment in this study. However, they could affect your health in other ways. If there are changes found that could cause health problems, then your study doctor will discuss your options with you.

Some exams, tests, and procedures are a necessary part of the research study, but would not be included in usual care. Listed below are procedures that will be done for research purposes only.

Your study doctor will need to use some of the tissue left over from your biopsy when you were diagnosed with cancer. This sample is a required part of the study and will determine if you are eligible to participate in the study. You and your study doctor will not get the results of this testing.

You will need to have biopsies and blood samples taken for the study. On Day 7 of Cycle 2, you will have a biopsy that takes small pieces of cancer tissue from your body. This is like the biopsy you had that helped diagnose your cancer. You will also have blood samples taken before you begin the study drug, on Day 1 of every odd cycle, on Day 7 of Cycle 2, and when your cancer gets worse. These biopsies and blood draws are mandatory and will be used to see if the study treatment is working. You and your study doctor will not get the results of this testing. If you agree to take part in the study, you may need to sign a separate consent form for the study biopsy at the hospital or clinic where the biopsy is done.

A patient study calendar is attached at the end of this document. It shows how often these blood and biopsy collections will be done.

What 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 the usual approach for your cancer at shrinking or stabilizing your cancer.

You also may have the following discomforts:

- 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.

The study drugs used in this study could be very harmful to an unborn or newborn baby. There may be some risks that doctors do not yet know about. 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 5 months after the last dose of pembrolizumab and 28 days after the last dose of ipatasertib.

This study will use a sample of your tissue. Generally, your hospital will keep some of your tissue. This tissue may be used to help treat your cancer in the future. Because this study will need to use some of this tissue, there is a small risk that it could be used up.

Biopsy Risks

Common side effects of a biopsy are a small amount of bleeding at the time of the procedure, bruising, and pain at the biopsy site. Pain can be treated with regular pain medications. Rarely, an infection can occur. You may sign a separate consent form for the study biopsy that describes the risks in more detail.

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 test your blood and let you know if changes occur that may affect your health.

There is also a risk that you could have other side effects from the study drugs.

Here are important things to know about side effects:

1. The study doctors do not know who will or will not have side effects.
2. Some side effects may go away soon, some may last a long time, and some may never go away.
3. Some side effects may make it hard for you to have children.
4. Some side effects may be mild. Other side effects may be very serious and even result in death.

You can ask your study doctor questions about side effects at any time. Here are important ways to make side effects less of a problem:

- If you notice or feel anything different, tell your study doctor. He or she can check to see if it is a side effect.
- Your study doctor will work with you to treat your side effects.
- Your study doctor may adjust the study drugs to try to reduce side effects.

This study is looking at a combination of the usual drugs used to treat this type of cancer plus a study drug. This new combination of drugs may increase your side effects or may cause new side effects.

You should notify your doctor immediately at the first sign of poorly formed or loose stools or an increased frequency of bowel movements. Loperamide (Imodium) should be kept on hand and should be taken as recommended by your doctor.

Drug Risks

The tables below show the most common and most serious side effects doctors know about. Keep in mind that there might be other side effects doctors do not yet know about. If important new side effects are found, the study doctor will discuss these with you.

Study Group 1 and Group 2 – Possible side effects of pembrolizumab are listed in the tables below. This drug is part of the usual approach for treating this type of cancer:

Possible Side Effects of pembrolizumab (MK-3475)
(Table Version Date: January 31, 2025)

COMMON, SOME MAY BE SERIOUS In 100 people receiving pembrolizumab (MK-3475), more than 20 and up to 100 may have:
• Tiredness Pembrolizumab (MK-3475) may cause your immune system to attack normal organs and cause side effects in many parts of the body. These problems may include but are not limited to: • Anemia which may require blood transfusion

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving pembrolizumab (MK-3475), from 4 to 20 may have:
• Constipation, nausea • Loss of appetite • Pain in back • Joint stiffness • Cough • Swelling and redness of the skin Pembrolizumab (MK-3475) may cause your immune system to attack normal organs and cause side effects in many parts of the body. These problems may include but are not limited to: • Pain in lymph nodes • Blood clot which may cause bleeding, confusion, paralysis, seizures and blindness • Hormone gland problems (especially the thyroid, pituitary and adrenal glands, and pancreas). Signs and symptoms may include: headaches that will not go away or unusual headaches, extreme tiredness or changes in mood or behavior decreased sex drive; weight loss or weight gain; excessive thirst or urine; dizziness or fainting • Intestinal problems (colitis) that can rarely lead to tears or holes in your intestine. Signs and symptoms of colitis may include: diarrhea or increase in bowel movements, blood in your stools or dark, tarry, sticky stools, severe belly pain or tenderness • Diarrhea • Sores in the mouth which may cause difficulty swallowing • Pain in belly • Sores in the bowels • Chills, fever • Reaction during or following a drug infusion which may cause fever, chills, rash, low blood pressure

- Liver problems (hepatitis) which can cause liver failure. Signs and symptoms of hepatitis may include: yellowing of your skin or the whites of your eyes, severe nausea or vomiting; drowsiness; pain in the right upper belly
- Lung problems (pneumonitis and other conditions). Symptoms may include: new or worsening cough, chest pain, shortness of breath
- Pain or swelling of the joints
- Problem of the muscle, including swelling, which can cause muscle pain and severe muscle weakness sometimes with dark urine
- Skin: itching; acne; rash (can be severe); blisters and peeling on the skin; skin changes; hives

RARE, AND SERIOUS

In 100 people receiving pembrolizumab (MK-3475), 3 or fewer may have:

- A syndrome starting with flu-like symptoms and followed by swelling, tenderness which may cause flu-like symptoms, blurred vision, ringing in the ears, changes in hair or hair loss
- Inability to digest food which may cause bloating
- Swelling of the gallbladder
- Swelling of the spinal cord
- Feeling of "pins and needles" in arms and legs
- Redness, pain or peeling of palms and soles

Pembrolizumab (MK-3475) may cause your immune system to attack normal organs and cause side effects in many parts of the body. These problems may include but are not limited to:

- Heart problems including swelling and heart failure. Symptoms and signs of heart problem may include: Shortness of breath, swelling of the ankle and body
- Swelling and redness of the eye which may cause blurred vision with a chance of blindness
- Swelling of the bowels
- Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat
- Damage to organs in the body when donor cells attack host organs which may cause yellowing of eyes and skin, itchy dry skin
- Damage to organs in the body when the body produces too many white cells
- A condition with high blood sugar which leads to tiredness, frequent urination, excessive thirst, headache, nausea and vomiting, and can result in coma
- Problem of the nerves that can cause paralysis. Signs and symptoms may include: numbness, tingling of hands and feet; weakness of the arms, legs
- Swelling of the brain (encephalitis/meningitis) which may cause headache, confusion, sleepiness, seizures and stiff neck
- Kidney problems, including nephritis and kidney failure requiring dialysis. Signs of kidney problems may include: decrease in the amount of urine, blood in your urine, ankle swelling
- Skin rash developing 1-8 weeks after a drug is given which may be accompanied by fever, lymph node swelling and organ failure
- Swelling or tenderness of blood vessels

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.

Study Group 1 - In addition to side effects listed above, people who are in Group 1 may also have some side effects from ipatasertib. These side effects are listed below.

Possible Side Effects of Ipatasertib (GDC-0068)
(Table Version Date: October 28, 2024)

COMMON, SOME MAY BE SERIOUS In 100 people receiving ipatasertib, more than 20 and up to 100 may have:
• Diarrhea, nausea • Tiredness

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving ipatasertib, from 4 to 20 may have:
• Anemia which may require blood transfusion • Pain • Heartburn, vomiting • Weight loss, loss of appetite • Changes in taste • Headache • Muscle weakness • Numbness, tingling or pain of the arms and legs • Rash

RARE, AND SERIOUS In 100 people receiving ipatasertib, 3 or fewer may have:
• Sores in the mouth, which may cause difficulty swallowing • Liver damage which may cause yellowing of the eyes and skin • Bruising, bleeding • Dehydration • Damage to the lungs which may cause shortness of breath

Risks Associated with Ipatasertib

The side effects associated with ipatasertib are listed below. There may be side effects that are not known at this time.

High levels of glucose (sugar) in the blood (hyperglycemia) in patients being treated with ipatasertib have resulted in serious consequences, including one death (your study doctor can provide further details as needed).

There is a small chance that you will have an allergic reaction to ipatasertib. Allergic reactions may range from mild, such as skin rash or hives, to severe, such as breathing difficulties or shock. A severe allergic reaction would require immediate medical treatment and could result in permanent disability or death.

Other Side Effects Potentially Associated with Ipatasertib

The following are side effects that may be associated with ipatasertib. Although it has not yet been established whether ipatasertib causes these reactions, these side effects could be experienced by patients receiving ipatasertib.

- Elevated liver enzymes, which may indicate inflammation of the liver
- Increase of cholesterol or triglycerides (fats) in blood
- Decrease in the number of white blood cells
- Decrease in the number of platelets in the blood; in severe cases, this could lead to bleeding
- Decrease in the number of red blood cells
- Inflammation of the lungs (pneumonitis)
- Inflammation of the large intestine (colitis)
- Causing malformation of fetus (developing baby still inside the mother's body)

Additional Drug Risks

Your study doctor will give you a clinical trial wallet card that lists the study drugs that you are taking. Share this information with your family members, caregivers, other health care providers, and pharmacists.

Rarely, there are problems getting enough supplies of the study drug. If that happens, your doctor will talk with you about your options.

What are my responsibilities 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.
- Write down in your medication diary when you take the study drug at home.

For women: Do not get pregnant or breastfeed while taking part in this study. **For men:** Do not father a baby while taking part in this study. **For all:** Tell your study doctor right away if you think that you or your partner have become pregnant during the study or within 5 months after the last dose of pembrolizumab and 28 days after the last dose of ipatasertib.

What are the costs of taking part in this study?

You and/or your insurance plan will need to pay for the costs of medical care you get as part of the study, just as you would if you were getting the usual care for your cancer. This includes:

- the costs of tests, exams, procedures, and drugs that you get during the study to monitor your safety, and prevent and treat side effects.
- the costs of getting the pembrolizumab and ipatasertib ready and giving it to you.
- the cost of pembrolizumab
- your insurance co-pays and deductibles.

Talk to your insurance provider and make sure that you understand what your insurance pays for and what it doesn't pay for if you take part in this clinical trial. Also, find out if you need approval from your plan before you can take part in the study.

Ask your doctor or nurse for help finding the right person to talk to if you are unsure which costs will be billed to you or your insurance provider.

You and/or your insurance provider will not have to pay for exams, tests, and procedures done for research purposes only or that are covered by the study. These include:

- The biopsy collection for research purposes on Day 7 of Cycle 2.
- The blood collection for research purposes at the beginning of the study, on Day 1 of each odd cycle, on Day 7 of Cycle 2, and during progression.

You or your insurance provider will not have to pay for ipatasertib while you take part in this study.

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 because I took part in this study?

If you are injured as a result of taking part in this study and need medical treatment, please talk with your study doctor right away about your treatment options. The study sponsors will not pay for medical treatment for injury. Your insurance company may not be willing to pay for a study-related injury. Ask them if they will pay. If you do not have insurance, then you would need to pay for these medical costs.

If you feel this injury was caused by medical error on the part of the study doctors or others involved in the study, you have the legal right to seek payment, even though you are in a study. Agreeing to take part in this study does not mean you give up these rights.

Who will see my medical information?

Your privacy is very important to us. The study doctors will make every effort to protect it. The study doctors have a privacy permit to help protect your records if there is a court case. However, some of your medical information may be given out if required by law. If this should happen, the study doctors will do their best to make sure that any information that goes out to others will not identify who you are.

Some of your health information, such as your response to cancer treatment, results of study tests, and medicines you took, will be kept by the study sponsor in a central research database. However, your name and contact information will not be put in the database. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used.

There are organizations that may look at or receive copies of some of the information in your study records. Your health information in the research database also may be shared with these organizations. They must keep your information private, unless required by law to give it to another group.

Some of these organizations are:

- The study sponsor and any company supporting the study agent now or in the future. This would include any organization helping the company with the study.
- The NCI Central IRB, which is a group of people who review the research with the goal of protecting the people who take part in the study.
- The FDA and the groups it works with to review research.
- The NCI and the groups it works with to review research.
- The NCI's National Clinical Trials Network and the groups it works with to conduct research.

In addition to storing data in the study database, data from studies that are publicly funded may also be shared broadly for future research with protections for your privacy. The goal of this data sharing is to make more research possible that may improve people's health. Your study

records may be stored and shared for future use in public databases. However, your name and other personal information will not be used.

Some types of future research may include looking at your information and information from other patients to see who had side effects across many studies or comparing new study data with older study data. However, right now we don't know what research may be done in the future using your information. This means that:

- You will not be asked if you agree to take part in the specific future research studies using your health information.
- You and your study doctor will not be told when or what type of research will be done.
- You will not get reports or other information about any research that is done using your information.

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. For more information about the laws that protect you, ask your study doctor.

Where can I get more information?

You may visit the NCI web site 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 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.

You can talk to the study doctor about any questions or concerns you have about this study or to report side effects or injuries. Contact the study doctor (*insert name of study doctor[s]*) at (*insert telephone number, and email address if appropriate*).

For questions about your rights while in this study, call the (*insert name of organization or center*) Institutional Review Board at (*insert telephone number*).

My signature agreeing to take part in the study

I have read this consent form or had it read to me. I have discussed it with the study doctor and my questions have been answered. I will be given a signed and dated copy of this form. I agree to take part in the main study.

Participant's signature

Date of signature

Signature of person(s) conducting the informed consent discussion

Date of signature

Patient Study Calendar

Cycle = 21 days	Before Treatment Begins	Cycle 1		Cycle 2		Cycles 3 and Beyond	Off Study
Cycle / Visit Day		1	8	1	7 (+/-3 days)	1	
Pembrolizumab		A		A		A	
Ipatasertib		B		B		B	
Informed consent, demographics, height, and medical history	X						
Evaluation of medications taken during treatment	X	X----------X					
Physical exam and vital signs	X	X	X	X		X	X
Weight	X	X	X	X	X	X	X
Performance status[a]	X	X		X		X	
Blood draws for complete blood count and general health status	X	X	X	X	X	X	X
Thyroid tests[b]	X	X		X		X	
EKG (as indicated)	X						
Side effects evaluation		X----------X					
Medical imaging scans for tumor measurements	X	Tumor measurements are repeated every 9 weeks.					
Blood or urine collection for pregnancy test	X	X		X		X	
Tumor biopsy					X		
Left over tumor tissue from your previous biopsy	X						
Blood collection for research purposes		X			X	X	X
Medication Diary		X		X		X	

A: You will receive pembrolizumab through a vein in your arm on Day 1 of each 21-day cycle.
B: If you are assigned to receive ipatasertib plus pembrolizumab, you will take ipatasertib as tablets by mouth every day for Days 1-14 of each 21-day cycle.
a: Performance status evaluations are done before the study and at the beginning of every cycle. Assessment will be taken as your doctor indicates it is necessary.
b: For patients receiving pembrolizumab.