NATIONAL CANCER INSTITUTE
Center for Cancer Research

TO: Cancer Therapy Evaluation Program/PIO

FROM: Anish Thomas, MBBS, M.D., DTB, CCR, NCI

DATE: 07/31/20206

RE: **Amendment Request Protocol Version Date: 07/31/2026 for Protocol 10445**: "Phase I Dose Escalation and Expansion Study of Tazemetostat in Combination with Topotecan and Pembrolizumab in Recurrent Small Cell Lung Cancer"

NOTE: Spelling, grammar and formatting changes may have been made throughout the protocol and consent; these are not tracked below.

SUMMARY OF CHANGES

1. **Version date:** Updated in all headers.

Research Study Informed Consent Document

Study Title for Participants: Testing of Tazemetostat in Combination with Topotecan and Pembrolizumab in Patients with Recurrent Small Cell Lung Cancer

Official Study Title for Internet Search on http://www.ClinicalTrials.gov: Protocol 10445, Phase I Dose Escalation and Expansion Study of Tazemetostat in Combination with Topotecan and Pembrolizumab in Recurrent Small Cell Lung Cancer (NCT pending)

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 been diagnosed with relapsed small cell lung cancer (SCLC). “Relapsed” means that the disease has grown or spread after prior treatment. Small cell cancers are an aggressive (fast-growing) cancer that can arise in the lungs and less commonly in “extrapulmonary” sites, also known as other parts of the body outside of the lungs.

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 lower the chance of your relapsed SCLC growing or spreading by finding a safe dose of the combination of pembrolizumab, tazemetostat and topotecan combination therapy?

We are doing this study because we want to find out if a new approach is better or worse than the usual approach for your relapsed SCLC. The usual approach is defined as care most people get for relapsed SCLC.

What is the usual approach to my relapsed small cell lung cancer?

The usual approach for patients who are not in a study is treatment with either topotecan or lurbinectedin. The usual approach is proven to help patients with your health condition live longer.

Tazemetostat is being investigated to find out if it can overcome treatment resistance and increase the efficacy of both pembrolizumab and topotecan in second line treatment.

Tazemetostat and pembrolizumab are investigational drugs that have not been approved by the FDA for this type of cancer.

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 get the combination treatment of pembrolizumab, tazemetostat and topotecan as long as the cancer remains under control (*i.e.*, shrinking or not growing).

After you finish your study treatment, your doctor will continue to follow your condition and watch you for side effects and worsening of your condition by phone every 3 months until the study is completed.

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 may not be as good as the usual approach for your cancer at shrinking or stabilizing your cancer or preventing your cancer from coming back.

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 of pembrolizumab that the study doctors know about are:

- Tiredness

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

- Anemia which may require blood transfusion
- Constipation, diarrhea, nausea, vomiting
- Tiredness
- Bruising, bleeding
- Loss of appetite, weight loss
- Hair loss
- Dry skin

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

- Shortness of breath
- Infection, especially when white blood cell count is low
- Bruising, bleeding
- Anemia which may require a blood transfusion
- Constipation, diarrhea, nausea, vomiting
- Fever
- Pain
- Tiredness
- Hair loss

There may be some risks that the study doctors do not yet know about the use of these three drugs in SCLC as this combination has never been studied before.

Benefits

There is some evidence in people with another type of cancer that this combination treatment can shrink or stabilize that type of cancer, but we do not know if this will happen in people with your type of cancer. However, it is not possible to know now if this treatment combination will extend your life or your time without disease compared to the usual approach. This study may help the study doctors learn things that may help other 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. 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 test the safety of a combination of drugs called pembrolizumab, tazemetostat and topotecan. This study tests different doses of the drug to see which dose is safer for people. There will be about 60 people taking part in this study.

What are the study groups?

There are two parts in this study, a dose escalation part and a dose expansion part. Your doctor will tell you which part you are in.

In the dose escalation part of this study, different people will get different doses and schedule of the study drugs. The first 3 people taking part in this study will get the lowest dose. If the drug does not cause serious side effects, the next group of people in the study will get a higher dose. The study doctor will watch each group carefully as they increase the dose. If people have serious side effects, the dose will be lowered and the next group may continue on the lower dose. Once the dose that causes the least side effect is found, this part of the study is stopped.

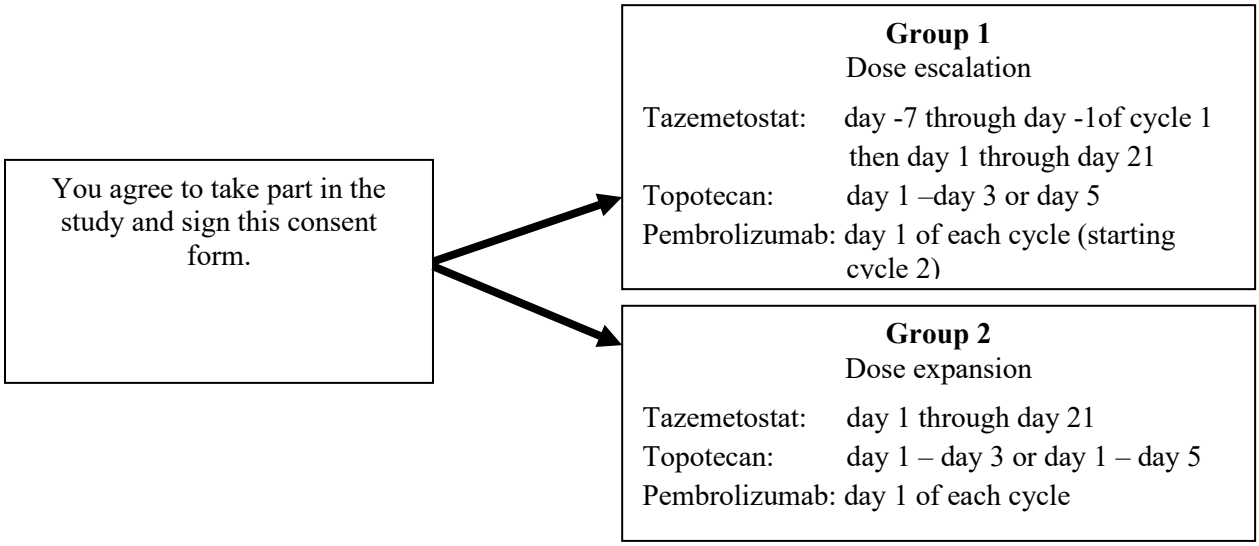
In the dose expansion part of this study, the highest dose with manageable side effects will be given to 15 more people. This will help study doctors better understand the side effects that may happen with this drug.

Pembrolizumab will be given through a vein in your arm on the first day of each cycle. You will take tazemetostat orally twice a day for 7 days before cycle 1 (days -7 through -1) and every day

(days 1-21) during each cycle. You will receive topotecan through a vein in your arm on days 1-3 or days 1-5 (depending on which part of the study you are in) of each cycle. Each cycle lasts 21 days. You will receive treatment until your disease progresses, you experience an unacceptable side effect, or you decide to no longer be part of the study.

You will not be able to get additional doses of pembrolizumab or tazemetostat. These drugs are not approved by the FDA for treatment of your disease.

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. Samples will be collected before you begin taking tazemetostat (day -7), on the first day you start taking tazemetostat and topotecan together (cycle 1 day 1), and on the first day of your second cycle (cycle 2 day 1). 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.

This study will use genetic tests that may identify changes in the genes in your DNA and RNA. 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. If the changes in your genes were inherited, the changes could also affect the health of your family members.

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.

You will need to have mandatory CT guided biopsies for the study. Samples will be collected before you begin taking tazemetostat, on the first day you start taking tazemetostat and topotecan together (cycle 1 day 1), and on the first day of your second cycle (cycle 2 day 1). The study biopsy takes small pieces of cancer tissue from your body. This is like the biopsy you had that helped diagnose your cancer. Researchers will obtain genetic material (DNA and ribonucleic acid [RNA]) from your tumor tissue. Your DNA and RNA will be sequenced to evaluate changes in your DNA and RNA. 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.

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 investigational treatment 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. For women, adequate contraception should be used and women should avoid becoming pregnant for at least 6 months after the last dose of tazemetostat or topotecan and 4 months after the last dose of pembrolizumab. Women should not breastfeed for 1 week after the last dose of tazemetostat. For men, adequate contraception should be used and sperm should not be donated for at least 3 months after the last dose of tazemetostat or topotecan.

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.

Genetic Testing Risks

The genetic test used in this study will test your tumor and normal tissue for change of genes. Changes found in your normal tissue may be passed down in families. For example, these genetic changes may be passed down to your children in the same way that eye and hair color are passed down.

Genetic tests of normal tissue can reveal information about you and also about your relatives. Your doctor will talk with you about what the tests results may mean for you and your family.

He or she also may suggest you talk with a genetics counselor to learn more. You or your insurance plan would have to pay for visits to a genetic counselor.

Biopsy Risks

Common side effects of a tumor 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.

Leftover tissue from your study may also be used for optional studies discussed later in this document under “Optional Studies”.

Side Effect Risks

The study 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:

- The study doctors do not know who will or will not have side effects.
- Some side effects may go away soon, some may last a long time, and some may never go away.
- Some side effects may make it hard for you to have children.
- 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 two study drugs. This different combination of drugs may increase your side effects or may cause new side effects.

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, tazemetostat and topotecan are listed in the tables below. These drugs are part of the usual approach for treating this type of cancer:

Possible Side Effects of Pembrolizumab (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.

Possible Side Effects of Tazemetostat (Table Version Date: October 29, 2024)

COMMON, SOME MAY BE SERIOUS In 100 people receiving tazemetostat, more than 20 and up to 100 may have:
• Anemia which may require blood transfusion
OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving tazemetostat, from 4 to 20 may have:
• Pain • Constipation, diarrhea, nausea, vomiting • Tiredness, fever • Cold symptoms such as stuffy nose, sneezing, sore throat • Bruising, bleeding • Infection, especially when white blood cell count is low • Loss of appetite, weight loss • Headache • Hair loss, dry skin
RARE, AND SERIOUS In 100 people receiving tazemetostat, 3 or fewer may have:
• Cancer of the bone marrow caused by chemotherapy • Damage to the bone marrow (irreversible) which may cause infection, bleeding, may require transfusions • A new cancer resulting from treatment of earlier cancer • Cough, shortness of breath • Increased risk of sunburn

Photo-reactive Potential:

There are nonclinical data supporting a potential for phototoxicity, which has not been evaluated in humans. Hence, prolonged exposure to sunlight should be avoided during treatment. In addition, subjects should take other measures to avoid ultraviolet (UV)

exposure such as wearing sunscreen and sunglasses, wearing protective clothing, and avoiding tanning beds.

Side Effects or Risks of Special Interest:

The following side effects or risks have been identified, requiring additional monitoring, or tests, to potentially minimize the occurrence of these events.

T-cell lymphoblastic lymphoma or T-cell acute lymphoblastic leukemia (T-LBL/T-ALL)

- A 9-year-old subject treated with tazemetostat in a study being conducted in children developed a type of non-Hodgkin lymphoma, which is also called T-cell lymphoblastic lymphoma (T-LBL), after receiving tazemetostat for 14 months.

During pre-clinical animal testing, T-LBL, including lymphoid hyperplasia in the thymus, was observed in one model, rats, but not in other animal models. It was noted by the company that in rats, these events were observed at the highest doses, doses higher than have been used in humans.

B-cell acute lymphoblastic leukemia

- A patient with diffuse large B-cell lymphoma developed B-cell ALL after approximately 46 months of treatment with tazemetostat. The observed development of B-cell ALL may be due to the underlying diffuse large B-cell lymphoma or prior therapy for the lymphoma.

According to the tazemetostat Investigator Brochure, V10.0, this is the only case of T-cell lymphoma that has occurred out of a total of 90 children enrolled in tazemetostat clinical trials. In addition, there have been no cases of T-LBL/T-ALL or B-cell ALL in the 725 adult patients treated across multiple studies conducted in different types of cancer. The company will continue to monitor all patients treated with tazemetostat very carefully for the development of secondary malignancies.

Treatment related secondary malignancies includes Peripheral T-cell lymphoma (PTCL), T-cell lymphoblastic lymphoma (T-LBL), and B-cell acute lymphoblastic leukemia (B-ALL). It may be worth noting that the adult patient observed with B-ALL may be due to an underlying Diffuse large B-cell lymphoma (DLBCL).

Possible Side Effects of Topotecan (Table Version Date: August 29, 2024)

COMMON, SOME MAY BE SERIOUS In 100 people receiving Topotecan, more than 20 and up to 100 may have:
• Infection, possibly in the blood, especially when white blood cell count is low • Bruising, bleeding • Anemia which may require a blood transfusion • Diarrhea, nausea, vomiting

COMMON, SOME MAY BE SERIOUS In 100 people receiving Topotecan, more than 20 and up to 100 may have:
• Tiredness • Hair loss

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving Topotecan, from 4 to 20 may have:
• Shortness of breath • Blockage of the bowels • Sores in mouth which may cause difficulty swallowing • Constipation • Loss of appetite • Pain, including pain in the belly or joints • Fever • Swelling or redness at the site of medication injection

RARE, AND SERIOUS In 100 people receiving Topotecan, 3 or fewer may have:
• Damage to the lungs which may cause shortness of breath, cough, wheezing • Swelling of the bowels which may require surgery • Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat

Additional Drug Risks

The study drugs could interact with other drugs. Certain other drugs can change how your body processes one of the study drugs (tazemetostat). This could decrease the effect of tazemetostat, or it could increase the side effects from tazemetostat. Your study doctor will give you a wallet card. 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.

Imaging Risks

The CTs and CT guided biopsies 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 CTs and CT-guided biopsies that you get in this study will expose you to more radiation than you get from everyday background radiation. The amount of radiation from this scan is the same as 41 years’ worth of background radiation. Most of the time, this amount of extra radiation is not harmful to you. However, scientists believe that being exposed to too much radiation can

cause harmful side effects. This could include getting a new cancer. We estimate that this could happen in about 1 out of every 1000 people who get a very large amount of extra radiation.

As part of the CTs that you get in this study, iodine will 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.

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: Adequate contraception should be used and women should avoid becoming pregnant for at least 6 months after the last dose of tazemetostat or topotecan and 4 months after the last dose of pembrolizumab. Women should not breastfeed for 1 week after the last dose of tazemetostat. **For men:** Adequate contraception should be used and sperm should not be donated for at least 3 months after the last dose of tazemetostat or topotecan. **For all:** Tell your study doctor right away if you think that you or your partner have become pregnant during the study or within 6 months after your last dose of study treatment.

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.
  - this includes the EKG(s) at any time that your study doctor determines it is necessary to do so.
- the costs of getting pembrolizumab, tazemetostat and topotecan ready and giving them to you.
- 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 blood tests performed every cycle.
- The three biopsies to test for genetic changes.

You or your insurance provider will not have to pay for pembrolizumab and tazemetostat 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 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.

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*).

Optional studies that you can choose to take part in

This part of the consent form is about optional studies that you can choose to take part in. They are separate from the main study described above. These optional studies will not benefit your health. The researchers leading these optional studies hope the results will help other people with relapsed SCLC in the future. The results will not be added to your medical records and you or your study doctor will not know the results.

Taking part in these optional studies is your choice. You can still take part in the main study even if you say "no" to any or all of these studies. 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.

Circle your choice of "yes" or "no" for each of the following studies.

Optional sample collections for known laboratory studies and/or storage for possible future studies

Researchers are trying to learn more about cancer and other health problems using blood and tissue samples from people who take part in clinical trials. By studying these samples, researchers hope to find new ways to prevent, detect, treat, or cure diseases.

Some of these studies may be about how genes affect health and disease. Other studies may look at how genes affect a person's response to treatment. Genes carry information about traits that are found in you and your family. Examples of traits are the color of your eyes, having curly or straight hair, and certain health conditions that are passed down in families. Some of the studies may lead to new products, such as drugs or tests for diseases.

Known future studies

If you choose to take part in this optional study, researchers will use leftover tumor tissue and collect blood for research on your DNA and RNA, your immune system and other markers in your body.

Researchers will use a test called immunohistochemistry on your tumor tissue to evaluate how tazemetostat and topotecan are being processed in your body.

Your tumor tissue and blood will also be used for another test called whole exome sequencing to assess for changes in your DNA and RNA which may be useful to predict how certain people may respond to treatment better than others.

Your blood will be used to perform a test called fluorescence activated cell sorting to evaluate how your immune system responds to treatment.

Unknown future studies

If you choose to take part in this optional study, any tumor tissue or blood sample left over will be collected and stored. Storing samples for future studies is called "biobanking." The biobank is being run by the Nationwide Children's Hospital in Columbus, Ohio and is supported by the NCI. This is a publicly funded study. Samples from publicly funded studies are required to be shared as broadly as possible. However, we will protect your privacy. The goal of this is to make more research possible that may improve people's health.

The biobank is a public research resource. It has controlled access. This means that researchers who want to get samples and data from it must submit a specific research request. The request identifies who they are and what their planned research project is. Before getting the samples and data, the researchers must agree to keep the data private, only use it for their planned research project, and never use it to try to identify you.

Right now, we don't know what research may be done in the future using your blood and/or tissue samples. This means that:

- You will not be asked if you agree to take part in the future research studies.
- 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 samples.

Unknown future research studies may include sequencing of all or part of your DNA. This is called genomic sequencing. Sequencing allows researchers to identify your genetic code. Changes in your genetic code may just be in your tumor tissue. These are called somatic changes. Changes may also be in your normal tissue and passed down through your family. For example, these genetic changes may be passed down to your children in the same way that eye and hair color are passed down. These are called germline changes. If only tumor tissue is sequenced, we will not know if a genetic change in your tumor is also in your normal tissue. This is why sometimes both normal tissue and tumor tissue are sequenced. This helps researchers understand if a genetic change happened only in your cancer tissue, or in your normal tissue as well.

What is involved in this optional sample collection?

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

1. About 2 teaspoons of blood will be collected from a vein in your arm on the first day before your tazemetostat monotherapy (day-7), on day 1 of each cycle and when your disease progresses. A sample from the tissue collected during your mandatory biopsies (first day of the tazemetostat monotherapy (day-7), cycle 1 day 1 and cycle 2 day 2) will be sent to the biobank.

2. Your sample will be stored in the biobank. There is no limit on the length of time we will keep your samples and research information. The samples will be kept until they are used for research or destroyed.
3. Researchers can only get samples from the biobank after their research has been approved by experts. Researchers will not be given your name or contact information.
4. Some of your genetic and health information may be placed in central databases for researchers to use. The databases will not include your name or contact information.

What are the risks in this optional sample collection?

- The most common risks related to a needle 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, significant bleeding, or collapsing of the lung can occur. The most common risks related to drawing blood from your arm are brief pain and maybe a bruise.
- Generally, hospitals will keep some of your tissue. This tissue may be used to help treat your cancer in the future. There is a small risk that when this tissue sample is submitted to the biobank for this optional sample collection, your tissue could be used up.
- Your medical and genetic information is unique to you. There is a risk that someone outside of the research study could get access to your study records or trace information in a database back to you. They could use that information in a way that could harm you. Researchers believe the chance that someone could access and misuse your information is very small. However, the risk may increase in the future as people find new ways of tracing information.
- In some cases, this information could be used to make it harder for you to get or keep a job and get or keep health insurance. There are laws against the misuse of genetic information, but they may not give full protection. For more information about the laws that protect you, ask your study doctor or visit: https://www.genome.gov/10002328/

How will information about me be kept private?

Your privacy is very important to the study researchers and biobank. They will make every effort to protect it. Here are just a few of the steps they will take:

1. They will remove identifiers, such as your initials, from your sample and information. They will replace them with a code number. There will be a master list linking the code numbers to names, but they will keep it separate from the samples and information.
2. Researchers who study your sample and information will not know who you are. They also must agree that they will not try to find out who you are.
3. Your personal information will not be given to anyone unless it is required by law.
4. If research results are published, your name and other personal information will not be used.

What are the benefits to taking part in this optional sample collection?

You will not benefit from taking part.

The researchers, using the samples from you and others, might make discoveries that could help people in the future.

Are there any costs or payments to this optional sample collection?

There are no costs to you or your insurance. 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 if I change my mind about this optional sample collection?

If you decide you no longer want your samples to be used, you can call the study doctor, (*insert name of study doctor for main trial*), at (*insert telephone number of study doctor for main trial*), who will let the biobank know. Then, any sample that remains in the biobank will be destroyed or returned to your study doctor. This will not apply to any samples or related health information that have already been given to or used by researchers.

What if I have questions about this optional sample collection?

If you have questions about the use of your samples for research, contact the study doctor, (*insert name of study doctor for main trial*), at (*insert telephone number of study doctor for main trial*).

Please circle your answer below to show if you would or would not like to take part in each optional study:

Samples for known future studies:

I agree that my samples and related health information may be used for the laboratory studies described above.

YES NO

Samples for unknown future studies:

I agree that my samples and related health information may be kept in a biobank for use in future health research.

YES NO

Contact for Future Research

I agree that my study doctor, or someone on the study team, may contact me or my doctor to see if I wish to participate in other research in the future.

YES NO

This is the end of the section about optional studies.

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. I also agree to take part in any additional studies where I circled "yes".

_____

Participant's signature

_____

Date of signature

_____

Signature of person(s) conducting the informed consent discussion

_____

Date of signature