SUMMARY OF CHANGES – Consent

NCI Protocol #: 10327
Local Protocol #: PhI-113
Protocol Version Date: December 19, 2023

Protocol Title: A Phase 1 Trial of MLN0128 (sapanisertib) and Telaglenastat (CB-839) HCL in Advanced NSCLC Patients

Informed Consent Version Date: December 19, 2023

#	Section	Changes (7/31/2023 and 12/19/2023)
1.	N/A	The consent version date was updated to match the protocol version date of December 19, 2023.
2.	What will happen if I decide…? Are there other reasons why…? What are the study group? Patient Study Calendar	Removed references on how long a patient can be on study as drug is now available.
3.	What are the study groups? What are the costs in taking part in the study?	Sections have been updated to include the original expansion cohorts 1) [redacted] mutations (LSCC); 2) [redacted] mutations (LSCC); [redacted] or [redacted] co-mutations (non-squamous NSCLC); or 3) LSCC WT for [redacted]) as sufficient drug is now available.

Research Study Informed Consent Document

Study Title for Participants: Testing of the safety and tolerability of anti cancer drugs Telaglenastat (CB-839) HCL and MLN0128 (sapanisertib) in advanced stage non-small cell lung cancer

Official Study Title for Internet Search on http://www.ClinicalTrials.gov: Protocol 10327, "A Phase I Trial of MLN0128 (sapanisertib) and Telaglenastat (CB-839) HCL in Advanced NSCLC Patients" (NCT#04250545)

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 non-small cell lung 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:

What is the highest dose of Telaglenastat (CB-839) HCL that can be given safely (with manageable side effects) when added to MLN0128 (sapanisertib) for your non-small cell lung cancer?

We are doing this study because we want to find out if this approach is better or worse than the usual approach for your non-small cell lung cancer. The usual approach is defined as care most people get for non-small cell lung cancer.

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

The usual approach for patients who are not in a study is treatment with more chemotherapy or immunotherapy. There are several chemotherapy and/or immunotherapy drugs approved by the Food and Drug Administration (FDA).

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 study drugs until your disease gets worse or the side effects become too severe.

After you finish your study treatment your doctor will continue to follow you until your cancer grows and watch you for side effects or you start a new treatment for your cancer. Follow up will occur quarterly by phone call until your disease gets worse or the next line of therapy has been started.

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.

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:

- Diarrhea, nausea, vomiting
- Sores in the mouth which may cause difficulty swallowing

- Tiredness
- Loss of appetite
- Itching, rash
- High blood sugar

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

Benefits

There is some evidence in animals and in living human cells, that this treatment may shrink or stabilize lung cancer with squamous cells. It is unlikely that Telaglenastat (CB-839) HCL and MLN0128 (sapanisertib) will help you live longer. 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), 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 drug called Telaglenastat (CB-839) HCL in combination with the drug MLN0128 (sapanisertib). This drug combination has been tested in animals but has not been tested in people. This study tests different doses of the drug to see which dose is safer for people.

There will be about 85 people taking part in this study.

What are the study groups?

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

In the dose finding part of this study, different people will get different doses of the study drugs MLN0128 (sapanisertib) and Telaglenastat (CB-839) HCL.

The first 3 people taking part in this study will get the starting 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. The doses will continue to increase for every new group until people have serious side effects that require the dose to be lower. Once this dose is found, the dose finding 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 a total of 56 people. This will help study doctors better understand the side effects that may happen with this drug. You might need to take drugs to prevent vomiting and diarrhea before you take these study drugs.

Treatment schedule: You will get Telaglenastat (CB-839) HCL and MLN0128 (sapanisertib) both as a pill you take by mouth. Each cycle lasts 28 days.

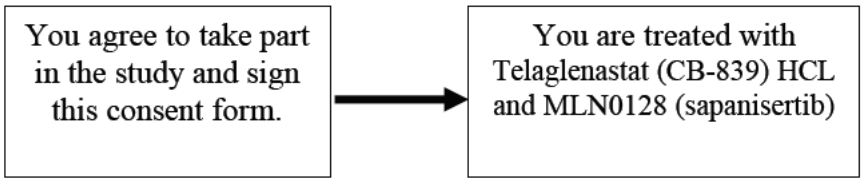
Telaglenastat (CB-839) HCL should be taken with food about 12 hours apart (*i.e.* immediately after breakfast and dinner). MLN0128 (sapanisertib) should be taken at bedtime at least 2 hours after eating with no consumption of food or liquids other than water for at least one hour after dosing.

You will need to take Telaglenastat (CB-839) HCL in the clinic on days when your blood is drawn to determine drug levels (before study treatment; Cycle 1, Day 15; Cycle 2, Day 1; Cycle 3+, Day 1; and at the end of the study). See the patient study calendar for more information.

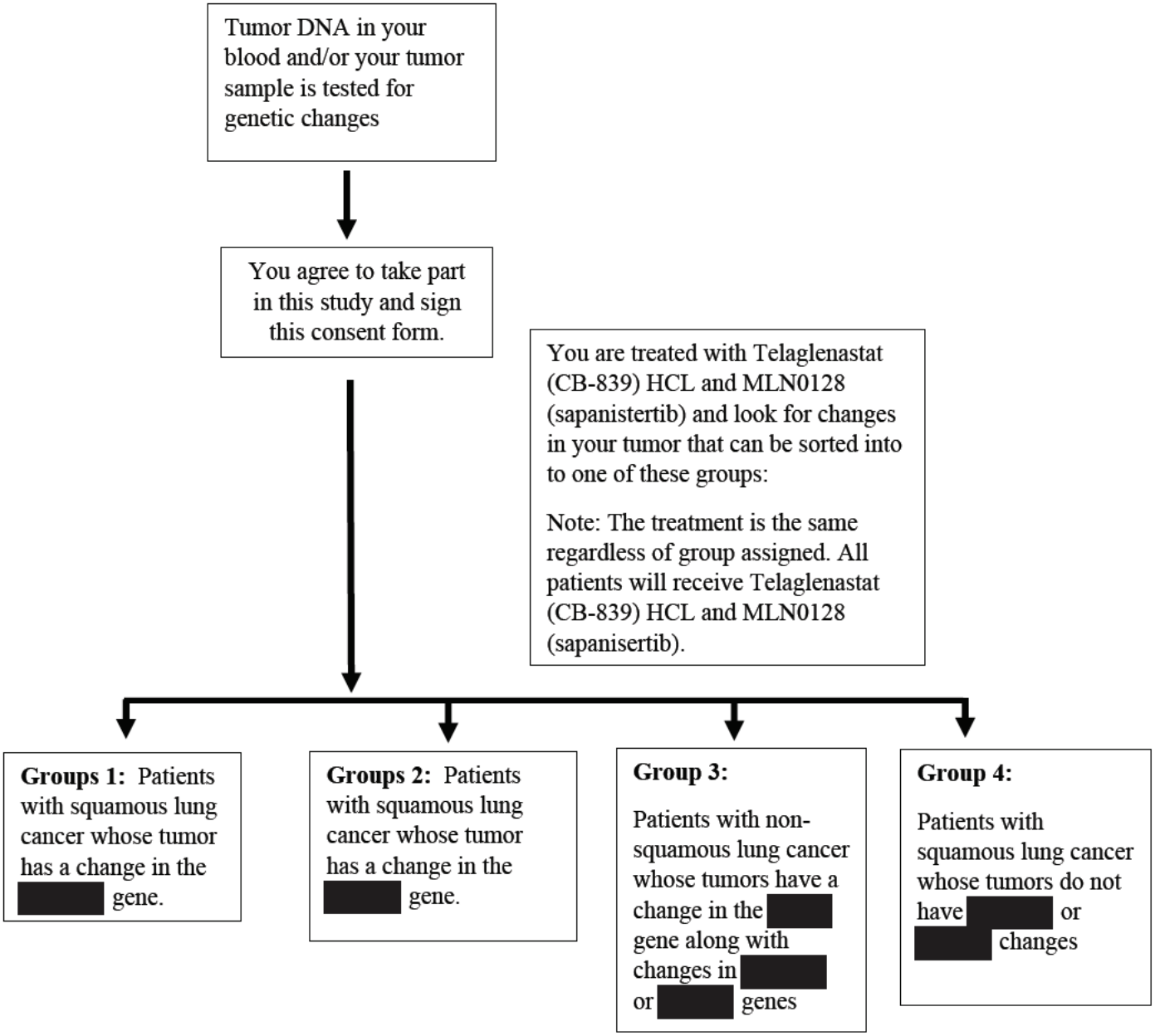
You will not be able to get additional doses of the drugs after your disease gets worse or your side effects become too severe to continue on the study. These drugs are not approved by the FDA for treatment of your disease.

Another way to find out what will happen to you during this study is to read the chart below. Start reading from the top and read to the bottom, following the lines and arrows.

Dose Finding



Dose Expansion



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:

- Complete blood counts and blood draws for general health status done weekly during the first cycle and then every cycle thereafter.
- Physical exams done weekly during the first cycle and then every cycle thereafter.
- Electrocardiogram (EKG) before you begin study treatment, at the start of the first and second cycle 4-5 hours after you take CB-839 study medication that day and then every other cycle after cycle 2.
- Fasting blood glucose testing to be performed in the clinic every two weeks during the first cycle, on the first day of the second cycle, on the 15th day of the second cycle, and then the first day of every cycle thereafter.
- Home blood glucose testing. Your doctor will tell you when and how frequent this needs to be performed. To be performed every day starting predose on dosing days if you have prediabetes, and at approximately the same time each day- prior to breakfast

This study will use genetic tests that may not be FDA approved to identify changes in the genes in your 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 the changes in your genes were inherited, the changes could also affect the health of your family members.

You and your family may want to know about any genetic test findings that may be important to your health. You may use this form to grant us permission in advance to give this information to your doctor. If a genetic test result about you seems to be medically important and you have granted us permission to contact you, the following steps will occur:

- Researchers will study the result further to decide if it may be medically important to you or your relatives.
- The research laboratory that performed the genetic test will contact your doctor about the finding. The research laboratory, which will not have any identifying information about you, will provide your doctor with a code number assigned to your genetic test sample.

- Your doctor will use the code number to identify you, and will then contact you about the medically important finding. Your doctor may try to contact you several times.
- You will require another genetic test to confirm the results. This test must be paid for at your own expense.
- If it is confirmed that there are changes found that could cause health problems, then your doctor will discuss your options with you. We strongly suggest that you also talk to a genetic counselor. Genetic counseling services must be paid for at your own expense.

It is more likely, however, that you will not be contacted by us about a medically important finding. Even if we do not contact you, it does not mean that your genes do not contain changes that are important to your health. Researchers are always learning about new and medically important changes in genes and some information may be learned in the future. Researchers will only decide to contact you about genetic test results at the time your DNA is initially sequenced. You will not be contacted or consented for any research done using your samples in the future, and you will not receive any reports or information about any medically important findings learned in the future. Also, sometimes the meaning of genetic test results can be uncertain, and we may not know for sure what the results mean for your future health. Sharing an uncertain genetic test result with you could offer little benefit, no benefit at all, or could even be harmful.

Results from genetic testing will not be a part of your medical records, unless the results are confirmed by additional testing that you agreed to. See "Who will see my medical information?" for laws and risks in protecting your genetic information.

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. 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.

You will need to have blood samples taken for the study before you begin study treatment, on the fifteenth day of the first cycle, and the first day of the second, third, and fifth cycle of treatment.

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. The specimen will be to look for gene and protein changes in your tumor.

If you are in the dose expansion group and if there is not enough tissue left over from your biopsy, your study doctor will need to do another biopsy to get this tissue. The sample will be taken, before you begin study drug. The study biopsy takes small pieces of cancer tissue from your body. This is like the biopsy you had that helped diagnose your cancer. The specimen will be to look for gene and protein changes in your tumor. You and your study doctor will get the results of the gene testing

Researchers will obtain genetic material (DNA and RNA) from your tumor tissue and blood samples. Your DNA and RNA will be sequenced to evaluate changes in your DNA and RNA that may occur during treatment. You and your study doctor will not get any results of this

testing.

A patient study calendar is attached at the end of this document. It shows how often these exams and procedures 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 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 drugs Telaglenastat (CB-839) HCL and MLN0128 (sapanisertib) 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 90 days for women and 120 days for men after you have completed the study.

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

As part of this study, we are also using a genetic test. The test is designed to find out if your tumor has the genetic changes that are needed for this study. If it does, we will assign you to a study group based on the genetic changes in your tumor if you are in the dose expansion group.

Because this genetic test is still being studied, there is a risk that the test results may be wrong. If the test results are wrong, you may be included in this study even though it may not offer the best treatment option for you. Or, you may not be included in this study even though it may offer a good treatment option for you.

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, significant bleeding, or collapsing of the lung 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 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 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.

Possible side effects of Telaglenastat (CB-839) HCL and MLN-0128 (sapanisertib) are listed in the tables below.

Possible Side Effects of Telaglenastat (CB-839) HCl
(Table Version Date: July 21, 2019)

COMMON, SOME MAY BE SERIOUS In 100 people receiving Telaglenastat (CB-839) HCl , more than 20 and up to 100 may have:
• Tiredness

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving Telaglenastat (CB-839) HCl, from 4 to 20 may have:
• Anemia which may require blood transfusion • Discomfort from light • Nausea, vomiting • Bruising, bleeding • Loss of appetite

Possible Side Effects of MLN0128 (sapanisertib, TAK-228)
(Table Version Date: July 28, 2019)

COMMON, SOME MAY BE SERIOUS In 100 people receiving MLN0128 (sapanisertib, TAK-228), more than 20 and up to 100 may have:


OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving MLN0128 (sapanisertib, TAK-228), from 4 to 20 may have:


RARE, AND SERIOUS In 100 people receiving MLN0128 (sapanisertib, TAK-228), 3 or fewer may have:


High Blood Sugar Risks

[redacted].

Additional Drug Risks

The study drug could interact with other drugs. Your study doctor will give you a drug information handout and wallet card that lists these possible interactions. 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.
- Fill out the glucose monitoring diary when you take the MLN0128 (sapanisertib)

For women: Do not get pregnant or breastfeed while taking part in this study. Contraception use is required up to 90 days after the last dose of study drugs for women of childbearing potential. Do not to donate egg(s) during the course of this study or within 90 days after the last dose of study drugs.

Acceptable Birth Control Methods if you are of child bearing potential:

- Condoms AND one of the following:
    - Oral contraceptive or hormonal therapy (*e.g.*, hormone implants, skin patches, intravaginal device, hormone shots).
    - Placement of an intra-uterine device (IUD; *e.g.*, Mirena®). OR
- Total sexual abstinence, when this is in line with your usual and/or preferred lifestyle. **Periodic abstinence** (*e.g.*, calendar, ovulation), the rhythm method, **and withdrawal are not acceptable methods of contraception**.

For men: Do not father a baby while taking part in this study. Contraception use is required up to 120 days after the last dose of study drugs. Do not donate sperm during the course of this study or within 120 days after the last dose of study drugs.

Acceptable Birth Control Methods:

Even if you had a vasectomy with assurance that it was successful, you must agree to the following:

- Condoms OR
- Total sexual abstinence, when this is in line with your usual and/or preferred lifestyle. **Periodic abstinence** (*e.g.*, calendar, ovulation), the rhythm method, **and withdrawal are not acceptable methods of contraception**.

For all: Tell your study doctor right away if you think that you or your partner have become pregnant during the study or within 4 months after your last dose of study drug.

What 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 Telaglenastat (CB-839) HCL and MLN0128 (sapanisertib) ready and giving it to you.
- the cost of the glucometer and the supplies needed for the glucose blood testing
- 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 extra EKGs in this study done before you begin study treatment, at the start of the first and second cycle 4-5 hours after you take CB-839 study medication that day and then every other cycle after cycle 2.
- [redacted]
- The research blood draws

You or your insurance provider will not have to pay for the Telaglenastat (CB-839) HCL and MLN0128 (sapanisertib) 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 lung cancer 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 imaging study – research scan or procedure

If you choose to take part in this study and you are part of the dose expansion group at Memorial Sloan Kettering Cancer Center (MSKCC) or UC Davis, you will have extra ^{18}Fluoroglutamine-PET CT and ^{18}Fluorodeoxyglucose PET CT. PET CT is already used in medical care. In this study, the scan will be done at another time in your treatment than with the usual care. Researchers would use this imaging study to try to learn more about how treatment works on cancer. ^{18}Fluoroglutamine is an investigational agent that is not FDA approved. The scan would only be used for research and not to guide your medical care.

If you agree to have this extra scan, it would involve an additional PET CT with additional time for imaging. These scans would be performed prior to the start of treatment, on or around Cycle 1 Day 8, Cycle 3 Day 1, and shortly before the end of the study. The risks would be additional radiation risk. Ask your study doctor if you would like to learn more about this type of scan.

Please circle your answer: I choose to take part in the imaging study and will have the PET CT:

YES NO

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 collect your tumor tissue to look at changes in your DNA and RNA that occur during treatment. Researchers will obtain DNA and RNA from both your tumor cells and your blood. These studies will be done by an NCI-supported laboratory in Frederick, Maryland, known as the National Clinical Laboratory Network (NCLN) Genomics Laboratory at the Frederick National Laboratory for Cancer Research. The laboratory will compare the DNA and RNA from your tumor and blood cells. These studies may help explain why you did or did not respond to the treatment you received. This optional study may improve the ability to select future treatments or treatment combinations for others in the future. This optional study will not affect the cancer treatment that you receive.

Neither you nor your study doctor will be informed when this research will be done. You and your study doctor will not receive reports of these studies, as they are intended for research purposes only and cannot be used to plan treatment.

What is involved in this optional sample collection?

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

1. A sample of tissue will be collected from optional extra biopsies. Two biopsy procedures will be performed on any time during Day 8 and 21 first cycle and when your disease gets worse. If you are in the dose finding group, you will have an additional biopsy taken before you begin treatment unless there is some tissue left over from your biopsy when you were diagnosed with cancer. For the biopsy procedure, the study doctor will use a needle to take pieces of your tumor. This process may be repeated several times in the same appointment in order to get enough tissue.

2. Your samples 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 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, 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 samples 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 need my tissue samples to be returned?

Tumor tissue or blood samples that remain in the biobank can be returned if needed for medically necessary events or procedures to assure appropriate medical care, such as for DNA or RNA analysis. Specimens may also be returned if tissue is needed to determine eligibility for enrollment in a research protocol or clinical trial. Every effort will be made to facilitate medically necessary events or procedures to assure appropriate medical care for a patient with a serious or life-threatening illness.

Tumor tissue or blood samples and genetic material (DNA and RNA) that is no longer in the biobank or that has already been given to or used by researchers cannot be returned. No samples will be returned for matters related to patients needing or wanting genetic testing to determine medically important risks.

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

I agree that my study doctor, or someone on the study team, may contact me or my doctor to see if I wish to learn about results from these studies.

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