To: CTEP PIO

From: Naoko Takebe, MD, PhD

Date: March 3, 2021

Re: Amendment to Protocol #10349: "A Phase I Trial of the P97 Inhibitor CB-5339 in Patients with Advanced Solid Tumors and Lymphomas"

This amendment includes information about the recently opened Cleave-sponsored CB-5339 trial of patients with AML/myelodysplastic syndrome and proposes inpatient evaluation of the first three patients entered on the NCI trial. It also addresses CIRB stipulations on the format of the consent form from the March 2, 2021 amendment review (all accepted with the exception of 10d) . The version date of this submission is 3/3/21. No changes have been mde to the protocol except to the date.

1	What exams, tests, and procedures are involved in this study? What will happen if I decide to take part in this study? Risks Patient Study Calendar	Added text explaining that CB-3339 has been given to a small number of patients on Cleave's phase 1 trial of patients with AML/myelodysplastic syndrome.
2	What exams, tests, and procedures are involved in this study? What will happen if I decide to take part in this study? Patient Study Calendar	Added text that the first three patients on study will be admitted to the NIH Clinical Center for 5 days of in-patient evaluation followed by out-patient evaluation at the day hospital on days 6 and 7. These patients will return to the Clinical Center on 8 (C1W2) and will have additional routine blood draws on Days 2, 5, and 6.

Response to CIRB Stipulations

Consent Form(s):

1.	Throughout the study documents, correct pagination. **Response**: This change has been made to the clean and track-changes documents (not track-changed).
2.	In the study title, remove the word "Study" before "Participants". **Response**: This change has been made on page 1.
3.	In the official study, remove "NCI" and add "(NCT04449562)" at the end of the title to comply with NCI CF template. **Response**: This change has been made on page 1.
4.	Page 2, revise the header "What are my other choices…?" to "What are my choices if I *decide* not to take part in this study?" a. Delete the 1st sentence. b. Revise 3rd bullet to make the 3rd and 4th bullet comply with NCI CF template.

	Response: These changes have been made on page 2
5.	Page 2 under "What will happen if I decide…?", revise the 5th paragraph to comply with NCI CF template. **Response**: This change has been made on page 2
6.	Page 3, under "Risks": a. Insert the 2nd paragraph from the NCI CF template. b. 2nd paragraph, revise 2nd sentence to state: "Some of the most common side effects that the study doctors know about are:" **Response**: These changes have been made on page 2
7.	Page 3, under "If I decide to take part…?": a. Revise 2nd paragraph to comply with NCI CF template. b. 3rd paragraph, replace "The" with "Your" **Response**: These changes have been made on page 3
8.	Page 3, under "Are there other reasons…?", revise to comply with NCI CF template: a. Insert "Yes." before the 1st sentence. b. Revise 1st sentence by replacing "out" with "off" and adding "if" after "study". c. In each bullet delete "If" at the beginning of the sentence. d. Revise 4th bullet to: "New information becomes available and the study is no longer in your best interest." **Response**: These changes have been made on page 3
9.	Page 4, under "What is the purpose…?": a. 1st paragraph delete the 2nd sentence. b. 2nd paragraph, insert as the last sentence "There will be about 40 people taking part in this study." **Response**: These changes have been made on page 4
10.	Page 4, under "What are the study groups?", revise to comply with NCI CF template: a. Insert as the 1st paragraph "Different people taking part in this study will get different doses of the study drug CB-5339." b. 1st paragraph delete the 1st sentence. c. 2nd sentence, revise to: "Different doses of the study drug CB-5339 will be given to some study participants." d. 3rd sentence, revise to: "The first 3 people taking part in this study will get the lowest dose." e. 4th sentence, delete "it will be given to" after the comma and replace "study participants at" with "group of people in the study will get" f. Insert as the 5th sentence, "The study doctor will watch carefully as they increase the dose." g. Delete the 2nd paragraph. **Response**: These changes have been made on page 4 with the exception of d. because we are following an accelerated titrationdesign (one patient per dose level).
11.	Page 4-5, under "What exams, tests, and procedures…?": a. This section states: "You can take CB-5339 at home, so overnight stays in the hospital

	or clinic except at the beginning of the study are not planned." Clarify if this is referring to overnight hospitalization for hour 8 PK assessment on C1D1 and (for some) C1D4? If so, add a reference to this information in the description of research blood tests. b. Under "Blood will be drawn:", 2nd bullet, add a parenthesis after "afterwards". c. Under "You may have additional blood drawn:", 2nd bullet add a parenthesis after "afterwards". d. Last paragraph 1st sentence, capitalize "hospital", and 2nd sentence, replace "retun" with "return". **Response**: Overnight hospitalization is not required for the PK assessments so no changes have been made to the consent form. The other changes have been made starting on page 4
12.	Page 6, under "General Risks", revise the 1st paragraph to comply with NCI CF template. **Response**: This change has been made on page 5
13.	Page 6, under "Side Effects": a. 3rd paragraph, 2nd sentence replace "points about how you and the study doctor can" with "ways to". b. 2nd and 3rd bullets, replace "The" with "Your". **Response**: These changes have been made on page 5
14.	Page 6, under "Drug Risks" 2nd paragraph: a. 1st sentence replace "that researchers" with "doctors". b. 2nd sentence, add "Keep in mind that" at the beginning of the sentence and replace "that researchers" with "doctors" **Response**: These changes have been made on page 6
15.	Page 7, under "Imaging Risks", 1st paragraph, 2nd sentence remove the extra "s" in "scans". **Response**: This change has been made on page 6
16.	Page 8, under "What are the costs…?": a. Revise 1st and 2nd paragraphs to comply with NCI CF template. b. 3rd paragraph, 1st sentence, revise to: "You and/or your insurance provider" c. Insert as the 4th paragraph "You or your insurance provider will not have to pay for CB-5339 while you take part in this study." **Response**: These changes have been made on page 8
17.	Page 9 remove "or hurt" from the header "What happens if I am injured…?" to comply with NCI CF template. And revise the 1st paragraph, as follows: a. 1st sentence remove "or hurt" and replace "please tell your study doctor" with "please talk with your study doctor right away about your treatment options.". b. 2nd sentence remove "offer to" before "pay". c. Revise the 5th sentence to state "If you do not have insurance, then you would need to pay for these medical costs." d. 2nd paragraph, revise the 1st sentence to comply with NCI CF template. **Response**: These changes have been made on page 9
18.	Page 9, under "Who will see my medical information?", revise as follows to comply with NCI CF

	template: a. 1st paragraph: i. Replace the 1st sentence with "Your privacy is very important to us. The study doctors will make every effort to protect it." ii. Delete the 4th sentence. iii. Revise 5th sentence to state "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." iv. Create a 2nd paragraph beginning with the 6th sentence. b. New 2nd paragraph: i. 1st sentence add "by the study sponsor" before "in a central database", add "research" before "database", and delete "for research" after "database". ii. 2nd sentence, add "However," before "your" and replace "or" with "and". c. Replace the paragraph before the bullets with the NCI CF template language and revise the 1st set of bullets to comply. d. New 4th paragraph, revise as follows: i. 3rd sentence replace "also will" with "may", add "and shared" after "stored", and add "in public database" after "future use". e. Start a new paragraph starting with the 5th sentence. New 5th paragraph, revise as follows: i. 1st sentence replace "records" with "information" and replace "those of" with "information from". ii. 2nd sentence insert "right now" after "However,". iii. Add a space between this paragraph and the 1st bullet. **Response**: These changes have been made starting on page 9
19.	Page 10, under "Where can I get more information?", 3rd paragraph, 2nd sentence add "*, and email address if appropriate"* after "*telephone number"*. **Response**: This change has been made 9
20.	Page 12, under "What if I change my mind…?"and "What if I have questions…?", replace "Dr. Takebe," with "(*insert name of study doctor for main trial*)," and replace "(240) 781-3398" with "(*insert telephone number of study doctor for main trial*)". **Response**: These changes have been made on page 12
21.	Page 13, remove "Main" in the header "My Signature Agreeing to Take Part in the Study". **Response**: This change has been made on page 14
22.	Page 13, under "My Signature Agreeing to Take Part in the Study", revise as follows: a. 4th sentence add "main" before "study". b. Add 5th sentence to state "I also agree to take part in any additional studies where I circled "Yes"." **Response**: These changes have been made on page 14
23.	Page 14, "Cycle 1, Day 1": a. 10th bullet, add "be" before "taken". b. 11th bullet delete extra space between "Questionnaire" and "will". **Response**: These changes have been made starting on page 15

24.	Page 15, Cycle 1, Day 5, 1st bullet, delete the extra space between "on" and "day. **Response**: This change has been made on page 15
25.	Page 16, Cycle 3 and onwards: a. 5th bullet delete the extra space between "will" and "be". b. 6th bullet, delete the extra space before "for". **Response**: These changes have been made starting on page 15

Research Study Informed Consent Document

Study Title for Participants: Testing the Safety of CB-5339 in Patients With Solid Tumors and Lymphomas

Official Study Title for Internet Search on http://www.ClinicalTrials.gov:
Protocol 10349: A Phase I Trial of the p97 Inhibitor CB-5339 in Patients With Advanced Solid Tumors and Lymphomas (NCT04449562)

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 solid tumors(s) or advanced lymphoma.

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 doses of the study drug CB-5339 can safely be given to patients with advanced solid tumor(s) or lymphoma?

There might be a safe dose of CB-5339 that can kill the cancer cells in your body. We are doing this study because we want to find out if this drug can be safely given to patients with advanced solid tumor(s) or lymphoma and to determine the dose of CB-5339 to be used for future studies.

What is the usual approach to my cancer?

The usual approach for patients who are not in a study is treatment with surgery, radiation, or chemotherapy drugs that have been approved for your type of cancer by the FDA. You are being asked to take part in this study because you have cancer that is spreading or does not respond to the usual treatment options. People with your type of advanced cancer usually don't have effective treatment options, such as radiation or chemotherapy.

What are my other 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 your 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 begin taking the study drug CB-5339 by mouth. You can take CB-5339 at home except for the first 3 patients on the study. These 3 patients will be admitted to the NIH Clinical Center in Bethesda for 5 days and then asked to visit the Clinical Center Day Hospital on days 6 and 7 for a check up. We will tell you if you are one of these patients.

The drug is given in 28-day (4-week) periods called cycles. You will take CB-5339 once a day for four days, then you will not take it for three days (4-on/3-off). This 4-on/3-off pattern will repeat four times in a cycle. Your treatment dose may vary from one cycle to another.

You should take CB-5339 on an empty stomach, either 1 hour before or 2 hours after a meal, at about the same time each day. You will be asked to record each CB-5339 dose that you take and to make notes if you have any side effects.

You will continue to take the study drug for as long as your cancer does not get worse, the side effects are tolerable, and you agree to stay on study.

After you finish your treatment, your doctor and study team will watch you for side effects for 30 days, or until any drug-related side effects you may have experienced during treatment stabilize. This follow up will be a phone call from the study team

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 drug may not be as good as the usual approach for your cancer at shrinking or stabilizing your cancer

If you choose to take part in this study, there is a risk that you could have side effects from the study drug CB-5339. These side effects may be worse and may be different than you would get with the usual approach for your cancer.

CB-5339 has been given to a small number of patients with leukemia myelodysplastic syndrome, so we do not know much yet about what side effects it might cause.
Some of the most common side effects that the study doctors know about are:

- Vision changes
- Nausea and/or vomiting
- Fatigue

There may be some risks that the study doctors do not yet know about, including potentially serious side effects or death.

Benefits

There is some evidence in animals that this treatment can shrink cancer, but we do not know if this will happen in people. It is unlikely that this drug 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 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. Your study doctor may take you off the study if:

- Your health changes and the study is no longer in your best interest
- Your disease gets worse during treatment
- You have side effects from the treatment that your doctor thinks are too severe
- New information becomes available and the study is nolonger in your best interest
- You do not follow the study rules
- For women: if you become pregnant while on the study
- If the study is stopped by the sponsor, the IRB (people who review the research to protect the people taking part in the study), or the FDA. 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 CB-5339. "Dose" is defined as the amount of drug you get. CB-5339 is an experimental drug; it is not yet approved by the Food and Drug Administration. Because CB-5339 has only been given to a small number of patients , we do not know what side effects you may have. This will be reviewed with you by your medical team before you sign the consent form.

Proteins have many important jobs in your body, but sometimes there are proteins that are not working right or are no longer needed. Your body has a way to remove those proteins. Cancer cells need that protein removal process even more than healthy cells. In laboratory experiments, CB-5339 blocked protein removal and killed tumor cells. We don't know if CB-5339 works to treat cancer in people, but it has shrunk several types of tumors in animals. Researchers hope to learn if the drug can be given safely and cause cancer cell death in humans. There will be about 40 people taking part in this study.

What are the study groups?

All of the participants in the study will receive CB-5339. Different doses of the drug will be given to different study participants based on when they enter the study. The first study participants will receive the lowest dose. If the drug does not cause serious side effects, the next study participants will get a higher dose. The study doctor will watch carefully as they increase the dose. The dose will continue to increase until side effects occur that require the dose to be lowered. Once the appropriate dose is identified, up to 15 additional patients will be treated with CB-5339 at that dose.

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.

You will need to have the following extra tests to find out if you can be in the study:

- An EKG (electrocardiogram) and ECHO (echocardiogram) to check your heart
- Pregnancy test in women who are able to become pregnant
- An eye exam and questionnaire to check your vision

If the exams, tests, and procedures show that you can take part in the study, and you choose to take part, then you will need the following extra tests to monitor your safety and health. They are not part of the usual approach for your type of cancer. We will use them to carefully follow the effects of the study treatment, including preventing and managing side effects.

During the study:

- Physical exams done weekly in the first cycle and the first week of every cycle after that
- Blood counts done every week of the first cycle and the first week of every cycle after that
- An EKG (electrocardiogram) will be done at the beginning of each cycle,
- Eye exams after your dose on the first or second day of treatment and any other time the study doctor thinks it is necessary for your eye health

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.

- Blood and urine tests to measure the way your body handles the study drug and to measure the effect of the study drug on cells in your blood. These samples are required in order for you to take part in this study because the research on the samples is an important part of the study.
    - Your urine will be collected before your first dose of CB-5339 on Day 1 and every time that you urinate in the 24 hours after that first dose.
    - Blood will be drawn:
        - before your first dose of CB-5339 on Day 1,
        - at several times after the first dose on day 1 (15 and 30 minutes and then 1, 2, 4, 6, and 24 hours afterwards).

      The total blood for all of these tests will be about 1 tablespoon.

    - You may have additional blood drawn:
        - 8 hours after your CB-5339 dose on Day 1.
        - Before your Day 4 dose and at several times afterwards (15 and 30 minutes and then 1, 2, 4, 6, and 24 hours afterwards). Please do **not** take your Day 4 dose at home so that blood can be drawn first.
        - If it is determined that your cancer has gotten worse.

      The total blood for all of these additional tests will be about 1 tablespoon.

    - Additional blood collections will be required from some patients who have had side effects before and a few hours after the new dose. The amount of blood for these additional collections will be about 0.5 tablespoons per collection.

- Biopsies to measure the effect of CB-5339 on your tumor. Tumor biopsies are not required from all patients; they will only be collected from patients receiving certain doses of study drug. We will tell you if biopsies are required before you decide to take part in the study.

At the NCI, the first 3 patients will be admitted to the NIH Clinical Center Day Hospital on days 1-5 so that we can monitor your health. These patients will go home or to a hotel on day 5 but will be asked to return to the Clinical Center Day Hospital for blood tests on days 6 and 7 (the first weekend of the study only). Blood draws will be more frequent for these patients. Your study doctor will tell you if you are one of these patients and will explain the additional monitoring. A study calendar that shows how often these tests will be done is attached.

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 drug may not be as good as the usual approach for your cancer at shrinking or stabilizing your cancer
You may also have the following discomforts:

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

The CB-5339 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 4 months after you have completed the study.

Your study doctor will give you a drug information handout and wallet card that lists possible drug interactions. Please share this information with your family members, caregivers, other health care providers, and pharmacists.

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

CB-5339 has only been tested in a small number of patients with leukemia and myelodysplastic syndrome and its side effects are unknown. There is a risk that you could have side effects. CB-5339 may affect how different parts of your body work such as your eyes, liver, kidneys, heart, and blood. The study doctor will test your blood and let you know if changes occur that may affect your health.

Here are important points 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, or 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 serious and may even result in death.

You can ask your study doctor questions about side effects at any time. Here are 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.

Drug Risks

CB-5339 has only been given to a small number of patients with leukemia and myelodysplastic syndromebut, a similar drug caused temporary changes in vision and sensitivity to color and light during a clinical trial. CB-

5339 did not cause vision problems in animal studies. An ophthalmologist (eye doctor) has been added to the study team for CB-5339 and will perform eye exams before you take your first dose, after your dose on day 1 or 2, and any time the study team thinks it is necessary. Please tell your study team if you notice any changes in your vision, and please consider avoiding bright light and wearing sun glasses for eye protection.

The table below shows the most likely side effects that doctors expect with this study drug. Keep in mind that there might be other side effects that 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 CB-5339:

POSSIBLE, SOME MAY BE SERIOUS
• Anemia which may require blood transfusion • Change in color vision • Visual loss, including blurred vision • Seeing flashing lights • Discomfort from light • Constipation, diarrhea, nausea, vomiting • Swelling of arms, legs • Tiredness • Pain • Kidney damage which may require dialysis

This list may not include all possible side effects of CB-5339. This is an investigational agent being given to humans with your type of cancer for the first time and its side effects are unknown. If you experience symptoms that are worrying you, contact the study doctor immediately.

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

Imaging Risks

Some patients on this study will be required to have CT scans in order to collect biopsy samples from their tumors. Up to 2 CT-guided biopsy scans may be required and a third may be requested. We will tell you if CT-guided biopsies are required before you decide to take part in this study.

The CT scans that you get in this study will expose you to low amounts of radiation. Every day, people are exposed to low levels of radiation that come from the sun and the environment around them. This type of radiation is called "background radiation." No one knows for sure whether exposure to these low amounts of radiation is harmful to your body.

The CT scans that you get in this study will expose you to more radiation than you get from everyday background radiation. The total amount of radiation from three CT scans is the same as 8 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.

What are my responsibilities in this study?

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

- Keep your study appointments.
- Maintain a study diary to document:
  - the date and study day
  - time at which the dose is taken
  - whether or not the dose was taken
  - additional comments (e.g., side effects)
- 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

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 4 months after your last dose of study drug.

What are the costs of taking part in this study?

(Note to Local Investigator: Revise this section as appropriate for patients at your site.)

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 CB-5339 ready and giving it 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. These include:

- Blood tests to measure how your body handles the drug and the effect of the study drug on cells in your blood.
- CT scans and biopsies to measure the effect of the study drug on your tumor and immune cells.

- Eye exams

You and/or your insurance provider will not have to pay for the CB-5339 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 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 otherswill 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.
- 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 other groups it works with to review research
- The NCI and other 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 maybe stored and shared for future use in a public database. However, your name and other personal information will not be used.

Some types of future research may include looking at your information and information fromother 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.

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 e-mail address).*

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 your condition in the future.

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 the following study.

Unknown future studies

If you choose to take part in this optional study, any of your tumor tissue or blood samples left over from protocol-specific research will be 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 do not know what research may be done in the future using your tumor tissue and blood 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 be 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.

What is involved in this optional sample collection?

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

1. A sample from the tissue that was collected at the time of your tumor biopsy 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 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?

- 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 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 doctor for main trial*).

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

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

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 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_____

Patient Study Calendar

Time Point	Patient Activity
Before starting study drugs	• Check in at _____ [*name of center*] • Have a history taken of how you feel and undergo a physical examination by a Health Care Provider • Echocardiogram (ECHO) and EKG to test your heart • Pregnancy test for women who are able to become pregnant • Routine blood tests • Routine urine tests • Eye exam and questionnaire about your vision • Tumor measurements by CT or MRI scans for patients with measurable disease • Tumor biopsy taken from some patients -we will tell you if this applies to you.
Cycle 1, Day 1	• Check in at _____ [*name of center*] • Some patients will be admitted to the NIH Clinical Center for 5 days • Physical exam • Routine blood tests • Routine urine tests • Take the first dose of CB-5339 by mouth • Record the time you took CB-5339 in your patient diary • Research urine samples will be collected before you take CB-5339 and every time that you urinate in the next 24 hours. • Research blood samples will be collected before you take CB-5339 and at several times over the next 24 hours. • Tumor biopsy will be taken from some patients -we will tell you if this applies to you. • Questionnaire will be done on day 1 or day 2
Cycle 1, Day 2	• Routine blood tests for patients admitted to the NIH Clinical Center • Take CB-5339 • Record the time you took the dose in your diary • Research blood samples will be taken
Cycle 1, Day 3	• Routine blood tests may be performed on patients admitted to the NIH Clinic Center • Take CB-5339 • Record the time you took the dose in your diary
Cycle 1, Day 4	• Research blood samples may be taken before you take CB-5339 and at several times over the next 24 hours. We will tell you if this applies to you. If it does, please do **not** take your day 4 dose at home so that blood can be drawn first. • Routine blood tests for patients admitted to the NIH Clinical Center • Take CB-5339 • Record the time you took the dose in your diary

Time Point	Patient Activity
Cycle 1, Day 5-	• Do not take CB-5339 on day 5 • Patients at the Clinical Center will be sent home/to a local hotel
Cycle 1, Days 6, 7-	• Do not take CB-5339 on these days • The first 3 patients will come to the Bethesda Day Hospital on both days for routine blood tests
Cycle 1, Days 8-11	• Take CB-5339 each day • Record the time you took CB-5339 in your diary • On Day 8, physical exam and routine blood tests
Cycle 1, Days 12-14	• Do not take CB-5339 on these days
Cycle 1, Days 15-18	• Take CB-5339 each day • Record the time you took CB-5339 in your diary • On Day 15, physical exam and routine blood tests
Cycle 1, Days 19-21	• Do not take CB-5339 on these days
Cycle 1, Days 22-25	• Take CB-5339 each day • Record the time you took CB-5339 in your diary • On Day 22, physical exam and routine blood tests
Cycle 1 Days 26-28	• Do not take CB-5339 on these days
Cycle 2 Day 1	• Check in at _____ [*name of center*] • Physical exam and medication history • Routine blood tests • Routine urine tests • Take CB-5339 • Record the time you took CB-5339 in your diary • Pregnancy test for women who are able to become pregnant • Research blood samples will be taken • EKG will be done •

Time Point	Patient Activity
Cycle 2 Days 1-28	• Take CB-5339 each day for 4 days, followed by a 3-day break • Record the time you took CB-5339 in your diary
Cycle 3 and onwards	• Physical exam and medication history • Routine blood tests • Take CB-5339 each day for 4 days, followed by a 3-day break for 28 days • Record the time you took CB-5339 in your diary • EKG will be done on Day 1 of every cycle • Tumor measurements by CT or MRI scans every 2 cycles (less often if you are on study for over one year) for patients with measurable disease • Pregnancy test for women who are able to become pregnant • Research blood samples will be taken at the start of each cycle
If your cancer gets worse	• You may choose to have a blood draw and/or biopsy collected for research
After finishing treatment	• You will be followed for 30 days after your last dose of drug is taken