To: CTEP Protocol and Information Office

From: Sarah Shin, MD, MPH, DTC/DCTD/NCI

Date: November 26, 2024

Re: Amendment to Protocol 10346: Pilot Study of DS-8201a Pharmacodynamics in Patients with HER2-expressing Advanced Solid Tumors

This amendment is being submitted in response to the CTEP request for rapid amendment dated 11/18/2024.

The version date is now November 26, 2024. Thank you for your consideration.

I. Changes from the CTEP Request for Rapid Amendment Dated 11/18/2024:

#	Section	Comments
1.	General	We have updated the consent version date to match the protocol version date.

2.	Drug Risks	Revision of the Condensed Risks List to Match the Revised Protocol CAEPR:
		• Added New Risk:
		  ◦ Occasional: Blurred vision; Changes in taste; Heart failure, which may cause shortness of breath, swelling of ankles, and tiredness; Itching; Rash; Skin changes
		• Increase in Risk Attribution:
		  ◦ Changed to Common from Occasional: Infection, especially when white blood cell count is low
		  ◦ Changed to Occasional from Also Reported on DS-8201a Trials But With Insufficient Evidence for Attribution (i.e. Added to Risk Profile): Bloating; Weight loss
		• Provided Further Clarification:
		  ◦ Reaction during or following a drug infusion which may cause chills, rash, low blood pressure (under Occasional) is now reported as Reaction during or following a drug infusion which may cause chills, low blood pressure (under Occasional)
		  ◦ Belly pain (under Occasional) is now reported as Pain (under Common)

3.	Risks	Updated the summary of the most common side effects to match the revised protocol CAEPR (added "Pain").

Research Study Informed Consent Document

Study Title for Participants: Testing how the body responds to the drug DS-8201a in HER2-positive patients with advanced solid cancers

Official Study Title for Internet Search on http://www.ClinicalTrials.gov/:
Protocol 10346, "Pilot Study of DS-8201a Pharmacodynamics in Patients with HER2-expressing Advanced Solid Tumors" (NCT #04294628)

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 cancer and because your cancer has a particular protein (HER2) for which the study drug may be an effective targeted therapy.

Taking part in this study is your choice.

You can choose to take part in this study 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:

How does the study drug, called **DS-8201a** (also known as **Enhertu** or **fam-trastuzumab deruxtecan-nxki**), affect the levels of certain proteins and immune cells in your tumor, and how well does the drug work against the cancer cells in your tumor?

We will answer this question by examining cells from a small piece of your tumor taken before DS-8201a is given and again after DS-8201a is given. The Food and Drug Administration (FDA) has approved DS-8201a for the treatment of patients with advanced HER2-positive breast cancer.

What is the usual approach to my cancer?

The usual approach for patients who are not in a study is treatment with surgery, radiation, immunotherapy drugs, or chemotherapy drugs. Sometimes, combinations of these treatments are used. Your doctor can explain which treatment may be best for you. These treatments can reduce symptoms and may stop the tumor from growing for a few months or longer. For patients with advanced HER2-positive breast cancer, the usual approach may be treatment with DS-8201a, which is FDA-approved for this disease and has been proven to help patients with advanced HER2-positive breast cancer live longer. For patients with advanced solid cancers other than breast cancer, there are no treatments that are proven to help patients with your health condition live longer.

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 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 be given the drug DS-8201a through a vein in your arm on Day 1 of each 21-day cycle until your disease gets worse or the side effects become too severe. The study tests the same dose of DS-8201a in each patient to see if it is safe and tolerable for people with HER2-expressing, advanced solid tumors.

Tumor biopsies are required before you begin receiving DS-8201a and twice while you are receiving DS-8201a. We may also collect a fourth biopsy (optional) if your disease comes back or shows signs of coming back.
Your doctor will continue to watch you for side effects and follow how you are feeling for 30 days after you finish the study. 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 will give you more information in the "What possible 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 DS-8201a 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 DS-8201a. 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:

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

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

Benefits

This study is unlikely to help you. 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 the 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 and whether or not to let the study doctor continue to provide your medical information to the organization running the study.

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: if 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 (National Cancer Institute (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 main purpose of this study is to look at how DS-8201a may affect the levels of certain proteins and immune cells in your tumor and how well the drug works against cancer cells by examining cells from a small piece of your tumor taken before DS-8201a is given and again after DS-8201a is given. Other purposes of this study are to find out how safe and tolerable the study drug is, to see what good or bad effects the study drug has on your cancer, and to see how the levels of DS-8201a in your blood affect how well the drug works against cancer cells.

DS-8201a works by binding to a protein called HER2 that is present on the surface of your cancer cells. This allows DS-8201a to kill the cancer cells by damaging their DNA, resulting in cancer cell death.

The Food and Drug Administration (FDA) has approved DS-8201a for the treatment of patients with advanced HER2-positive breast cancer.

What are the study groups?

Each patient taking part in this study will receive the same dose of DS-8201a. You will be able to receive additional doses of the drug for as long as you remain in the study.

Treatment will be given in the outpatient setting, so you won't have to stay overnight in the hospital or clinic. DS-8201a is administered IV (through a vein in your arm) and is given in 3-week (21-day) cycles. Your study doctor will explain how the drugs are given and when you will need to come to the clinic for study tests and procedures.

Up to 63 patients will take part in this study at the NIH Clinical Center, Dana-Farber Cancer Institute, Ohio State University Comprehensive Cancer Center, and University of Pittsburgh Cancer Institute.

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 tests and scans 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:

- An ECG (electrocardiogram), troponin-I test, and ECHO (echocardiogram) or MUGA (multigated acquisition) scan before you begin the study and during the study to check your heart
- If you have a history of eye problems, an eye exam will be done before you begin the study and at the end of the study to check for eye problems (as eye abnormalities were found in some prior animal studies)
- Pregnancy test in women who are able to become pregnant before you begin the study and during the study

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 blood samples taken to test drug levels. These blood samples will be collected by inserting a needle in your arm at various time points during the first, second, third, and fourth cycles of treatment, and optionally if your disease comes back or shows signs of coming back. Blood samples will be drawn:
    - Before your first dose of DS-8201a on Cycle 1 Day 1
    - Two times after the first dose on Cycle 1 Day 1 (immediately after you finish receiving DS-8201a and 5 hours afterwards)
    - On Cycle 1, Day 2, 3, or 4
    - Two times each on Day 1 of Cycles 2, 3, and 4 (before the dose of DS-8201a and immediately after you finish receiving DS-8201a)

- Biopsies to measure the effect of DS-8201a on your tumor cells and immune cells within your tumor. Tumor biopsies are a very important part of this trial, as it is the only way for study scientists to learn more about how DS-8201a potentially works against your cancer. We will collect a tumor biopsy before you begin receiving DS-8201a and twice while you are receiving DS-8201a. We may also collect a fourth biopsy (optional) if your disease comes back or shows signs of coming back, as specified in the section below. We are collecting these samples to study the effects of DS-8201a and to search for any gene variations in your tumor that may help us understand how it responds to DS-8201a.

A Patient Study Calendar is attached at the end of this document. It shows how often these tests 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 DS-8201a 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 DS-8201a 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 7 months (women) or 4 months (men) after you have completed the study.

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. Biopsies for this study may also involve exposure to radiation from CT scans (see "Imaging Risks," below, for more information). You may sign a separate consent form for the study biopsy that describes the risks in more detail.

Side Effect Risks

The DS-8201a 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 will let you know if changes occur that may affect your health.

There is also a risk that you could have side effects from the study drug(s)/study approach.

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.

Drug Risks

The tables below show the most common and the 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.

Risk Profile for DS-8201a
(CAEPR Version 2.2, September 18, 2024)

COMMON, SOME MAY BE SERIOUS In 100 people receiving DS-8201a, more than 20 and up to 100 may have:
• Anemia which may require blood transfusion • Constipation, diarrhea, nausea, vomiting • Tiredness • Bruising, bleeding • Infection, especially when white blood cell count is low • Loss of appetite • Pain • Hair loss

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving DS-8201a, from 4 to 20 may have:
• Heart failure, which may cause shortness of breath, swelling of ankles, and tiredness • Blurred vision • Dry eye • Bloating, heartburn • Sores in the mouth which may cause difficulty swallowing • Fever • Cold symptoms such as stuffy nose, sneezing, sore throat • Reaction during or following a drug infusion which may cause chills, low blood pressure • Change in heart function • Weight loss • Dizziness, headache • Changes in taste • Cough, shortness of breath • Nose bleed • Damage to the lungs (including interstitial lung disease [ILD]) which may cause shortness of breath. In rare cases, this can be life-threatening or fatal • Itching, rash, skin changes

Imaging Risks

This research study involves exposure to radiation from up to 4 CT scans (used in research biopsy collections). This radiation exposure is not required for your medical care and is for research purposes only.

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 4 CT scans is the same as 11 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.

Please tell your doctor if you have had any radiation exposure in the past year, either from other research studies or from medical tests or care, so we can make sure that you will not receive too much radiation. Radiation exposure includes x-rays taken in radiology departments, cardiac catheterization, and fluoroscopy as well as nuclear medicine scans in which radioactive materials were injected into your body.

If you are pregnant, you may not participate in this protocol, as the fetus is more sensitive to radiation than children or adults.

Blood Sample Risks

Possible side effects from drawing the blood sample include mild pain, bleeding, bruising, and infection at the site of the needle insertion. Fainting or light-headedness can sometimes occur, but usually last only a few minutes. The frequent blood sampling for research purposes may be burdensome, inconvenient, and painful.

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.

For women: Do not get pregnant or breastfeed while taking part in this study; if you are a woman on this study who may become pregnant, you need to use birth control from the time you sign the study consent form, while on this study, and for 7 months after receiving the last dose of study drug. **For men:** Do not father a baby while taking part in this study; if you are a man on this study, you need to use effective barrier contraception while you are on this study and for 4 months after receiving the last dose of study drug. **For all:** Tell your study doctor right away if you think that you or your partner have become pregnant during the study or within 7 months (women) or 4 months (men) 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 DS-8201a 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 or your insurance provider will not have to pay for the DS-8201a while you take part in this study.

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:

- Blood tests to measure study drug levels and the effect of the study drug on circulating tumor DNA (ctDNA) in your blood stream
- CT scans and biopsies to measure the effect of the study drug on your tumor and immune cells
- Eye exams

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 or hurt 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.
- Similar regulatory agencies if other countries are involved in the study.

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)*.

For questions about your rights while in this study, call the _____ (insert name of center) Institutional Review Board at _____ (insert telephone number). *(Note to Local Investigator: Contact information for patient representatives or other individuals at a local institution who are not on the IRB or research team but take calls regarding clinical trial questions can also be listed here.)*

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 cancer and other diseases 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 biopsy study

If you choose to take part in this optional biopsy study, you will have an extra (fourth) tumor biopsy at the time that your disease comes back or shows signs of coming back. Researchers would use this tumor biopsy to look for any changes in the genes, proteins, or immune cells in your tumor that may explain why your disease is showing signs of coming back, and these results would be used for research only and not to guide your medical care.

If you agree to have this extra biopsy, it would involve a fourth biopsy procedure similar to the mandatory biopsy procedures described above. The risks would be a small amount of bleeding at the time of the procedure, bruising, pain at the biopsy site, and (if a CT scan is used for the biopsy) exposure to radiation from the CT scan; rarely, an infection can occur. In addition, there are risks associated with genomic sequencing of your biopsy sample. 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/. Ask your study doctor if you would like to learn more about this optional biopsy procedure.

Please circle your answer: I choose to take part in the biopsy study and will undergo the extra biopsy:

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 these optional studies, researchers will:

1) Collect blood specimens for research to test levels of circulating tumor DNA (ctDNA) in your blood stream.
2) Collect blood specimens for research to look for anti-drug antibodies (ADA). These are antibodies against DS-8201a that your body's immune system may make in response to DS-8201a therapy.
3) Use any existing tumor biopsy specimens to measure additional effects of DS-8201a on tumor cells, including genomic sequencing studies (see "Genomic Sequencing," below).

Genomic Sequencing:

One of the optional tests performed on your biopsy and blood samples will be genomic sequencing. Your tumor contains genes, which are made up of DNA (**d**eoxy**r**ibonucleic **a**cid) and serve as the "instruction book" for the cells that make up our bodies. Genomic sequencing of your tumor tissue, or of small pieces of tumor DNA that can be found circulating in your blood, will determine the exact order of the DNA building blocks in your tumor DNA. We know that variations in some tumor genes play an important role in how cancers respond to drugs. Determining whether different tumor gene variations affect how DS-8201a works against tumors will help scientists understand which patients might respond best to this drug.

The information collected from genomic sequencing of your tumor DNA will be for research purposes only, and we will not give you any individual results from this sequencing or add this information to your medical records.

What is involved in this optional sample collection?

If you choose to take part in these studies, here is what will happen next:

1) Additional blood samples (about half of a tablespoon each) will be collected from a vein in your arm throughout the study, as noted in the Patient Study Calendar below, to test levels of circulating tumor DNA (ctDNA).
2) Additional blood samples (about one teaspoon each) will be collected from a vein in your arm throughout the study, as noted in the Patient Study Calendar below, to test levels of anti-drug antibodies (ADA) to DS-8201a.
3) Existing tumor biopsy specimens left over after the mandatory studies are completed may be used to measure additional effects of DS-8201a on tumor cells, including genomic sequencing studies.
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 drawing blood from your arm are brief pain and possibly a bruise.
- There is a risk that someone could get access to the personal information in your medical records or other information researchers have stored about you.
- 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 more 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)*.

Samples for known future studies:

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

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

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 copy of this form. I agree to take part in the study.

Participant's signature_____

Date of signature_____

Signature of person(s) conducting the informed consent discussion_____

Date of signature_____

I agree that an optional fourth tumor biopsy may be collected from me if my disease comes back or shows signs of coming back.

Participant's signature_____

Date of signature_____

Signature of person(s) conducting the informed consent discussion_____

Date of signature_____

Patient Study Calendar

The study drug is given over 21-day periods of time called cycles. The chart below shows what will happen to you during each cycle after you sign the consent form and start the study.

Day	Patient Activity
Before starting study drugs	• Check in at the Outpatient Clinic • Have a history taken of how you feel and undergo a physical examination by a Health Care Provider • Routine blood tests • ECG, ECHO/MUGA, and troponin-I test to examine your heart • Eye exam (if you have a history of eye problems) • Pregnancy test for women who are able to become pregnant • Tumor measurements by CT or MRI scans • Research blood samples will be taken • Tumor biopsy will be taken
Cycle 1, Day 1	• Check in at the Outpatient Clinic • Physical exam and routine blood tests • Receive DS-8201a • Research blood samples will be taken
Cycle 1, Day 2, 3, or 4	• Check in at the Outpatient Clinic • Physical exam and routine blood tests • Research blood samples will be taken • Tumor biopsy will be taken
Cycle 2 and onwards, Day 1	• Check in at the Outpatient Clinic • Physical exam and routine blood tests • Receive DS-8201a • Research blood samples will be taken during Cycles 2, 3, and 4
Cycle 3, Day 1	• Check in at the Outpatient Clinic • Physical exam and routine blood tests • Research blood samples will be taken • Tumor biopsy will be taken before receiving DS-8201a • Receive DS-8201a
Cycle 4 and onward	• CT scan to determine how your tumor is responding to the drugs will be done every 9 weeks (12 weeks if on study more than 1 year) • Research blood samples may be taken on Day 1 of Cycle 4 and every 4 cycles thereafter (Cycles 8, 12, 16, etc.), and at the time of your follow-up appointment after stopping treatment • An eye exam will be performed at the end of the study treatment if you have a history of eye problems

Day	Patient Activity
	• ECHO to check your heart will be performed at the beginning of Cycle 5 and every 4 cycles afterward • Optional tumor biopsy for research will be obtained if your disease comes back or shows signs of coming back • Optional blood draws for research will be obtained if your disease comes back or shows signs of coming back • You will be followed for 30 days after your last dose of drug is administered