SUMMARY OF CHANGES - Consent

To: CTEP Protocol and Information Office

From: Matthew Ingham, M.D.

Date: March 25, 2025

Re: Response to Disapproval of Amendment #8 of Protocol #10330: "A Phase 2 Study of Belinostat and SGI-110 (Guadecitabine) or ASTX727 for the Treatment of Unresectable and Metastatic Conventional Chondrosarcoma"

SUMMARY OF CHANGES – Consent

I. Comments Requiring a Response– Administrative & Editorial Issues:

#	Section	Comments
1.	**ICD Risks**	Please add ASTX727 risk list (CAEPR version 2.2, December 19, 2024), as attached. **PI Response:** Risks updated in applicable consent. ASTX727 risks not described in SGI-110 consent.

II. Consent form changes in response to the RRA dated 02/25/25:

#	Section	Comments
1.	Global	The informed consent version date was updated.
2.	How will information about me be kept private	In response to the Executive Order regarding Defending Women, the term 'gender' has been replaced by 'sex.'

Research Study Informed Consent Document
Belinostat and SGI-110 (guadecitabine) Version

Study Title for Participants: Testing the combination of belinostat and SGI-110 (guadecitabine) or ASTX727 for the treatment of unresectable and metastatic conventional chondrosarcoma

Official Study Title for Internet Search on http://www.ClinicalTrials.gov: NCI Protocol 10330, A Phase 2 Study of Belinostat and SGI-110 (Guadecitabine) or ASTX727 for the Treatment of Unresectable and Metastatic Conventional Chondrosarcoma (NCT# TBD)

Overview and Key Information

What am I being asked to do?

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

We are asking you to take part in this research study because you have been diagnosed with chondrosarcoma that cannot be removed by surgery.

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:

Is the combination of the drugs belinostat and SGI-110 (guadecitabine) effective at lowering the chance of your chondrosarcoma growing or spreading?

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

What is the usual approach to my chondrosarcoma?

There are no treatments approved by the U.S. Food and Drug Administration (FDA) for advanced chondrosarcoma. The usual approach for patients who are not in a study is treatment with a chemotherapy drug such as doxorubicin or the combination of gemcitabine with docetaxel. Sometimes, radiation is also used to treat advanced chondrosarcomas. Unfortunately, neither chemotherapy nor radiation is very effective for the treatment of chondrosarcoma.

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 receive two drugs, belinostat and SGI-110 (guadecitabine). Belinostat is administered through a vein in your arm (IV) over approximately 30 minutes, and SGI-110 (guadecitabine) is administered by subcutaneous injection (*i.e.*, under your skin). Both drugs will be given together, once daily for 5 consecutive days in your doctor's office. This 5-day treatment is repeated every 28 days. The treatment will continue for as long as your disease remains under control, you do not develop unacceptable side-effects, and you want to continue participating in the study.

Belinostat and SGI-110 (guadecitabine) are both "epigenetic" drugs. This means that the drugs modify the expression of genes in the cancer cell. Cancer cells often turn on certain genes and turn off other genes to allow the cancer to grow and spread. Epigenetic drugs may work by reversing these changes in gene expression in the cancer cell.

The status of your cancer will be evaluated by imaging tests (*e.g.*, by a CT scan or an MRI scan) every 8 weeks while you are receiving the treatment. After you finish your study treatment, your doctor will continue to follow your condition. Specifically, the study team will follow up with you in the clinic or by telephone approximately once every 3 months for information related to the status of your cancer and any new treatments you are receiving, for a period of up to 24 months after you finish treatment on this study.

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 combination of belinostat and SGI-110 (guadecitabine) may not be as good as chemotherapy at shrinking or stabilizing your cancer.

There is also a risk that you could have side effects from the belinostat and SGI-110 (guadecitabine) combination. These side effects may be worse and may be different than you would get with the usual approach for chondrosarcoma.

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

- Belinostat:
  - tiredness
  - low appetite
  - lower than normal blood cells
  - diarrhea, nausea, or vomiting
- SGI-110 (guadecitabine):
  - tiredness
  - swelling or redness at the site where the drug is injected
  - low levels of blood cells that fight infection, low levels of blood cells that stop bleeding
  - bruising, low appetite

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

Benefits

The combination of belinostat and SGI-110 (guadecitabine) has shrunk chondrosarcoma in cell and animal models of chondrosarcoma. It may work in a subset of patients with chondrosarcoma, but it is unlikely that it will work in everyone with chondrosarcoma. 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:

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

It is important that you understand the information in the informed consent before making your decision. Please read, or have someone read to you, the rest of this document. If there is anything you don't understand, be sure to ask your study doctor or nurse.

SGI-110 supply may no longer be suitable for clinical use after 31-AUG-2021. The pharmaceutical company, Astex, has decided not to continue to develop the drug or conduct clinical trials with the drug. This decision does not reflect any new information on side effects. This decision also does not reflect any information on how well the drug may work in chondrosarcoma. If SGI-110 is no longer available from the drug manufacturer as of 31-AUG-2021, further treatment options will be discussed with subjects enrolled to the belinostat/SGI-110 regimen who remain on treatment as of 31-AUG-2021.

Patients who remain on study with SGI-110 (guadecitabine) and belinostat in August 2021 will discuss treatment options with their doctor at that time. ASTX727 is a new drug that works in a very similar way to SGI-110 (guadecitabine). Patients may be allowed to change treatment to ASTX727 and belinostat in August 2021 if the overall assessment of risks versus benefits support that change, primarily related to any observations of adverse safety and tolerability of ASTX727 and belinostat at that time. However, we cannot guarantee that patients who remain on SGI-110 (guadecitabine) and belinostat in August 2021 will be allowed to change treatment to ASTX727 and belinostat.

What is the purpose of this study?

The purpose of this study is to test the good and bad effects of the drugs called belinostat and SGI-110 (guadecitabine). These drugs could shrink your cancer, but they could also cause side effects, which are described in the risks section below. The study doctors hope to learn if the study drugs will shrink the cancer more often than observed with other standard treatment options.

We don't know if belinostat or SGI-110 (guadecitabine) work to treat chondrosarcoma in people, but they have been used in other clinical trials and are noted to be well-tolerated in patients with other types of cancer.

There will be approximately 26 people taking part in this study.

What are the study groups?

In this study, you will get the study drugs belinostat and SGI-110 (guadecitabine).

Treatment schedule: You will get belinostat through a vein in your arm on days 1 through 5 of each cycle (one cycle is 28 days). You will also get SGI-110 (guadecitabine) injections subcutaneously (*i.e.*, under your skin) on the same days, days 1 through 5, of each cycle. The treatment is given in the outpatient setting.

Belinostat is FDA-approved but not for the treatment of your type of cancer. SGI-110 (guadecitabine) is an experimental drug; it is not approved by the FDA.

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

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

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

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

- Blood counts checked every 2 weeks for the first 8 weeks on the study, then every 4 weeks.
- Office visits and a physical examination every 4 weeks. An additional office visit and physical examination are conducted during the third week of the study.

This study will use genetic tests that may 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:

1. Researchers will study the result further to decide if it may be medically important to you or your relatives.
2. 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.
3. 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.
4. You will require another genetic test to confirm the results. This test must be paid for at your own expense.
5. 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.

You will need to have two biopsies that are mandatory for participation in this study. These biopsies will be done before you begin the treatment and during your second cycle of treatment on Day 3, 4, or 5. The study biopsies take small pieces of cancer tissue from your body. This is like the biopsy you had that helped diagnose your cancer.

A blood sample (about 2 teaspoons of blood) will also be taken for the study. The blood sample is mandatory for participation in the study and will be collected before you begin the study drugs.

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 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 belinostat and SGI-110 (guadecitabine) combination may not be as good as chemotherapy 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 medications 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 3 months after you have completed the study.

Genetic Testing Risks

The genetic test used in this study will test your tumor and normal tissue for genetic changes, including changes in the IDH1 and IDH2 genes. *IDH1* and *IDH2* are two genes that the investigators think may be important in chondrosarcoma. Changes found in your normal tissue may be passed down in families. For example, these genetic changes may be passed down to your children in the same way that eye and hair color are passed down.

Genetic tests of normal tissue can reveal information about you and also about your relatives. Your doctor will talk with you about what the tests results may mean for you and your family. He or she also may suggest you talk with a genetics counselor to learn more. You or your insurance plan would have to pay for visits to a genetic counselor.

Biopsy Risks

During this study, core needle biopsies will be performed from a site where the cancer is located. Depending on the site of the biopsy, an imaging test such as a CT scan may be used during the procedure to guide the biopsy. The study team will explain the procedure to you. Common side effects of the core needle biopsies that you will have performed on this study are a small amount of bleeding at the time of the procedure, bruising, and pain at the biopsy site. Pain can be treated with regular pain medications. Rarely, an infection can occur. You may sign a separate consent form for the study biopsy that describes the risks in more detail.

Side Effect Risks

The medications 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 medications.

Here are important things to know about side effects:

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

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

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

This study is looking at a combination of drugs which have been previously studied in human trials, either alone or in combination with other drugs. However, these two study drugs have not been studied in combination with each other. This new combination of drugs may increase your side effects or may cause new side effects.

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

Drug Risks

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

Possible Side Effects of SGI-110 (Guadecitabine)
(Table Version Date: May 8, 2019)

COMMON, SOME MAY BE SERIOUS In 100 people receiving SGI-110 (guadecitabine), more than 20 and up to 100 may have:
• Tiredness • Swelling and redness at the site of the medication injection • Bruising, bleeding

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving SGI-110 (guadecitabine), from 4 to 20 may have:
• Anemia which may require blood transfusion • Infection, especially when white blood cell count is low • Constipation, diarrhea, nausea, vomiting • Sores in the mouth which may cause difficulty swallowing • Fever • Pain • Loss of appetite • Dizziness, headache • Difficulty sleeping • Shortness of breath • Nose bleed • Rash

RARE, AND SERIOUS In 100 people receiving SGI-110 (guadecitabine), 3 or fewer may have:
• Swelling of the eye • Swelling of the face • Kidney damage which may require dialysis

Possible Side Effects of Belinostat
(Table Version Date: October 29, 2018)

COMMON, SOME MAY BE SERIOUS In 100 people receiving belinostat (PXD-101), more than 20 and up to 100 may have:
• Diarrhea, nausea, vomiting • Tiredness • Loss of appetite

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving belinostat (PXD-101), from 4 to 20 may have:
• Anemia which may require blood transfusion • Belly pain • Constipation • Dry mouth • Swelling of arms, legs • Fever • Swelling and redness at the site of the medication injection • Infection, especially when white blood cell count is low • Change in the heart rhythm • Bruising, bleeding • Weight loss • Dehydration • Dizziness, headache • Changes in taste • Shortness of breath • Rash • Flushing

RARE, AND SERIOUS In 100 people receiving belinostat (PXD-101), 3 or fewer may have:
• Kidney damage which may require dialysis

Additional Drug Risks

The study drugs could interact with other drugs. Your study doctor will monitor for any interactions.

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.

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 3 months after your last dose of study drugs.

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 chondrosarcoma. 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.
- 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 biopsies done before study treatment begins and during cycle 2 of this study.
- Blood collection done before study treatment begins.

You or your insurance provider will not have to pay for the belinostat or SGI-110 (guadecitabine) 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 school or 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 your condition in the future. The results will not be added to your medical records and you or your study doctor will not know the results.

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

your insurance company will not be billed for these optional studies. If you sign up for but cannot complete any of these studies for any reason, you can still take part in the main study.

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

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

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

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

Unknown future studies

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.

If you choose to take part in this optional study, any of your tumor tissue or blood samples left over from the genomic sequencing 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. Also, any health-related information, such as your response to cancer treatment, results of study tests, and medicines you took, will be stored for future use. Your genomic sequence will also be stored in a secure NIH database for future use. 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. 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 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.
- Future research studies may include genomic sequencing.
- You will not get reports or other information about any research that is done using your samples.

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 before you begin study treatment and during Cycle 2 on Day 3, 4, or 5 will be sent to the biobank. No new or additional biopsies for tissue collection will occur.
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.
- 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. Only your study doctor and a few study researchers will have access to the master list linking the code numbers to names. The biobank and the genomic sequencing laboratory will receive your samples with the following information only: your sample code number; your age, race/ethnicity, and sex; your type of cancer; any previous treatments you received for your cancer; and the treatment you will receive for this current study.
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. The researchers must be trained in the handling of private information. Any researcher who wants to study your stored samples and genetic information must apply and be approved to do so.
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 for exams, tests, and procedures done for research purposes only; these include the biopsy, blood draw, DNA/RNA sequencing, and biobanking of your specimen(s). 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 or blood 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 study described above.

YES NO

Samples for unknown future studies:

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

YES NO

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

Patient Study Calendar

	Before you begin study treatment[A]	Cycle 1[B]				Cycle 2[B]				Cycle 3+[B]				Off Study[C]
		Week 1	Week 2	Week 3	Week 4	Week 1	Week 2	Week 3	Week 4	Week 1	Week 2	Week 3	Week 4	
Belinostat		X				X				X				
SGI-110 (guadecitabine)		X				X				X				
Pre-study (before you begin study treatment) procedures, including informed consent, demographics, and medical history	X													
Concurrent meds	X	X				X				X				X
Physical exam, vital signs, and weight	X	X		X		X				X				X
Assessment of how you perform everyday tasks and activities	X													
Height	X													X
Blood draws for complete blood count and general health status	X	X		X		X		X		X				X
Pregnancy test	X													X
ECG[D]	X													X
Side effects evaluation	X	Throughout study												X
Medical imaging scans for tumor measurements	X								X					X
Tumor biopsy for research purposes	X					X[E]								
Blood draw for research purposes	X													

A. All of your assessment will be performed within 21 days of the first cycle.
B. All your assessments will be performed on Day 1 of the specified week unless noted otherwise.
C. All of your assessments will be performed within 21 days of receiving the last doses of study drugs.
D. Additional ECGs may be performed if your doctor indicates this is necessary.
E. The tumor biopsy can be collected on Day 3, 4, or 5.