SUMMARY OF CHANGES – Triplet Combination Consent

NCI Protocol #: 10404
Local Protocol #: PhI-117
Protocol Version Date: January 10, 2025

Protocol Title: A Phase 1 Trial of the ATR Inhibitor BAY 1895344 in combination with cisplatin and with cisplatin plus gemcitabine in advanced solid tumors with an emphasis on urothelial carcinoma

Informed Consent Version Date: January 10, 2025

Section	Comments
General	No changes were made to the consent besides the version date to match the protocol. The study is closed to accrual with all patients off treatment.

Research Study Informed Consent Document (Triplet Combination)

Study Title for Participants: Testing the addition of an anti-cancer drug, BAY 1895344, to the usual chemotherapy treatment (cisplatin and gemcitabine) for advanced solid tumors with emphasis on urothelial carcinoma

Official Study Title for Internet Search on http://www.ClinicalTrials.gov: P10404 "A Phase I Trial of the ATR inhibitor BAY 1895344 in combination with cisplatin and with cisplatin plus gemcitabine in advanced solid tumors with an emphasis on urothelial carcinoma" (NCT # NCT04491942)

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 urothelial carcinoma.

Taking part in this study is your choice.

You can choose to take part or you can choose not to take part in this study. You also can change your mind at any time. Whatever choice you make, you will not lose access to your medical care or give up any legal rights or benefits.

This document has important information to help you make your choice. Take time to read it. Talk to your doctor, family, or friends about the risks and benefits of taking part in the study. It's important that you have as much information as you need and that all your questions are answered. See the "Where can I get more information?" section for resources for more clinical trials and general cancer information.

Why is this study being done?

This study is being done to answer the following question:

What is the highest dose of BAY 1895344 that can be given safely in combination with cisplatin and gemcitabine in patients with advanced solid tumors, including urothelial carcinoma?

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

What is the usual approach to my advanced solid tumor or urothelial carcinoma?

The usual approach for patients who are not in a study is treatment with cisplatin alone or in combination with other agents such as gemcitabine. The combination of cisplatin with gemcitabine has been approved by the FDA. About 25 to 45 patients out of 100 have a response to this treatment, depending on the tumor type.

What are my choices if I decide not to take part in this study?

- You may choose to have the usual approach described above.
- You may choose to take part in a different research study, if one is available.
- You may choose not to be treated for cancer.
- You may choose to only get comfort care to help relieve your symptoms and not get treated for your cancer.

What will happen if I decide to take part in this study?

If you decide to take part in this study, you will get BAY 1895344 in combination with cisplatin and gemcitabine as a triplet combination for six (6) cycles [each cycle is 3 weeks long]. You may also stop the drugs if you have side effects that are too difficult for you.

After you finish BAY 1895344 with cisplatin and gemcitabine triplet combination treatment, your doctor will continue to follow your condition for 30 days and watch you for side effects and every 3 months to monitor for progression of cancer. Ideally, we will monitor you every 3 months during a follow-up clinic visit, but if there are circumstances that prevent you from being able to these follow-up appointments, you may have the option to follow-up with a phone call. If you have evidence of progression of cancer, then you will no longer have to follow-up with us.

What are the risks and benefits of taking part in this study?

There are both risks and benefits to taking part in this study. It is important for you to think carefully about these as you make your decision.

Risks

We want to make sure you know about a few key risks right now. We give you more information in the "What risks can I expect from taking part in this study?" section.

If you choose to take part in this study, there is a risk that the study drugs may not be as good as the usual approach for your cancer shrinking or stabilizing your cancer.

There is also a risk that you could have side effects from the study drugs. These side effects may be worse and may be different than you would get with the usual approach for your cancer.

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

- Nausea, vomiting
- Anemia that may cause tiredness or may require blood transfusions
- Bruising or bleeding
- Diarrhea
- Numbness and tingling of the arms and legs
- Damage to kidney function
- Infection, especially when white blood cell count is low

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

Benefits

There is some evidence based on a clinical study that BAY 1895344 may have benefit to patients with various types of cancers, and that adding BAY 1895344 to the usual approach can shrink or stabilize cancer for longer than the usual approach alone. However, we do not know if this will happen in people. It is unlikely that this combination will help you live longer than the usual approach alone. 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. This means stopping the study treatment while undergoing careful monitoring of your health with laboratory tests and a physical examination. If you stop, you can decide if you want to keep letting the study doctor know how you are doing.

Your study doctor will tell you about new information or changes in the study that may affect your health or your willingness to continue in the study.

Are there other reasons why I might stop being in the study?

Yes. The study doctor may take you off the study if:

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

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

What is the purpose of this study?

The purpose of this study is to test the safety of a drug called BAY 1895344 in combination with cisplatin and gemcitabine. This study tests different doses of the drugs to see which dose is safer for people. "Dose" is defined as the amount of drug you get, such as 10 mg. There will be about 37 people taking part in this part of the study.

Cisplatin is FDA-approved in the case of patients with non-small cell lung cancer and pancreatic cancer, however during this study you may receive less than the typical dose of chemotherapy.

What are the study groups?

There are two parts in this study, one with two drugs (BAY 1895344 and cisplatin) and a triplet combination with three drugs (BAY 1895344, gemcitabine and cisplatin). This consent is only for triplet combination with three drugs (BAY 1895344, gemcitabine and cisplatin) part of the study. There are two groups for the triplet combination, a dose escalation group and a dose expansion group. Your doctor will tell you which group you are in.

Different people taking part in this study will get different doses of the study drugs BAY 1895344 with cisplatin and gemcitabine as a triplet combination. See the patient calendar for more information on the timing and duration of your treatments, and how your treatments will be administered.

The first 3 people taking part in this study will get the first dose. If the drug does not cause serious side effects, the next group of people in the study will get a higher dose. The study doctor will watch each group carefully as they increase the dose. The doses will continue to increase for every new group until people have serious side effects that require the dose to be lower. Once this dose is found, this part of the study is stopped.

The highest dose with manageable side effects will be given to 12 more people who have advanced urothelial carcinoma. This will help study doctors better understand the side effects that may happen with this drug combination.

You will not be able to get additional doses of BAY 1895344. This drug is not approved by the FDA for treatment of your disease.

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:

- An electrocardiogram (EKG) at the beginning of the study to evaluate your heart as your doctor indicates it is necessary.
- Blood counts done weekly for the first two weeks of each cycle.
- Physical exams done on or around day 1 of each cycle

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 make 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.

Your study doctor will need to use some of the tissue left over from your biopsy when you were diagnosed with cancer. This sample is a required part of the study. The sample will be tested to look for the presence of any mutations that might suggest you are more or less likely to respond to cancer treatment. You and your study doctor will get the results of this testing upon request.

- Research blood samples will also be taken for the study during Cycle 1 only.
- The first blood collection will be before you begin study treatment.
- Blood samples will be collected on Day 1 before you receive your first dose of cisplatin and gemcitabine. There will be an additional collection on Day 1 to check the levels of gemcitabine in your blood. Specifically, on Day 1, the timepoints are as follows: pretreatment, 25 minutes into infusion of gemcitabine, 15 minutes, 30 minutes, and 60 minutes after infusion of gemcitabine.
- If you are in the dose escalation group, you will have blood collections on Days 2 and 9 to check the level of BAY1895344 in your blood. On Days 2 and 9 the timepoints are as follows: before you receive your BAY 1895344 dose, and 30 minutes, 1 hour, 1.5 hours, 2 hours, 4 hours, 6 hours, 8 hours, and 24 hours after your BAY 1895344 dose.
- If you are in the dose expansion group, you will have blood collections on Day 2 to check the level of BAY1895344 in your blood. On Day 2 the timepoints are as follows: before you receive your BAY 1895344 dose, and 30 minutes, 1 hour and 1.5 hours after your BAY 1895344 dose.

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 the study drugs may not be as good as the usual approach to 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 study intervention 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 6 months after you have completed the study.

This study will use a sample of your tissue. Generally, your hospital will keep some of your tissue. This tissue may be used to help treat your cancer in the future. Because this study will need to use some of this tissue, there is a small risk that it could be used up.

Blood Draw Risks

Some of the risks from drawing blood from your arm may include pain, bruising, light-headedness, and rarely, infection. The multiple, and frequent blood draws taken from your arm for research testing may be burdensome and inconvenient given the time you need to stay in the hospital. In addition, the frequent needle sticks may be uncomfortable as your infusion line cannot be used. For most people, needle punctures to get blood samples do not cause any serious harm. 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.

Side Effect Risks

The study drugs used in this study may affect how different parts of your body work such as your liver, kidneys, heart, and blood. The study doctor will test your blood and let you know if changes occur that may affect your health.

There is also a risk that you could have other side effects from the study drugs.

Here are important things to know about side effects:

1. The study doctors do not know who will or will not have side effects.
2. Some side effects may go away soon, some may last a long time, and some may never go away.
3. Some side effects may 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 the usual drugs used to treat this type of cancer plus a study drug. This different combination of drugs may increase your side effects or may cause new side effects.

Drug Risks

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

Possible Side Effects of BAY 1895344 (Table Version Date: September 5, 2020)

COMMON, SOME MAY BE SERIOUS **In 100 people receiving BAY 1895344, more than 20 and up to 100 may have:**
• Anemia which may require blood transfusion • Nausea • Tiredness • Bruising, bleeding • Infection, especially when white blood cell count is low
OCCASIONAL, SOME MAY BE SERIOUS **In 100 people receiving BAY 1895344, from 4 to 20 may have:**
• Diarrhea, vomiting • Loss of appetite

Possible Side Effects of Cisplatin
(Table Version Date: November 8, 2019)

COMMON, SOME MAY BE SERIOUS In 100 people receiving Cisplatin, more than 20 and up to 100 may have:
• Infection, especially when white blood cell count is low • Bruising, bleeding • Anemia which may cause tiredness, or may require blood transfusions • Kidney damage which may cause swelling, may require dialysis • Hearing loss including ringing in the ears • Nausea, vomiting • Confusion

COMMON, SOME MAY BE SERIOUS In 100 people receiving Cisplatin, more than 20 and up to 100 may have:
• Numbness and tingling of the arms and legs
OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving Cisplatin, from 4 to 20 may have:
• Diarrhea • Change in taste • Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat • Hair loss
RARE, AND SERIOUS In 100 people receiving Cisplatin, 3 or fewer may have:
• Brain damage, Posterior Reversible Encephalopathy syndrome, which may cause headache, seizure, blindness • Seizure • A new cancer resulting from treatment of a prior cancer

Possible Side Effects of Gemcitabine
(Table Version Date: October 17, 2019)

COMMON, SOME MAY BE SERIOUS In 100 people receiving Gemcitabine, more than 20 and up to 100 may have:
• Infection, especially when white blood cell count is low • Bruising, bleeding • Anemia which may require a blood transfusion • Blood in urine • Nausea, vomiting • Flu-like symptoms of muscle pain, fever, headache, chills and fatigue • Muscle weakness • Feeling of "pins and needles" in arms and legs • Numbness and tingling of the arms and legs • Swelling of arms, legs • Tiredness • Difficulty sleeping • Rash • Hair loss

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving Gemcitabine, from 4 to 20 may have:
• Fluid in the organs which may cause low blood pressure, shortness of breath, swelling of ankles • Scarring of the lungs

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving Gemcitabine, from 4 to 20 may have:
• Shortness of breath • Liver damage which may cause yellowing of eyes and skin, swelling • Diarrhea, constipation • Sores in mouth which may cause difficulty swallowing • Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat • Swelling and redness of the area of radiation • Blisters on the skin

RARE, AND SERIOUS In 100 people receiving Gemcitabine, 3 or fewer may have:
• Brain damage, Posterior Reversible Encephalopathy syndrome, which may cause headache, seizure, blindness • Blockage of the airway which may cause cough • Blood clot • Severe blood Infection • Anemia, kidney problems which may require dialysis

Additional Drug Risks

The study drug BAY 1895344 may also make you more sensitive to sunlight, so you should take protective measures to minimize sun exposure while taking BAY 1895344.Your study doctor will give you a drug information handout and wallet card that lists these possible interactions. Share this information with your family members, caregivers, other health care providers, and pharmacists.

Rarely, there are problems getting enough supplies of the study drug. If that happens, your doctor will talk with you about your options.

What are my responsibilities in this study?

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

- Keep your study appointments.
- Tell your doctor about:
  - all medications and supplements you are taking
  - any side effects
  - any doctors' visits or hospital stays outside of this study
  - if you have been or are currently in another research study.
- Write down in your medication diary when you take the study drug at home.

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 6 months after your last dose of study drug.

What are the costs of taking part in this study?

You and/or your insurance plan will need to pay for the costs of medical care you get as part of the study, just as you would if you were getting the usual care for your cancer. This includes:

- the costs of tests, exams, procedures, and drugs that you get during the study to monitor your safety, and prevent and treat side effects.
- the costs of getting the BAY 1895344 ready and giving it to you.
- the cost of getting the cisplatin ready and giving it to you.
- the cost of getting the gemcitabine 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 or that are covered by the study. These include:

- Blood collections before you begin study treatment and on Days 1, 2, and 9 of Cycle 1.
- Left over tumor tissue from your previous biopsy

You or your insurance provider will not have to pay for the BAY 1895344 while you take part in this study.

Taking part in this study may mean that you need to make more visits to the clinic or hospital than if you were getting the usual approach to treat your cancer. You may:

- Have more travel costs.
- Need to take more time off work.
- Have other additional personal costs.

You will not be paid for taking part in this study. The research may lead to new tests, drugs, or other products for sale. If it does, you will not get any payment.

What happens if I am injured because I took part in this study?

If you are injured as a result of taking part in this study and need medical treatment, please talk with your study doctor right away about your treatment options. The study sponsors will not pay for medical treatment for injury. Your insurance company may not be willing to pay for a study-related injury. Ask them if they will pay. If you do not have insurance, then you would need to pay for these medical costs.

If you feel this injury was caused by medical error on the part of the study doctors or others involved in the study, you have the legal right to seek payment, even though you are in a study. Agreeing to take part in this study does not mean you give up these rights.

Who will see my medical information?

Your privacy is very important to us. The study doctors will make every effort to protect it. The study doctors have a privacy permit to help protect your records if there is a court case. However, some of your medical information may be given out if required by law. If this should happen, the study doctors will do their best to make sure that any information that goes out to others will not identify who you are.

Some of your health information, such as your response to cancer treatment, results of study tests, and medicines you took, will be kept by the study sponsor in a central research database. However, your name and contact information will not be put in the database. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used.

There are organizations that may look at or receive copies of some of the information in your study records. Your health information in the research database also may be shared with these organizations. They must keep your information private, unless required by law to give it to another group.

Some of these organizations are:

- The study sponsor and any company supporting the study or the study agent now or in the future. This would include any organization helping the company with the study.
- The NCI Central IRB (Institutional Review Board), 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 (Food and Drug Administration) 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 get reports as requested 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 cancer in the future. The results will not be added to your medical records and you or your study doctor/will not know the results.
Taking part in these optional studies is your choice. You can still take part in the main study even if you say "no" to any or all of these studies. There is no penalty for saying "no." You and your insurance company will not be billed for these optional studies. If you sign up for, but cannot complete any of these studies for any reason, you can still take part in the main study.

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

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

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

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

Known future studies

If you choose to take part in this optional study, researchers will use some of the tissue left over from your biopsy when you were diagnosed with cancer and blood for research on evaluating the changes in your DNA and RNA that occur during treatment. Researchers will obtain genetic material (DNA and RNA) from both your tumor cells and your blood. Your DNA and RNA will be used for genomic sequencing. Genomic sequencing is a method of recording information in all or part of your genes, piece by piece. This is usually done to look for changes in your genes that may cause health problems.

The genomic sequencing will be done by an NCI-supported laboratory in Frederick, Maryland, known as the National Clinical Laboratory Network (NCLN) Genomics Laboratory at the Frederick National Laboratory for Cancer Research. The laboratory will compare the genetic material from your tumor and blood cells to identify how they differ. These differences may be important to understand why you did or did not respond to the treatment you received. By identifying these changes, researchers hope to discover changes within your tumor that could be used to predict how patients with your type of cancer may respond to current or future treatments. This optional study may improve the ability to select future treatments or treatment combinations for others in the future. This optional study will not affect the cancer treatment or approach that you receive.

Your study doctor will not be informed when the genetic sequencing research will be done. Your study doctor will not receive reports of these studies, as they are intended for research purposes only and may not significantly impact your future treatment.

Unknown future studies

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 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. This is a publicly funded study. Samples from publicly funded studies are required to be shared as broadly as possible. However, we will protect your privacy. The goal of this is to make more research possible that may improve people's health.

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

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

- You will not be asked if you agree to take part in the future research studies.
- You and your study doctor will not be told when or what type of research will be done.
- You will not get reports or other information about any research that is done using your samples.

Unknown future research studies may include sequencing of all or part of your DNA. This is called genomic sequencing. Sequencing allows researchers to identify your genetic code. Changes in your genetic code may just be in your tumor tissue. These are called somatic changes. Changes may also be in your normal tissue and passed down through your family. For example, these genetic changes may be passed down to your children in the same way that eye and hair color are passed down. These are called germline changes.

What is involved in this optional sample collection?

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

1. About 2 teaspoons of blood will be collected from a vein in your arm if your disease gets worse if you are in the dose expansion group.
2. A sample from the tissue that was collected at the time of a previous biopsy of your tumor will be sent to the biobank.
3. 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.
4. 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.
5. Some of your genetic and health information may be placed in central databases for researchers to use. The databases will not include your name or contact information.

What are the risks in this optional sample collection?

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

How will information about me be kept private?

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

1. They will remove identifiers, such as your initials, from your sample and information. They will replace them with a code number. There will be a master list linking the code numbers to names, but they will keep it separate from the samples and information. 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 gender; 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 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, Mamta Parikh, at 916-734-3772, 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.

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

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, Mamta Parikh, at 916-734-3772.

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

Samples for known future studies:

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

YES NO

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

YES NO

Contact for Future Research

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

YES NO

This is the end of the section about optional studies.

My signature agreeing to take part in the study

I have read this consent form or had it read to me. I have discussed it with the study doctor and my questions have been answered. I will be given a signed and dated copy of this form. I agree to take part in the main study. I also agree to take part in any additional studies where I circled "yes".

Participant's signature

Date of signature

Signature of person(s) conducting the informed consent discussion

Date of signature

Patient Study Calendar

		Cycle 1 (Cycle Length = 21 days)						Cycles 2-6 (Cycle Length = 21 days)						Follow-up visits every 3 months	After you finish study treatment
	Before you begin study treatment	Day 1	Day 2	Day 8	Day 9	Day 14	Day 21	Day 1	Day 2	Day 8	Day 9	Day 14	Day 21		
BAY1895344[A]			X		X				X		X				
Cisplatin[B]		X		X				X		X					
Gemcitabine[C]		X		X				X		X					
Pre-study procedures including informed consent, demographics, medical history, height, and blood or urine collection for pregnancy test for women of childbearing potential)	X														
Concurrent meds	X	X----------X													
Physical exam, vital signs, and assessment of how you perform everyday tasks and activities[D]	X	X						X						X	X
Weight[D]	X	X						X							X
Blood draws for general health status[D]	X	X		X				X		X					X
Blood draws for complete blood count	X	X		X			X			X					X
EKG (as indicated)	X														
Side effects evaluations		X----------X													X

		Cycle 1 (Cycle Length = 21 days)						Cycles 2-6 (Cycle Length = 21 days)						Follow-up visits every 3 months	After you finish study treatment
	Before you begin study treatment	Day 1	Day 2	Day 8	Day 9	Day 14	Day 21	Day 1	Day 2	Day 8	Day 9	Day 14	Day 21		
Medical imaging scans for tumor measurements	X	Medical imaging scans for tumor measurements are repeated every 9 weeks.													X
Completion of Medication Diary			X		X				X		X				
Collection of left-over tumor tissue from your previous biopsy	X														
Optional Blood collection for research purposes															
Blood collection for research purposes check the level of study drugs in your blood (BAY1895344)			X[E]		X[E,F]										
Blood collection for research purposes check the level of study drugs in your blood (Gemcitabine)		X[G]													
Mandatory Blood collection for research purposes		X													
Optional Blood collection for research purposes (dose escalation group only)															X

		Cycle 1 (Cycle Length = 21 days)						Cycles 2-6 (Cycle Length = 21 days)						Follow-up visits every 3 months	After you finish study treatment
	Before you begin study treatment	Day 1	Day 2	Day 8	Day 9	Day 14	Day 21	Day 1	Day 2	Day 8	Day 9	Day 14	Day 21		

A: BAY1895344: Dose as assigned; Take on Day 2 and Day 9 of every 21-day cycle.

B: Cisplatin*:* Dose as assigned through a vein in your arm on Day 1 and Day 8 of every 21-day cycle for 6 cycles.

C: Gemcitabine. Dose as assigned, through a vein in your arm on Day1 and Day 8 of every 21-day cycle for 6 cycles.

D: May be performed within ±3 days, but must be obtained prior to receiving cisplatin treatment.

E: If you are in the dose escalation group: To be collected before treatment and then 30 minutes, 1h, 1.5h, 2h, 4h, 6h, 8h, and 24h after BAY1895344 treatment

F: If you are in the dose expansion group: To be collected before treatment and then 30 minutes, 1h, and 1.5h after BAY1895344 treatment

G: To be collected before treatment, 25 minutes into infusion (of Gemcitabine), 15 minutes, 30 minutes, and 60 minutes after infusion (of gemcitabine)