SUMMARY OF CHANGES- Consent

NCI Protocol #: 10402
Local Protocol #: PH110402
Protocol Version Date: July 31, 2024

Protocol Title: BAY1895344 Plus Topoisomerase-1 (Top1) Inhibitors in Patients with Advanced Solid Tumors, Phase I Studies with Expansion Cohorts in Small Cell Lung Carcinoma (SCLC), Poorly Differentiated Neuroendocrine Carcinoma (PD-NEC) and Pancreatic Adenocarcinoma (PDA)

Informed Consent Version Date: July 31, 2023

#	Section	Comments
1.	Header	The protocol version date and consent version date were changed to match the updated version date of the protocol. No other changes to the consent were made.

Research Study Informed Consent Document

Study Title for Participants: Testing the addition of an anti-cancer drug, BAY 1895344, to usual chemotherapy for advanced stage solid tumors, with a specific focus on patients with small cell lung cancer, poorly differentiated neuroendocrine cancer and pancreatic cancer.

Official Study Title for Internet Search on http://www.ClinicalTrials.gov: P10402, BAY 1895344 Plus Topoisomerase-1 (Top1) Inhibitors in Patients with Advanced Solid Tumors, Phase I Studies with Expansion Cohorts in Small Cell Lung Carcinoma (SCLC), Poorly Differentiated Neuroendocrine Carcinoma (PD-NEC) and Pancreatic Adenocarcinoma (PDA), (NCT#- NCT04514497)

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 an advanced solid tumor or small cell lung cancer, poorly differentiated neuroendocrine cancer or pancreatic cancer.

Taking part in this study is your choice.

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

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

Why is this study being done?

This study is being done to answer the following question:

Is it safe and tolerable to give BAY 1895344 in combination with topotecan or irinotecan in patients with advanced small cell lung cancer, poorly differentiated neuroendocrine cancer, and pancreatic cancer?

The combination of the experimental drug BAY 1895344 and topotecan or irinotecan is not approved by the Food and Drug Administration (FDA) for your cancer or any cancer.

What is the usual approach to my advanced solid tumor or advanced small cell lung cancer, poorly differentiated neuroendocrine cancer or pancreatic cancer?

The usual approach for patients with advanced solid tumors or these specific cancers, who are not enrolled in a study, is treatment with standard chemotherapy which targets DNA of cancer cells.

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 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 one of the following treatments until your disease gets worse, the side effects become too severe, your doctor believes it is no longer safe for you, or you desire to discontinue the study drugs:

1. BAY 1895344 on Days 1* and 2 plus irinotecan on Day 1 of each 14 day cycle
2. BAY 1895344 on Days 2 and 3, 9 and 10 and 16 and 17 plus irinotecan on Day 1,8 and 15 of each 21 day cycle (after cycle 2, Days 16 and 17 of BAY 1895344 and Day 15 of irinotecan will be dropped)
3. BAY 1895344 on Days 2 and 5* plus topotecan on Days 1-5 of each 21 day cycle

*Some people may only receive BAY 1895344 on Day 2 of each cycle.

Your doctor will tell you which treatment you are taking.

After you finish your treatment, your doctor and study team will watch you for side effects for 6 months. This follow up could occur by visiting your doctor or over the phone. If you stop treatment because you cannot tolerate it, we will check you every 6 weeks after your treatment and monitor disease response using CT scans.

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 BAY 1895344 plus irinotecan or topotecan may not be as good as the usual chemotherapy used to slow the spread of your cancer.

There is also a risk that you could have side effects from the combination of BAY 1895344 plus irinotecan or topotecan. 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 a blood transfusion
- nausea
- diarrhea
- vomiting
- constipation

There may be some risks that the study doctors do not yet know about. Combining BAY 1895344 with topotecan or irinotecan can result in some greater side effects experienced by the drug alone.

Benefits

There is some evidence in animals and in living human cells, that adding BAY 1895344 to irinotecan or topotecan can slow the growth of cancer for longer than seen with those drugs alone. However, we do not know if this will happen in people. It is unlikely that the combination of BAY 1895344 combined with irinotecan or topotecan 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 is important that you stop safely. This may mean slowly stopping the study drugs so that there is not a sudden unsafe change (e.g. risk to your health). 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.
- The study is stopped by the Food and Drug Administration (FDA), or study sponsor (NCI). The study sponsor is the organization who oversees the study.
- For women: You become pregnant while on 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 and tolerability of a drug called BAY 1895344 in combination with irinotecan or topotecan at different doses. There will be about 96 people taking part in this study, with up to 63 people in the first part of the study (Dose Escalation) and up to 33 people in the 2nd part (Dose Expansion) to further assess the safety and tolerability of the study drugs.

Irinotecan has already been approved by the FDA to treat pancreatic cancer while topotecan has already been approved by the FDA to treat small cell lung cancer.

We don't know if the combination of BAY 1895334 and irinotecan or topotecan works to treat cancer in people, but it has shrunk several types of tumors in animals.

Another purpose of the study is to check the level of the study drugs in your blood called pharmacokinetics or PK and to see if there are changes in levels of circulating tumor cells in your blood. To assess what effect the study drugs have on damaging the DNA of your cancer, pharmacodynamic or PD studies will be performed from the on-treatment tumor biopsies for patients in the expansion group. In addition, another objective of the study is for future biobanking studies related to your tumor and blood samples such as a biomarker study.

What are the study groups?

There are two parts in this study, a dose escalation (or dose-finding) part and a dose expansion part (further testing the safety and tolerability of the established dose found in the first part). Your doctor will tell you which part you are in.

The dose escalation part of this study involves two different drug combinations. Different people will get different doses of either BAY 1895344 and irinotecan or BAY 1895344 and topotecan. You will be told which combination and dose you will be receiving.

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

In the dose expansion parts of this study, the highest dose of BAY 1895344 and irinotecan with manageable side effects will be given to 11 more people with pancreatic cancer. The highest dose of BAY 1895344 and topotecan with manageable side effects will be given to 11 people with small cell lung cancer and 11 people with poorly differentiated neuroendocrine cancer. This will help study doctors better understand the side effects that may happen with these drug combinations. Depending on how BAY 1895344 is being supplied at your institution, you will take either two 10 mg tablets, or one 20 mg tablet. Your doctor will tell you how many tablets to take.

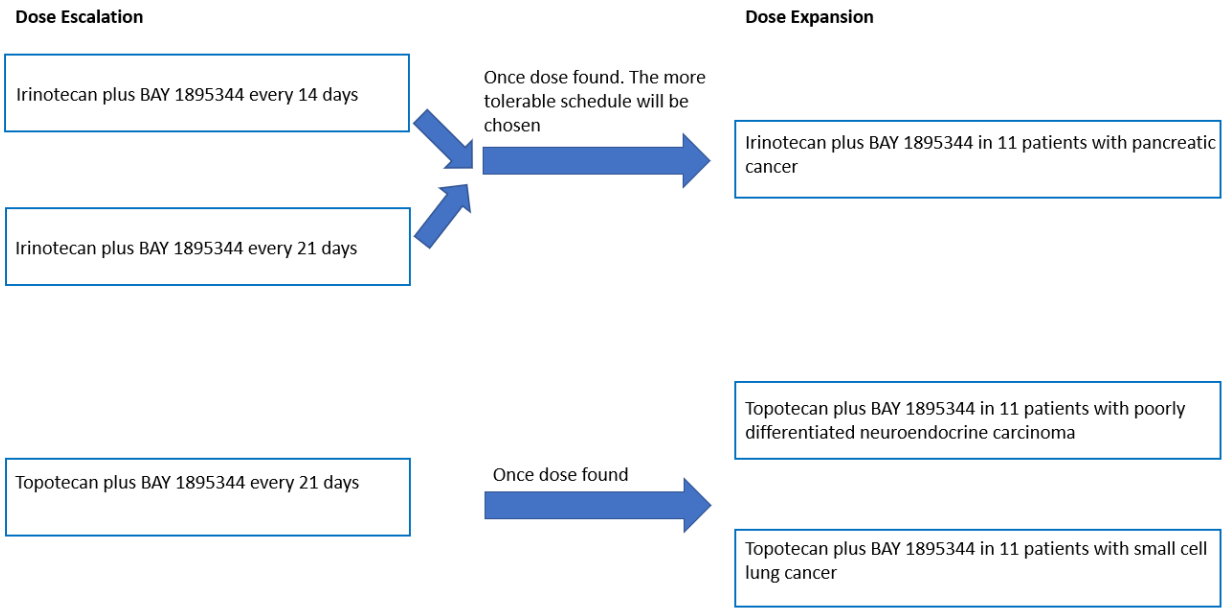
Dosing schedule (irinotecan group #1): You will get BAY 1895344 as a pill you will take by mouth twice a day on the first and second day of each cycle. Some people may only get BAY 1895344 on Day 2 of each cycle. You will also get irinotecan through a vein in your arm on the first day of each cycle. Each cycle lasts 14 days. Please see the patient study calendar for more information.

Dosing schedule (irinotecan group #2): You will get BAY 1895344 as a pill you will take by mouth once daily day 2, 3, day 9, 10 and day 16, 17 for cycle 1 and 2. You will also get irinotecan through a vein in your arm on the day 1, 8 and 15 of cycle 1 and 2. Each cycle lasts 21 days. After cycle 2, day 16, 17 of BAY 1895344 and day 15 of irinotecan will be dropped. Please see the patient study calendar for more information.

Dosing schedule (topotecan group): You will get BAY 1895344 as a pill you will take by mouth twice a day on the second and fifth day of each cycle. Some people may only get BAY 1895344 on Day 2 of each cycle. You will also get topotecan through a vein in your arm on days 1-5 of each cycle. Each cycle lasts 21 days. Please see the patient study calendar for more information.

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

Another way to find out what will happen to you during this study is to read the chart below. Start reading at the left side and read across to the right, following the lines and arrows.



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.

Some exams, tests, and procedures are a necessary part of the research study but would not be included in usual care. Listed below are procedures that will be done for research purposes only.

If you are in the dose expansion part of the study, you will need to have two biopsies for the study. The study biopsy takes small pieces of cancer tissue from your body. This is like the biopsy you had initially that helped diagnose your cancer. For patients in the irinotecan arm, the first biopsy will be done before you begin the study drug. The second biopsy will be taken on Day 3 of Cycle 1 or on Day 2 of Cycle 1, depending on which irinotecan dose schedule you are receiving. For patients in the topotecan arms, the first biopsy will be done before you begin the study drug. The second biopsy will be taken on Day 3 of Cycle 1 (prior to infusion). DNA damage markers will be measured from these biopsies to assess how the drugs you are receiving may damage the DNA of your cancer. These test results will be returned to your doctor however not to you. If you are unable to undergo the biopsies for technical reasons (difficulty reaching the tumor) or if you decide against undergoing the biopsies, you may be able to continue the study treatment.

Blood samples will also be taken for the study to check the levels of the study drugs in your blood and additional research studies (such as looking for the number of circulating tumor cells in your bloodstream). These will be taken on different days and times depending on whether you

are receiving irinotecan or topotecan. These blood samples will be taken through a needle in your arm.

For patients in the every 14 day irinotecan group:

- The first blood sample will be collected before you begin the study drug. You will have blood samples taken on Day 1 Cycle 1 before you begin treatment and at 30 minutes, 1 hour, 1 hour 20 minutes, 2 hours, 4 hours, 6 hours and 8 hours after you start the irinotecan. Additional blood samples will be taken on Day 2 of Cycle 1 at 24 hours after you took the first dose of the oral BAY 1895344 drug and Day 3 of Cycle 1 at 48 hours after you took the first dose of the oral BAY 1895344 drug.

  For patients in the every 21 day irinotecan group:

  The first blood sample will be collected before you begin the study drug. You will have blood samples taken on Day 1 Cycle 1 before you begin irinotecan treatment and at 30 minutes, 1 hour and 1 hour 20 minutes after the infusion start. You will also have blood samples drawn 30 minutes, 2 hour and 30 minutes and 4 hour and 30 minutes after completion of the irinotecan. Additional blood samples will be taken on Day 2 of Cycle 1 prior to the dose of the oral BAY 1895344 drug and at 30 minutes, 1 hour, 1 hour 20 minutes, 2 hour, 4 hour and 6 hour-post dose. You will also have blood samples taken on Day 3 of C1 prior to your second dose of the BAY 1895344 drug.

For patients in the topotecan group:

- The first blood sample will be collected before you begin the study drug. You will have blood samples taken on Day 1 Cycle 1 before you begin treatment, at 5 minutes, 15 minutes, 25 minutes after the start of topotecan, and at 5 minutes, 15 minutes, 1 hour, 2 hour, 4 hour and 6 hours after you finish topotecan. This will be repeated on Day 2 Cycle 1. Finally, on Days 3 and 4 of Cycle 1, you will have additional blood samples drawn prior to your topotecan infusion.

The results of these blood samples will not be returned to your doctor nor to you.

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 combination of BAY 1895344 and irinotecan and BAY 1895344 and topotecan may not be as good as the usual approach for your cancer at slowing the spread of 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 combination of BAY 1895344 and irinotecan or topotecan 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 that was obtained during your biopsies. 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.

Biopsy Risks

Common side effects of a biopsy include 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 lung collapse can occur. You may sign a separate consent form for the study biopsy that describes the risks in more detail.

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 drugs used in this study may affect how different parts of your body work such as your liver, kidneys, heart, and bone marrow. The study doctors will test your blood to see how these organs are affected 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.

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 about the study drugs 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 Irinotecan (Table Version Date: August 8, 2021)

COMMON, SOME MAY BE SERIOUS In 100 people receiving Irinotecan, more than 20 and up to 100 may have:
• Cholingeric syndrome, which may cause increased sweating, flushed skin, watering eyes, runny nose, drooling

COMMON, SOME MAY BE SERIOUS In 100 people receiving Irinotecan, more than 20 and up to 100 may have:
• Shortness of breath • Infection, especially when white blood cell count is low • Bruising, bleeding • Anemia which may cause tiredness, or may require blood transfusions • Severe diarrhea • Constipation, nausea, vomiting, loss of appetite, weight loss • Sores in mouth which may cause difficulty swallowing • Fever, pain • Dizziness, tiredness, weakness headache, chills • Hair loss, rash

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving Irinotecan, from 4 to 20 may have:
• Swelling of the body, including the belly • Low blood pressure which may cause feeling faint • Scarring of the lungs • Cough • Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat • Blood clot which may cause swelling, pain, shortness of breath • Yellowing of eyes and skin • Dehydration • Heartburn, passing gas • Difficulty sleeping

RARE, AND SERIOUS In 100 people receiving Irinotecan, 3 or fewer may have:
• Kidney damage which may cause swelling, may require dialysis • Confusion

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

COMMON, SOME MAY BE SERIOUS In 100 people receiving Topotecan, more than 20 and up to 100 may have:
• Shortness of breath • Infection, especially when white blood cell count is low

COMMON, SOME MAY BE SERIOUS In 100 people receiving Topotecan, more than 20 and up to 100 may have:
• Bruising, bleeding • Anemia which may require a blood transfusion • Constipation, diarrhea, nausea, vomiting • Fever • Pain • Tiredness • Hair loss

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving Topotecan, from 4 to 20 may have:
• Cough • Blockage of the bowels • Sores in mouth which may cause difficulty swallowing • Headache • Rash

RARE, AND SERIOUS In 100 people receiving Topotecan, 3 or fewer may have:
• Scarring of the lungs • Swelling of the bowels which may require surgery • Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat

Additional Drug Risks

The study drug could interact with other drugs. BAY 1895344 is broken down by the CYP3A4 system in the liver and other drugs which inhibit this enzyme could increase levels of the study drug. Furthermore, strong inducers of the CYP3A4 system can also affect levels of 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.

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.

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 you may be experiencing
    - 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 and for 4 months after the last dose of BAY 1895344. **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 the study treatment.

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 cost of the irinotecan and topotecan
- the costs of preparing the BAY 1895344, irinotecan or topotecan and the costs of administering the drugs
- 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 biopsy before you begin study treatment and on Day 3 of Cycle 1 or Day 4 of Cycle 1
- The research blood samples collected during the study on Days 1, 2 or Days 1, 2, 3 and 4 of Cycle 1.

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 sponsor will not pay for the medical treatment that may be needed to manage the 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 extremely 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 agent 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. These studies are separate from the main study described above. These optional studies will likely 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 likely will not know the results. Your study doctor may receive information about some of these results and choose to share them with you if he or she feels they may impact future treatments for you down the road.

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.

Known future studies

If you choose to take part in this optional study, researchers will collect your tumor tissue and blood for research in order to evaluate 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, which is sequencing of all or part of your DNA. All your genetic information makes up your genome. Genomic sequencing is a test that records all or part of the pieces of DNA that are in your genes, piece by piece. This is usually done to look for changes in your genome 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 genomic sequences from your tumor and blood cells to identify how they differ. The differences between genomic sequences of your tumor and blood cells may be important to understand why you did or did not respond to the treatment you received. Researchers hope to find potential "biomarkers" (changes present in tumor tissue that predict how patients with your type of cancer

may respond to current or future treatments). These optional studies may help improve the ability of study doctors to select future treatments or treatment combinations for others. These optional studies will not affect the cancer treatment you receive on the study.

Neither you nor your study doctor will be informed when the genetic sequencing research will be done. Your study doctor will receive reports of these studies and can decide, if he or she feels they may influence future treatment, to reach out to you about the results.

ATM Expression Loss in Tumor
A test to look at how much of a specific protein, ATM, is expressed by your tumor to see if it helps determine who responds to the study treatment.

DNA Damage Response Mutations
A test to look at whether your tumor possesses mutations in certain genes which may make it more sensitive to the study treatment.

Unknown future studies

If you choose to take part in this optional study, tumor and blood will be collected and 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 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.
- Future research studies may include genomic sequencing.
- 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.

If only tumor tissue is sequenced, we will not know if a genetic change in your tumor is also in your normal tissue. This is why sometimes both normal tissue and tumor tissue are sequenced. This helps researchers understand if a genetic change happened only in your cancer tissue, or in your normal tissue as well.

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 before you begin treatment. If you are in the dose expansion group, blood samples will also be taken if your disease gets worse at any time while you are on the study. A sample of tissue left over from your biopsy when you were diagnosed with the cancer will be sent to the biobank.
2. Your samples will be stored in the biobank. There is no limit on the length of time we will keep your samples and research information. The samples will be kept until they are used for research or destroyed.
3. Researchers can only get samples from the biobank after their research has been approved by experts. Researchers will not be given your name or contact information.
4. Some of your genetic and health information may be placed in central databases for researchers to use. The databases will not include your name or contact information.

What are the risks in this optional sample collection?

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

How will information about me be kept private?

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

1. They will remove identifiers, such as your initials, from your sample and information. They will replace them with a code number. There will be a master list linking the code numbers to names, but they will keep it separate from the samples and information. 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. If your doctor feels that a finding from these studies (for example, a mutation that is discovered in your tumor) may help with a future treatment for you, he or she will notify you individually.

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 a possible biopsy, blood draw, DNA/RNA sequencing from tumor and blood, test looking at how much ATM protein is in your tumor, 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 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

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

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 Calendars

Irinotecan Group #1

	Before You Begin Study Treatment	Cycle 1		Cycle 2		Cycle 3		Cycle 4		Cycle 5		Cycle 6+		When You Finish Study Treatment
		Wk 1	Wk 2	Wk 1	Wk 2	Wk 1	Wk 2	Wk 1	Wk 2	Wk 1	Wk 2	Wk 1	Wk 2	
BAY 1895344		A		A		A		A		A		A		
Irinotecan		B		B		B		B		B		B		
Pre-study (before you begin study treatment) procedures, including informed consent, demographics and medical history	X													
Height	X	X		X		X		X		X		X		
Check of all medications that you are taking		X----------											-----X	
Physical exam and vital signs	X	X		X				X		X		X		X
Weight	X	X		X		X		X		X		X		X
An assessment of how you perform everyday tasks and activities	X	X		X		X		X		X		X		X
Blood draws for complete blood count and general health status	X	X		X		X		X		X		X		X
EKG (as your doctor indicates is necessary)	X													
Side effect evaluation		X----------											-----X	X
Medical imaging scan for tumor measurements	X	Measurements are repeated every 6 weeks												X
Pregnancy test (for women of childbearing potential only)	X													
Collection of left over tumor tissue from previous biopsy	X													
Tumor Biopsy[a] for research purposes	X	X												
Blood collection for research purposes to check the level of study drug in your blood[b]		X												
Blood collection for additional research purposes (mandatory)	X													
Blood collection for additional research purposes (optional – dose expansion group only)														X
A: BAY 1895344: Dose as assigned. Take twice a day on Days 1 and 2 of each cycle (Some people may only take BAY 1895344 on Day 2 of each cycle. This will be conveyed to you by your														

doctor). Cycle Length = 14 days.

B: Irinotecan: Dose as assigned. IV on Day 1 of each cycle. Cycle Length = 14 days.

a: The first biopsy will be collected within 7 days (± 3 days) of study initiation. The second biopsy will be collected on Cycle 1 Day 3

b: Blood collection will occur on Cycle 1 Days 1, 2 and 3

Irinotecan Group #2

	Pre-Study	Cycle 1			Cycle 2			Cycle 3*			Cycle 4+			When You Finish Study Treatment
		Wk 1	Wk 2	Wk 3	Wk 1	Wk 2	Wk 3	Wk 1	Wk 2	Wk 3	Wk 1	Wk 2	Wk 3	
BAY 1895344		A	A	A	A	A	A	A	A		A	A		
Irinotecan		B	B	B	B	B	B	B	B		B	B		
Pre-study (before you begin study treatment) procedures, including informed consent, demographics and medical history	X													
Height	X	X			X			X			X			
Medical history	X													
Check of all medications that your are taking	X	X----------X												
Physical exam and vital signs	X	X			X			X			X			X
Weight	X	X			X			X			X			X
As assessment of how you perform your everyday tasks	X	X			X			X			X			
Blood draws for complete blood count and general health status	X	X	X	X	X	X	X	X	X		X	X		
EKG (as your doctor indicates is necessary)	X													
Side effect evaluation		X----------X												X
Medical imaging scan for tumor measurements	X	Tumor measurements are repeated every _6_ weeks. Documentation (radiologic) must be provided for patients removed from study for progressive disease.												X
Pregnancy test (for women of child bearing potential)	X													
Collection of left over tumor tissue from previous biopsy	X													
Tumor Biopsy[a]	X	X												

Blood collection for research purposes to check the level of study drug in your blood[b]		X												
Blood collection for additional research purposes (mandatory)	X													
Blood collection for additional research purposes (optional-dose expansion group)														X

*Please note after C2 patients will receive a 1 week treatment break (7 days) prior to starting C3

A: BAY 1895344: Dose as assigned; Take once per day on D2,3, D9,10 and D16,17 by mouth. After cycle 2, D16,17 doses are dropped. Cycle Length = 21 days.

B: Irinotecan: Dose as assigned D1,8, 15 IV. After cycle 2, D15 dose is dropped. Cycle Length= 21 days.

a: The first biopsy will be collected within 7 days (± 3 days) of study initiation. The second biopsy will be collected on Cycle 1 Day 2

b: Blood collection will occur on Cycle 1 Days 1,2 and 3

Topotecan Group

	Before You Begin Study Treatment	Cycle 1			Cycle 2			Cycle 3			Cycle 4+			When You Finish Study Treatment
		Wk 1	Wk 2	Wk 3	Wk 1	Wk 2	Wk 3	Wk 1	Wk 2	Wk 3	Wk 1	Wk 2	Wk 3	
BAY 1895344		A			A			A			A			
Topotecan		B			B			B			B			
Pre-study (before you begin study treatment) procedures, including informed consent, demographics, and, medical history	X													
Height	X	X		X		X		X		X		X		
Check of all medications that you are taking		X----------X												
Physical exam and vital signs	X	X			X			X			X			X
Weight	X	X			X			X			X			X
An assessment of how you perform everyday tasks and activities	X	X			X			X			X			X
Blood draws for complete blood count and general health status	X	X			X			X			X			X
EKG (as your doctor indicates is necessary)	X													
Side effect evaluation		X----------X												X
Medical imaging scans for tumor measurements	X	Measurements are repeated every 6 weeks												X
Pregnancy test (for women of childbearing potential only)	X													
Collection of left over tumor tissue from previous biopsy														
Tumor Biopsy[a] for research purposes	X	X												
Mandatory blood collection for research purposes to check the level of study drug in your blood[b]		X												
Mandatory blood collection for additional research purposes	X													
Optional blood collection for additional research purposes (dose expansion group only)														X

A: BAY 1895344: Take pill twice a day on Days 2 and 5 of each cycle (Some people may only take BAY 1895344 on Day 2 of each cycle. This will be conveyed to you by your doctor). Dose as assigned
B: Topotecan: IV on days 1-5 of each cycle. Dose as assigned
a: The first biopsy will be collected within 7 days (± 3 days) of study initiation. The second biopsy will be collected on Cycle 1 Day 3 (prior to infusion)
b: Blood collection will occur on Cycle 1 Days 1, 2, 3 and 4