SUMMARY OF CHANGES – Consent

NCI Protocol #: 10211
Local Protocol #: VICC LOI #18012
Protocol Version Date: December 2, 2022

Protocol Title: A Phase 2 Single-Arm Study of M6620 in Combination with Irinotecan in Patients with Progressive TP53 Mutant Gastric and Gastro-Esophageal Junction Cancer

This consent is being amended:

- Update version date of protocol
- To address a CTEP recommendation per review on September 14, 2022

Informed Consent Version Date: 12/02/2022

#	Section	Page	Request for Amendment (RA)
1	**Footer**	**All**	**OLD TEXT: Version Date: August 17, 2022** **NEW TEXT: Version Date: December 2, 2022** **RATIONALE: Updated version date in footer**
2	Side effects of irinotecan	**8**	Please update the irinotecan risk list to the latest version (August 8, 2021) available on our website: **https://ctep.cancer.gov/protocolDevelopment/sideeffects/drugs.htm** **PI Response:** Updated as requested

Research Study Informed Consent Document

Study Title for Participants: Testing the addition of M6620 to Irinotecan in TP53 mutant stomach and gastro-esophageal junction (GEJ) cancer

Official Study Title for Internet Search on http://www.ClinicalTrials.gov: 10211, "A Phase 2 Single-Arm Study of M6620 in Combination with Irinotecan in Patients with Progressive TP53 Mutant Gastric and Gastro-Esophageal Junction Cancer," (NCT03641313)

Overview and Key Information

What am I being asked to do?

We are asking you to take part in this research study because you have gastric or gastro-esophageal cancer and your tumor has a TP53 mutation. TP53 is a gene that plays a role in the regulation of cell growth. We do research studies to try to answer questions about how to prevent, diagnose, and treat diseases like 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:

Will patients like you, with progressive stomach and GEJ cancers (TP53 mutation positive) benefit from adding a treatment that blocks a molecule involved in repairing tumor DNA when it is damaged (M6620) to standard-of-care chemotherapy with irinotecan?

What is the usual approach to my stomach or gastro-esophageal junction (GEJ) cancer?

The usual approach to treating stomach or GEJ cancer is chemotherapy. You have already been treated with chemotherapy and your disease is growing. People who are not in a study are

usually treated with more chemotherapy, which could include the Food and Drug Administration (FDA)-approved irinotecan.

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

If you decide not to take part in this study, you have other choices. For example:

- you may choose to have the usual approach described above
- you may choose to take part in a different study, if one is available
- or you may choose not to be treated for cancer but you may want to receive comfort care to relieve symptoms.

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

If you decide to take part in this study, you will receive intravenous irinotecan followed by intravenous M6620 twice per month, with 14 days in between doses, until your disease gets worse or the side effects become too severe.

After you finish your study treatment, your doctor and study team will watch you for side effects. They will check you at approximately 30 days after you stop treatment for any side effects that may have occurred. They will also check you every 2 months for up to 1 year after treatment. This means you will either see your doctor in clinic or speak to someone from the study team on the telephone for up to 1 year. If you have a serious side effect during the study, the study doctor may ask you to visit the office for follow-up examinations, even after you have completed your regular study visits.

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 M6620 plus irinotecan may not be as good as chemotherapy alone with irinotecan at shrinking your tumor or stabilizing your disease.

There is also a risk that you could have side effects from the M6620 and irinotecan. These side effects may be worse and may be different than you would get with the usual approach with irinotecan or other chemotherapy approaches for stomach and GEJ cancer.

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

- Low red cells which may require blood transfusion

- Diarrhea, nausea, vomiting
- Tiredness
- Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat
- Infection which may cause painful and frequent urination

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

Benefits

The combination of M6620 and irinotecan has been shown to be safe in a limited number of people with your cancer and has shown increased effectiveness compared to chemotherapy alone in animals or in living human cells with TP53 mutations. We hope that this strategy will work in some patients with your cancer. This study may help the study doctors learn things that may help other people in the future.

If I decide to take part in this study, can I stop later?

Yes, you can decide to stop taking part in the study at any time.

If you decide to stop, let your study doctor know as soon as possible. It's important that you stop safely. If you stop, you can decide if you want to keep letting the study doctor know how you are doing.

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

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

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

- 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 get bad side effects from the treatment that you cannot tolerate.
- You do not follow the study rules.
- For women: You become pregnant while on the study.
- The study is stopped by the Institutional Review Board (IRB), Food and Drug Administration (FDA), or study sponsor (National Cancer Institute). The study sponsor is the organization who oversees the study.

Because of these reasons, we cannot predict the length of time that you will be on study. However, your anticipated participation time on this study is up to 1 year after you finish your study treatment.

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?

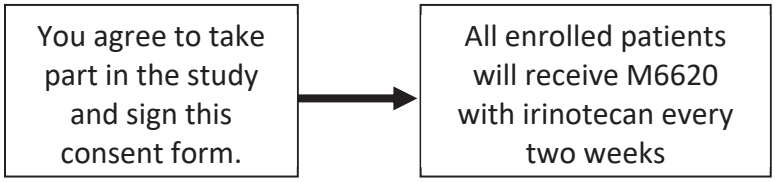
TP53 mutant tumors are particularly aggressive and the hope of this study is to identify a treatment approach that can take advantage of some of the characteristics of these tumors to improve patient outcomes.

The purpose of this study is to test any good and bad effects of the study drug called M6620 when given with irinotecan. The combination of M6620 and irinotecan could shrink your cancer, but it could also cause side effects. Researchers hope to learn if the study drug will shrink the cancer by at least one-quarter compared to its present size. Irinotecan has already been FDA-approved to treat your cancer. M6620 has not been FDA-approved to treat any types of cancer. We don't know if M6620 plus irinotecan works to treat cancer in people, but it has shrunk several types of TP53 mutant tumors in animals. There will be about 18 people taking part in this study.

What are the study groups?

All study participants will get the same study intervention. It will include the usual chemotherapy irinotecan and the study drug M6620, as follows:

- On Days 1 and 15 of each 28-day cycle, you will receive the study drugs through a vein.
- Irinotecan will be given first over 90 minutes.
- M6620 will be given immediately following irinotecan over 60 minutes.



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

Most of the exams, tests, and procedures you will have are part of the usual approach for your cancer. CT scans will be done to see the size of your tumor before you start irinotecan and M6620. Blood samples will also be needed before you start therapy to see how your organs and other body systems are functioning. These are part of your standard treatment if you were not in a study.

However, there are some extra procedures that you will need to have if you take part in this study.

You will need to have the following extra research-related procedures:

- Biopsy (9 patients) on day 1 of your first cycle of treatment after getting the first drug (irinotecan)
- Biopsy (9 patients) on day 2 of your second cycle of treatment

Small pieces of your cancer will be collected through two biopsy procedures, one after getting the first drug on day 1 of your treatment and one on day 2 after your second cycle of therapy. These samples are required from 9 patients in order to evaluate if M6620 is working to block the intended target. The research biopsy is done in a similar way to biopsies done for diagnosis. A doctor will use an endoscopic procedure called an endoscopic biopsy that uses a flexible thin tube (endoscope) entered through your mouth in order to collect samples from your stomach or GEJ cancer.

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 for your cancer at shrinking or stabilizing your cancer.

You also may have the following discomforts:

- Spend more time in the hospital or doctor's office.
- Be asked sensitive or private questions about things you normally do not discuss
- May not be able to take part in future studies.
- There is a risk someone could get access to the personal information in your medical records or other information researchers have kept about you. Someone might be able to trace this information back to you. The researchers believe the chance that someone will identify you is very small, but the risk may change in the future as people come up with new ways of tracing information.

The drugs 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 sue during the study and for 6 months after you have completed the study.

Biopsy Risks

Gastrointestinal endoscopy is a very low risk procedure. However, all of the possible common side effects are listed below:

- Bleeding: Bleeding, if it occurs, is usually a complication of biopsy, polyp removal, dilation, or fine needle aspiration. Management of this complication may consist only of careful observation. Blood transfusions and surgery are rarely needed.
- Perforation: Passage of the endoscope may result in an injury or tear to the gastrointestinal tract wall, with possible leakage of gastrointestinal contents into the body cavity. Perforations can be small requiring a few days of hospitalization, but could be severe requiring prolonged hospitalization and/or surgery.

- Infection: Infection or irritation resulting in inflammation (phlebitis) may occur at the intravenous site and may require treatment. Rarely, passage of the endoscope and manipulations may cause infection elsewhere in the body. Fine needle biopsy could possibly cause a serious infection.
- Sedation: Risks of sedation include aspiration pneumonia, cardiac or respiratory arrest from the sedatives or potential allergic reactions to the drugs. Post procedure complications can include nausea and vomiting.
- Other risks: Complications from other diseases you may already have. Instrument failure could occur rarely, requiring a repeat procedure. Aspiration or dental injury is a possible risk of upper endoscopy procedures. Serious or fatal complications from endoscopy are extremely rare.

Your privacy is very important and the researchers will make every effort to protect it. Your test results will be identified by a unique code and the list that links the code to your name will be kept separate from your sample and health information. The results from the biopsy are for research purposes only and will be assessed by the study doctor during the initial analysis not be made available to you or your study doctor after the first nine patients complete treatment.

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 blood. The study doctor will be testing your blood and will let you know if changes occur that may affect your health.

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

Here are important points about side effects:
- The study doctors do not know who will or will not have side effects.
- Some side effects may go away soon, some may last a long time, or some may never go away.
- Some side effects may interfere with your ability to have children.
- Some side effects may be mild. Other side effects may be very serious and may even result in death.

You can ask your study doctor questions about side effects at any time. Here are important points about how you and the study doctor can make side effects less of a problem:
- Tell the study doctor if you notice or feel anything different so they can see if you are having a side effect.
- The study doctor may be able to treat some side effects.
- The study doctor may adjust the study drugs to try to reduce side effects.
- The study doctor will provide you with information about other drugs you may need to avoid while receiving the study drug.

This study is looking at a combination of a usual treatment used to treat your 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 the most serious side effects that researchers know about. There might be other side effects that researchers do not yet know about. If important new side effects are found, the study doctor will discuss these with you.

Possible Side Effects of M6620

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 • Severe diarrhea • Constipation, nausea, vomiting • Infection, especially when white blood cell count is low • Hair loss • Loss of appetite, weight loss • Anemia, which may cause tiredness or may require blood transfusions • Fever, pain • Dizziness, tiredness, weakness, headache, chills • Shortness of breath • Sores in mouth, which may cause difficulty swallowing • Rash • Bruising, bleeding

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 • 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 • Scarring of the lungs • 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

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.

What are my responsibilities in this study?

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

- Keep your study appointments.
- Tell your doctor about:
  - all medications and supplements you are taking
  - any side effects
  - any doctors' visits or hospital stays outside of this study
  - if you have been or are currently in another research study.

For women: Do not get pregnant or breastfeed while taking part in this study. **For men:** Do not father a baby while taking part in this study. **For all:** Tell your study doctor right away if you think that you or your partner have become pregnant during the study or within 6 months after your last dose of 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 costs of getting the irinotecan 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.

M6620 will be supplied at no charge while you take part in this study. The cost of getting the M6620 ready and giving it to you is not paid by the study sponsor so you or your insurance company may have to pay for this. It is possible that M6620 may not continue to be supplied while you are on the study. Although not likely, if this occurs, your study doctor will talk to you about your options.
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:

- research biopsies.

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.

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 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 of M6620 and irinotecan now or in the future.
- The Investigational Review Board (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 Federal Drug Administration (FDA) and the groups it works with to review research.
- The National Cancer Institute (NCI) and the groups it works with to review research.

Your study records also will be stored for future use. However, your name and other personal information will not be used. Some types of future research may include looking at your records and those of other patients to see who had side effects across many studies or comparing new

study data with older study data. However, we don't know what research may be done in the future using your information. This means that:

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

Where can I get more information?

You may visit the NCI web site at http://cancer.gov/ for more information about studies or general information about cancer. You may also call the NCI Cancer Information Service to get the same information at: 1-800-4-CANCER (1-800-422-6237).

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

You can talk to the study doctor about any questions or concerns you have about this study or to report side effects or injuries. Contact the study doctor (*insert name of study doctor[s]*) at (*insert telephone number, and 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*).

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.

Participant's signature

Date of signature

Signature of person(s) conducting the informed consent discussion

Date of signature