FOX CHASE CANCER CENTER
TEMPLE HEALTH

FOX CHASE CANCER CENTER
AT TEMPLE UNIVERSITY HOSPITAL
All hospital services provided by Temple University Hospital

INFORMED CONSENT DOCUMENT

Quinacrine–Capecitabine Combinatorial Therapy for Advanced Stage Colorectal Adenocarcinoma: A Phase I/II Investigator Initiated Clinical Trial

Principal Investigator: Crystal Denlinger, MD

This is a clinical trial, a type of research study. Research studies are voluntary and include only people who choose to take part. Please read this consent form carefully and take your time making your decision. As your study doctor or and study staff discusses this consent form with you, please ask him/her to explain any words or information that you do not clearly understand. We encourage you to talk with your family, friends or family doctor before you decide to take part in this research study.

You are being asked to take part in this research study because you have advanced stage colorectal cancer that is metastatic, meaning it has spread.

The sponsor of this study is the Fox Chase Cancer Center.

Why is this research study being done?

The purpose of the first part of this research study, (Phase 1) is to find the maximum dose of quinacrine and capecitabine that can be given together without causing severe or intolerable side effects. Study doctors will determine the safety and side effects of the combination of quinacrine and capecitabine in patients with advanced metastatic colorectal cancer.

The purpose of the second part of this study (Phase 2) is to see how well patients being treated with quinacrine and capecitabine respond to treatment.

We do not know if you will benefit from this research study. It is possible that your condition will get better, but it is also possible that there will be no effect on your condition or that your condition will get worse. We can use what we learn from this research study to help other people with the same disease.

How many people will take part in this research study?

Between 3 and 18 people will be a part of Phase 1 and between 10 and 29 additional patients will be a part of Phase 2.

What will happen if you take part in this research study?

Before you begin the research study

You will need to have the following exams, tests or procedures to find out if you can be in the research study.

These exams, tests, or procedures are part of regular cancer care and may be done even if you do not join the research study. If you have had some of them recently, they may not need to be repeated. This will be up to your study doctor.

- Medical history including and medications or supplements you may be taking
- Physical exam
- Vital signs including
    - Heart rate or pulse
    - Blood Pressure
    - Breathing rate
    - Temperature
- Height
- Weight
- Blood Counts: (1 teaspoon of blood)
- Blood Chemistry: (2 teaspoons of blood)
- CEA and CA 19-9 Blood tests (about 4 teaspoons)
- ECG (as needed, this is a test to measure the electrical activity of your heart)
- Tumor Imaging and measurements using a CT Scan or MRI
    - A CT scan is a computerized x-ray that gives your study doctor pictures of the inside of your body
    - A MRI scan uses a magnetic field and radio waves to take pictures of the inside of your body
- Blood Pregnancy Test (2 teaspoons of blood)
- Study Related Blood Tests
- Blood collection for future research (about 7 tablespoons of blood)
- If you choose to agree, tissue from your tumor will be sent to Caris Life Sciences for biomarker testing and mutational analysis. Mutational analysis or testing identifies changes or abnormalities in the DNA of your cancer tissue.
    - This information will become a part of your permanent medical records, your clinical trial records and a copy of the report will be given to your study doctor.
    - Your tumor tissue may be from a previous biopsy or a new biopsy if you are scheduled to have one. You will not be asked to have a new biopsy solely for this optional tissue collection.
    - You will be asked to sign a separate consent form for this optional testing.
    - Your decision will not affect your ability to participate in this clinical research study.

During the research study

Study Treatment

- Treatments will be given in a 21-day period called a cycle.
- On day 1 of every cycle, you will receive both study drugs, quinacrine and capecitabine.
- Both quinacrine and capecitabine are pills that are taken orally.
- Quinacrine should be taken after a meal with water.
- You will take quinacrine each day of the cycle (Days 1-21).
- Capecitabine should be taken within 30 minutes after a meal with water.
- You will take capecitabine days 1-14 of the cycle.

If you are in the phase I part of this study, you will have up to 6 cycles of treatment. Once the safe level of quinacrine is found in phase I, you may be able to be a part of phase 2. Your treatment may last up to a year in total.

If you start in the phase 2 part you will have up to 1 year of treatments.

Your study doctor will tell you your dose and how many pills of capecitabine and quinacrine to take. The capecitabine dose is based on your height and weight.
You should not drink alcohol or use medicines that have alcohol in them like cough syrup or dental mouthwashes while taking the study medications.

Tests and Procedures

If the exams, tests and procedures show that you can be in the research study, and you choose to take part, then you will need the following tests and procedures. They are part of regular cancer care.

- Physical exam
- Vital signs
    - Heart rate or pulse
    - Blood Pressure
    - Breathing rate
    - Temperature
- Weight
- Blood Counts: (1 teaspoon of blood)
- Blood Chemistry: (2 teaspoons of blood)
- CEA and CA 19-9 Blood tests (about 4 teaspoons) (Day 1 of every cycle)
- Tumor Imaging and measurements using a CT Scan or MRI (After every 3 Cycles)
    - A CT scan is a computerized x-ray that gives your study doctor pictures of the inside of your body
    - A MRI scan uses a magnetic field and radio waves to take pictures of the inside of your body

You will need these tests and procedures that are either being tested in this research study or being done to see how the research study is affecting your body.

- Study Related Blood Tests
    - Pharmacokinetic (PK) study (to measure the amount of quinacrine and capecitabine in your blood. (about 2 teaspoons of blood)
        - This will be done several times:
            - Before you receive study drugs on day 1 of your first treatment
            - 1 Hour after your first treatment
            - 2 Hours after your first treatment
            - 4 Hours after your first treatment
            - 8 Hours after your first treatment
            - Cycle 2 Day 1
            - Cycle 3 Day 1

After you are finished study treatment

You will be followed for the rest of your life.

How long will you be in the research study?

You will be asked to take quinacrine and capecitabine as long as you are benefitting from treatment. After you are finished treatments, the research study will involve long-term follow-up. We would like to keep track of your medical condition for the rest of your life. We would like to do this by calling you on the telephone once a year to see how you are doing. Keeping in touch with you and checking on your condition every year helps us look at the long-term effects of the study.

Can you stop being in the research study?

Yes. Your participation in this research is completely voluntary. If you agree to participate now and change your mind later, you may withdraw at any time. Tell the study doctor if you are thinking about stopping or decide to stop. He or she will tell you how to stop safely and will discuss with you options for withdrawal such as continuing to provide further data collection from routine medical care.
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Can you be removed from this research study?

The study doctor may stop you from taking part in this research study at any time if he/she believes it is in your best interest; if you do not follow the research study rules; or if the research study is stopped.

What side effects or risks can you expect from being in the research study?

You may have side effects while on the research study. Everyone taking part in the research study will be watched carefully for any side effects. However, doctors don't know all the side

effects that may happen. Side effects may be mild or very serious. Your health care team may give you medicines to help lessen side effects. Many side effects go away soon after you stop taking the quinacrine and capecitabine. In some cases, side effects can be serious, long lasting, or may never go away. There is also a risk of death.

You should talk to your study doctor about any side effects that you have while taking part in the research study. The combination of quinacrine and capecitabine may involve risks that are unknown.

It is not clear how often or severe the side effects quinacrine will be. However, some risks and side effects possibly related to the quinacrine include those which are:

Likely (≥ 20%)

- loss of appetite
- nausea (Feeling sick to your stomach)
- vomiting (Throwing Up)
- diarrhea
- dizziness
- stomach pain
- fever

Less likely (5% to 19%)

- headache
- nervousness
- black and blue skin
- blurred vision or visual 'halos'
- emotional or mood changes
- nightmares
- trouble sleeping
- seizures (convulsions)
- skin rash, itching, peeling skin
- yellowing of the eyes or skin
- hepatitis
- abnormal heart rhythm (beating slow, fast or irregularly)
- yellow nails or urine (this will go away when you stop taking the medicine)

Rare but Serious (< 5%)

- confusion
- Aplastic anemia
    - A condition where the bone marrow does not make enough blood cells

Risks and side effects related to the Capecitabine include those which are:

Likely (≥ 20%)

- Tiredness
- Palmar-Plantar Erythrodyesthesia (Hand-Foot-Syndrome) Redness, tenderness, pain and possible peeling of the palms of the hands and soles of the feet. The redness looks like a sunburn. The affected area can become dry and peel with numbness or tingling developing
- Diarrhea – increased frequency of bowel movements with loose, watery stools
- Skin inflammation

- Abnormal sensation of the skin that may include numbness, tingling, pricking, burning, or creeping feeling on the skin
- Anemia (low hemoglobin, low hematocrit or low red blood cell count) Red blood cells carry oxygen and nutrients throughout the body. Symptoms that may be experienced as a result of low red blood cell counts may include feeling tired and weak, shortness of breath, increased heart rate, dizziness or lightheadedness, headache, chest pain and pale skin
- Leukopenia/Neutropenia: (low white blood cell count) A low white blood cell count makes it hard for you to fight off infections
- Thrombocytopenia (low platelet count) Platelets are important in stopping bleeding. A low platelet count can increase the time to form a blood clot
- Mucositis/stomatitis- sores in the lining of your mouth and/or throat that can be painful and make it hard to swallow
- Nausea-feeling sick to your stomach
- Vomiting- throwing up
- Decrease or Loss of appetite
- Belly pain
- Elevated liver enzymes: Liver enzymes are proteins made by the liver that are measured in the blood, with a blood draw. Liver enzymes indicate how well your liver is functioning. Elevated liver enzymes may or may not indicate damage to your liver. You may not feel any symptoms, however higher liver enzyme levels may cause you to feel overly tired or weak, you may bruise or bleed more easily, and you may experience abdominal pain or have a yellowing of the skin or eyes

Less Likely (5% to 19%)

- Swelling of the extremities
- Fever
- Pain
- Irritation of the eyes
- Shortness of breath
- Loss of hair
- Changes in skin color or nail changes
- Heartburn
- Constipation – difficulty having a bowel movement
- Blood clots
- Headache
- Dizziness
- Difficulty falling asleep
- Change in mood or depression
- Skin redness
- Skin rash
- Dehydration – loss of water in the body which can cause weakness, dry mouth, increased thirst, dark urine, and decreased urination
- Bleeding
- Changes in taste
- Muscle or joint pain
- Pain in back, arms or legs
- Vision changes
- Cough
- Difficulty swallowing

Rare But Serious (< 5%)

- Chest pain
- Heart attack – symptoms may include chest pain/tightness, shortness of breath, nausea, sweating, dizziness
- Abnormal heart rhythm that could cause your heart beat differently (too fast or slow) – symptoms may include make you feel tired or short of breath
- Stroke
- Difficulty breathing
- Clotting disorders
- Bowel inflammation or obstruction causing death of tissue
- Radiation recall reaction – a sunburn-like reaction in an area that has received radiation
- Death

Radiation Risk for Diagnostic Imaging

- It is unlikely that there will be any harmful effects from the radiation exposure you will receive from participating in this study.
- At high levels of exposure, scientists agree that radiation can cause cancer.
- At low exposure levels most scientists agree that the risk, if any, is very low. You will have low levels of radiation exposure with diagnostic imaging procedures.
- Risks from exposure to radiation may accumulate over a lifetime.

Blood Draw Risks

- Fainting
- Bleeding
- Bruising at the place on your arm where the blood was drawn or needle inserted
- Pain
- Swelling
- Infection (rare)

Reproductive Risks

- Study treatment may make you sterile (unable to have children).
- The drugs in this study may affect a baby, before or after the baby is born.
- You should not become pregnant or father a baby while on this research study because the drugs you take could possibly hurt an unborn baby.
- If you are pregnant now or if you are breast-feeding now, you may not take part in this research study.
- If you become pregnant while you are on the research study, you may not continue to take part in the research study.

<u>For women who can become pregnant</u>:

- You should not become pregnant while you are in this study.
- You should not breast-feed your baby while taking drugs for this research study.

<u>For men:</u>

- You should not make a woman pregnant while you are in this study.

<u>For women and men:</u>

- If you are having sex that could lead to pregnancy, you should use birth control while you are in this study.

- Check with the study doctor about birth control methods and how long to use them. Some methods might not be approved for use in this study.

Are there benefits to taking part in the study?

Taking part in this study may or may not make your health better. While doctors hope that quinacrine and capecitabine will be more useful against cancer compared to the usual treatment, there is no proof of this yet. We do know that the information from this study will help doctors learn more about quinacrine and capecitabine as a treatment for cancer. This information could help future cancer patients.

What other choices do you have if you do not take part in this research study?

Your other choices may include:
- Getting treatment or care for your cancer without being in a study
- Taking part in another study
- Getting no treatment

Talk to your doctor about your choices before you decide if you will take part in this study.

Will your medical information be kept private?

We will do our best to make sure that the personal information in your medical record will be kept private. However, we cannot guarantee total privacy. Your personal information may be given out if required by law. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used.

Organizations that may look at and/or copy your medical records for research, quality assurance, and data analysis include:
- Fox Chase Cancer Center and affiliated Joint Centers, The Institutional Review Boards of The Fox Chase Cancer Center and Temple University, Temple University, Temple University Health System, Inc., and its affiliates or subsidiaries and other authorized representatives of these organizations.
- The National Cancer Institute (NCI) and other government agencies, like the Food and Drug Administration (FDA), involved in keeping research safe for people

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 will be given a separate form to review regarding the steps we will take to guard your privacy as part of your participation in the research study. By signing that additional authorization, you will be providing your consent to use and disclose information described in that form connected with your participation in this research study.

What are the costs?

You and/or your health plan/insurance company will need to pay for some or all of the costs of treating your cancer in this study. Some health plans will not pay these costs for people taking part in studies. Check with your health plan or insurance company to find out what they will pay for. Taking part in this study may or may not cost your insurance company more than the cost of getting regular cancer treatment.

Even though it probably won't happen, it is possible that the manufacturer may not continue to provide the quinacrine for this study. If there is no quinacrine available at all, no one will be able to get more and the study would close.

If your insurance will not pay for medicines you may need to help with side effects, you may have to pay for them.

For more information on clinical trials and insurance coverage, you can visit the National Cancer Institute's Web site at http://cancer.gov/clinicaltrials/understanding/insurance-coverage . You can print a copy of the "Clinical Trials and Insurance Coverage" information from this Web site.

Another way to get the information is to call 1-800-4-CANCER (1-800-422-6237) and ask them to send you a free copy.

Will you be compensated?

You will not be paid for taking part in this research study.

What if you are injured while taking part in this research study?

If you are injured as a result of your participation in this research study, seek immediate medical care. Temple University Health System or its subsidiaries will treat the injury, though there is no commitment to provide monetary compensation or free medical care. Other financial compensation (such as lost wages or pain and suffering) for such injuries is not available. In the case of injury resulting from this study, you do not lose any of your legal rights to seek payment by signing this form.

What are your rights if you take part in this research study?

Taking part in this research study is your choice. You may choose either to take part or not to take part in the research study. If you decide to take part in this study, you may leave the study at any time. No matter what decision you make, there will be no penalty to you and you will not lose any of your regular benefits. Leaving the study will not affect your medical care. You can still get your medical care from our institution.

In the case of injury resulting from this study, you do not lose any of your legal rights to seek payment by signing this form.

New findings

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

Who can answer your questions about the research study?

Important Contact Numbers	
If you are enrolled at the Fox Chase location (333 Cottman Ave)	
If you have questions about:	Please Call:

This study, including if you get sick or hurt	Dr. Crystal Denlinger at 215-728-4300
If you have a concern or complaint	Risk Management Department at 215-728-2591
Your rights as a research participant on this study	FCCC Institutional Review Board at 215-214-3754
Your bills or health insurance coverage	Clinical Trial Financial Counselor at 215-214-3768

Where can you get more information?

You may call the National Cancer Institute's Cancer Information Service at:

1-800-4-CANCER (1-800-422-6237)

You may also visit the NCI website at http://cancer.gov

- For NCI's clinical trials information, go to: http://cancer.govclinicaltrials/
- For NCI's general information about cancer, go to: http://cancer.gov/cancerinfo/

By signing below, you tell us that you have gotten all of the information you need; that you have received clear answers to your questions, and that you agree to take part in the research study. You will receive a copy of this form. You may also request a copy of the research plan.

Signature of Participant	Print Name of Participant	Date

By signing this form the Physician obtaining consent indicates that the research participant has been fully informed of all aspects of the research study.

Signature of Physician Obtaining Consent	Print Name of Physician Obtaining Consent	Date

By signing this form the person obtaining consent indicates that the research participant has been fully informed of all aspects of the research study.

Signature of Person Obtaining Consent	Print Name of Person Obtaining Consent	Date

Informed Consent Document for Use of Tissue for Research

Please note: This section of the informed consent form is about additional research studies that are being done with people who are taking part in the main study. You may take part in these additional studies if you want to. You can still be a part of the main study even if you say 'no' to taking part in any of these additional studies.

You can say "yes" or "no" to each of the following studies. Please mark your choice for each study.

About Using Tissue for Research

We would like to use some of the tissue that is left over from your previous biopsy if you have had one, or if you are going to have a biopsy for future research. If you agree, this tissue will be sent to Caris Life Sciences to learn more about cancer and other diseases. If you would like to read more about how tissue is used for research, you can visit the National Cancer Institutes' website at http://www.cancer.gov/clinicaltrials/learningabout/providingtissue

The research that may be done with your tissue is not designed specifically to help you. The results from this testing will be stored in your medical record and might help you or people who have cancer and other diseases in the future.

Reports about research done with your tissue will be given to your doctor. These reports will be put in your health record. The research will not have an effect on your care.

Things to Think About

The choice to let us use your tissue for this research is up to you. No matter what you decide to do, it will not affect your care.

If you decide now that your tissue can be used for research, you can change your mind at any time. Just contact us and let us know that you do not want us to use your tissue. Then any tissue that remains will no longer be used for research.

Tissue that is used for genetic testing may reveal information about diseases that are passed on in families. Even if your tissue is used for this kind of research, the results will not be put in your medical records.

Your tissue will be used only for testing and will not be sold.

The information or results gathered from the testing of you tissue may be sold. It may help to develop new products in the future.

Even if your information from the testing of your tissue is sold, leads to a treatment or future research, you will not be paid.

Benefits

The benefits of research using tissue include learning more about what causes cancer and other diseases, how to prevent them, and how to treat them.

Risks

The greatest risk to you is the release of information from your health records. We will do our best to make sure that your personal information will be kept private. The chance that this information will be given to someone else is very small.

Making Your Choice

Please read each sentence below and think about your choice. After reading each sentence, circle "Yes" or "No." If you have any questions, please talk to your doctor or nurse, or call our research review board 215-214-3754.

No matter what you decide to do, it will not affect your care.

1. My tissue may be sent to Caris Life Sciences for genetic testing. The results of this testing will be placed in my health record and made available to my study doctor

YES NO

2.. The results of my tumor's genetic or mutational analysis may be for use in research to learn about, prevent, or treat cancer. This may mean that information about my health and my family's health could be discovered by someone reviewing this information.

YES NO

3. Someone may contact me in the future to ask me to take part in more research.

YES NO

By signing below, you tell us that you have gotten all of the information you need; that you have received clear answers to your questions, and that you agree to take part in the research study. You will receive a copy of this form. You may also request a copy of the research plan.

Signature of Participant	**Print Name of Participant**	**Date**

By signing this form the Physician obtaining consent indicates that the research participant has been fully informed of all aspects of the research study.

Signature of Physician Obtaining Consent	**Print Name of Physician Obtaining Consent**	**Date**

By signing this form the person obtaining consent indicates that the research participant has been fully informed of all aspects of the research study.

Signature of Person Obtaining Consent	**Print Name of Person Obtaining Consent**	**Date**