Certification of Completion of the Informed Consent

IRB #

Title:

I have discussed the "Informed Consent for Participation in Research Activities" in its entirety for the above referenced research study, with the research participant listed below (or the research participant's legally authorized representative). During the review of the consent form, the possible benefits, risks and discomforts involved in his/her participation on the study, as well as potential alternatives were reviewed.

The research participant has been encouraged to ask questions, and all questions asked by the participant have been answered. The research participant affirmed that he/she has received all information that he/she desires at this time, and a copy of the signed consent form has been provided to the participant.

PRINTED NAME of Person Obtaining Informed (Consenter)	SIGNATURE	TITLE	DATE	TIME

ADULT INFORMED CONSENT

COH Protocol # 20664
TITLE: A Phase II Study of Cabozantinib and Temozolomide in Patients with Unresectable or Metastatic Leiomyosarcoma and Other Soft Tissue Sarcomas

Protocol Version date: 03/01/2022

PRINCIPAL INVESTIGATOR: Mark Agulnik, MD

24-HOUR TELEPHONE NUMBER: (626) 256-HOPE (4673) ext. 95200
DAY TIME TELEPHONE NUMBER FROM THE HOURS OF 8:00 AM TO 5:00 PM: (626) 256-HOPE (4673) ext. 89200

EXPERIMENTAL PARTICIPANT'S BILL OF RIGHTS

The rights below are the rights of every person who is asked to be in a research study, also known as an experiment or clinical trial. As a research participant, you have the following rights:

1. To be told what the research study is trying to find out.
2. To be told what will happen to you and whether any of the procedures to be used are different from what would be used in standard practice.
3. To be told about the discomforts, side effects and risks of the things that will happen to you as part of the research study.
4. To be told if you can expect any benefit from participating in the research study.
5. To be told of the other choices you have and how they may be better or worse than being in the research study.
6. To be told what medical treatment is available if any complications arise.
7. To be allowed to ask any questions concerning the research study, both before agreeing to be in the study and during the course of the study.
8. To refuse to participate in the research study or to change your mind about participation after the study is started. To be informed that this decision will not affect your right to receive the care you would receive if you were not in the study.
9. To receive a copy of the signed and dated research study consent form.
10. To be free of pressure when considering whether you wish to agree to be in the research study.

ADULT INFORMED CONSENT

COH Protocol # 20664

TITLE: A Phase II Study of Cabozantinib and Temozolomide in Patients with Unresectable or Metastatic Leiomyosarcoma and Other Soft Tissue Sarcomas

PRINCIPAL INVESTIGATOR: Mark Agulnik, MD

KEY INFORMATION

You are invited to participate in a research study. The purpose of this research study is to determine if Cabozantinib, given together with Temozolomide is able to stop or reduce the rate of cancer growth in participants with Leiomyosarcoma (cancer of the smooth muscles) or non-leiomyosarcoma (another kind of soft tissue cancer) better than Temozolomide alone. The information we learn by doing this research study may help doctors understand your condition better and may help future participants with this medical condition.

Participants in this study will be given an investigational drug or drugs and asked to come in for approximately 35 study visits. Participation is expected to last for up to 5 years or your condition worsens. The major risks associated with study include:

- Abdominal pain
- Alterations of thyroid function tests (hypothyroidism)
- Blisters, rash, or pain in hands or feet (palmar-plantar erythrodysesthesia syndrome)
- Hemorrhage (escape of blood from blood vessel)
- Hypertension (abnormally high blood pressure)
- Lymphopenia (lacking a blood cell type called a lymphocyte)
- Thrombocytopenia (lack of platelets in the blood that cause bleeding into tissues, bruising, and slow blood clotting after injury)
- Neutropenia (fewer neutrophils in the blood leading to potential infections)
- Leukopenia (less white cells in the blood which could lead to difficulty fighting off germs and cause sickness)
- Risks of the combination of using these drugs together is unknown as this has not been previously studied.

You do not have to join this research study. You can choose to receive standard methods to treat cancer instead of participating on this study. If you are interested in learning more about this study, please continue to read below.

INTRODUCTION

You are invited to take part in a clinical trial, a type of research study, because you have been diagnosed with leiomyosarcoma (cancer of the smooth muscles) or non-leiomyosarcoma (another kind of soft tissue cancer), and your type of cancer cannot be removed through surgery or has spread to a different part of your body.

This research study is sponsored by City of Hope. Exelixis, Inc. is the company that makes the drug being tested. They provide funding to cover the costs of conducting this study.

It is expected that about 72 people will take part in this research study.

We encourage you to take some time to think this over, to discuss it with other people and your primary doctor, and to ask questions now and at any time in the future. Please take as much time as you need to read the consent form. If you find any of the language difficult to understand, please ask questions. If you decide to participate, you will be asked to sign this form. We will give you a copy so that you can refer to it while you are involved in this research study. If you choose not to participate in this research study, the research doctors will discuss other treatment options with you and/or refer you back to your primary doctor.

A. WHY IS THIS RESEARCH STUDY BEING DONE?

This research study is a Phase II clinical trial. Phase II clinical trials test the safety and effectiveness of an investigational (experimental) intervention to learn whether the intervention works in treating a specific disease. "Investigational" means that the intervention is being studied.

The FDA (the U.S. Food and Drug Administration) has not approved Cabozantinib in combination with Temozolomide for your specific disease but it has been approved for other uses. Cabozantinib is approved by the FDA for liver cancer, kidney, and differentiated thyroid cancer while Temozolomide is approved to treat adult patients with brain cancer and brain tumors. The combination of both drugs are considered investigational.

The purpose of this study is to determine if Cabozantinib, given together with temozolomide is able to stop or reduce the rate of cancer growth in participants with your kind of cancer better than temozolomide alone. Preclinical and clinical evidence shows that adding antiangiogenic agents (substances, drugs, or compounds which get rid of parts of the blood vessels needed by tumors to grow and spread) to chemotherapy, enhances anti-tumor and antiangiogenic effects. The combination of Cabozantinib with oral temozolomide is expected to shrink your cancer cells or lower the chance of your cancer cells growing and spreading. This study will also look at any possible side effects that this combination of temozolomide and Cabozantinib may have.

B. WHAT IS INVOLVED IN THE STUDY?

If you decide to take part, this is what will happen:

If you take part in this research study you will be given a drug diary. You will be asked to document information in the drug diary about the study drug you are being asked to take.

If you take part in this research study you will be given a study calendar. Information about what to expect during and between study visits will be included in the study calendar.

After signing this consent form, you will be asked to undergo screening tests or procedures to find out if you can be in the research study. This may take up to 3-4 hours.

Before the research starts (screening):

After signing this consent form, you will be asked to undergo some screening tests or procedures to find out if you can be in the research study. Many of these tests and procedures are likely to be part of regular cancer care and may be done even if it turns out that you do not take part in the research study. If you have had some of these tests or procedures recently, they may or may not have to be repeated.

- A medical history, which includes questions about your health, current medications, and any allergies.
- Physical examination, including a measurement of your vital signs: blood pressure, heart rate, temperature, and breathing rate, height and weight.
- Documentation of current medication list.
- Performance status, which evaluates how you are able to carry on with your usual activities.
- An assessment of your tumor by MRI (magnetic resonance imaging) which is a type of scan that uses magnetic fields and radio waves to take a picture or CT (CAT Scan) which is an X-ray procedure where a high-speed computer is used to take multiple images or pictures of your body. Both the MRI and CT scan are part of your standard of care.
- Blood tests, about 2-3 teaspoons.
- Urine sample, for routine safety tests.
- Pregnancy test, via urine sample.
- Heart assessment with electrocardiogram (ECG) which is a test that gives us a measure of the heart's electrical activity.
- Questionnaires, to check your quality of life which should take less than fifteen minutes.

If these tests show that you are eligible to participate in the research study, you will begin the study treatment. If you do not meet the eligibility criteria, you will not be able to participate in this research study.

Study Procedures:

If you are eligible to participate in this research study, the following test and procedures will occur. A chart summarizing the timing of these tests and procedures is also provided below. Some tests and procedures may be part of your standard of care.

After the screening procedures confirm that you are eligible to participate in the research study:

The following tests and procedures will be done on cycle 1 day 1:

- Physical Examination.
- Performance status, which evaluates how you are able to carry on with your usual activities.
- Blood tests, Blood will be drawn (about 4 tablespoons) for tests to monitor your health, including blood counts and chemistry.
- Urine tests, Urine will be collected for tests to monitor your health.
- Cabozantinib pills administration, taken orally daily
- Temozolomide pills, administration, taken orally on days 1 – 5.
- Pregnancy test.
- Heart assessment, with electrocardiogram (ECG) which is a test that gives us a measure of the heart to test your heart health.
- Questionnaires, to check your quality of life.

The following tests and procedures will be done on cycle 1 day 15, cycle 2 day 1, cycle 2 day 15, cycle 3 day 1, and day 1 of every following cycle:

- Physical Examination.
- Performance status, which evaluates how you are able to carry on with your usual activities.
- Urine tests, Urine will be tested during screening and every 2 cycles.
- Blood tests, Blood will be drawn (about 4 tablespoons) for tests to monitor your health, including blood counts and chemistry.
- Heart assessment, with electrocardiogram (ECG) which is a test that gives us a measure of the heart to test your heart health.
- ECG will be done every 3 cycles, starting from cycle 3 day 1 until end of treatment.
- Pregnancy test.
- An assessment of your tumor, by MRI (magnetic resonance imaging) which is a type of scan that uses magnetic fields and radio waves to take a picture or CT (CAT Scan) which is an X-ray procedure where a high-speed computer is used to take multiple images or pictures of your body.
- CT or MRI will be done at week 6, week 12, week 20, and then every 8 weeks thereafter.
- After one year of receiving treatment, the scans may be obtained every 12 weeks as per your study doctor.

Treatment plan:

Participants will take the study drug by mouth once daily for 28 days and temozolomide by mouth on Days 1-5 of each 28 day cycle. Treatment will continue until either your cancer gets worse, the study drug has too many side effects or your doctor decides it is in your best interest to take you off the study.

The chart below shows what will happen to you during treatment, as previously explained. The top row shows the time period, left hand column show the test/procedure and the right-hand columns indicate when the test/procedure is performed with an "X".

Research Study Calendar:

1. Screening assessments should be done within 28 days of first dose of study treatment (unless otherwise specified).
2. Cycle 1 Day 1 assessments should be done within 7 days of starting treatment. Pre-study procedures completed within 7 days of C1D1 do not need to be repeated. If a pre-study procedure was done more than 7 days prior to C1D1, then procedure needs to be repeated, but may be done within 5 days of starting therapy.

	Study Treatment Period			Post- Treatment Period
	Screening	Cycle 1 Day 1	C1D15, C2D1, C2D15, C3D1 and Day 1 of every following cycle (± 5 days)	30 Days after Last Dose/ Survival Follow-up
Informed Consent	X			
Demographics	X			
Medical and Cancer History/Demographics	X			
Physical Examination	X	X	X	X
Height	X			
Weight	X	X	X	X
Vital Signs	X	X	X	X
ECOG Performance Status	X	X	X	X
Complete Blood count Testing	X[a]	X	X	X
Chemistry Panel Blood Testing	X[a]	X	X	X
Urine Testing	X			X

Urine Protein/Urine Creatinine Testing	X[f]	X[f]	X[f] every 8 weeks	X
PT/INR, PTTk Blood Test	X[k]			
TFTs (TSH, FT3, FT4) Blood Test	X		X[d] every other cycle	
12-lead ECGc	X[c]		X[c]	
Cabozantinib Administration j		X	X (daily)	
Temozolomide Administration j		X	X (Days 1-5)	
Pregnancy Test	X	X	X[e]	X
Questionnaire	X[h]	X[h]	X[h]	X
Correlative Blood Sample		X[i]	X[i]	X[i]
Tumor Assessment	X		X[b]	
Concomitant Medications	X	X	X	X
NGS Report (a useful tool that determines the sequence of your DNA), if available	X			
Adverse Events	Continuous			X
Follow-up/Survival				X[g]

Planned Follow-up:

We would like to keep track of your medical condition. Once you have come off of study treatment, we would like you to return for a follow up visit 30 days after last dose of treatment or before starting a new treatment. Each visit should last up to 30 minutes. The following will be assessed during your follow-up visits:

- Physical examination,
- Blood tests, Blood will be drawn (about 4 tablespoons) for tests to monitor your health, including blood counts and chemistry
- Urine sample, for routine safety tests,
- Pregnancy test,
- Questionnaires.

We would then like to either see you in clinic or call you on the telephone every six months to see how you are doing. Keeping in touch with you and checking your condition every six months for up to 2 years if your disease has progressed, and up to 5 years if no disease progression has occurred. This will help us look at the long-term effects of the research study.

C. HOW LONG WILL I BE IN THIS RESEARCH STUDY?

You will be in this research study for about study for up to 5 years or your condition worsens

D. WHAT ARE THE POSSIBLE RISKS AND DISCOMFORTS?

There are risks to taking part in any research study. One risk is that you may get a study drug that does not help treat your disease or that makes your condition or disease worse. Another risk is that there may be side effects.

All cancer treatments can have side effects, which can range from mild and reversible to severe, long lasting and possibly life-threatening. There is a great deal of variability among side effects of different cancer treatments and between individuals. In a research study, all of the risks or side effects may not be known before you start the study. **You need to tell your doctor or a member of the study team immediately if you experience any side effects.**

Everyone in the research study will be monitored carefully for side effects. You will be monitored during the administration of study drugs to keep track of your blood counts and organ function, particularly your kidney and liver function. If you experience side effects, they may go away after you stop taking the study drug. You will be monitored closely for any severe, life-threatening side effects listed below. Some of these side effects may be permanent. Appropriate medical care will be provided, if necessary, including additional treatment, hospitalization and/or surgery.

Possible risks and discomforts you could experience during this study include:

Risks associate with the Study Drug Cabozantinib Commonly Occurring Side Effects (reported in 1 in 10 research participants)

- Abdominal pain (for example cramping)
- Alteration of thyroid function tests (hypothyroidism, blood thyroid stimulating hormone increased)
- Blisters, rash, or pain in hands or feet
- Changes in blood tests used to monitor the liver, which may indicate liver damage (AST increased, ALT increased, GGT increased, hepatic enzyme increased, transaminases increased, liver function test increased)
- Change in voice (dysphonia, vocal cord paralysis)
- Changes to the way things taste (dysgeusia, ageusia, hypogeusia)
- Bowel movements that are infrequent or hard to pass.
- Loose watery stool
- feeling tired
- Hair color changes or hair loss
- High blood pressure (hypertension)
- Inflammation of mucus membranes (mucosal inflammation, anal inflammation, genital tract inflammation, gingival swelling, laryngeal inflammation, nasal inflammation, oral mucosal erythema, pharyngeal inflammation, vulvovaginal inflammation)

- Loss of appetite
- Mouth and throat sores or swelling (stomatitis, mouth ulceration, cheilitis, glossitis, tongue blistering)
- Upset stomach
- Rash
- Vomiting
- Weakness
- Weight loss
- Abnormal thickening of the outer layer of the skin (hyperkeratosis)
- Change in the feeling of touch (paranesthesia, dysesthesia, hyperesthesia, hypoesthesia)
- Cough
- Bleeding, including bleeding from stomach or intestines which may look like coffee grounds or black sticky bowel movements and bleeding within the brain
- Blood clot in a large vein, usually in the leg (deep vein thrombosis, portal vein thrombosis, pelvic venous thrombosis, venous thrombosis limb)
- Blood clot that travels from a vein to the lung (pulmonary embolism, embolism)
- Confusion and disorientation (confused state, mental status changes, delirium)
- Decreased amounts of red blood cells (anemia), which may cause feelings of tiredness or shortness of breath
- Decreased amounts of calcium or sodium in the blood (hypocalcemia, blood calcium decreased, hyponatremia)
- Decreased or increased amounts of potassium in the blood (hypokalemia, blood potassium decreased, hyperkaliemia)
- Decreased amounts of magnesium or phosphorus in the blood (hypomagnesaemia, blood magnesium decreased, hypophosphatemia, blood phosphorus decreased)
- Decreased level of albumin in the blood (hypoalbuminemia, blood albumin decreased)
- Decreased platelet counts, which increases the risk of bleeding or make bleeding more difficult to stop (thrombocytopenia, platelet count decreased)
- Decreased white blood cell counts, which may increase chances of infection (neutropenia, leukopenia, lymphocyte count decreased, lymphopenia, neutrophil count decreased, white blood cell count decreased)
- Dermatitis acneiform, a type of acne
- Loss of water fluids in the body
- Difficulty swallowing
- Dizziness
- Dry mouth
- Dry skin
- Fever
- Fungal infections including mouth, lung, and other locations (aspergilloma, oral candidiasis)
- Swollen veins in your lower rectum and bleeding hemorrhoids
- Headache
- Increased amounts of pancreas enzymes in the blood, which may indicate damage to the pancreas (lipase increased, amylase increased, pancreatitis, pancreatitis acute)
- Increased levels of bilirubin in the blood, which may indicate complications with the liver (blood bilirubin increased, hyperbilirubinemia)
- Increased levels of creatinine in the blood, which may indicate complications with the kidneys

(blood creatinine increased)
- Mouth or throat pain (oral pain, oropharyngeal pain, glossodynia, oral discomfort)
- Muscle spasm
- Muscle weakness
- Pain in a joint or muscle (arthralgia, musculoskeletal chest pain)
- Pain in extremities
- Protein in the urine, which may indicate kidney damage
- Shortness of breath
- Stomach acid coming up from the stomach into the esophagus (gastroesophageal reflux disease, oesophagitis)
- Swelling of the limb(s)
- Ulcer (anal ulcer, oesophageal ulcer, skin ulcer)
- Upset stomach or indigestion

Occasional Side Effects (1 in 50-100 research participants)

- Abnormal electrical activity in the heart that could cause a potentially serious change in heart rhythm (ventricular arrhythmia, electrocardiogram QT prolonged, atrioventricular block)
- Abnormal opening between two organs or from an organ to the outside of the body (acquired tracheoesophageal fistula, gastrointestinal fistula, oesophageal fistula, anal fistula, enterocutaneous fistula, enterovesical fistula, tracheal fistula, fistula)
- Abscesses, infected cavities filled with pus (gingival abscess, lung abscess, colonic abscess, perirectal abscess, rectal abscess, anal abscess, pharyngeal abscess, periumbilical abscess, tooth abscess)
- Blood clot in an artery (peripheral artery thrombosis, intestinal ischaemia, carotid artery thrombosis, cerebral ischaemia, transient ischaemic attack)
- Chest discomfort originating from the heart (angina pectoris)
- Clouding of the lens in the eye that affects vision (cataract)
- Damage to skeletal muscle tissue (rhabdomyolysis)
- Decreased brain function or decreased alertness and ability to think (encephalopathy, hepatic encephalopathy)
- Decrease in all blood counts (red blood cells, white blood cells and platelets)
- Destruction of bone tissue, in particular, bone in the jaw (osteonecrosis of jaw, osteonecrosis)
- Feelings of unease or fear (anxiety)
- Gallstones (cholelithiasis)
- Heart attack (acute myocardial infarction, myocardial infarction, myocardial ischaemia)
- Heart failure (cardiac failure)
- Holes in the stomach or intestines (diverticular perforation, gastric perforation, gastrointestinal perforation, intestinal perforation, small intestinal perforation, large intestine perforation, appendicitis perforated, rectal perforation)
- Infections (osteomyelitis, wound infection, postoperative wound infection, sepsis, septic shock)
- Inflammation of the intestine, appendix, gall bladder or thin tissue lining the inner wall of the abdomen and most of the abdominal organs (appendicitis, colitis, colitis ischaemic, cholecystitis, enterocolitis, peritonitis, proctitis)
- Reduced kidney function (renal failure, renal failure acute, prerenal failure, renal failure chronic, nephrotic syndrome, nephropathy)
- Liver failure
- Loss of consciousness, fainting episode

- Pneumonia and inflammation of the lungs
- Rapid heart rhythm (supraventricular tachycardia, atrial fibrillation)
- Re-opening of wounds after surgery (wound dehiscence, postoperative wound complication, impaired healing)
- Respiratory failure
- Convulsion, fits
- Stroke / mini-stroke (cerebral infarction, cerebral ischaemia, ischaemic stroke)
- Tear or inflammation in skin that lines the anus (anal fissure, anal inflammation)
- Uncoordinated movements

Side effects that occurred in less than 0.1% of patients but were considered medically important or severe or life-threatening and rarely fatal are listed in the tables below. These events occurred in studies of Cabozantinib given alone. If you are at the clinical site and notice any signs or symptoms of the side effects listed below, check with the staff in the clinic immediately; if you are no longer at the clinical site, call your doctor or go immediately to the nearest hospital.

Rarely Seen Side Effects (less than 1 in 100 research participants)

- Air in the chest between lungs and chest wall (pneumothorax, pneumomediastinum)
- Allergic reaction (hypersensitivity)
- Anemia caused by destruction of red blood cells (Hemolytic uremic syndrome)
- Blocked intestines (intestinal obstruction, gastrointestinal obstruction)
- Brain dysfunction caused by brain swelling (posterior reversible encephalopathy syndrome, leukoencephalopathy)
- Cancer of the mouth or skin (squamous cell carcinoma of the oral cavity, squamous cell carcinoma)
- Damage to the outermost surface of the eye (corneal epithelium defect)
- Enlargement and weakening of a blood vessel wall or a tear in a blood vessel wall
- Inflammation and blockage of channels that carry bile from the liver (hepatitis cholestatic)
- Severe swelling of the mouth, lips, tongue, eyes and throat, or difficulty swallowing or breathing
- Very high blood pressure that comes on suddenly and quickly and which can lead to serious injury to the heart and brain (hypertensive crisis, malignant hypertension)
- Temporary paralysis of the intestines
- Throat swelling
- Blood vessel inflammation associated with possible bleeding, bruising, and/or rash

Risks associate with the STUDY DRUG temozolomide

Commonly Occurring Side Effects **(reported in 1 in 10 research participants)**

- Constipation, nausea, vomiting, diarrhea
- Dizziness
- Muscle weakness, paralysis, difficulty walking
- Trouble with memory
- Tiredness
- Difficulty sleeping
- Hair loss

- Headache, seizure
- Infection, especially when white blood cell count is low
- Anemia which may cause tiredness
- Bruising, bleeding

Occasional Side Effects (1 in 50-100 research participants)

- Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat
- Cancer of bone marrow caused by chemotherapy
- Headache, seizure
- Infection, especially when white blood cell count is low
- Anemia which may cause tiredness
- Bruising, bleeding

Side effects that occurred in less than 0.1% of patients but were considered medically important or severe or life-threatening and rarely fatal are listed in the tables below. These events occurred in studies of Cabozantinib given alone. If you are at the clinical site and notice any signs or symptoms of the side effects listed below, check with the staff in the clinic immediately; if you are no longer at the clinical site, call your doctor or go immediately to the nearest hospital.

Rarely Seen Side Effects (less than 1 in 100 research participants)

- Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat
- Cancer of bone marrow caused by chemotherapy
  Hepatotoxicity (fatal and severe hepatotoxicity)

Since the effect of the study drug(s) taken with other medications may not be known, it is important that you tell the research doctor about all prescription and non-prescription drugs that you are taking or planning to take. There may also be some foods that you should avoid while on this research study and your research doctor will review this information with you.

Risks Associated with Blood Draw

Risks of blood draws include mild pain or discomfort, bruising and swelling around the puncture site, dizziness or fainting, or infection (rare).

Incidental Findings:

It is possible the research procedures could find a medical problem unrelated to the purpose of this study that you did not know about before. If during the research procedures we learn information that may be important for you to know about, such as the possibility of a previously unknown medical condition, we will tell you. You may authorize the release and communication of the findings to your personal doctor. These findings may require additional testing or treatment. You will be responsible for the cost of any additional tests or related treatment.

Results of genetic research will not be used in your medical care. The results will not be given to you, the study doctor, or your personal doctor.

Reproductive Risks:

We do not know whether this study drug might hurt an unborn child. While participating in this research study, you should not become pregnant or father a baby., and should not nurse a baby. We can provide counseling about preventing pregnancy for either male or female study participants. Let your doctor know immediately if you become pregnant or find out that you are going to be the father of a child.

In the event that your partner becomes pregnant, it may be critical to share information regarding your participation in this research study with that person. Your research doctor should also be told if this happens. The study sponsor may want to collect data on your partner's pregnancy.

You must use birth control while on this study. These are some birth control measures that you can use:

If you are pregnant or nursing a baby and do not want to stop, you cannot take part in this study. If you are a woman who can become pregnant, a urine pregnancy test will be obtained before treatment is started. If you are sexually active and capable of bearing or fathering a child, both you and your partner must agree to use two medically effective forms of birth control while you are on this study. The investigational drug(s) may involve risks to you (or to the embryo or fetus, if you or your partner become pregnant), which is currently unforeseeable.

You must use birth control while on this study. Acceptable medically effective forms of birth control are:

- Abstinence,
- Surgical sterilization (tubal ligation or hysterectomy for women, or vasectomy for men),
- Double-barrier methods (i.e. condoms, diaphragm, cervical cap, or sponge used with spermicidal gel or foam),
- Intrauterine device (IUD) (i.e. Progestin, Copper),
- Hormonal Contraceptives (Birth control patches, implants, pills, rings, or injections)

Other Risks:

Because of side effects or the time required for tests and clinic visits while you are on this research study, you may be unable to keep up with your normal daily activities.

Risks Associated with Questionnaires: The quality of life questionnaires used in this study may be upsetting. If you find the questionnaires upsetting, you may speak with the research doctor or ask to be referred for additional emotional support. Some of the questions may make you feel uneasy or embarrassed. You can choose to skip or stop answering any questions that make you uncomfortable.

Risks associated with Breach of Confidentiality:
There is a small risk that people who are not connected with this study will learn your identity or your personal information.

Results of this genetic research will not be used in your medical care. The results will not be given to you, the study doctor, or your personal doctor.

The Genetic Information Nondiscrimination Act of 2008 (GINA) is a federal law that protects Americans from being treated unfairly because of differences in their DNA that may affect their health, and may prevent discrimination by health insurers and employers based on genetic information. GINA is intended to ease concerns about discrimination that might keep some people from getting genetic tests that could benefit their health, and enable people to take part in research studies such as this without fear that their DNA information might be used against them by health insurers or their workplace. This protection does not extend to disability or life insurance. Additional information can be found at http://www.genome.gov/10002328.

Genetic Data Sharing Risks:

Who else will have access to my genetic information?
The researchers may decide to share data gathered from your samples to help further research into cancer and other diseases. One way to do this is by putting information into scientific databases where it is stored along with information from participants in other studies. Researchers can then study the combined information to learn even more about science and health. If you agree to take part in the study, some of your genetic and health information might be placed into a controlled access scientific database and shared with other researchers. Controlled access means that only researchers who apply for and get permission to use the information for a specific research project will be able to access the information.

Your name and other information that could directly identify you will never be placed into a scientific database. However, because your genetic and health information is unique to you, there is a small chance that someone could trace it back to you. The risk of this happening is very small, but may grow in the future. There are many safeguards in place to protect your information while is it stored in data repositories and used for research.

E. WILL YOU RECEIVE NEW INFORMATION ABOUT THIS STUDY?

During the research study, you will be notified of newly discovered side effects or significant findings, which may affect your health or willingness to participate. You may be asked to sign a new consent form that shows that you have been informed of new information relating to this research study.

F. HOW WILL YOUR INFORMATION BE KEPT CONFIDENTIAL?

Any information learned from this study in which you might be identified will be confidential and disclosed only with your permission. Every effort will be made to keep any information collected about you confidential. However, it is impossible to guarantee that information about you will not be mistakenly released. If, despite our best efforts, identifying information about you is released, it could negatively impact you or your family members. This risk is small.

There are organizations that may inspect your records. These organizations are required to make sure your information is kept private, unless required by law to provide information. Some of these organizations are:

- The study sponsor, City of Hope, and any drug company Exelixis, Inc. supporting the study The Institutional Review Board, IRB, is a group of people who review the research with the goal of protecting the people who take part in the study.
- Regulatory agencies such as the Office for Human Research Protections (OHRP), the Food and Drug Administration (FDA), and the National Cancer Institute (NCI) in the U.S., and similar ones if other countries are involved in the study as required by law.

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.

Future Use of Research Information and Specimens

The information or specimens that have been collected for this study will not be used for future research studies or shared with other researchers beyond the research activities described in this consent form.

G. WHAT ARE THE POSSIBLE BENEFITS OF TAKING PART IN THIS RESEARCH STUDY?

There is no guarantee that you will receive any benefits from this study. The possible benefit of the study drug in the treatment of leiomyosarcoma (cancer of the smooth muscles) or non-leiomyosarcoma (another kind of soft tissue cancer), is not known. If you decide to participate in this study, your health will be monitored very closely. By being in this study, you will give doctors more information about how well the study drug works. It may help doctors understand your condition better and may help future patients with this medical condition.

H. WHAT OTHER OPTIONS ARE THERE?

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

- You may choose to have the usual approach for your cancer,
- 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.

I. ARE THERE ANY PAYMENTS TO YOU FOR TAKING PART IN THE STUDY?

You will not receive any monetary compensation for taking part of this study.

Possible Commercial Products
We may use your samples and information to develop a new product or medical test to be sold. The sponsor and hospital may benefit if this happens. Donors of blood, tissue and other biological materials do not retain any property rights to the materials. Therefore, you would not share in any money or other benefits that any entity might receive for these inventions or discoveries.

J. WHAT ARE THE COSTS?

Taking part in this research study might lead to added costs to you or your insurance company.

Cabozantinib will be provided to you at no cost while you take part in the study. It is possible that the Cabozantinib may not continue to be supplied while you are on the study. If this occurs, the research doctor will talk to you about your options. The commercially available drug, temozolomide will be the responsibility of you and/or your insurance company
Most of the tests, procedures, and/or drugs provided to you as part of this study are routinely used to treat your illness. You would receive these tests, procedures, and/or drugs even if you were not participating in this study. You or your health plan/insurance company will need to pay for this routine care. You will also be responsible for any co-payments or deductibles required by your health plan/insurance company. Some health plans/insurance companies will not pay the costs associated with these tests, procedures, and/or drugs because you are in a research study. If your health plan/insurance company will not pay these costs, you will have additional expenses from being in this study, such as the costs associated with treating side effects.

If you have questions about your insurance coverage, or the items you might be required to pay for, please call financial services for information. The contact information for financial services are:

- City of Hope Financial Support Services: 626-256-HOPE (4673), extension: 80258.

The National Cancer Institute provides an online resource to help people participating in cancer clinical trials understand which services their insurance company is required by law to pay. This can be found at the website below or can be provided by the study team:

www.cancer.gov or 1-800-4-CANCER (1-800-422-6237)

K. WHAT HAPPENS IF YOU GET INJURED AS A RESULT OF THIS STUDY?

If you think you have been hurt by taking part in this study, tell the person in charge of this research study as soon as possible. The research doctor's name and phone number are listed in this consent form. City of Hope will offer you the care needed to treat injuries directly resulting from taking part in this research. This care will be billed to you or your insurance company. You will be responsible for deductible and co-payments, or any costs not paid by your insurer. There are no plans to pay you or give you other compensation for the injury. You do not give up your legal rights by signing this form.

There are no plans for any of the sponsors of this study to pay you or give you other compensation for the injury. You do not give up your legal rights by signing this form.

L. WHAT ARE YOUR RIGHTS IF YOU TAKE PART IN THIS STUDY AND WHAT WILL HAPPEN IF YOU DECIDE NOT TO PARTICIPATE? Your participation in this research study is voluntary. You are free to withdraw your consent for participation in this study without any loss of benefits, penalty, or interference with any future treatment at City of Hope.

You can decide to stop at any time and you may still be treated at your hospital or clinic. Tell your study doctor if you are thinking about stopping or decide to stop. You should talk to the study doctor about leaving the study before you decide so that he/she can find out if you are having any side effects from study treatment. Another reason to tell your study doctor that you are thinking about stopping is so that he/she can talk to you about any other treatments that could be helpful to you.

If you decide to stop being in this study, you will still be asked to come back to the hospital or clinic for the end of treatment tests described above. You may also be asked to take part in the follow-up phone calls and/or visits. This information is important to make sure that there are no lasting side effects from the study treatment and to see if your cancer got better, stayed the same, or got worse after treatment.

M. CAN YOU BE REMOVED FROM THE STUDY

You may be removed from this study without your consent for any of the following reasons: you do not follow the investigator's instructions, at the discretion of the investigator or the sponsor, your disease gets worse, or the sponsor closes the study. If this happens, the investigator will discuss other options with you.

N. WHOM DO YOU CALL IF YOU HAVE QUESTIONS OR CONCERNS?

The principal investigator, Dr. Mark Agulnik responsible for your care or treatment, has offered to and has answered any and all questions regarding your participation in this research study. If you have any further questions or in the event of a research related injury, you can contact Dr. Mark Agulnik at (626) 256-HOPE (4673) ext. 88972

This study has been reviewed and approved by the Institutional Review Board (IRB). If you have any questions regarding your rights as a research participant, you may contact a representative of that Board, from the Office of Human Research Subjects Protection, at (626) 256-HOPE (4673) ext. 62700.

P. SIGNATURE SECTION

SIGNATURE FOR CONSENT: By signing this consent form, you are making a decision to participate in this research study. Your signature on this informed consent form indicates that you:

1. Have read and understood the information in this form.
2. Have had the information in this form explained to you.
3. Have had a chance to ask questions and these questions were answered to your satisfaction.
4. Have been informed that you will receive a copy of this signed consent form, which includes the "Experimental Subject's Bill of Rights."

I hereby agree to be a research participant in this research study:

_____ _____ _____

Research Participant's Signature Date Time

(For paper consent only, date and time must be in research participant's handwriting)

_____

Print Research Participant's Name

INDIVIDUAL OBTAINING CONSENT SIGNATURE

_____ _____ _____

Signature of Individual Obtaining Consent Date Time

_____

Print Name of Individual Obtaining Consent

FOR USE WITH IRB APPROVED TRANSLATED SHORT/LONG CONSENT FORMS FOR NON ENGLISH SPEAKING PARTICIPANTS ONLY

NOTE: To determine who should sign below, review the guidance document, *Consenting Non English Speaking Research Participants (Pediatric or Adult) – Who Signs What?*

Interpreter: By signing here, I attest that I have acted as interpreter and facilitated this consent process.

_____ _____ _____

Interpreter's Signature Date Time

_____

Print Interpreter's Name

FOR USE WHEN A WITNESS IS REQUIRED:

Witness: By signing here, I attest that I witnessed the consent process and that the entire consent form was discussed.

_____ _____ _____

Witness' Signature Date Time

_____

Print Witness' Name

A Phase II Study of Cabozantinib and Temozolomide in Patients with Unresectable or Metastatic Leiomyosarcoma and Other Soft Tissue Sarcomas

AUTHORIZATION TO USE AND DISCLOSURE OF YOUR PROTECTED HEALTH INFORMATION (PHI) FOR PURPOSES OF THIS STUDY:

I. **Purpose of this Authorization**: The information about your health is something that is protected by law and cannot, except for certain purposes, be disclosed (shared) without your permission. As part of this research, you are agreeing to allow City of Hope, its affiliated research doctors, healthcare providers, and physician network to use and share with others your protected health information ("PHI"), as needed for the research. If you agree to participate in the study named above (called the "Study"), you must sign this authorization in addition to the *Study Consent Form*.

II. **The Information About You that is Covered By this Authorization**: PHI refers to information that we maintain about you that identifies you and includes the information contained in your medical record. Your medical record consists of information related to your health and the treatment we provide to you, such as your medical history, the results of physical exams, blood tests, x-rays and other diagnostic and medical procedures. If you sign this authorization, you are allowing City of Hope and the individuals indicated below to use and share any PHI we maintain about you that is required for your participation in the Study.

III. **Purposes for Uses and Sharing of your PHI; Who Will Use, Share and Receive your PHI**: Your PHI will be used and shared with others for the purpose of doing this research as described in the *Study Consent Form*. Your PHI will also be used to keep the research sponsor informed about this Study, for reporting to those individuals and authorities responsible for overseeing our research activities to make sure that the activities are properly conducted, and to report to regulatory agencies as required by the Study.

The people authorized to use and share your PHI for purposes of the Study include the Principal Investigator and the research staff supporting the Study; your City of

Hope physicians and the health care team; the Health Information Management Services Department (i.e., Medical Records Department), and affiliated research doctors and other medical centers participating in the research, if applicable. This also includes any agents or contractors used by these individuals or groups for purposes of conducting or managing this Study. At the City of Hope, the Institutional Review Board ("IRB"), and other City of Hope research regulatory committees will have access to your PHI as necessary to monitor research.

You are also allowing your PHI to be shared with the Office for Human Research Protections ("OHRP") and with any person or agency as required by law. In addition, certain other regulatory agencies, including, ***as applicable,*** the Food and Drug Administration ("FDA"); the National Cancer Institute ("NCI"), will have access to your PHI.

Use and disclosure of your PHI may also continue for as long as the sponsor needs to maintain the PHI for purposes of obtaining approval of the drug from the FDA or for other FDA reporting.

Your information will also be shared, with Exelixis, Inc**,** the "Research Sponsor" and its employees, agents or contractors who are involved in the administration of the Study.

This authorization will allow us to use and share your PHI for the Study. No other additional uses and disclosures other than for the purposes of the Study is included in this authorization. City of Hope's Notice of Privacy Practices will continue to protect your non-Study information. If necessary, another separate permission will be obtained from you for any non-Study uses or sharing of your PHI.

IV. **<u>Expiration of this Authorization</u>**: This authorization to use and share your PHI will expire twenty-five (25) years from the date that you sign this authorization.

V. **<u>Further Sharing of Your PHI</u>**: Your privacy is important and this is the reason for having rules which control who can use or see your PHI. City of Hope maintains control over your PHI at present, but once we share this information with a third party (for example, an individual or agency outside of the City of Hope), then it is no longer possible to maintain the same level of protection. The persons outside

our control may not be governed by federal or state privacy laws and it is possible that they could share your PHI with others for whom you have not given permission.

The information from this Study may be published in scientific journals or presented at scientific meetings but your identity will be kept confidential.

VI. **<u>Your Rights Under this Authorization</u>**: You may cancel this permission to use and share your PHI at any time by contacting City of Hope's Privacy Officer at (626) 256-HOPE (4673) ext. 64025. You should ask for the form, *Revocation (Cancellation) of Authorization for Use of Protected Health Information for Research*. Fill this form out and return it as the form instructs. Your cancellation begins when the Health Information Management Department of City of Hope receives this form. If you cancel this authorization to use and share your PHI, you will no longer be able to participate in the Study. This is because the research under this Study cannot be conducted without your PHI.

Once you cancel your permission to use and share your PHI, the researchers and others involved in conducting the Study will no longer be able to use or share your PHI for this research. PHI already used and shared up to this point as part of this Study will continue to be used for purposes of this research. This means that any uses of your PHI and any PHI shared about you by City of Hope prior to receiving your cancellation (revocation) form cannot be taken back. While no further PHI about you will be shared for the Study, your PHI already shared will continue to be used in the overall Study.

VII. **<u>Signing this Authorization is Your Choice</u>:** Your ability to obtain care at the City of Hope will not be affected by your decision to sign this authorization form. You will be able to continue to receive health care at City of Hope if you choose not to sign this authorization form or if you sign this form and later cancel your permission to use and share your PHI.

If you agree to the use and sharing of your PHI, please sign below. You will be given a copy of this authorization form.

_____ _____ _____

Research Participant's Signature Date Time

(date and time must be in research participant's handwriting)

_____

Print Research Participant's Name

INDIVIDUAL OBTAINING CONSENT SIGNATURE

_____ _____ _____

Signature of Individual Obtaining Consent Date Time

_____

Print Name of Individual Obtaining Consent

FOR USE WITH IRB APPROVED TRANSLATED SHORT/LONG CONSENT FORMS FOR NON ENGLISH SPEAKING PARTICIPANTS ONLY

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FOR USE WHEN A WITNESS IS REQUIRED:

Witness: By signing here, I attest that I witnessed the consent process and that the entire consent form was discussed.

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Witness' Signature Date Time

_____

Print Witness' Name