The Ohio State University Consent to Participate in Research + HIPAA Authorization

Study Title:	A Phase I Study of Riluzole in Combination with mFOLFOX6/Bevacizumab in Patients with Metastatic Colorectal Cancer
Principal Investigator:	Dr. Ning Jin
Sponsor:	OSU

- **This is a consent form for research participation.** It contains important information about this study and what to expect if you decide to participate. Please consider the information carefully. Feel free to discuss the study with your friends and family and to ask questions before making your decision whether or not to participate.
- **Your participation is voluntary.** You may refuse to participate in this study. If you decide to take part in the 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 usual benefits. Your decision will not affect your future relationship with The Ohio State University. If you are a student or employee at Ohio State, your decision will not affect your grades or employment status.
- **You may or may not benefit as a result of participating in this study.** Also, as explained below, your participation may result in unintended or harmful effects for you that may be minor or may be serious depending on the nature of the research.
- **You will be provided with any new information that develops during the study that may affect your decision whether or not to continue to participate.** If you decide to participate, you will be asked to sign this form and will receive a copy of the form. You are being asked to consider participating in this study for the reasons explained below.

Key Information About This Study
The following is a short summary to help you decide whether or not to be a part of this study. More detailed information is listed later in this form.

You are being asked to participate in this clinical trial because you have been diagnosed with advanced colorectal cancer that has spread beyond your colon.

The standard of care (SOC) treatment, meaning what is usually done to treat this kind of disease, is the chemotherapy drugs mFOLFOX6 and bevacizumab (or FDA approved bevacizumab biosimilars).

mFOLFOX6 is a chemotherapy regimen that consists of three drugs: oxaliplatin, leucovorin and 5-FU. Bevacizumab is an antibody that targets the blood vessel by blocking the activity of

a protein called vascular endothelial growth factor alpha (VEGF-A). It helps to make the mFOLFOX6 more effective. Each medication in the chemotherapy as well as bevacizumab (or bevacizumab biosimilar) will be given as an intravenous (IV) infusion through a vein. You will receive medications to help decrease the risk of side effects such as nausea and vomiting.

This study is looking at whether Riluzole can help these drugs be more effective in treating advanced colorectal cancer. Riluzole is a well-tolerated oral medication used to treat a disease called amyotrophic lateral sclerosis (ALS). Non-clinical research has demonstrated that riluzole may make chemotherapy work better.

This study will test whether riluzole can be given safely with chemotherapy in patients with colorectal cancer that has spread to other parts of the body. This study may help us develop more effective treatment for patients with colorectal cancer. As part of the study, we will attempt to develop tests that will predict how well the study drug works.

If you are determined to be eligible for this trial, you will start the treatment period, which will consist of approximately 16 weeks where you will take the study drug (riluzole), as well as standard chemotherapy mFOLFOX. You will then be followed up with for 30 days. More details on this can be found in section 3 of this informed consent form.

Assessments for this study include physical exams, pregnancy tests, blood tests, urine tests, blood samples, ECGs, CT scans, and tumor biopsies. A full description of these tests can be found in section 3, and their risks can be found in section 6.

Common side effects of Riluzole include tiredness, nausea, decreased lung function. Vomiting, high blood pressure, dry mouth, abdominal pain, dizziness, and increased liver enzymes. There are also side effects to the mFOLFOX regimen that you would be exposed to even if you do not take part in this study. These risks are listed out in section 6 of this form.

The effect of riluzole on pregnant women and their babies is not known at this time. All persons in this study will need to use a highly effective form of birth control during study participation and for 6 months after the last dose of study drug.

It is not known what side effects may occur when Riluzole is taken in combination with mFOLFOX and bevacizumab.

You may or may not receive any benefit from taking part in this study, but it is the researchers' hope that the information gained from this study may be used to improve treatment for people with advanced colorectal cancer.

You do not have to take part in this study to receive care for your cancer, even after signing this consent form.

1. Why is this study being done?

This study is designed to test if riluzole in combination with one of the standard chemotherapies (mFOLFOX/bevacizumab) will be safe and effective in patients with advanced colorectal cancer.

This study has several purposes:

- To determine if the combination will be safe.
- To determine the highest safe dose of the study drug (riluzole) when it is combined with SOC chemotherapy
- To determine how the body processes the study drug ("pharmacokinetics")
- To evaluate how well the study drug works when it is combined with chemotherapy
- To evaluate how the tumor responds to the combination treatment
- To examine what the study drug does to the body ("pharmacodynamics")

2. How many people will take part in this study?

At the Ohio State University, approximately 15 patients will participate in this trial.

3. What will happen if I take part in this study?

If you decide to take part in the study, you will first be asked to sign this consent form.

The study will then include three main periods:

- Screening period
- Treatment period
- Follow-up period

The details of each period are described below.

Screening period

The screening period can last up to 4 weeks. You will be checked to see if the study is suitable for you and to assess your current health status. This will take a single visit to the study center.

At the screening visit, you will be asked if you agree to participate in the study by signing this consent form. If you agree, you will have several assessments to check whether the study is suitable for you, these are outlined in the table of study assessments (Table 1).

During the screening period, your study doctor will take your personal information, review your complete medical history and all the medication that you are currently taking, and ask about any previous treatments for your colorectal cancer.

Treatment period

The treatment period will start within 4 weeks of the screening visit and will consist of approximately 16 weeks of treatment. During this time, you will take the study drug (riluzole), as well as standard chemotherapy. The study drug is a tablet that should be taken by mouth twice a day, in the morning and at night, with a full glass of water and at least 1 hour before or 2 hours after a meal. You must swallow the study drug whole, and should not crush, chew, or bite it.

Different doses of the study drug will be investigated. The initial small group of participants (3 patients) will receive a dose of the study drug starting at 50 mg twice a day. A group of healthcare professionals, known as a Safety Monitoring Committee (SMC), will decide when and whether the next dose level can be started. The SMC will make this decision by reviewing the data of patients that are already receiving treatment in the study. The SMC may approve the next dose level, or decide that the study should be stopped or modified to ensure patient safety.

It is important to know that the SMC may meet during the time that you are having the screening assessments, and may review the next dose level before you are able to begin treatment. If you found to be eligible for the study, you will not be able to receive treatment until the SMC gives the approval to move forward with treating the next group of patients.

It is therefore important to understand that starting the screening process is not a guarantee for being treated in this study.

In addition, you will receive the chemotherapy drug called mFOLFOX6 in combination with the drug bevacizumab/or bevacizumab biosimilar, which is the standard of care in colorectal cancer.

mFOLFOX6 is a chemotherapy regimen that consists of three drugs: oxaliplatin, leucovorin, and 5-FU. Bevacizumab is an antibody that targets the blood vessel by blocking the activity of a protein called vascular endothelial growth factor alpha (VEGF-A). It helps to make the mFOLFOX6 more effective. Each medication in the chemotherapy, as well as bevacizumab, will be given as an intravenous (IV) infusion through a vein.

You will receive 85 mg/m2 of oxalipaltin and 400 mg/m2 of leucovorin over 2 hours on day 1, then 5 mg/kg of Bevacizumab. You will then 400 mg/m2 of 5-FU and then another 2400 mg/m2 of 5-FU over 46 hours. This will be done every 2 weeks for 8 cycles.

Follow-up period

The follow-up period will last for up to 30 days. This is to check your health after you stop receiving the study medication. The study investigators will continue to follow all patients after the 30-day follow up visit for treatment benefits for the rest of your life.

Early termination

If you finish the study treatment early for any reason, you will be asked to attend an early termination visit to make sure it is being done safely. This will happen as soon as possible after your last dose of the study drug.

Below is the schedule of study visits and assessments.

Table 1. Study calendar

Trial Period	**Screen Visit**	**Treatment[1] Visit**								**End of Study Visit[2]**
Study Period		C 1 D 1	C 2 D 1	C 3 D 1	C 4 D 1	C 5 D 1	C 6 D 1	C 7 D 1	C 8 D 1	
Schedule Window (Days):	Day -28 to Day -1	Each cycle: 14 days								After the last dose of Riluzole (30 days +/- 7 days)
Informed Consent	x									
Demographics and Medical History	x									
Medication Review	x	x		x		x		x		x
Review of Adverse Events	x	x		x		x		x		x
Full physical exam,	x	x		x		x		x		x
Vital Signs and Weight	x	x	x	x	x	x	x	x	x	x
ECOG Performance Status	x	x		x		x		x		x
Pregnancy Test – Urine or Serum beta-HCG	x									
[5]CBC with Differential	x	x	x	x	x	x	x	x	x	x
[6]Comprehensive Metabolic Panel	x	x	x	x	x	x	x	x	x	x
Urine test	x			x				x		x
[3]Blood Samples		x		x		x		x		
12-Lead ECG	x									
CT Scan	x					x				x

Tumor biopsy[4] for biomarkers	x	x								

[1] The dosage of riluzole will be determined by your doctor.

[2]End of study visit: This is to check your health after you stop receiving the study medication, which is around 30 days after the last dose of riluzole.

[3]Blood sample: Blood work will be collected for pharmacokinetic study for riluzole on day 1 of cycle 1, at 6 different time points. Blood work will be collected for pharmacokinetic study for bevacizumab on day 1 of odd cycles, at 2 different time points. Also, blood samples will be collected to examine immune cells and protein levels.

[4]Pre-treatment tumor tissue biopsy will be obtained before starting the study, and post-treatment tumor tissue biopsy will be obtained after the completion of cycle 1 and before completion of cycle 3. If biopsy is risky, unsafe or difficult to obtain, your doctor will waive the biopsy for you.

[5]CBC with differential: A complete blood count, also known as a full blood count, is a set of medical laboratory tests that provide information about the cells in a person's blood. The CBC indicates the counts of white blood cells, red blood cells and platelets, the concentration of hemoglobin, and the hematocrit.

[6]Comprehensive metabolic panel: Comprehensive Metabolic Panel (CMP) measures a panel of the chemical in the blood to assess liver function, kidney function, electrolytes, proteins, and calcium.

Study assessments and procedures

Some or all the following assessments may take place at your study visits:

Blood tests

Blood samples will be taken for a number of different tests:

- To check your blood cells and the health of your liver and kidneys, as well as a potential tumor marker Carcinoembryonic Antigen (CEA).
- To see how the study drug works in your body.

The amount of blood that will be taken during the study is estimated at about 20-30 ml (one to two tablespoons) on treatment cycles 1, 3, 5 and 7. This amount may vary if you have any abnormal results or if the test needs to be repeated for any reason.

Urine tests

Urine samples will be taken to monitor your general health.

Pregnancy test

It is not known how the study drug may affect an unborn child. Therefore, women who are able to have children will be required to have blood samples taken for a pregnancy test before beginning treatment.

Vital signs
This will include checks of your body temperature, breathing rate, heart rate, and blood pressure. You will need to rest for about 5 minutes in a quiet place (without distraction from television or cell phone) before your heart rate and blood pressure are measured. Blood pressure and heart rate will be measured while you are lying down.

Physical exam
An external examination will be carried out to check your overall health. This will include checks of your general appearance, skin, head, neck, cardiovascular and pulmonary system (heart and blood vessels, and lungs), gastrointestinal system (gut and intestines), genitourinary system (reproductive organs and urinary system), lymphatic system, muscles and bones, arms, legs, eyes, nose, throat, and nervous system.
Your body weight will also be checked when the physical examination is performed. Your height will be checked at the screening visit only.

Questions about your health and medications
The study doctor will ask if you have had any new symptoms or changes in your health or medications since your last visit. They will also ask if you have taken any new medications or experienced any new side effects in this time.

ECOG performance status
Your Eastern Cooperative Oncology Group (ECOG) performance status will be assessed. This is a scale used by doctors and researchers to see how the disease affects your daily activities. Your study doctor will ask you questions about what you are able to do in your daily life. This is to check how the cancer is progressing, how it is affecting your day-to-day activities, and your general well-being.

12-lead Electrocardiogram (ECG)
This is a test that looks at the rhythm of your heart by putting small, sticky patches on certain areas of your body while you are lying down. These patches are connected to thin wires that are also connected to a machine, which interprets the activity of your heart and prints a report. The test takes about 5 to 10 minutes and it will be done before you have taken the study drug and after you have been lying down on your back for 5 minutes.

Biopsy samples
The study doctor will request a sample of tumor tissue before starting the study. In addition, you will also be asked for another fresh biopsy after you have taken the study drug for about two weeks to 6 weeks.

A biopsy is a procedure where a small sample of the tumor tissue is removed for examination. Before taking the sample, the study doctor will numb the area of skin over the tumor with an “anesthetic” so that you cannot feel the sample being taken. A special needle will be used to take the tumor sample, which will measure approximately the size

of a grain of rice (5 mm^3). The procedure will take about 20 minutes. The stored tumor tissue sample or the freshly collected tumor tissue sample at screening will be used only for research purposes.

The biopsy is mandatory. If you have had tumor tissue saved previously that can be used, you can forgo the pre-treatment biopsy. The procedure may cause some discomfort or pain, however, it is generally safe. We will analyze your tumor tissue to examine how your tumor responds to the study drug. Your tumor tissue will be stored and accessible to you for other tests, which may provide more treatment options in the future. If your doctor feels it is unsafe to do the biopsy or technically difficult to do the biopsy, then biopsy procedure will be waived.

Tumor assessments
The possible growth and/or spread of the cancer will be monitored during the study by using a CT (computed tomography) scan.

A CT scan makes use of computer-processed combinations of many X-ray measurements taken from different angles to produce cross-sectional images of specific areas of a scanned object, allowing the user to see inside the object. After the scan is done, the study doctor will evaluate the images of your tumor with the appropriate criteria for your tumor.

4. How long will I be in the study?

You will be asked to visit the study center approximately 9 times. You will be in the study for approximately 20 weeks, with the treatment lasting about 16 weeks with regular study center visits, and with a follow up visit after 30 days of the last dose of riluzole. Your regular chemotherapy will continue, following the completion of study drug administration.

5. Can I stop being in the study?

Yes, you may leave the study at any time. If you decide to stop participating in the study, there will be no penalty to you, and you will not lose any benefits to which you are otherwise entitled. Your decision will not affect your future relationship with The Ohio State University.

6. What risks, side effects or discomforts can I expect from being in the study?

Below is a list of risks and side effects for this study.

It is impossible to predict every risk or side effect that may happen in this study because each person's reaction to a study drug may be different. You may have a side effect or be at risk for symptoms, illnesses and/or complications that could not be predicted by your study doctor. If such side effects occur, you must inform your study doctor immediately.

Side effects of Riluzole

Riluzole is well-studied in terms of side effects in patients with a disease called amyotrophic lateral sclerosis (ALS). However, the side effects of riluzole taken in combination with chemotherapy (like mFOLFOX and bevacizumab) are not known. Your study doctor will monitor you for side effects while you are on this study. The drugs that may increase the level of riluzole (increase the side effects of riluzole) include: ciprofloxacin, enoxacin, fluvoxamine, methoxsalen, mexiletine, oral contraceptives, thiabendazole, vemurafenib, zileuton. The drugs that may decrease the level of riluzole (decrease the effectiveness of riluzole) include: carbamazepine, phenobarbital, phenytoin, rifampin, ritonavir.

In addition to drug interactions which may increase or decrease the level of riluzole in your body, riluzole may cause elevated liver enzymes. Therefore, we recommend avoiding drugs that can cause liver damage while you are taking riluzole, including rifampicin, isoniazid, fibrates. Please notify your physicians if you have new medications or supplements you are about to start during the study.

Based on clinical studies from over 1000 patients, some of the side effects from the study drug can be anticipated:
Very common (occurring in more than 1 in 10 participants):

- Feeling tired
- Feeling sick (nausea)
- Decreased lung function

Common (occurring in more than 1 in 100 but less than 1 in 10 participants):

- Being sick (vomiting)
- High blood pressure
- Dry mouth
- Abdominal pain
- Dizziness
- Increased liver enzymes

Very rare (occurring in less than 1 in 10,000 participants):

- Decreased white blood cell counts

Side effects of mFOLFOX6 (*oxaliplatin, fluorouracil (5-FU), and leucovorin*):

Common side effects (may affect more than 20 in 100 people):

- Hair loss
- Redness, pain or peeling of palms and soles
- Rash, increased risk of sunburn, and itching
- Diarrhea, nausea, vomiting, constipation, and loss of appetite
- Difficulty swallowing
- Sores in mouth
- Heartburn
- Infection, especially when white blood cell count is low
- Decrease in red blood cells (anemia) which may require a blood transfusion
- Decrease in white blood cells (neutropenia) which can lead to infections
- Bruising, bleeding
- Headache
- Tiredness
- Numbness, tingling or pain, "pins and needles" of the hands, feet, arms and legs
- Cough
- Fever, pain

Occasional side effects (may affect 4-20 in 100 people):

- Chest pain
- Abnormal heartbeat which may cause fainting
- Swelling and redness at the site of the medication injection
- Hives
- Skin changes
- Weight gain, weight loss, belly pain
- Internal bleeding which may cause black tarry stool, blood in vomit or urine, or coughing up blood
- Changes in taste
- Blood clot which may cause swelling, pain, shortness of breath
- Bleeding from multiple sites including vaginal bleeding, bleeding of the testis, or bleeding of the brain
- Liver damage which may cause yellowing of eyes and skin
- Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat
- Change in voice
- Confusion, dizziness
- Muscle weakness
- Inability to move shoulder or turn head
- Blurred vision, watering eyes
- Discomfort from light
- Abnormal body movement including the eye and eyelid
- Difficulty walking, using your hands, opening mouth, talking, with balance and hearing, smelling, eating, sleeping, emptying the bladder

- Hearing loss
- Swelling of the body which may cause shortness of breath
- Kidney damage which may require dialysis
- Scarring of the lungs
- Blockage of the airway which may cause shortness of breath, cough, wheezing
- Dehydration

Rare and serious side effects (may affect less than 3 in 100 people):

- Damage to the heart which may cause shortness of breath
- A new cancer resulting from treatment of a prior cancer
- Sensation of difficulty swallowing or breathing which may be made worse by exposure to cold
- Breakdown of muscle tissue and leaking of breakdown products into the blood, which may cause kidney damage
- Change in the heart's electrical activity (known as QTc prolongation) that rarely may lead to abnormal heart rhythms that can be fatal

Side effects of Bevacizumab:

COMMON, SOME MAY BE SERIOUS

In 100 people receiving bevacizumab, more than 20 and up to 100 may have:

- High blood pressure which may cause headaches, dizziness, blurred vision

OCCASIONAL, SOME MAY BE SERIOUS

In 100 people receiving bevacizumab, from 4 to 20 may have:

- Anemia which may require blood transfusion
- Low white cell count that may increase the risk of infection
- Infection, including collection of pus in the belly or rectum
- Abnormal heartbeat which may cause palpitations or fainting
- Pain in the belly, rectum, chest, joints, muscles, or tumor
- Low appetite, constipation, diarrhea, heartburn, nausea, vomiting, or dehydration
- Internal bleeding which may cause black tarry stool, blood in vomit, coughing up blood, or blood in urine
- Bleeding from other sites, including the vagina or nose
- Blockage of internal organs which may cause vomiting or inability to pass stool
- Sores in the mouth
- Allergic reaction during or after infusion of bevacizumab which may cause fever, chills, rash, itching, hives, low blood pressure, wheezing, shortness of breath, swelling of the face or throat
- Delay in healing of wounds or spontaneous opening of wounds
- Weight loss, tiredness, or dizziness
- Muscle weakness
- Damage to the jawbone which may cause loss of teeth

- Headache
- Numbness, tingling or pain in the fingers or toes
- Hoarseness, stuffy nose, or cough
- Dry skin
- Swelling and redness of the skin
- Blood clot in limbs or lungs which may cause swelling, pain, shortness of breath
- Leakage of protein in the urine, which can rarely lead to damage to the kidney

RARE, AND SERIOUS
In 100 people receiving bevacizumab, 3 or fewer may have:

- Clots in the arteries, causing stroke (which may cause paralysis or weakness) or heart attack (which may cause chest pain or shortness of breath). This risk is significantly increased in patients who are elderly or with history of diabetes
- Heart failure which may cause shortness of breath, swelling of ankles, and tiredness
- Bowel perforation (a tear in the bowel) that can cause pain or bleeding and require surgery to repair
- A tear or hole (fistula) in internal organs such as the nose, throat, lungs, esophagus, rectum, or vagina. These conditions may cause serious infections or bleeding and require surgery to repair
- Sores in the throat
- Flesh-eating bacteria syndrome, an infection in the deep layers of skin
- Damage to organs (bone, lungs, others) which may cause loss of motion
- Bleeding in the tumor, brain, belly or lungs which may cause confusion, blood in stool or coughing up blood
- Brain damage which may cause headache, seizure, blindness (also known as Reversible Posterior Leukoencephalopathy Syndrome)
- Kidney damage which may require dialysis
- Redness, pain or peeling of palms and soles

Additional information on possible side effects for bevacizumab:

- Risk in children or adolescents: abnormal bone changes which may interfere with growth.
- Risk in pre-menopausal women: more likely to develop menopause when taking bevacizumab

<u>Reproductive Risks:</u>
The effect and safety of the study drugs on a developing baby is not known at this time. There may be unknown risks to you, the embryo, the unborn baby, or a nursing infant if you (or your partner) become pregnant or are breastfeeding during your study treatment.

Women who are pregnant, breastfeeding or plan on becoming pregnant during the study should not take part in the study (or stop breastfeeding in order to take part). At screening,

you will be asked to take a pregnancy test to confirm you are not pregnant if you are a woman of childbearing potential.

Women who could become pregnant must agree to use an effective contraceptive during the course of this study and for 6 months after their last dose of study drug. Any woman who finds that she has become pregnant while taking part in the study or 6 months after their last dose of study drug should immediately tell her study doctor.

If you are a man who is sexually active, you must inform your partner(s), if they are able to have children, that the effects of the investigational product on sperm are unknown. You or your partner(s) should use one (1) form of highly effective method of birth control, so your partner(s) does not become pregnant. Any man whose partner becomes pregnant while taking part in the study should immediately tell his study doctor.

If you are a woman of childbearing potential, or if you are a man whose partner is a woman of childbearing potential, you and your partner must be willing to consistently and correctly use 1 form of highly effective birth control starting at screening and throughout the study period, and for 6 months after you stop taking study drug.

Highly effective forms of birth control include:

- Consistent and correct usage of established hormonal methods of birth control (e.g. “the pill”)
- Established intrauterine device (IUD) or intrauterine system (IUS)
- Surgically blocking of fallopian tubes to prevent the egg from being fertilized (“having one’s tubes tied”)
- Male partner who has had a vasectomy
    - A vasectomy is a highly effective contraception method provided the absence of sperm has been confirmed. If not, an additional highly effective method of contraception should be used.
- Removal of both testicles
- Sexual abstinence is considered a highly effective method only as defined as refraining from heterosexual activity during the entire period of risk associated with the study treatment. The reliability of sexual abstinence needs to be evaluated in relation to the duration of the study and must be the preferred and usual lifestyle of the participant.

If you are a woman, you must not donate ova or eggs or breastfeed during this study and for 6 months after your last dose of study treatment.

If you are a man, you must not donate sperm during this study and for 6 months after your last dose of study drug.

Electrocardiogram (ECG):
The ECG test is a recording of the electrical activity of your heart. The sticky pads used may be cold when applied and sometimes cause some discomfort such as redness or itching. If the hair under the patches needs to be shaved, irritation from shaving also could occur.

Blood Draws:
During the collection of blood samples, you may experience pain and/or bruising at the needle injection site. Although rare, localized clot formation and infections may occur. Lightheadedness and/or fainting may also occur during or shortly after the blood draw or catheter insertion.

Risks of Using an Intravenous (IV) Catheter:
- Infection
- Pain
- Redness
- Bruising
- Vein irritation from the fluids or medication being given
- Local swelling due to IV fluid accidentally entering the tissue rather than the vein
- Blood clots, which may cause inflammation, swelling and pain

CT Scan:
CT scans send x-rays through the body at different angles. You will be exposed to small doses of radiation. This dose of radiation could be potentially harmful, but the risks are so small that they are difficult to measure.

Some people may feel "closed in" while lying in the scanner. However, the scanner is open at both ends and an intercom allows you to talk with the doctors and staff. If you feel anxious during the scan, medical staff may provide comfort or the scan may be stopped. If a CT scan is being done of the abdomen, you will usually drink a liquid to help define various abdominal organs. This liquid may cause hives, itching, or other allergic symptoms, nausea and/or vomiting and/or diarrhea. You may also receive an IV contrast to make the x-ray pictures more accurate. This IV solution may cause flushing, nausea, and/or very infrequent severe allergic reactions. Please inform the study doctor if you have a history of allergic reactions while getting ready for a CT scan.

Tumor Biopsy:
Tumor biopsy is a minimally invasive procedure. Possible risks at biopsy site may include pain, bruising, swelling, inflammation, infection, bleeding or scarring. Some of these risks may be severe. There is a rare possibility of the tumor cells spreading into the nearby area. Your study doctor will further discuss the risks involved if you are providing a sample of your tumor tissue for a biopsy.

The risks associated with other treatment for your cancer are similar to those described in this consent. The possible risks of getting no treatment, or getting comfort care, include your disease getting worse or death. Your doctor will discuss these alternatives in detail, including the benefits and risks of each option.

Other Risks

Treatment with this study drug/SOC Combination may involve risks that are currently unexpected and may interact with other medications you are taking. Side effects that have not been reported and have not been anticipated may occur due to the investigational nature of this treatment. Therefore, you must report all changes in your condition to your study doctor as soon as possible. During the study, you will be thoroughly and regularly examined.

7. What benefits can I expect from being in the study?

You may or may not receive any benefit from taking part in this study, as this is a study to test the safety and effectiveness of the study drug. Your disease could get worse, stay the same, or improve. The potential benefits to you may include improvement of your condition and better effectiveness of the standard chemotherapy.

There is no guarantee that you will receive a medical benefit from participating in this study, but the information we get from this study may help us in the future to better treat people with advanced colorectal cancer.

8. What other choices do I have if I do not take part in the study?

You may choose:

- To take part in a different clinical trial, if one is available
- Not to take part in a clinical trial
- Not to receive treatment for your disease
- To receive palliative treatment, also called comfort care, which aims to increase patient comfort but not treat the underlying condition

You may choose not to participate without penalty or loss of benefits to which you are otherwise entitled.

9. Will my study-related information be kept confidential?

Efforts will be made to keep your study-related information confidential. However, there may be circumstances where this information must be released. For example, personal

information regarding your participation in this study may be disclosed if required by state law.

Also, your records may be reviewed by the following groups (as applicable to the research):

- Office for Human Research Protections or other federal, state, or international regulatory agencies;
- U.S. Food and Drug Administration;
- The Ohio State University Institutional Review Board or Office of Responsible Research Practices;
- The sponsor supporting the study, their agents or study monitors; and
- Your insurance company (if charges are billed to insurance).

If this study is related to your medical care, your study-related information may be placed in your permanent hospital, clinic, or physician's office records. Authorized Ohio State University staff not involved in the study may be aware that you are participating in a research study and have access to your information.

If we find information that significantly impacts your health during your participation in this study, we will share it with you by asking you to re-consent to this trial by signing an updated version of this consent form.

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

10. Will my de-identified information (and bio-specimens) be used or shared for future research?

Yes, it/they may be used or shared with other researchers without your additional informed consent.

11. What are the costs of taking part in this study?

The study drug, riluzole, will be provided to you and will not be billed to you or your insurance company. You and/or your insurance company will not be charged for the cost of any tests or procedures that are required as part of this research study and are outside the standard of care for your condition.

You and/or your insurance company will still be responsible for the cost of routine medications, tests and procedures that you would receive even if you were not in this

research study. You and/or your insurance company will be billed for the costs of these routine tests and procedures in the usual manner. You will be responsible for any co-payments, co-insurance and deductibles that are standard for your insurance coverage. You will be responsible for any charges not reimbursed by your insurance company.

Some insurance companies will not pay for routine costs for people taking part in research studies. Before deciding to be in this research study, you should check with your insurance company to find out what they will pay for. Participating in this research study may lead to additional costs to you. In some cases, it is possible that your insurance company will not pay for these costs because you are taking part in a research study.

12. Will I be paid for taking part in this study?

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

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

If you suffer an injury from participating in this study, you should notify the researcher or study doctor immediately, who will determine if you should obtain medical treatment at The Ohio State University Wexner Medical Center.

The cost for this treatment will be billed to you or your medical or hospital insurance. The Ohio State University has no funds set aside for the payment of health care expenses for this study.

14. What are my rights if I take part in this study?

If you choose to participate in the study, you may discontinue participation at any time without penalty or loss of benefits. By signing this form, you do not give up any personal legal rights you may have as a participant in this study.

You will be provided with any new information that develops during the course of the research that may affect your decision whether or not to continue participation in the study.

You may refuse to participate in this study without penalty or loss of benefits to which you are otherwise entitled.

An Institutional Review Board responsible for human subjects research at The Ohio State University reviewed this research project and found it to be acceptable, according to applicable state and federal regulations and University policies designed to protect the rights and welfare of research participants.

HIPAA AUTHORIZATION TO USE AND DISCLOSE INFORMATION FOR RESEARCH PURPOSES

I. What information may be used and given to others?

- Past and present medical records;
- Research records;
- Records about phone calls made as part of this research;
- Records about your study visits;
- Information that includes personal identifiers, such as your name, or a number associated with you as an individual;
- Information gathered for this research about:
  HIV / AIDS
  Hepatitis infection
  Sexually transmitted diseases
  Other reportable infectious diseases
  Physical exams
  Laboratory, x-ray, and other test results
  The diagnosis and treatment of a mental health condition
- Records about any study drug you received

II. Who may use and give out information about you?

Researchers and study staff.

III. Who might get this information?

- The sponsor of this research. "Sponsor" means any persons or companies that are:
  - working for or with the sponsor; or
  - owned by the sponsor.
- Authorized Ohio State University staff not involved in the study may be aware that you are participating in a research study and have access to your information;
- If this study is related to your medical care, your study-related information may be placed in your permanent hospital, clinic, or physician's office record;
- Other research team members including study monitor (CRO, SMO), healthcare providers, persons or organizations that analyze health information for the study, data safety monitoring boards, etc.

IV. Your information <u>may</u> be given to:

- The U.S. Food and Drug Administration (FDA), Department of Health and Human Services (DHHS) agencies, and other federal and state entities;
- Governmental agencies in other countries;
- Governmental agencies to whom certain diseases (reportable diseases) must be reported; and
- The Ohio State University units involved in managing and approving the research study including the Office of Research and the Office of Responsible Research Practices.

V. Why will this information be used and/or given to others?

- To do the research;
- To study the results; and
- To make sure that the research was done right.

VI. When will my permission end?

There is no date at which your permission ends. Your information will be used indefinitely. This is because the information used and created during the study may be analyzed for many years, and it is not possible to know when this will be complete.

VII. May I withdraw or revoke (cancel) my permission?

Yes. Your authorization will be good for the time period indicated above unless you change your mind and revoke it in writing. You may withdraw or take away your permission to use and disclose your health information at any time. You do this by sending written notice to the researchers. If you withdraw your permission, you will not be able to stay in this study. When you withdraw your permission, no new health information identifying you will be gathered after that date. Information that has already been gathered may still be used and given to others.

If you wish to withdraw from this study, you must do so in writing to:

Dr. Ning Jin
1800 Cannon Dr.
13th Floor, Lincoln Tower
Columbus, OH 43210

VIII. What if I decide not to give permission to use and give out my health information?

Then you will not be able to be in this research study and receive research-related treatment. However, if you are being treated as a patient here, you will still be able to receive care.

IX. Is my health information protected after it has been given to others?

There is a risk that your information will be given to others without your permission. Any information that is shared may no longer be protected by federal privacy rules.

X. May I review or copy my information?

Signing this authorization also means that you may not be able to see or copy your study-related information until the study is completed.

15. Who can answer my questions about the study?

For questions, concerns, or complaints about the study you may contact Dr. Ning Jin at (614) 346-6259 (24 hour/pager).

For questions related to your privacy rights under HIPAA or related to this research authorization, please contact:

HIPAA Privacy Manager,
The Ohio State University Medical Center
600 Ackerman Road
Suite E2140
Columbus, OH 43202
614-293-4477.

For questions about your rights as a participant in this study or to discuss other study-related concerns or complaints with someone who is not part of the research team, you may contact the Office of Responsible Research Practices at 1-800-678-6251.

If you are injured as a result of participating in this study or for questions about a study-related injury, you may contact Dr. Ning Jin at (614) 293-6529 or (614) 346-6259 (24 hour/pager).

Signing the consent form

I have read (or someone has read to me) this form and I am aware that I am being asked to participate in a research study. I have had the opportunity to ask questions and have had them answered to my satisfaction. I voluntarily agree to participate in this study.

I am not giving up any legal rights by signing this form. I will be given a copy of this form**.**

Printed name of participant	**Signature of participant**
	AM/PM
	Date and time
Printed name of person authorized to consent for participant (when applicable)	**Signature of person authorized to consent for participant (when applicable)**
	AM/PM
Relationship to the participant	**Date and time**

Investigator/Research Staff

I have explained the research to the participant or his/her representative before requesting the signature(s) above. There are no blanks in this document. A copy of this form has been given to the participant or his/her representative.

Printed name of person obtaining consent	**Signature of person obtaining consent**
	AM/PM
	Date and time

Witness(es) - *May be left blank if not required by the IRB*

Printed name of witness	**Signature of witness**
	AM/PM
	Date and time
Printed name of witness	**Signature of witness**
	AM/PM
	Date and time