PennState Cancer Institute

CONSENT FOR RESEARCH
Penn State College of Medicine
Penn State Health

Title of Project: A Pilot Study to Evaluate the Response and Tolerability of Verzenio™ (Abemaciclib) in Patients with Advanced Biliary Tract Carcinoma

Principal Investigator and Study Sponsor: Nelson Yee, M.D., Ph.D.

Address: Penn State Cancer Institute – Clinical Trials Office
Rm T2200, MC: CH56
500 University Drive
Hershey, PA 17033

Telephone Numbers: Weekdays: 8:00 a.m. to 5:00 p.m. (717) 531-8678. After hours call (717) 531-8521. Ask for the Hematology/Oncology doctor on 24-hour call.

Subject's Printed Name: _____

We are asking you to be in a research study.

Whether or not you take part is up to you. You can choose not to take part. You can agree to take part and later change your mind. Your decision will not be held against you, and there will be no penalty or loss of benefits to which you are entitled.

This form gives you information about the research. Please ask questions about anything that is unclear to you and take your time to make your choice.

KEY INFORMATION

The following is a short summary of this study to help you decide whether or not to be a part of this research. More detailed information is provided later in this form. If you have any questions, be sure to ask the study team.

Why am I being invited to take part in this research study?

You have been asked to participate in this study because you have advanced biliary tract carcinoma that has progressed (worsened) despite initial treatment, or you did not tolerate the previous chemotherapy, or you are considered not a good candidate for first-line systemic therapy.

What is the purpose of this research study?

The purpose of this voluntary research study is to investigate the use of a medication called Verzenio™ or Abemaciclib for your disease. Abemaciclib is a medicine that targets certain proteins in cancer cells and stops the cancer cells from growing.

How long will the research study last?

If you agree to take part, it will take you about 3 years to complete this research study. You may continue to take part in the study until your disease progresses (or gets worse), you experience serious side effects or you decide to withdraw from the study.

What will I need to do?
If you choose to participate there is a screening period, treatment period and a long term follow up period. You will need to take the study medication by mouth twice a day as directed, you will be asked to keep a study drug diary while you are taking the study medication, you will need to come to all your scheduled study visits, and make sure you talk to your study doctor or study staff about any side effects you are experiencing while participating in this study.

What are the main risks of taking part in the study?
You may have side effects while on the study. There are side effects of the study drug Abemaciclib. In addition, you may have side effects from other medication you are receiving as part of your routine care for your disease. Some of the common side effects are as follows: loose stools, belly pain or swelling, lack of energy, weakness, fatigue, feeling sick to the stomach, low appetite, decreased number of white blood cells, low red blood cell count, decreased number of platelets, bruising, difficulty with blood clotting, or bleeding easily, dry mouth, inflammation or ulcers inside the mouth, taste changes or bad taste in the mouth, hair loss, headache, jaundice (or the yellowing of the eyes and skin), fever, joint pain, cough, and dark-colored urine.

Everyone taking part in the study will be watched carefully for any side effects. However, researchers don't know all the side effects that may happen. You may experience none, some, or many of the side effects listed below. Side effects may be mild or very serious, including a risk of death. Your health care team may give you medicines to help lessen side effects.

What are the possible benefits to me that may reasonably be expected from being in the research?
There is no guarantee that you will benefit from this research. It is possible that the medication Abemaciclib may help to prevent your cancer from growing. However, the information from this study will help investigators learn more about the medication Abemaciclib and its effect on advanced biliary tract carcinoma.

What happens if I do not want to be in this research?
Participation in research is completely voluntary. You can decide to participate or not to participate. Instead of participating in this research, you could:

- Be part of a different research study, if one is available.
- Receive standard of care treatment that is FDA approved.
- Choose not to be treated for your medical condition and only receive care to make you more comfortable.

DETAILED INFORMATION
The following is more detailed information about this study in addition to the information listed above.

1. Why is this research study being done?
You have been asked to participate in this study because you have advanced biliary tract carcinoma that has progressed (worsened) despite initial treatment, or you did not tolerate the previous chemotherapy. We are studying the use of a medication called Verzenio™ or Abemaciclib for your disease. Abemaciclib is a medicine that targets certain proteins in cancer cells and stops the cancer cells from growing.

The United States Food and Drug Administration (FDA) has approved Abemaciclib as a type of treatment for patients with advanced breast cancer. Researchers have found that some of the genetic mutations (changes in DNA) present in breast cancer cells are also found in biliary tract cancer. For this reason, the doctors would like to find out if use of Abemaciclib can help stop the growth of your disease. Because Abemaciclib has not been FDA approved for biliary tract carcinoma, use of this medication for your disease is considered research (or investigational).

We expect about 10 people will take part in this research study at Penn State Cancer Institute in Hershey, PA over the next few years.

2. What will happen in this research study?

Study Screening:

If you agree to participate, the research team will evaluate you to see if you are able (or eligible) to take part in this study. As part of this screening you will need to have the following exams and tests. These exams and tests are part of regular cancer care and may be done even if you did not join the study. If you have had some of them recently, they may not need to be repeated.

- Your doctors will ask you about your medical history, surgical and psychiatric history, any previous cancer treatments, smoking history, and other medications you are taking.
- A physical examination, which includes your vital signs (heart rate, breathing rate, temperature, and blood pressure), height, weight
- How you are performing in terms of your activities of daily living (called a "performance status assessment"), and your overall health status (heart, lungs, kidneys, liver, etc.).
- Blood tests to look at how your blood, immune system, kidneys, and liver are functioning. About 2 teaspoons of blood are needed for these tests.
- A urinalysis used to test for abnormalities like infection or kidney problems.
- Females who are able to have a child will be required to take a pregnancy blood test within 7 days prior to the study treatment. About 1 teaspoon of blood is needed for this test.
- A 12-lead electrocardiogram (also called ECG, an electrical tracing of your heartbeat) and echocardiogram (sound waves to make pictures of your heart, which helps show how well your heart pumps blood) to check for signs of heart disease.
- Tumor evaluation include CT scans (Computerized series of x-rays), and/or MRI scans of your chest, belly, pelvis and brain (Magnetic resonance imaging, body pictures created by using magnetic energy rather than x-ray energy. To have the scans, you will lie on a table that slides into the scanner, which is like a large tube). A PET/CT (uses a small amount of a radioactive drug to show differences between healthy tissue and tumor tissue) can also be used to scan your chest, upper belly and lower belly to measure your disease.
- You either had or will have a tumor biopsy taken for your routine care. If there is enough sample left over, a piece of the tumor biopsy sample taken for your routine care will be requested for research testing. If there is not enough tissue from previous tumor samples then a fresh biopsy will be collected for diagnosis and to analyze the mutation of your cancer cells.

On the day you start the study medication-Abemaciclib

Before you receive your first dose of Abemaciclib, the following assessments are required:

- A physical examination including your weight, and vital signs which include temperature, heart rate, breathing rate and blood pressure
- Your performance status assessment

- Blood tests to look at how your blood, immune system, kidneys, and liver are functioning and if there are any changes that may be related to the study medication. About 2 teaspoons of blood are needed for these tests
- ECG (12-lead electrocardiogram, as clinically indicated)
- Your doctors will ask you about other medications you are taking
- Your doctor will ask about any symptoms you might experience.
- A questionnaire about your health called EORTC-QLQ-C30. You may skip any questions on this questionnaire that you would prefer not to answer
- A blood test for biomarkers. Biomarkers are proteins found in the blood and on cancer cells that can tell your doctors how your body and disease are responding to different types of treatment. This test will require about 4.5 teaspoons of blood.

Study Medication - Abemaciclib

How do I take Abemaciclib?

- Take this study medication twice a day for 28 days (a "cycle') as ordered by your study doctor. Follow all instructions closely.
- Take with or without food.
- Take at a similar time of day, twice daily.
- Swallow as a whole capsule and do not chew, crush or split capsules before swallowing.
- Do not use if the capsule is broken or cracked.
- To gain the most benefit, do not miss doses.
- Keep taking this drug as directed, even if you feel well.
- Drink lots of liquids every day (about 8-10 glasses of clear liquid) unless told to drink less liquid by your doctor.
- Avoid grapefruit and products that contain grapefruit juice, orange juice or pomelo products during treatment with Abemaciclib. These products, such as grapefruit juice decreases the body's ability to breakdown the study drug resulting in increased blood level of the study drug that may result in the risk for new or worsened side effects.
- Do not take a medication called ketoconazole or any medication containing ketoconazole.
- If you throw up after taking a dose, do not repeat the dose. Take your next dose at your normal time.
- Write in your diary the dates and times of taking the drug and any symptoms you might experience.
- For your safety, you must tell the study doctor or nurse about all the prescription drugs, herbal products, over-the-counter drugs (OTC), vitamins and other supplements you are taking. Check with the study doctor before starting any new medicines (including prescription, OTC drugs, vitamins and herbal supplements) or changing doses of medications that you are already taking.

What do I do if I miss a dose?

Skip the missed dose and go back to your normal time.
Do not take 2 doses at the same time or extra doses to make up for missing a dose.

How do I store and/or throw out Abemaciclib?

Store at room temperature.
Store in a dry place. Do not store in a bathroom.
Keep all drugs in a safe place. Keep all drugs out of the reach of children and pets.
Return unused drug to the next clinic visit.

During Treatment Cycles (28-Day cycles)

The following procedures and assessments will be performed on days 1 (±3 days) of cycle 1 and 2.

- Review of all prescription drugs, herbal products, over-the-counter drugs, vitamins and other supplements and supplements you have taken along with Abemaciclib.
- Performance status
- Physical examination
- Body weight
- Vital signs measurements (including temperature, heart rate, breathing rate, and blood pressure)
- ECG (C1D1 only, as clinically indicated)
- Blood tests that include how your blood, immune system, kidneys, and liver are functioning and if there are any changes that may be related to the study medication. About 2 teaspoons of blood is needed for these tests
- A blood test for biomarkers. Biomarkers are proteins found in the blood and on cancer cells that can tell your doctors how your body and disease are responding to different types of treatment. This test will require about 4.5 teaspoons of blood (C1D1 only).
- Receipt of Abemaciclib on day 1 of each cycle
- Write in your diary the dates and times of taking the drug and any symptoms you might experience.
- Review of your diary (C2D1 only)
- Return any unused Abemaciclib (C2D1 only).
- A questionnaire about your health called EORTC-QLQ-C30. You may skip any questions on this questionnaire that you would prefer not to answer
- Your doctor will ask about any symptoms you might experience

The following procedures and assessments will be performed on day 15 (±3 days) of cycle 1 and 2.

- Review of all prescription drugs, herbal products, over-the-counter drugs, vitamins and other supplements and supplements you have taken along with Abemaciclib.
- Performance status
- Physical examination
- Vital signs measurements (including temperature, heart rate, breathing rate, and blood pressure)
- Blood tests that include how your blood, immune system, kidneys, and liver are functioning and if there are any changes that may be related to the study medication. About 2 teaspoons of blood is needed for these tests
- Your doctor will ask about any symptoms you might experience

The following procedures and assessments will be performed on cycle 3 through cycle 8 or subsequent cycles should you have clinical benefit, unless otherwise noted.

- Review of all prescription drugs, herbal products, over-the-counter drugs, vitamins and other supplements and supplements you have taken along with Abemaciclib.
- Performance status
- Physical examination
- Vital signs measurements (including temperature, heart rate, breathing rate, and blood pressure)

- Blood tests that include how your blood, immune system, kidneys, and liver are functioning and if there are any changes that may be related to the study medication. About 2 teaspoons of blood is needed for these tests
- A blood test for biomarkers. Biomarkers are proteins found in the blood and on cancer cells that can tell your doctors how your body and disease are responding to different types of treatment (every 8 weeks until end of treatment visit). This test will require about 4.5 teaspoons of blood.
- Tumor evaluation, including CT/MRI/PET of your chest, belly, pelvis and brain as applicable, every other cycle (every 8 weeks)
- Receipt of Abemaciclib on day 1 of each cycle
- Write in your diary the dates and times of taking the drug and any symptoms you might experience.
- Review of your diary
- Return any unused Abemaciclib and study diary on day 1 of each cycle except cycle 1.
- A questionnaire about your health called EORTC-QLQ-C30. You may skip any questions on this questionnaire that you would prefer not to answer
- Your doctor will ask about any symptoms you might experience

End of Treatment (up to 30 days (± 7 days) after last dose study drug)

If you complete the study or withdraw prematurely, final evaluations will be performed at the end-of-treatment visit or on the last day the you take Abemaciclib. The following procedures will be performed:

- Physical examination including body weight
- Vital signs measurements
- Performance status
- ECG (as clinically indicated)
- Your doctor will ask about any symptoms you might experience
- Your doctors will ask you about other medications you are taking
- Your doctors will ask you any anti-cancer therapy you had after completion of this study
- Blood tests that include how your blood, immune system, kidneys, and liver are functioning and if there are any changes that may be related to the study medication. About 2 teaspoons of blood are needed for these tests
- A blood test for biomarkers. This test will require about 4.5 teaspoons of blood.
- A urinalysis used to test for abnormalities like infection or kidney problems.
- Tumor evaluation, including CT/MRI/PET of your chest, belly, pelvis and brain as applicable
- Return any unused study medication Abemaciclib and study diary.
- A questionnaire about your health called EORTC-QLQ-C30. You may skip any questions on this questionnaire that you would prefer not to answer

Long Term Follow-Up Visits

A follow-up visit will be conducted every 3 months +/- 7 days x2 beginning 3 months after the last dose of Abemaciclib then every 6 months +/- 7 days thereafter. The following procedures will be performed at the follow-up visit:

- Tumor evaluation, including CT/MRI/PET of your chest, belly, pelvis and brain as applicable every 3 months until your disease progression.
- Your doctors will ask you have had any anti-cancer therapy.

Research Testing

In addition to all the other blood tests you will undergo at your visits, we will obtain some additional blood for research purposes only. One blood test will be done every 8 weeks. A total of 4.5 teaspoons of blood is needed for this test each visit. This test will be obtained at the same time as your routine blood testing. For this reason, no additional needle sticks should be required.

- A blood test will be done to look at different blood biomarkers called extracellular vesicles. When certain cells in the body grow, they produce (secrete) proteins called extracellular vesicles into the bodily fluids (blood, urine). Biliary tumors produce specific extracellular vesicles that can be found in the blood. The research doctors would like to find out if checking these extracellular vesicles will help show if the cancer is growing.

2a. What are my responsibilities if I take part in this research?
In order to obtain useful, complete data about how Abemaciclib works with your disease, you will be expected to do the following:

- Attend all of your routine visits as scheduled by your physician
- Let your physician know if you are having any new health concerns and when they started. For example, if you have recently started to have red patches on your skin, you should let your physician know as soon as possible and when it started.
- Tell your physician or research team member if you have any changes in medications or allergies while you are taking part on this study.
- Follow the directions of your treating physicians and research team
- Do not participate in other research studies while you are a subject in this study
- Tell the research team member if you wish to stop being in the study.
- Avoid consumption of grapefruit, grapefruit juice, orange juice and pomelo products while taking the study drug due to possible drug interactions.
- At the first sign of loose stools, start an antidiarrheal therapy as instructed by the study doctor and notifying the study doctor or study staff for further instructions and appropriate follow up.
- Drink plenty of fluids, it is recommended about 8-10 glasses of clear fluids each day.
- For your safety, you must tell the study doctor or nurse about all the prescription drugs, herbal products, over-the-counter drugs (OTC), vitamins and other supplements you are taking. Check with the study doctor before starting any new medicines (including prescription, OTC drugs, vitamins and herbal supplements) or changing doses of medications that you are already taking.
- **Males:** are advised to instruct patients to conduct regular self-examination of their testicles and report any new symptoms or changes to their investigator during clinical trial visits.
- If you experience vision changes, you are advised to see an eye doctor.

3. What are the risks and possible discomforts from being in this research study?
You may have side effects while on the study. There are side effects of the study drug Abemaciclib as noted below. In addition, you may have side effects from other medication you are receiving as part of your routine care for your disease.

Everyone taking part in the study will be watched carefully for any side effects. However, researchers don't know all the side effects that may happen. You may experience none, some, or many of the side effects listed below. Side effects may be mild or very serious, including a risk of death. Your health care team may give you medicines to help lessen side effects.

Side Effects of Abemaciclib

Very Common side effects (10% to 90%): (may occur in 10 or more of every 100 people taking the medication)

- Loose stools, may be severe
- Belly pain or swelling
- Lack of energy, weakness or fatigue
- Feeling sick to the stomach with a sense of wanting to throw up
- Low appetite
- Decreased number of white blood cells count in the blood; this may make infections more likely to occur
- Low red blood cell count in the blood that may make you feel more tired
- Decreased number of platelets in the blood; this may cause bruising, difficulty with clotting of blood, or bleeding easily
- Dry mouth
- Inflammation or ulcers inside the mouth
- Taste changes or bad taste in the mouth
- Hair loss
- Headache
- Jaundice (or the yellowing of the eyes and skin)
- Fever
- Joint pain
- Cough
- Dark-colored urine
- Diarrhea

Uncommon side effects (1% to 5%): (may occur in less than 5 of every 100 people taking the medication)

- Decreased number of lymphocytes in the blood; this may make infections more likely to occur
- Rare but severe inflammation of the lungs causing coughing and difficulty breathing
- Deep vein thrombosis (blood clot in the lower leg or thigh) which could be indicated by pain, swelling, redness or warmth in the area of the clot
- Pulmonary embolism (blood clot in the lung) which could be indicated by dry cough, lightheadedness, chest pain, shortness of breath

Very often, increases in creatinine levels, a substance in the blood that measures kidney function, were noted by laboratory testing. While Abemaciclib does not decrease kidney function, creatinine increases may indicate the need for other tests of kidney function.

In mice and rats, when abemaciclib was taken in doses that caused similar exposures to doses used in this study for three or six months, respectively, it caused cataracts and retinopathy. We are not sure how this applies to humans.

Risks in Women of Childbearing Potential and Nonsterile Men
Abemaciclib has been studied in animals to understand possible harmful effects. Information on harmful effects in animals can indicate possible risks to people. This information may be useful to you in considering whether to participate in the study.

Abemaciclib may harm a developing embryo, fetus, or child. When Abemaciclib was tested on pregnant rats, it was found to cause heart and bone birth defects and to decrease the weight of developing fetuses. No effects on female reproductive organs in mice, rats, or dogs were observed. No effects on female fertility and early embryonic development in rats were observed. Women with childbearing potential should use highly effective contraception during treatment and for 3 weeks after the last dose of Abemaciclib.

The effect of Abemaciclib on a fetus (unborn baby) or nursing children is unknown. For that reason if you are pregnant or breastfeeding, you will not be able to participate in this study. If you become pregnant while on study, the Abemaciclib will be stopped and you and your child will be followed closely until completion of the study.

Male animals given Abemaciclib had injury to their testes. Abemaciclib may affect your ability to have children, both while you are taking this drug and in the future.

Abemaciclib may cause fertility problems in males. This may affect your ability to father a child. Talk to your healthcare provider if this is a concern for you.

In rats, when abemaciclib was taken in doses that caused similar exposures to doses used in this study, it caused an increase in the number of Leydig cells in the testicles. When rats were exposed to similar or higher doses than used in this study, it caused an increase in non-cancerous tumors made of these cells. We are not sure how this applies to humans.

Risk of Venipuncture
There may be a risk related to obtaining the blood for the research tests. However, we will obtain the blood for those tests at the same time that your routine blood tests are obtained. For this reason, the physical risks for these blood tests are no more than what you would have in your daily life.

Risk of loss of confidentiality
There is a risk of loss of confidentiality if your information or your identity is obtained by someone other than the investigators, but precautions will be taken to prevent this from happening. The confidentiality of your electronic data created by you or by the researchers will be maintained as required by applicable law and to the degree permitted by the technology used. Absolute confidentiality cannot be guaranteed.

New Information
You have the right to know about new information concerning the study and the medication involved that may affect your health, welfare, or your willingness to take part. You will be informed in writing in a timely manner of any new information or findings that become available that may affect your choice to continue to take part in this study. You will be asked to sign a new (updated) informed consent form as soon as possible to document that this new information has been explained to you.

4. What are the possible benefits from being in this research study?

4a. What are the possible benefits to me?
There is no guarantee that you will benefit from this research. It is possible that the medication Abemaciclib may help to prevent your cancer from growing.

4b. What are the possible benefits to others?
The information from this study will help investigators learn more about the medication Abemaciclib and its effect on advanced biliary tract carcinoma.

5. What other options are available instead of being in this research study?

You do not have to take part in this study to be treated for your condition. Instead of participating in this research, you could:

- Be part of a different research study, if one is available.
- Receive standard of care treatment that is FDA approved.
- Choose not to be treated for your medical condition and only receive care to make you more comfortable.

Before you decide if you want to be in this research, we will discuss the other choices that are available to you. We will tell you about the possible benefits and risks of these choices. Because it is investigational, it's important that you know that the study drug Abemaciclib offered in this research is not available to you without taking part in this research study.

6. How long will I take part in this research study?

If you agree to take part, it will take you about 4 years to complete this research study. You will be asked to return to the Cancer Center Clinic several times throughout the study as noted above. You may continue to take part in the study until your disease progresses (or gets worse), you experience serious side effects or you decide to withdraw from the study.

7. How will you protect my privacy and confidentiality if I decide to take part in this research study?

7a. What happens to the information collected for the research?

Efforts will be made to limit the use and sharing of your personal research information. In our research files at The Milton S. Hershey Medical Center (HMC) and Penn State College of Medicine (PSU), we will include these identifiers your name, dates (e.g. date of birth), medical record number, and a code number.

- A list that matches your name with your code number will be kept in a limited access, password protected computer system within the Cancer Institute Clinical Trials Office.
- Your research records will be labeled with: your code number, your initials, & dates and will be kept in a secure area of the Cancer Institute Clinical Trials Office.
- Your research blood samples will be labeled with: a code number, and your initials, and kept in a secured limited access lab in the Penn State Cancer Institute. Your samples and data will be sent for processing at the laboratory of Penn State University at University Park.
- A copy of this signed consent form will be included in your HMC medical record. This means that other HMC healthcare providers will know you are in this study.
- Results of some of the research-related tests may be kept in your HMC medical record

For research records and specimens sent to Dr. He's laboratory at Captis Diagnostics, Inc, 5000 Forbes Avenue, Scott Hall 4N211, Pittsburgh, PA 15213, you will be identified by a code number.

In the event of any publication or presentation resulting from the research, no personally identifiable information will be shared.

7b. What will happen to my research information and/or samples after the study is completed?
We may use your research information and your biological samples in future studies or may share your information or biological samples with other investigators for future research without your additional informed consent. Before we use or share your information or samples we will remove any information that shows your identity.

Researchers can do studies that are more powerful when they share with each other the data or information they get from research studies. They share this information with each other by putting it into scientific databases. Your coded research information may be put in one or more databases and used for future research. Your information stored in these databases will not include any identifying information such as your name, address, telephone number, or social security number. Your research data will only be available to researchers who have received approval from data access committees and/or Institutional Review Boards. Some of these databases are maintained by PSH/PSU, some are maintained by the federal government, and some are maintained by private companies and other institutions.

Most tests done on samples in research studies are only for research and have no clear meaning for health care. If the research with your identifiable information or samples gives results that do have meaning for your health, the researchers will not contact you to let you know what they have found.

7c. How will my identifiable health information be used?
In general, under federal law (including the Health Insurance Portability and Accountability Act – HIPAA or privacy laws) your health information is private. By signing this form, you are authorizing us to collect, use, and disclose your identifiable health information, sometimes referred to as "Protected Health Information" or "PHI" under HIPAA, for the purposes of this research study. We will use and disclose your information only as described in this form, in the PSH Privacy Notice, and as may be required or allowed under the applicable privacy laws.

The research team may use the following health information:

- Past, present, and future medical records, including identifiable information
- New health information from tests, procedures, visits, interviews, or forms filled out as part of this research study.

The following people/groups may see, use, and share your identifiable health information:

- PSH/PSU research staff involved in this study
- The PSH/PSU Institutional Review Board (IRB), a group of people who review the research study to protect subjects' rights and welfare
- The PSH/PSU Human Subjects Protection Office
- The PSH/PSU Research Quality Assurance Office
- Non-research staff within PSH/PSU who need this information to do their jobs (such as for treatment, payment (billing), or health care operations)
- Federal and state agencies (such as the U.S. Food and Drug Administration, the Office for Human Research Protections, the Department of Health and Human Services, the National Institutes of Health, and other U.S. or foreign government bodies that oversee or review research)

- People or groups that we hire to do work for us, such as data storage companies, insurers, and lawyers
- Organizations that provide independent accreditation and oversight of hospitals and research
- Public health and safety authorities (for example, if we learn information that could mean harm to you or others, we may need to report this, as required by law)
- The PSH/PSU pharmacy
- Representatives from Eli Lilly and Company, the manufacturer of the study drug Abemaciclib used in this study.
- Researchers at the lab of Dr. He at Captis Diagnostics, Inc.
- Representatives from the diagnostic lab, Captis Diagnostics, Inc.
- A group that oversees the data (study information) and safety of this research

These groups may also review and/or copy your original PSH/PSU records while looking at the results of the research study. It is possible that some of the other people/groups who receive your health information may not be required by Federal privacy laws to protect your information. We share your information only when we must, and we ask anyone who receives it from us to protect your privacy.

Sometimes a Principal Investigator or other researcher moves to a different institution. If this happens, your identifiable health information and samples may be shared with that new institution and their oversight offices. PHI will be shared securely and under a legal agreement to ensure it continues to be used under the terms of this consent and HIPAA authorization.

We may remove identifying information from your protected health information. Once we do this, the remaining information will not be subject to the privacy laws. Information without identifiers may be used or disclosed with other people or organizations for purposes besides this study.

Because research is an ongoing process, your permission for the use, storage and sharing of your health information will continue indefinitely.

Your privacy rights:

- You have the right to refuse to sign this form that allows us to use and share your health information for research; however, if you don't sign it, you will not be able to take part in this research study.
- You have the right to withdraw your permission for us to use or share your health information for this research study. If you want to withdraw your permission, you must notify the person in charge of this research study in writing using the address on the front of this form. Once permission is withdrawn, you cannot continue to take part in the study.
- If you withdraw your permission, we will stop collecting health information about you for this study; we may continue to use and share your health information that we already have if it is necessary for safety and scientific soundness of the research study; and we will not be able to take back information that has already been used or shared with others.
- You have the right to see and get a copy of your health information that is used or shared for treatment or for payment. However, you may not be allowed to see or copy certain health information that is a part of this research study. This is only for the period

of the study. You will be allowed to see that information when the entire research study is complete.

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

8a. What will I have to pay for if I take part in this research study?

You and/or your insurance company will not be charged for the cost of Abemaciclib and any tests or procedures that are required as part of the research and are outside the standard of care (what is normally done) for your condition. This includes the following:

- The study drug Abemaciclib will be provided by the manufacturer, Eli Lilly and Company, at no cost to you while you take part in this study.
- The research-related tests and procedures that will be provided at no cost to you including the research blood tests noted above in Section 2, Research Testing.

For costs of medical services for care you would receive even if you were not in this research study:

- You and/or your insurance company will be responsible for the costs of routine medications and the tests and procedures that you would receive even if you were not in this research.
- 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 may not pay for routine costs for people taking part in research studies. Before deciding to be in this research you should check with your insurance company to find out what they will pay for.

If you have any questions about costs and insurance, ask the research study doctor or a member of the research team.

8b. What happens if I am injured as a result of taking part in this research study?

It is possible that you could develop complications or injuries as a result of being in this research study. If you experience a side effect or injury and emergency medical treatment is required, seek treatment immediately at any medical facility. If you experience a side effect or injury and you believe that emergency treatment is not necessary, you should contact the principal investigator listed on the first page of this consent form as soon as possible and the principal investigator will arrange for medical treatment. You should also let any health care provider who treats you know that you are in a research study.

<u>PSH/PSU compensation for injury</u>

- There are no plans for PSH/PSU to provide financial compensation or free medical treatment for research-related injury.
- If an injury occurs, medical treatment is available at the usual charge.
- Costs will be charged to your insurance carrier or to you.
- Some insurance companies may not cover costs associated with research injuries.
- If these costs are not covered by your insurance, they will be your responsibility.

When you sign this form you are not giving up any legal right to seek compensation for injury.

9. Will I be paid to take part in this research study?
You will not receive any payment or compensation for being in this research study.

It is possible that your research information and/or specimens may be used to develop products or tests that could be patented and licensed. There are no plans to provide financial compensation to you should this occur.

10. Who is paying for this research study?
The cost for carrying out this study is being paid for by the Penn State Cancer Institute. Eli Lilly and Company, the manufacturer of Abemaciclib, will provide some financial support. In addition, they will provide the medication to Penn State Cancer Institute at no cost to the institution or to you.

The Pennsylvania State University has a beneficial interest in a company which licenses the technology used in or developed by this research. This interest has been reviewed by the University's Institutional Conflict of Interest Committee and is being managed by the University

11. What are my rights if I take part in this research study?
Taking part in this research study is voluntary.
- You do not have to be in this research.
- If you choose to be in this research, you have the right to stop at any time.
- If you decide not to be in this research or if you decide to stop at a later date, there will be no penalty or loss of benefits to which you are entitled.

You may withdraw from the study at any time. If you decide to withdraw, your study doctor will discuss your treatment options with you and your future medical care will not be affected.
If you stop being in the research, already collected data may not be removed from the study database. You will be asked whether the investigator can collect medical information from your routine medical care. If you agree, this data will be handled the same as research data. If you withdraw completely from the research study, no further information will be collected and your participation will end. You may discontinue taking part at any time without penalty or loss of benefits to which you are otherwise entitled.

Your research doctor Dr. Nelson Yee may take you out of the research study without your permission.
- Some possible reasons for this are: continuing the research would be harmful, your condition has become worse, you become pregnant, you did not follow the instructions of the study doctor, or you experience serious side effects.
- Also, Penn State Cancer Institute could decide to end the research study early.
- If your participation ends early, you may be asked to visit the research doctor for a final visit.

During the course of the research you will be provided with any new information that may affect your health, welfare or your decision to continue participating in this research.

12. If I have questions or concerns about this research study, whom should I call?
Please call the head of the research study (principal investigator), Dr. Nelson Yee at 717-531-8678 or the Hematology/Oncology doctor on 24-hour call at 717-531-8521 if you:
- Have questions, complaints or concerns about the research.

- Believe you may have been harmed by being in the research study.

You may also contact the research protection advocate in the PSH Human Subjects Protection Office (HSPO) at (717) 531-5687 if you:

- Have questions regarding your rights as a person in a research study.
- Have concerns, complaints or general questions about the research.
- Have questions about your privacy and the use of your personal health information.
- You may also call this number if you cannot reach the research team or wish to offer input or to talk to someone else about any concerns related to the research.

You may visit the Penn State College of Medicine's Clinical Research web site at http://med.psu.edu/clinical-research/faqs for:

- Information about your rights when you are in a research study;
- Information about the Institutional Review Board (IRB), a group of people who review the research to protect your rights; and
- Links to the federal regulations and information about the protection of people who are in research studies. If you do not have access to the internet, copies of these federal regulations are available by calling the HSPO at (717) 531-5687.

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.

INFORMED CONSENT AND AUTHORIZATION TO TAKE PART IN RESEARCH

Signature of Person Obtaining Informed Consent

Your signature below means that you have explained the research to the subject or subject representative, provided the subject or subject representative an opportunity to discuss and consider whether or not to participate in the research, and have answered any questions about the research.

_____	_____	_____	_____
Signature of person who explained this research	Date	Time	Printed Name

Signature of Person Giving Informed Consent and Authorization

Before making the decision about being in this research you should have:

- Discussed this research study with an investigator,
- Read the information in this form, and
- Had the opportunity to ask any questions you may have.

Your signature below means that you have received this information, have asked the questions you currently have about the research and those questions have been answered. You will receive a copy of the signed and dated form to keep for future reference.

Signature of Subject

By signing this consent form, you indicate that you voluntarily choose to be in this research and authorize your information to be used and shared as described above.

_____	_____	_____	_____
Signature of Subject	Date	Time	Printed Name

Witness to Consent for Limited English Speaking Subjects (Using a "Short Form" written in the subject's own language)

Witness Statement: As someone who understands both English and the language spoken by the subject or subject representative, your signature indicates that the English version of the consent form was presented orally in the language of the subject or subject representative, and that the subject or subject representative was given the opportunity to ask questions.

_____	_____	_____	_____
Witness Signature	Date	Time	Printed Name

Witness to Consent of Subjects Who Cannot Read or Write

Witness Statement: Your signature indicates that you were present during the informed consent discussion of this research for the above named subject, that the information in the consent form and any other written information was presented orally to the subject or subject representative, that the subject or subject representative was given the opportunity to ask questions, that the informed consent decision was freely made by the subject or subject representative who indicated consent and authorization for participation by (check the box as applicable):

☐ Making a mark
☐ Other means: _____
(fill in above)

_____	_____	_____	_____
Witness Signature	Date	Time	Printed Name