Study Title for Study Participants:

Testing selumetinib in advanced and recurrent pancreatic cancer with KRAS G12R genetic change.

Official Study Title for Internet Search on http://www.ClinicalTrials.gov:

A Phase II Study of Selumetinib (AZD6244) for the Treatment of Advanced Pancreas Cancer harboring KRAS G12R Mutations. IND: [redacted]

What is the usual approach to my pancreatic cancer?

You are being asked to take part in this study because you have advanced pancreatic cancer which has grown or has recurred. People who are not in a study are usually treated with either surgery, radiation, or with drugs. Sometimes, combinations of these are used and your doctor can explain which may be best for you. These treatments can reduce symptoms and may stop the tumor from growing for several months or more. Sometimes your doctor may recommend comfort care only (no further treatment) to help relieve your symptoms.

What are my other choices if I do not take part in this study?

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

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

Why is this study being done?

The purpose of this study is to test any good and bad effects of the study drug called selumetinib (AZD6244). Selumetinib could shrink your cancer but it could also cause side effects.. Researchers hope to learn if the study drug will shrink the cancer by at least 30 %. Selumetinib has not been approved by the U.S. Food and Drug Administration (FDA) in the treatment of any cancer. It has not been tested in pancreatic cancer, but has shrunk tumors in patients with lung tumor, thyroid cancers, or in patients with a certain eye tumors.

Up to 60 people will take part in the screening study described in Group 1 below. Of those people, up to 25 people will have the KRAS G12R genetic change that is needed to take part in the testing of the study drug selumetinib (Group 2 below).

What are the study groups?

This study has two phases. Everyone who agrees to take part in the study will be in Group 1. Only patients with a tumor sample testing positive for the KRAS G12R genetic change will continue to the Group 2 phase of the study.

Group 1 (Screening Phase).

All participants must provide a test result from CLIA certified laboratory, confirming somatic KRAS G12R mutation or tumor sample to test for the KRAS G12R genetic change.

The tumor sample can be from:

- Archival tumor sample that was previously acquired at diagnosis (no biopsy required)

- Or a biopsy (if the archival sample is not available).

*The tumor sample is then tested for the KRAS G12R genetic change.

It is expected that for every 100 patients with pancreas cancer, about 15 samples of the tumor will be positive for the KRAS G12R genetic change. The risks of this genetic test are further explained below in "What extra tests and procedures will I have if I take part in this study?"

If the test is negative for the KRAS G12R genetic change you are then taken off study.

Group 2 (Testing Phase)

All participants having a tumor with the KRAS G12R genetic change will get selumetinib as a capsule at a dose of 75 mg to be taken twice a day.

The study doctor might lower the dose if you have serious side effects. The study drug is given over 4-week periods of time called cycles. The 4-week cycle will be repeated as long as you are tolerating the study drug and your cancer is either stable or getting better. No other therapy for pancreas cancer will be given while you are on study.

You will be given a Patient's Pill Diary that explains how to take the study drug and to record when you take the capsules at home. You will also be given a study drug handout and wallet card as a resource for yourself, caregivers and other health care providers.

How long will I be in this study?

The screening phase of this study can take up to 2 weeks for archival tumor samples, and up to 3 weeks if a biopsy is needed test for the KRAS G12R genetic change or no time at all if you already have test result of KRAS mutation ststus.

For participants having a tumor with the KRAS G12R genetic change, you will receive the selumetinib for as long as you are able to tolerate the study drug and it keeps your cancer from further growing for up to 27 cycles which is about two years. After you finish the study drug, your study team will call you every two months for up to one year to follow your condition. If you have any side effects from the study drug after you finish the study, your doctor will follow you until your symptoms get better.

What extra tests and procedures will I have if I take part in this study?

Most of the exams, tests, and procedures you will have are part of the usual approach for your cancer. However, there are some extra tests that you will need to have if you take part in this study.

Before you begin the study

You will need to have the following extra exams, tests, and procedures to find out if you can be in the study:

- Pregnancy test (if female)
- A genetic test of a tumor sample for the KRAS G12R genetic change. The tumor sample can be from archival tumor sample that was previously acquired at diagnosis (no biopsy required), or from a new biopsy (if the archival sample is not available) (not necessary for patients with confirmed KRAS G12R genetic change)

Tumor biopsy and genetic testing:

i. Small pieces of cancer tissue removed during a biopsy will be taken before you begin study drug. This sample is required in order for you to take part in this study.

ii. Common side effects of a biopsy are a small amount of bleeding at the time of the procedure, pain at the biopsy site, which can be treated with regular pain medications, and bruising. Rarely, an infection can occur."

iii. Any of the specimen left over will be stored for biobanking. This will be discussed in the section on optional studies.

iv. Your privacy is very important and the researchers will make every effort to protect it. Your test results will be identified by a unique code and the list that links the code to your name will be kept separate from your sample and health information. The results will be available to you and study doctor.

- Research blood test (Optional)

If the exams, tests, and procedures show that you can take part in the study, and you choose to take part, then you will need the following extra procedures. They are not part of the usual approach for your type of cancer.

During the study

Once we determine that you are eligible for taking study drug you will be given a 30-day supply of selumetinib in the form of capsules.

You will be asked to:

- complete the study drug Pill Diary every day and review every 4 weeks;
- return to the clinic at the end of every treatment cycle (4 weeks) for repeat labs and scans to evaluate your disease and to confirm that your tumor has not progressed;
- research blood test (optional) up to 3 teaspoon every two weeks for 8 weeks and monthly after that.

Following the study you may be asked to take part in telephone interviews (every 2 months during the first 52 weeks).

A study calendar that shows how often these tests and procedures will be done is attached.

What possible risks can I expect from taking part in this study?

If you choose to take part in this study, there is a risk that:

- You may lose time at work or home and spend more time in the hospital or doctor's office than usual
- You may be asked sensitive or private questions which you normally do not discuss
- There is a risk someone could get access to the personal information in your medical records or other information researchers have kept about you. Someone might be able to trace this information back to you. The researchers believe the chance that someone will identify you is very small, but the risk may change in the future as people come up with new ways of tracing information. In some cases, this information could be used to make it harder for you to get or keep a job. There are laws against misuse of genetic information,

but they may not give full protection. The researchers believe the chance these things will happen is very small, but cannot promise that they will not occur.

- There can also be a risk in finding out new genetic information about you. New health information about inherited traits that might affect you or your blood relatives could be found during a study.

The selumetinib used in this study may affect how different parts of your body work such as your liver, kidneys, heart, and blood. The study doctor will be testing your blood and will let you know if changes occur that may affect your health.

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

Here are important points about side effects:

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

Here are important points about how you and the study doctor can make side effects less of a problem:

- Tell the study doctor if you notice or feel anything different so they can see if you are having a side effect.
- The study doctor may be able to treat some side effects.
- The study doctor may adjust the study drugs to try to reduce side effects.
- The study doctor will provide you with information about other drugs you may need to avoid while receiving the study drug.

The tables below show the most common and the most serious side effects that researchers know about. There might be other side effects that researchers do not yet know about. If important new side effects are found, the study doctor will discuss these with you.

Possible Side Effects of selumetinib (AZD6244)

COMMON, SOME MAY BE SERIOUS In 100 people receiving selumetinib (AZD6244), more than 20 and up to 100 may have:
• Diarrhea, nausea
• Swelling of the body
• Tiredness
• Acne, rash

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving selumetinib (AZD6244), from 4 to 20 may have:
• Anemia which may require blood transfusion
• Pain
• Constipation, vomiting
• Dry mouth, skin
• Sores in mouth which may cause difficulty swallowing
• Fever
• Bruising, bleeding
• Infection, especially when white blood cell count is low
• Loss of appetite
• Dizziness, headache
• Cough, shortness of breath
• Hair loss, itching
• High blood pressure which may cause headaches, dizziness, blurred vision

RARE, AND SERIOUS In 100 people receiving selumetinib (AZD6244), 3 or fewer may have:
• Heart failure which may cause shortness of breath, swelling of ankles, and tiredness

Research Procedure Risks:

Blood Draw

Side effects of blood draws include pain and bruising in the area where the needle was placed, lightheadedness, and rarely, fainting. When large amounts of blood are collected, low red blood cell count (anemia) can develop.

Reproductive risks:

You should not get pregnant, breastfeed, or father a baby while in this study. The selumetinib used in this study could be very damaging to an unborn baby. Check with the study doctor about what types of birth control, or pregnancy prevention, to use while in this study.

If you are a woman who can become pregnant, or are the partner of a woman who can become pregnant, you will need to practice an effective form of birth control before starting study drug, during taking study drug, and for up to 4 weeks (female patients) or 12 weeks (male patients) after you finish study drug. If you think that you or your partner is pregnant, you should tell your study doctor or nurse at once.

Effective forms of birth control include:

- abstinence

- intrauterine device (IUD)
- hormonal [birth control pills, injections, or implants]
- tubal ligation
- vasectomy

Other risks:

- In case of diarrhea you can have additional tests to address the need for immediate, aggressive treatment of diarrhea such as measurement of blood pressure and heart rate, urine and blood tests to check your organ functions.
- Please, avoid excessive sun exposure and use adequate sun protection measures.

What possible benefits can I expect from taking part in this study?

This study has only a small chance of helping you because we do not know if the study drug/study approach is effective. This study may help researchers learn things that may help other people in the future.

Can I stop taking part in this study?

Yes. You can decide to stop at any time. If you decide to stop for any reason, it is important to let the study doctor know as soon as possible so you can stop safely. If you stop, you can decide whether or not to let the study doctor continue to provide your medical information to the organization running the study.

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

The study doctor may take you off study drug:

- If your health changes and the study is no longer in your best interest
- If you become pregnant
- If new information becomes available
- If you do not follow the study rules
- If the study is stopped by the sponsor, IRB or FDA.
- If the drug is no longer available.

What are my rights in this study?

Taking part in this study is your choice. No matter what decision you make, and even if your decision changes, there will be no penalty to you. You will not lose medical care or any legal rights.

For questions about your rights while in this study, contact the National Cancer Central Institute Institutional Review Board (NCI CIRB) at 888-657-3711

What are the costs of taking part in this study?

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

You and/or your health plan/insurance company will need to pay for all of the other costs of treating your cancer while in this study, including the cost of tests, procedures, or medicines to manage any side effects, unless you are told that certain tests are supplied at no charge. Before you decide to be in the study, you should check with your health plan or insurance company to find out exactly what they will pay for.

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

What happens if I am injured or hurt because I took part in this study?

If you are injured or hurt as a result of taking part in this study and need medical treatment, please tell your study doctor. The study sponsors will not offer to pay for medical treatment for injury. Your insurance company may not be willing to pay for study-related injury. If you have no insurance, you would be responsible for any costs.

If you feel this injury was a result of medical error, you keep all your legal rights to receive payment for this even though you are in a study.

Who will see my medical information?

Your privacy is very important to us and the researchers will make every effort to protect it. Your information may be given out if required by law. For example, certain states require doctors to report to health boards if they find a disease like tuberculosis. However, the researchers will do their best to make sure that any information that is released will not identify you. Some of your health information, and/or information about your specimen, from this study will be kept in a central database for research. Your name or contact information will not be put in the database.

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, CTEP and any drug company 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.
- The Food and Drug Administration and the National Cancer Institute in the U.S., and similar ones if other countries are involved in the study.

Where can I get more information?

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

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

Who can answer my questions about this study?

You can talk to the study doctor about any questions or concerns you have about this study or to report side effects or injuries. Contact the study doctor *insert local PI name & contact number*.

ADDITIONAL STUDIES SECTION:

This part of the consent form is about optional studies that you can choose to take part in. You will not get health benefits from any of these studies. The researchers leading this optional study hope the results will help other people with cancer in the future.

The results will not be added to your medical records and you or your study doctor will not know the results.

You will not be billed for these optional studies. You can still take part in the main study even if you say "no" to any or all of these studies. If you sign up for but cannot complete any of the studies for any reason, you can still take part in the main study.

Circle your choice of "yes" or "no" for each of the following studies.

1. Optional Tumor Biopsy

If you choose to take part in this study, we would like to collect a sample of your tumor after 2 weeks of taking study drug to see how the study drug might affect the functioning of a certain gene within the tumor.

If you agree to this tumor biopsy, it would involve collecting a small piece of tumor tissue from you. A hollow needle is used to withdraw small cylinders (or cores) of tissue from your tumor using a CT scan or ultrasound for guidance. The needle is put in 3 to 6 times to get the samples, or cores. This procedure usually causes only brief discomfort at the site from which the biopsy is taken and you will be offered medication to help numb the pain. Biopsy collection may cause bruising and bleeding, but usually does not leave scars. Rarely infection may occur at the needle site.

To collect the optional research biopsy (at two weeks), you may be exposed to one CT scan. This radiation exposure is not required for your medical care and is for research purposes only.

The CT scan that you will receive in this study will expose you to low amounts of radiation. Every day, people are naturally exposed to low levels of radiation that come from the sun and the environment. This type of radiation is called "background radiation". No one knows for sure whether exposure to low amounts of radiation is harmful for your body. However, scientists believe that being exposed to too much radiation can cause harmful side effects, including causing a new cancer.

The CT scan that you will receive in this study will expose you to extra radiation that is equal to about 2 – 3 years worth of background radiation. Most of the time, this low amount of extra radiation is not harmful to you. However, scientists believe that if you get extra radiation that is more than about 30 year's worth of background radiation, there is a chance of having a harmful

side effect, including causing a new cancer. It is estimated that this could occur in about 1 out of every 1000 people who get a very large amount of extra radiation.
Please inform the study team immediately if you notice bleeding at the biopsy site more than 2 days after the procedure or if there is evidence of infection - redness, swelling, warmth, pain or red streaking of the skin around the wound.

Please circle your answer: I choose to have a post study drug tumor biopsy.

YES NO

2.Optional Sample Collections for Laboratory studies and/or Biobanking for Possible Future Studies

Researchers are trying to learn more about cancer, diabetes, and other health problems. Much of this research is done using samples from your tissue, blood, urine, or other fluids. Through these studies, researchers hope to find new ways to prevent, detect, treat, or cure health problems.

Some of these studies may be about genes. Genes carry information about features that are found in you and in people who are related to you. Researchers are interested in the way that genes affect how your body responds to study drug.

If you choose to take part, some of your research specimens and data will also be saved for future research. The researchers ask your permission to store and use your samples and related health information (for example, your response to cancer study drug, results of study tests and medicines you are given) for medical research. The research that may be done is unknown at this time. Storing samples for future studies is called “biobanking”.

WHAT IS INVOLVED?

If you agree to take part in biobanking, here is what will happen next:

1) Your left over samples and some related health information may be stored in the Biobank, along with samples and information from other people who take part. The samples will be kept until they are used up. Information from your medical record will be updated from time to time.
2) Qualified researchers can submit a request to use the materials stored in the Biobank. There will also be an ethics review to ensure that the request is necessary and proper. Researchers will not be given your name or any other information that could directly identify you.
3) You will not be notified when future studies will be conducted or given reports or other information about any research that is done using your samples.
4) Some of your genetic and health information may also be placed in central databases that may be public, along with information from many other people. Information that could directly identify you will not be included.

WHAT ARE THE POSSIBLE RISKS?

1) There is a risk that someone could get access to the personal information in your medical records or other information researchers have stored about you.
2) There is a risk that someone could trace the information in a central database back to you. Even without your name or other identifiers, your genetic information is unique to you. The researchers believe the chance that someone will identify you is very small, but the risk may change in the future as people come up with new ways of tracing information.
3) In some cases, this information could be used to make it harder for you to get or keep a job or insurance. There are laws against the misuse of genetic information, but they may not give full protection. There can also be a risk in knowing genetic information. New health information about inherited traits that might affect you or your blood relatives could be found during a study. The researchers believe the chance these things will happen is very small, but cannot promise that they will not occur.
4) There is a risk that the sample used for unspecified future research could be needed to determine if you are eligible for other treatments or clinical trials.

HOW WILL INFORMATION ABOUT ME BE KEPT PRIVATE?

Your privacy is very important to the researchers and they will make every effort to protect it. Here are just a few of the steps they will take:

1) When your samples are sent to the researchers, no information identifying you (such as your name) will be sent. Samples will be identified by a unique code only.
2) The list that links the unique code to your name will be kept separate from your sample and health information.
3) Researchers to whom the Biobank sends your sample and information will not know who you are.
4) Information that identifies you will not be given to anyone, unless required by law.
5) If research results are published, your name and other personal information will not be used.

WHAT ARE THE POSSIBLE BENEFITS?

You will not benefit from taking part.

Your samples may be helpful to research. The researchers, using the samples from you and others, might make discoveries that could help people in the future.

ARE THERE ANY COSTS OR PAYMENTS?

There are no costs to you or your insurance. You will not be paid for taking part. If any of the research leads to new tests, drugs, or other commercial products, you will not share in any profits.

WHAT IF I CHANGE MY MIND?

If you decide you no longer want your samples to be used, you can call the study doctor, Udo Rudloff, MD at 240-760-6238 who will let the researchers know. Then, any sample that remains in the bank will no longer be used and related health information will no longer be collected.

Samples or related information that have already been given to or used by researchers will not be returned.

WHAT IF I HAVE MORE QUESTIONS?

If you have questions about the use of your samples for research, contact the study doctor, Udo Rudloff, MD at 240-760-6238.

Please circle your answer to show whether or not you would like to take part in each option:

SAMPLES FOR THE LABORATORY STUDIES:

I agree to have my specimen collected and I agree that my specimen sample(s) and related information may be used for the laboratory study(ies) described above.

YES NO

I agree that my study doctor, or their representative, may contact me or my physician to see if I wish to learn about results from this(ese) study(ies).

YES NO

SAMPLES FOR FUTURE RESEARCH STUDIES:

My samples and related information may be kept in a Biobank for use in future health research.

YES NO

I agree that my study doctor, or their representative, may contact me or my physician to see if I wish to participate in other research in the future.

YES NO

My Signature Agreeing to Take Part in the Main Study

I have read this consent form or had it read to me. I have discussed it with the study doctor and my questions have been answered. I will be given a signed copy of this form. I agree to take part in the main study and any additional studies where I circled 'yes'.

Participant's signature_____

Date of signature_____

Signature of person(s) conducting the informed consent discussion_____

Date of signature_____

Study Calendar

Day	What will happen to you
After signing the consent, before starting study drug	Provide a history of how you feel and undergo a physical examination by the research team's Health Care Provider. CT, MRI or Ultrasound imaging Blood will be taken for routine cancer care tests and research (optional) blood samples. Pregnancy test (if female) Tumor biopsy if previous specimens are not available.
CYCLE 1	**28 Days long**
Days 1 through 28	Take Selumetinib capsules twice a day, 12 hours apart. Complete study drug and side effects diary
Day 14	Routine blood tests and physical exam Research blood tests (optional) Optional tumor biopsy
Day 28	Return to the clinic to see your doctor. Provide a history of how you feel and have a physical exam by your Health Care Provider. Blood will be taken for routine cancer care tests and research (optional) blood samples. CT, MRI or Ultrasound imaging (to determine if selumetinib is causing your disease to shrink or be controlled) Review study drug diary with research nurse If you are tolerating the study drug, the next cycle will begin.
CYCLE 2	**28 Days long**
Days 1 through 28	Take Selumetinib capsules twice a day, 12 hours apart. Complete study drug and side effects diary.
Day 14	Routine blood tests and physical exam
Day 28	Return to the clinic to see your doctor. Provide a history of how you feel and have a physical exam by your Health Care Provider. Blood will be taken for routine cancer care tests and research (optional) blood samples. Review study drug diary with research nurse If you are tolerating the study drug, the next cycle will begin.
CYCLE 3	**28 Days long**

Days 1 through 28	Take Selumetinib capsules twice a day, 12 hours apart. Complete study drug and side effects diary
Day 14	Routine blood tests and physical exam
Day 28	Return to the clinic to see your doctor. Provide a history of how you feel and have a physical exam by your Health Care Provider. Blood will be taken for routine cancer care tests and research (optional) blood samples. CT, MRI or Ultrasound imaging (to determine if selumetinib is causing your disease to shrink or be controlled) Review study drug diary with research nurse If you are tolerating the study drug, the next cycle will begin.
CYCLES 4-27	**28 Days long**
Days 1 through 28	Take Selumetinib capsules twice a day, 12 hours apart. Complete study drug and side effects diary
Day 28	Return to the clinic to see your doctor. Blood will be taken for routine cancer care tests CT, MRI or Ultrasound imaging after every 2 completed cycles (to determine if selumetinib is causing your disease to shrink or be controlled) Review study drug diary with research nurse If you are tolerating the study drug, the next cycle will begin.
30 days after last dose	If your cancer continues to be better or stable after 27 cycles of therapy, you will be seen at the clinic for an end of your treatment visit 30 days after your last dose and then followed by a telephone interview every 2 months during the first 52 weeks. If we find that your tumor is growing during selumetinib therapy, we will ask you to stop taking the drug and remove you from study. We will look for other investigational therapies you may be eligible for, or refer you back to the care of your local physician.
every 2 months during the first 52 weeks.	Telephone interview to determine your disease status