The University of Texas Southwestern Medical Center
Parkland Health & Hospital System

Phase 1b Research Consent
CONSENT TO PARTICIPATE IN RESEARCH

Title of Research:	A phase1b/2 clinical trial of chemotherapy and the AXL-inhibitor bemcentinib for patients with metastatic pancreatic cancer
Funding Agency/Sponsor:	UT Southwestern Medical Center
Study Doctor:	Muhammad Beg, MD

You may call the study doctor or research personnel during regular office hours at 214-648-7097. At other times, you may call them at 214-645-4673.

Instructions:
Please read this consent form carefully and take your time making a decision about whether to participate. As the researchers discuss this consent form with you, please ask him/her to explain any words or information that you do not clearly understand. The purpose of the study, risks, inconveniences, discomforts, and other important information about the study are listed below. If you decide to participate, you will be given a copy of this form to keep.

Why is this study being done?
The purpose of this study is to test the effectiveness (how well the drug works), safety, and tolerability of the investigational drug combination of bemcentinib plus chemotherapy (nab-paclitaxel/gemcitabine/cisplatin) in patients with metastatic pancreatic adenocarcinoma.

Bemcentinib (also known as BGB324 or R428) is an experimental oral drug that has not yet been approved by the FDA. Bemcentinib inhibits (blocks) Axl, a surface membrane protein kinase receptor that is overexpressed in many human cancers including lung, breast, and pancreatic cancer. By inhibiting Axl, bemcentinib inhibits the growth of tumor cells and also makes cancer cells more sensitive to chemotherapy. Bemcentinib is currently being tested across various types of solid tumor and hematologic cancers in combination with chemotherapy and immunologic treatments.

Why is this considered research?
This is a research study because we would like to determine the disappearance of tumor(s) identified and measured prior to starting bemcentinib plus chemotherapy (nab-paclitaxel/gemcitabine/cisplatin) in patients with metastatic pancreatic cancer.

- Nab-paclitaxel, gemcitabine and cisplatin combination is an option for treatment for metastatic pancreatic adenocarcinoma. However, due to the addition of

bemcentinib to Nab-paclitaxel/gemcitabine/cisplatin, it is also considered investigational and is not approved by the U.S. Food and Drug Administration (FDA).

The following definitions may help you understand this study:

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- Standard medical care means the regular care you would receive from your personal doctor if you choose not to participate in this research.
- Researchers means the study doctor and research personnel at the University of Texas Southwestern Medical Center at Dallas and its affiliated hospitals.

Why am I being asked to take part in this research study?
You are being asked to take part in this study because you have pancreatic adenocarcinoma that is metastatic or recurrent.

Conflict of Interest
A member of the research team, Muhammad Beg, MD is a paid consultant of Bristol-Myers Squibb. Bristol-Myers Squibb is the company who manufactures the drug Cisplatin, which will be considered standard of care for this study and will be billed to your insurance.

Do I have to take part in this research study?
No. You have the right to choose whether you want to take part in this research study. If you decide to participate and later change your mind, you are free to stop participation at any time.

If you decide not to take part in this research study it will not change your legal rights or the quality of health care that you receive at this center.

How many people will take part in this study?
About 44 people will take part in this study at UT Southwestern and Parkland Health & Hospital System and a number of other medical facilities around the country. There will be a total of up to 44 people participating in this research study throughout the United States and/or other countries.

What is involved in the study?
If you volunteer to take part in this research study, you will be asked to sign this consent form and will have the following tests and procedures completed. Some of the procedures may be part of your standard medical care, but others are being done solely for the purposes of this study.

<u>Screening Procedures</u>
To help decide if you qualify to be in this study, the researchers will ask you questions about your health, including any medications (including vitamins and nutritional supplements) you take and any surgical procedures that you have had.

You may also have to fill out certain forms or have the following exams, tests or procedures:

- Medical History
- Assess your overall functioning using a specific scale for cancer patients (ECOG)
- Vital Signs
- Physical examination
- Blood draw (approx. 5 teaspoons) for the following:
    - Routine safety tests to evaluate blood count, liver, and kidney function.
    - CA 19-9 a test that measures the level of tumor-associated antigens (substances causing an immune response) found in the blood.
    - CPK – an enzyme found in your muscles
- Pregnancy test (either urine or serum (blood) pregnancy test).
    - If the urine pregnancy test is positive or cannot be confirmed as negative, a serum pregnancy test will be required.
- Electrocardiogram (ECG): an electrical tracing of your heart rhythm, done in triplicate.
    - Wires or “leads” will be attached to your chest with an adhesive and you will be asked to lie still while the machine prints out an electrical “record” of your heart’s activity
- Echocardiogram or MUGA: sonogram of the heart to determine how well the heart is pumping blood.
- Optional tumor tissue collection to assess the effect of chemotherapy and bemcentinib.

<u>Group Assignment</u>

This study is being conducted in two phases, Phase 1b and Phase 2. Phase 1b is a safety run in to check the safety in using the combination of bemcentinib and chemotherapy (gemcitabine/nab-paclitaxel/cisplatin). Based on the observed activity and tolerance of gemcitabine, nab-paclitaxel and cisplatin with bemcentinib in Phase 1b, cisplatin is being removed from the treatment regimen in Phase 2. Phase 2 is a single arm phase 2 clinical trial of chemotherapy (gemcitabine and nab-paclitaxel) with bemcentinib. A revised safety run in will be completed in Phase 2 to verify the safety of the combination. You are currently participating in Phase 1b.

Phase 1b: Safety run in (bemcentinib/gemcitabine/nab-paclitaxel/cisplatin)

- Three patients will be enrolled for the safety run in to determine the starting dose of bemcentinib.
    - -If none of the first 3 patients experience a side effect from the combination of bemcentinib and chemotherapy (gemcitabine/nab-paclitaxel/cisplatin), then the randomized portion (part 2) of the trial will begin.
    - If at least 1 of the first 3 patients experiences a side effect of the combination

of bemcentinib and chemotherapy (gemcitabine/nab- paclitaxel/cisplatin), then 3 additional patients will be treated at that dose level.
    - If no more than 1 of the first 6 patients experiences a side effect of the combination of bemcentinib and chemotherapy (gemcitabine/nab-paclitaxel/cisplatin), then the randomized portion of the trial will begin.
    - If 2 or more of the first 6 patient's experiences a side effect of the combination of bemcentinib and chemotherapy (gemcitabine/nab-paclitaxel/cisplatin) and the dosage is more than the maximum tolerated dose, a lower dose level will be explored.

Phase 2: Single Arm (bemcentinib/nab-paclitaxel/gemcitabine)

- Subjects in this phase will be assigned to receive the combination of bemcentinib and chemotherapy (gemcitabine/nab-paclitaxel). The first 6 patients in this phase will participate in a revised safety run in to ensure the safety of this combination.

Study Medication/Intervention

Subjects participating in phase 1 of the study you will take:

- Bemcentinib daily, orally (by mouth) starting on Cycle 1 day 2
    - You will be asked, not to eat for at least two hours before and one hour following the bemcentinib dose. You will take bemcentib at the same time each day.
- Nab-Paclitaxel given intravenously on Day 1 and 8 every 21 days
- Gemcitabine given intravenously on Day 1 and 8 every 21 days
- Cisplatin given intravenously on Day 1 and 8 every 21 days

Procedures for storing of extra or left over samples

Subject samples collected for this study will be retained at University of Texas Southwestern Medical Center. Specimens will be stored indefinitely or until they have been completely used. If future use is denied or withdrawn by you, best efforts will be made to stop any additional studies and to destroy the specimens.

Muhammad Beg, MD, will be responsible for reviewing and approving requests for clinical specimen from potential research collaborators outside of University of Texas Southwestern Medical Center.

Collaborators will be required to complete an agreement that states specimens will only be released for use in disclosed research. Any data obtained from the use of clinical specimen will be the property of University of Texas Southwestern Medical Center for publication and any licensing agreement will be strictly adhered to.

Do you agree to take part in the Optional Tissue for correlative analysis?

Please indicate your choice by completing your initials on the line next to your choice.

_____ Yes, I agree to take part in the optional tissue biopsy.

_____ No, I do not agree to take part in the optional tissue biopsy

Procedures and Evaluations during the Research

Please note each cycle of treatment is 21 days in length

Day 1

- Inclusion/exclusion review (Cycle 1 only)
- Physical exam
- Vital Signs
- Measurement of weight and Body Surface Area (BSA) calculation prior to dosing
- Assess your overall functioning using a specific scale for cancer patients (ECOG)
- Blood draw (approx. 4 teaspoons) for the following:
    - Routine safety tests to evaluate blood count, liver, and kidney function.
    - Blood for correlative analysis to assess the effect of chemotherapy and bemcentinib
    - CA 19-9 (C3 and every subsequent odd cycle Day 1)
    - CPK (C3 and every subsequent odd cycle Day 1)
- EKG (Cycle 2 and beyond)
- Pregnancy test
- Evaluation of your baseline sign/symptoms
- Review all medications that you are currently taking
- Administration of chemotherapy
- Blood draw for pharmacokinetic (PK) testing (approximately 1 teaspoons at cycles 2, 3 and 4 only). PK testing is testing that show how the body processes the drug. (1st 15 patients only)
- Tumor imaging will be completed to measure your tumor before C3 and prior to every odd cycle
- Optional Tissue biopsy for correlative analysis. The on-treatment tissue collection will be performed during Cycle 2 or Cycle 3 in patients who have consented to tissue collection.

Day 2 (Only cycle 1 for patients receiving bemcentinib)

- Vital Signs
- EKG
- Blood draw (approximately 4 teaspoons) for the following:
    - Routine safety tests to evaluate blood count, liver, and kidney function.
    - Blood for correlative analysis to assess the effect of chemotherapy and bemcentinib

- Adverse events or side effects will be evaluated
- Review all medications that you are currently taking
- Start bemcentinib- you will take this first dose in clinic.

Day 4 (Only cycle 1 for patients receiving bemcentinib)

- Vital Signs
- EKG
- Adverse events or side effects will be evaluated
- Blood draw to evaluate blood counts
- Blood draw for PK testing (approximately 1 teaspoon) (1st 15 patients only)
- Review all medications that you are currently taking
- Bemcentinib – you will be asked to take this in the clinic

Day 8 of each cycle

- Vital Signs
- Assess your overall functioning using a specific scale for cancer patients (ECOG) (Cycle 1 only).
- Blood draw (approximately 5 teaspoons) for the following:
    - Routine safety tests to evaluate blood count, liver, and kidney function.
    - Blood for correlative analysis (pre-bemcentinib treatment) to assess the effect of chemotherapy and bemcentinib (Cycle 1 and 2 only)
- Adverse events or side effects will be evaluated
- Blood draw for PK testing (Cycle 1 only) approximately 1.5 teaspoons (1st 15 patients only)
- EKG (to be completed on bemcentinib patients only)
- Administration of chemotherapy
- Bemcentinib -you will be asked to take this in the morning prior to coming to clinic.

Day 11 (Only cycle 1 for patients receiving bemcentinib)

- Vital Signs
- EKG
- Adverse events or side effects will be evaluated
- Blood draw for PK testing - approximately 1 teaspoon (1st 15 patients only)
- Review of all medications that you are currently taking
- Bemcentinib - you will be asked to take this in the clinic

Day 15 of each cycle

- Vital Signs
- Blood draw (approximately 5 teaspoons) for the following:
    - Routine safety tests to evaluate blood count, liver, and kidney function.

    - Blood for correlative analysis (pre-bemcentinib treatment) to assess the effect of chemotherapy and bemcentinib (Cycle 1 and 2 only)
- Blood draw for PK testing - approximately 1 teaspoon (1st 15 patients only)
- EKG for bemcentinib patients only
- Administration of chemotherapy
- Bemcentinib dosing – you will be asked to take this in the clinic

Day 18 (Only cycle 1 for patients receiving bemcentinib)

- Vital Signs
- EKG
- Adverse events or side effects will be evaluated
- Review of all medications that you are currently taking
- Bemcentinib dosing - you will be asked to take this at home

Off Treatment Visit (30 days after last dose)

- Physical exam
- Measurement of weight (kg) and BSA calculation
- Vital signs
- Assess your overall functioning using a specific scale for cancer patients (ECOG)
- CA 19-9 a test that measures the level of tumor-associated antigens (substances causing an immune response) found in the blood.
- CPK
- EKG (only for patients that received bemcentinib)
- Blood draw (approximately 5 teaspoons) for the following:
    - Routine safety tests to evaluate blood count, liver, and kidney function.
    - Blood for correlative analysis to assess the effect of chemotherapy and bemcentinib
    - Blood for RNA sequencing
- Adverse events or side effects will be evaluated
- Any medication that you are currently taking will be discussed

Follow-up Procedures

- You will be followed every month after completion of (or early withdrawal from) study treatment until resolution of treatment related side effects.
- You will be followed for long term status every 3 months (this may be done through either a medical record review or follow up phone calls), from your off treatment visit date, until death or you withdraw consent from follow-up.

How long can I expect to be in this study?

The estimated time you might be in the study is about 30 months. However, the Study Doctor

may discontinue study treatment at any time if it is determined your disease has worsened, you experience intolerable or unacceptable side effects, your doctor determines that your safety is at risk, you become pregnant, you have a disappearance of tumor(s) identified before starting the study medication, or the study ends.

You can choose to stop participating for any reason at any time. However, if you decide to stop participating in the study, we encourage you to tell the researchers. You may be asked if you are willing to complete some study termination tests.

What are the risks of the study?
As with all research studies, the study medication and study procedures may involve unknown risks. Any medication can have temporary and permanent side effects and can cause unforeseen adverse reactions.

Study Procedure/Intervention
Because of your participation in this study, you are at risk for the following side effects. You should discuss these with the researchers and your regular health care provider.

What are the risks that can be anticipated with bemcentinib:
The following side effects have been reported in other patients who have received bemcentinib alone or in combination with other cancer treatments.

Very common side effects (occurring in 20 of 100 people or more):
- Diarrhea
- Feeling sick
- Changes in liver enzymes which may indicate inflammation in the liver (particularly in combination with other drugs)
- Changes in the electrical activity of the heart, known as QT prolongation – more details are provided below

Common side effects (occurring in at least 5 but less than 20 of 100 people)
- Fatigue
- Vomiting
- Decreased red blood cells (anemia)
- Decreased appetite
- Changes in blood tests that may indicate altered kidney function
- Rash (particularly in combination with other drugs)

QT prolongation is when the heart muscle takes longer than normal to recharge its electrical impulses between beats. These electrical impulses are needed to help the heart to beat regularly. Most patients who experience QT prolongation do not experience any symptoms and only show signs on an ECG. If patients do have symptoms with QT prolongation, which are uncommon and due to erratic heart beats, these may include light headedness, heart palpitations, irregular heartbeat, weakness or blurred vision – such symptoms may precede fainting. Occasionally heart irregularities

can lead to fainting without warning. If heart rate abnormalities continue this may also result in epileptic-type seizures.

If you are considered to have any risk factors for the development of an abnormal heart rhythm, caused by a QTc prolongation, you will not be able to take part in this study. If you do participate in this study your heart function will be closely monitored through ECGs.

Side effects involving the digestive system experienced by patients in clinical trials with bemcentinib included nausea, vomiting and diarrhea. In almost all cases these side effects were controlled by medication, but occasionally treatment breaks were also required.

Many of the patients with leukemia who were treated with bemcentinib experienced infections or fever when their white blood cells were low, although in the majority of these cases, the cause of the infection was thought to be due to their leukemia rather than bemcentinib.

In some of the patients who were treated with bemcentinib in combination with other cancer treatments, increase in liver enzymes was noted on blood tests. This may indicate inflammation in the liver, however in almost all of the cases this was temporary, and the liver enzymes returned back to normal after few days either spontaneously or with treatment.

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Below listed are the risks associated with the chemotherapy medications that will be given in this study. It should be noted that the potential occurrence of adverse effects for each of the products stated may be increased when the three medications are used in combination.

What are the risks that can be anticipated with Nab-paclitaxel:
Very common side effects (occurring in > 1/10 of patients):

- Low white blood cell count - which may temporarily place you at risk for infections, including oral thrush, respiratory infection, and pneumonia.
- Low red blood cell count – which may cause you to feel tired, look pale, and have shortness of breath)
- Low platelet count - which may lead to bruising or bleeding)
- Changes in ECG tracings of the heart rhythm, or increased or decreased or irregular heart rate
- Increase in liver function tests (AST and ALT)
- Increase in kidney function tests (creatinine)
- Shortness of breath
- Pneumonitis or inflammation of the walls of the lungs

Common side effects (occurring in > 1/100 to 1/10 of patients)

- Fatigue

- Numbness, tingling or burning of hands and feet
- Fluid retention in the hands and feet
- Fever
- Nausea
- Vomiting
- Diarrhea
- Hair loss (reversible)
- Appetite loss
- Rash
- Dehydration
- Pneumonia
- Cardiac ischemia/infarction (heart attack)
- Chest pain, cardiac arrest, fast heart beat
- Blockage of a blood vessel
- Blockage of a vessel in the lung leading to shortness of breath, pain and potentially coughing up blood
- Hypertension
- Strokes or temporary blockages of vessels in the brain
- Cough
- Visual disorders including keratitis (inflammation of part of the eye), cystoid macular edema (painless edema in part of the eye)
- Muscle or joint pain
- Urinary tract infections
- Nail changes
- Nosebleeds

Uncommon side effects (occurring in > 1/1000 to 1/100 of patients):

- Serious allergic reaction that may include symptoms such as shortness of breath, flushing, low blood pressure, chest pain, irregular or slow heart beats, trouble breathing.

Rare side effects (occurring in $\geq$ 1/10,000 to <1/1,000 patients)

Nab- paclitaxel contains human albumin, a derivative of human blood. Based on effective donor screening and product manufacturing processes, it carries a remote risk from transmission of viral diseases. A theoretical risk for transmission of Creutzfeldt-Jakob Disease (CJD) also is considered extremely remote. No cases of transmission of viral diseases or CJD have ever been identified for albumin.

What are the risks that can be anticipated with Cisplatin

Very common side effects (occurring in > 1/10 of patients), some may be serious i.e. causing hospitalization, life-threatening or where noted, may cause death:

- Kidney (abnormal function or failure)
- Low platelet count - which may lead to bruising or bleeding

- Low white blood cell count - which may temporarily place you at risk for infection
- Low red blood cell count – which may cause you to feel tired, look pale, and have shortness of breath
- Fever associated with low white blood count
- Nausea
- Vomiting
- Diarrhea
- Loss of taste
- Loss of appetite
- Dry skin
- Dehydration
- Hair loss (reversible)

Common side effects (occurring in > 1/100 to 1/10 of patients):

- Low magnesium, low calcium and low potassium levels which may lead to muscle cramps
- Liver function test abnormal(increase in liver enzymes and bilirubin)
- Numbness, tingling, pain, or burning of hands and feet
- Sepsis (life threatening condition when body's response to infection causes organ damage)
- Irregular heartbeat
- Inflammation of a vein at injection site
- Difficulty breathing, inflammation of the lungs, and respiratory failure
- Tinnitus (ringing in ears)

Uncommon side effects (occurring in > 1/1000 to < 1/100 of patients):

- Myocardial infarction (heart attack)
- Heart block
- Heart failure
- Arterial vasospasm (constriction of the blood vessels)
- Low blood pressure
- Stroke
- Blockage in the kidney capillaries that may cause kidney failure
- Visual disturbances (temporary), Flashing light or blurry vision, altered color perception

Rare side effects <u>(occurring in > 1/10,000 to <1/1,000 patients)</u>

- Serious allergic reaction that may include symptoms such as: swelling of the face, tongue, throat, itching, wheezing, trouble breathing, dizziness, increased heart rate and low blood pressure.
- Toxicity of the eyes sometime severe but usually reversible (such as inflammation of the optic nerve, swelling of the optic disc and possible cerebral blindness).

- Soft tissue damage at the site of injection leading to irreversible tissue damage.
- Loss of certain types of brain function characterized by spasms and reduced levels of consciousness.
- Hearing loss
- Reduced albumin levels in blood
- Inflammation of the mucous membranes of the mouth
- Increased risk of leukemia

What are the risks that can be anticipated <u>Gemcitabine</u>
Very common side effects (occurring in > 1/10 of patients):

- Low red blood cell count – which may cause you to feel tired, look pale, and have shortness of breath)
- Low platelet count (which can lead to bruising or bleeding)
- Low white blood cell count (which may temporarily place you at risk for infection)
- Constipation
- Lack of appetite
- Fever
- Flu-like symptoms (fever, feeling tired, loss of appetite, chills and cough)
- Hair loss (reversible)
- Liver function tests abnormal
- Protein in urine
- Blood in urine
- Fluid retention in the hands and feet
- Muscle or joint pain
- Nausea
- Vomiting
- Rash
- Numbness, tingling, pain, or burning of hands and feet
- Inflammation of the mucous membranes of the mouth

Common side effects (occurring in > 1/100 to 1/10 of patients):
- Fever associated with low white blood cells

Uncommon side effects (occurring in > 1/1000 to < 1/100 of patients):
- Abnormal kidney function or failure
- Build up of urea in the kidneys
- Sepsis (life threatening condition when body's response to infection causes organ damage)
- Irritation or bruising at the site of the infusion
- Serious allergic reaction that may include symptoms such as: swelling of the face, tongue, throat, itching, wheezing, trouble breathing, dizziness, increased heart rate and low blood pressure
- Serious lung toxicity including inflammation of the lungs, spasm of the lungs, swelling of the lungs and adults respiratory distress syndrome (ARDS)

Rare side effects (occurring in > 1/10,000 to <1/1,000 patients)

- Increase of toxicities with radiation therapy
- Capillary leak syndrome a condition in which fluid and proteins leak out of tiny blood vessels into surrounding tissue. This can result in dangerously low blood pressure, low albumin and a decrease in plasma volume.
- Swelling of the brain that may lead to headache, confusion, seizures, and loss of vision.

Risks of Radiation – Diagnostic Test
The radiation dose that you will get from diagnostic tests is medically indicated for your condition and it is the same that you would get if you were not involved in this research study.
CT Scan: CT scans are used to create images of internal bones and organs using radiation. The contrast solution that may be given for a CT scan may cause an allergic reaction (rare). Severe allergic reactions can be life threatening. CT contrast solution can cause kidney damage, especially if you are diabetic, dehydrated (lost body water) or elderly.

Magnetic Resonance Imaging (MRI): There are no known risks from exposure to magnetic fields. You may experience nervousness and/or anxiety due to the loud banging made by the machine while it is taking pictures and from confinement in a tight space (claustrophobia). If you become anxious, you can stop the procedure at any time. You may also experience some discomfort and fatigue from lying still during imaging.

If you have any metal clips or plates in your body, you should tell the investigator. MRI may not be appropriate if you are pregnant or are trying to become pregnant. MRI may not be appropriate if you have permanent eyeliner or eyebrows or any pieces of metal in your body, such as the following:

- heart pacemaker, heart valve replacement, or aortic clips
- metal fragments in your eyes, skin, or elsewhere in your body
- brain clips or pieces of metal used in aneurysm surgery or intercranial bypass
- venous umbrella
- pieces of metal in the body resulting from work as a sheet-metal worker or welder
- clips placed in an internal organ
- prosthetic devices, such as middle ear, eye, joint, or penile implants
- joint replacement.
- hearing aid that cannot be removed
- neurostimulator
- insulin pump
- intrauterine device (IUD)
- shunts or stents
- metal mesh or coil implants
- metal plate, pin, screws, or wires, or any other metal implants

If you have a history of an implanted device or clips in your pelvis (involving your uterus or fallopian tubes) or under your skin, acting as a contraceptive to prevent pregnancy, the MRI technologist will obtain specific information about the make and model of your

Psychological Stress

Some of the questions we will ask you as part of this study may make you feel uncomfortable. You may refuse to answer any of the questions, take a break or stop your participation in this study at any time.

Loss of Confidentiality

Any time information is collected; there is a potential risk for loss of confidentiality. Every effort will be made to keep your information confidential; however, this cannot be guaranteed.

Risks to Sperm, Embryo, Fetus or Breast-fed Infant

Males: Being in this research may damage your sperm, which could cause harm to a child that you may father while on this study. If you take part in this study and are sexually active, you must agree to use a medically-acceptable form of birth control through 120 days following your last dose of study drug. Medically-acceptable forms of birth control include:

(1) surgical sterilization (vasectomy), or
(2) a condom used with a spermicide (a substance that kills sperm).

Females: If you are part of this study while pregnant or breast-feeding an infant, it is possible that you may expose the unborn child or infant to risks. For that reason, pregnant and breast-feeding females cannot participate in the study. If you can become pregnant, a pregnancy test will be done, and it must be negative before you participate in this study. If you take part in this study and you are sexually active, you and any person that you have sex with must use a medically-acceptable birth control (contraceptives) through 120 days your last dose of study drug. Medically-acceptable birth control (contraceptives) includes:

(1) surgical sterilization (such as hysterectomy or “tubes tied”),

(2) approved hormonal contraceptives (such as birth control pills, patch or ring; Depo-Provera, Implanon),

(3) barrier methods (such as condom or diaphragm) used with a spermicide (a substance that kills sperm), or

(4) an intrauterine device (IUD).

If you do become pregnant during this study, you must tell the researchers immediately.

Radiation exposure to a woman’s reproductive organs may harm an embryo or fetus. Also, if radioactive materials are used for certain types of scans, harm may come to an embryo, fetus, or an infant who is breast feeding.

Pregnancy tests performed during the early stages of pregnancy do not always reveal pregnancy. Therefore, radiation exposure that includes the reproductive organs will be

limited to the first ten days after a woman who can become pregnant has begun her most recent menstrual period. This is standard policy in clinics and hospitals within UT Southwestern. This policy applies unless there is an important medical reason requiring radiation outside this time frame

Risks of Blood Drawing

Risks associated with drawing blood from your arm include minimal discomfort and/or bruising. Infection, excess bleeding, clotting, and/or fainting also are possible, although unlikely.

You will have approximately 10 tablespoons of blood collected because you are in this research study.

Risk of Optional Tumor Samples (collected by biopsy)

The biopsy may cause some pain and discomfort and may result in some bleeding and bruising. It is possible, but not likely, that you could get an infection. In very rare cases, people might have an allergic reaction to the numbing medicine. The allergic reaction could include rash/hive, flushing of the face, itching, wheezing and tightness in the throat. There will be a small scar from the biopsy.

Other Risks

There may possibly be other side effects that are unknown at this time. If you are concerned about other, unknown side effects, please discuss this with the researchers.

How will risks be minimized or prevented?

Study risks will be minimized or prevented by several measures at the beginning of the study and throughout your participation in the study.

You will be screened prior to enrollment to ensure that you meet the safety requirements of the study. All treatments will be modified within the study parameters to match your treatment needs. These modifications will include the timing and technical details of your operation. Throughout your participation in the study you will be evaluated by personnel trained to recognize, minimize, and treat side effects of your treatment. You will be withdrawn from the study if you experience an adverse event which causes unacceptable risk as determined by the investigators. You will continue to receive standard medical care if you are no longer participating in the study.

What will my responsibilities be during the study?

While you are part of this study, the researchers will follow you closely to determine whether there are problems that need medical care. It is your responsibility to do the following:

- Ask questions about anything you do not understand.
- Keep your appointments.
- Follow the researchers' instructions.
- Let the researchers know if your telephone number or address changes.

- Tell the researchers before you take any new medication, even if it is prescribed by another doctor for a different medical problem or something purchased over the counter.
- Tell the study doctor or study staff about any changes in your health.
- Tell your regular doctor about your participation in this study.
- Report to the researchers any injury or illnesses while you are on study even if you do not think it is related.

If I agree to take part in this research study, will I be told of any new risks that may be found during the course of the study?
Yes. You will be told if any new information becomes available during the study that could cause you to change your mind about continuing to participate or that is important to your health or safety.

What should I do if I think I am having problems?
If you have unusual symptoms, pain, or any other problems while you are in the study, you should report them to the researchers right away. Telephone numbers where they can be reached are listed on the first page of this consent form.

If you have a sudden, serious problem, like difficulty breathing or severe pain, go to the nearest hospital emergency room, or call 911 (or the correct emergency telephone number in your area). Tell emergency personnel about any medications you are taking, including any medications you are taking for this study.

What are the possible benefits of this study?
If you agree to take part in this study, there may or may not be direct benefits to you. The researchers cannot guarantee that you will benefit from participation in this research.

We hope the information learned from this study will benefit others with pancreatic cancer in the future. Information gained from this research could lead to better treatment.

What options are available if I decide not to take part in this research study?
You do not have to participate in this research to receive care for your pancreatic cancer. Instead of being in this study, you have the following options:
- Evaluation by a medical oncologist for chemotherapy regimens such as Nab-Paclitaxel/ gemcitabine and FOLFIRINOX for metastatic/ recurrent pancreatic cancer
- Evaluation by a radiation oncologist for standard radiation treatment
- Observation and supportive care
- Participation in another research study

By participation in this research, you may be forgoing other standard options with known clinical benefit.

Will I be paid if I take part in this research study?
No. You will not be paid to take part in this research study. There are no funds available to pay for parking expenses, transportation to and from the research center, lost time away from work and other activities, lost wages, or child care expenses.

Costs – Will taking part in this study cost anything?
You or your health insurance company will be responsible for the cost of treatments and procedures that would be done whether or not you took part in this study, such as standard of care procedures described in the procedures section above. It is important to understand that some insurance companies do not cover some costs (for example, approved drugs used in a way different from the package instructions). If your insurance company does not cover these treatments or procedures, you will be required to pay for them.

Ask the researchers if you have any questions about what it will cost you to take part in this study (for example bills, fees, or other costs related to the research).

The sponsor will provide the study drug, bemcentinib, free of charge during this study. At the end of your participation you must return all unused study drug to the researcher.

What will happen if I am harmed as a result of taking part in this study?
Compensation for an injury resulting from your participation in this research is not available from the University of Texas Southwestern Medical Center at Dallas or Parkland Health & Hospital System.

The sponsor, UT Southwestern, has expressed a willingness to help pay the medical expenses necessary to treat such an injury.

You retain your legal rights during your participation in this research.

If you have any questions concerning the availability of medical care or if you think you have experienced a research-related illness, injury or emergency, contact the research team listed at the top of this form immediately.

Can I stop taking part in this research study?
Yes. If you decide to participate and later change your mind, you are free to stop taking part in the research study at any time.

If you decide to stop taking part in this research study, it will not affect your relationship with the UT Southwestern staff or doctors. Whether you participate or not will have no effect on your legal rights or the quality of your health care you receive.

If you are a medical student, fellow, faculty, or staff at the Medical Center, your status will not be affected in any way.

Your doctor is a research investigator in this study. He is interested in both your

medical care and the conduct of this research study. At any time, you may discuss your care with another doctor who is not part of this research study. You do not have to take part in any research study offered by your doctor.

If I agree to take part in this research study, can I be removed from the study without my consent?

Yes. The researchers may decide to take you off this study if:

- Your medical problem remains unchanged or becomes worse.
- The researchers believe that participation in the research is no longer safe for you.
- The researchers believe that other treatment may be more helpful.
- The sponsor or the FDA stops the research for the safety of the participants.
- The sponsor cancels the research.
- If you become pregnant.
- You are unable to keep appointments or to follow the researcher's instructions.

Will my information be kept confidential?

Medical information collected during this study and the results of any test or procedure that may affect your medical care may be included in your medical record. The information included in your medical record will be available to health care providers and authorized persons including your insurance company.

You should know that certain organizations that may look at and/or copy your medical records for research, quality assurance, and data analysis include:

- UT Southwestern Medical Center
- BerGenBio ASA, collaborator and provider of bemcentinib.
- Representatives of government agencies, like the U.S. Food and Drug Administration (FDA), involved in keeping research safe for people; and
- The UT Southwestern Institutional Review Board.

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.

In addition to this consent form, you will be asked to sign an "Authorization for Use and Disclosure of Protected Health Information." This authorization will give more details about how your information will be used for this research study, and who may see and/or get copies of your information.

Are there procedures I should follow after stopping participation in this research?

- Let the researchers know immediately that you wish to withdraw from the research.
- Return to the research center for any tests that may be needed for your safety.
- Return any unused study materials, including empty containers.

- Discuss your future medical care, if any, with the researchers and/or your personal doctor.

Whom do I call if I have questions or problems?
For questions about the study, contact Muhammad Beg, MD at (214) 648.7097 during regular business hours and at (214) 645.4673 after hours and on weekends and holidays.

For questions about your rights as a research participant, contact the UT Southwestern Institutional Review Board (IRB) Office at 214-648-3060.

SIGNATURES:

YOU WILL BE GIVEN A COPY OF THIS CONSENT FORM TO KEEP.

Your signature below certifies the following:

- You have read (or been read) the information provided above.
- You have received answers to all of your questions and have been told who to call if you have any more questions.
- You have freely decided to participate in this research.
- You understand that you are not giving up any of your legal rights.

_____

Name of Participant (Printed)

_____ _____ _____ AM / PM

Signature of Participant Date Time

_____

Name of Person Obtaining Consent (Printed)

_____ _____ _____ AM / PM

Signature of Person Obtaining Consent Date Time

Witness

I attest that the information in the consent form was accurately explained to, and apparently understood by the subject or the subject's legal authorized representative, and that informed consent was freely given by the subject or the subject's legal authorized representative.

_____ _____ _____AM / PM

Name of Witness (Printed) Date Time

_____ _____ _____AM / PM

Signature of Witness Date Time