RESEARCH SUBJECT INFORMATION AND CONSENT FORM

TITLE:	A PHASE II TRIAL OF NAB-PACLITAXEL PLUS CISPLATIN PLUS GEMCITABINE IN PATIENTS WITH PREVIOUSLY UNTREATED METASTATIC PANCREATIC DUCTAL ADENOCARCINOMA
PROTOCOL NO.:	AX-CL-PANC-PI-13301 IRB Protocol #20190955 1421182
SPONSOR:	HonorHealth Research Institute
INVESTIGATOR:	Gayle Jameson, MSN, ACNP-BC, AOCN 10510 North 92nd Street Scottsdale, AZ 85258 USA
STUDY-RELATED PHONE NUMBER(S):	Gayle Jameson, MSN, ACNP-BC, AOCN 480-323-1350 (24 hours)

INTRODUCTION

You are being asked to take part in a clinical trial, a type of research study because you have been diagnosed with advanced pancreatic cancer. Your participation is entirely voluntary. To allow you to make an informed decision as to whether you want to take part in this research study, this document describes the purpose of the study, your rights and obligations, the procedures needed by the study, and the possible benefits and risks of participating. You should read all of this information carefully and discuss your questions and concerns with your study doctor or healthcare team. You may take home an unsigned copy of this consent form to think about or discuss your decision with your family, friends and anyone you choose. You should not join this research study until all of your questions are answered. A person who takes part in a research study is called a research or study subject. In this consent form, "you" always refers to the research subject.

Clinical trials include only people who choose to take part. Please take your time to make your decision. If you have any questions, you can ask your study doctor for more explanation about the clinical trial, this form, or your disease. This consent form may contain words that you do not understand. Please ask the study doctor or study staff to explain any words or information that you do not understand.

You are being asked to participate in a research study of nab-paclitaxel, cisplatin and gemcitabine for the treatment of pancreatic cancer. The combination of nab-paclitaxel plus gemcitabine has been approved for the treatment of pancreatic cancer. The combination of nab-paclitaxel, cisplatin and gemcitabine is experimental and has not been approved for the use described in this study by the Food and Drug Administration (FDA).

Things to know before deciding to take part in a research study:

- The main goal of a research study is to learn things to help patients in the future.
- The main goal of regular medical care is to help each patient.
- The decision to join or not join the research study will not cause you to lose any medical benefits. If you decide not to take part in this study, your doctor will continue to treat you.
- Parts of this study may involve standard medical care. Standard care is the treatment normally given for a certain condition or illness.
- Other parts of this study may involve experimental (investigational) drugs or procedures that are being tested for a certain condition or illness. An investigational drug is one that has not been approved by the U.S. Food & Drug Administration (FDA).
- After reading the consent form and having a discussion with the research staff, you should know which parts of the study are experimental and which are standard medical care.
- Your medical records may become part of the research record. If that happens, your medical records may be looked at and/or copied by the sponsor of this study and government agencies or other groups associated with the study.
- Your medical insurance may be billed for any standard medical care you receive during the research study. If your insurance company is billed then it may have access to the research records. Insurance companies may not pay for treatment that is part of a research study.

PURPOSE OF THE STUDY

The purpose of this study is to find out if the study drugs nab-paclitaxel, cisplatin, and gemcitabine given together are safe and effective. The combination of nab-paclitaxel plus gemcitabine has been studied in treating patients with pancreatic cancer, and as of September 2013 is approved for the treatment of advanced pancreatic cancer. In this study, cisplatin will be added to nab-paclitaxel plus gemcitabine, and tested in people who have not yet had any cancer therapy for the diagnosis of advanced pancreatic cancer, with the goal of improving response.

Another name for nab-paclitaxel is Abraxane®. Nab-paclitaxel contains the same medication as the prescription chemotherapy drug Abraxane®. Nab-paclitaxel is approved by the FDA for the treatment of advanced breast cancer, and in September 2013 nab-paclitaxel, combined with gemcitabine, was approved by the FDA for the treatment of advanced pancreatic cancer.

Cisplatin is approved by the FDA for the treatment of advanced bladder cancer, advanced ovarian cancer, and advanced testicular cancer and other childhood cancers. However, cisplatin is not approved by the FDA for the treatment of advanced pancreatic cancer.

Gemcitabine was approved by the FDA in 1996 for the treatment of pancreatic cancer. It is also an approved treatment for ovarian cancer, lung cancer, and breast cancer.

The Food and Drug Administration (FDA) has determined that this study meets the requirements for Investigational New Drug (IND) Exemption.

Who can participate in this study?
This study will be conducted in up to 4 cancer centers in the US. Up to 50 subjects in the US will take part in this study.

PROCEDURES
If you decide to participate in this study, you will be asked to sign this consent form. This form must be signed before any study-related tests are performed.

The study will consist of the following parts:

- Screening Evaluation
- Study Treatment Assessments
- Office Visit after Last Dose of Study Treatment
- Post-Study Follow-up

Screening Evaluation
In the first part of the study, you will have an extensive evaluation of your medical condition. The purpose of this evaluation is to find out if you qualify for this research study. Screening procedures for this study include:

- Review of this consent form
- Complete medical history, including your prior cancer treatments
- Physical examination
- Blood pressure, heart rate, respiratory rate, temperature and height and weight measurements
- Review of all of the medications you are taking or have taken within the past 30 days
- 12-lead ECG (electrocardiogram). An ECG is a record of the electrical activity of the heart.
- Assessment of your overall general health (performance status)
- CT (Computed Tomography) scan of your chest, abdomen, and pelvis. CT scanning uses X-rays to create images of tissue below the skin. Other tumor imaging tests if considered necessary by your study doctor. These tests could include MRI (magnetic resonance imaging). MRI uses magnetic fields to produce images of tissue below the skin.
- Blood draw (approximately 3 teaspoons) for the following:
    - routine safety tests to evaluate blood count, liver and kidney function
    - CA 19-9, (or CA 125, or CEA if not expressers of CA 19-9), a test that measures the level of tumor associated antigens (substance causing an immune response) found in the blood
- Serum (blood) pregnancy test if you are a woman of childbearing potential to make sure you are not pregnant. It will be done within 72 hours prior to the first dose of study drug.
- About 1-2 teaspoons of blood will be taken.
- Collect urine sample for urinalysis
- Study staff will obtain a sample of tumor tissue along with a copy of the pathology report, related to your diagnosis from a previous or recent surgery or biopsy, if available, and send to an outside laboratory for next generation sequencing.
- Complete two questionnaires related to your quality of life, pain, and symptoms related to your pancreatic cancer. It is expected that this will take you about 10 minutes to complete.

- Additionally if you are scheduled to undergo a biopsy and your study doctor determines that additional tumor tissue may be obtained with minimum risk and discomfort to you, he or she will ask you if a small sample of your tumor tissue may be obtained during the biopsy for research purposes. This is an optional portion of the study. The tumor tissue will be studied to help researchers understand if the combination of nab-paclitaxel, cisplatin and gemcitabine is changing the tumor. This testing may involve looking at the genes or proteins in the tumor. You will be asked to confirm whether or not you agree to take part in this optional part of the study in a separate Optional Tissue informed consent form. If you choose not to provide additional fresh tumor samples, you can still take part in this study.

Study Treatment Assessments

If you meet the study requirements during the screening period, you will then begin the study treatment phase of the study. You will receive the following study treatment regimen.

Nab-paclitaxel, cisplatin, and gemcitabine will be given weekly for 2 weeks (days 1 and 8) followed by 13 days of rest. Nab-paclitaxel 125 mg/m2 will be given IV (intravenously- through a vein in the arm) for about 30 minutes. Cisplatin at a dose of 25 mg/m2 will be given IV for about 60 minutes after the nab-paclitaxel dose is completed. Gemcitabine 1000 mg/m2 will be given IV for about 30 minutes after the cisplatin dose is completed. You will be given a total of about 5 hours of hydration (IV fluids) with each treatment day to reduce the risk of kidney damage. On treatment days, you will be given 2 hours of hydration prior to the chemotherapy and up to 3 hours of hydration after the chemotherapy has completed. On the days after chemotherapy, Day 2 and 9 of each treatment cycle, you will return to the clinic for a total of 3 hours of hydration. You will also receive medication to help prevent nausea and vomiting prior to the chemotherapy.

21-Day (3-week) Cycle:

- Day 1: nab-paclitaxel 125 mg/m2 followed by cisplatin 25mg/m2 followed by gemcitabine 1000 mg/m2
- Day 2: IV hydration
- Day 8: nab-paclitaxel 125 mg/m2 followed by cisplatin 25mg/m2 followed by gemcitabine 1000 mg/m2
- Day 9: pegfilgrastim 6mg and IV hydration
- Day 15: Day of rest
- Day 22: Repeat cycle- this is day 1 of the next cycle.

During dosing in this study treatment, you may receive another medicine called granulocyte colony-stimulating factor (G-CSF). G-CSF helps your body form more white blood cells and may help some of the common side effects of the study drugs.

On your first visit, you will be provided ahead of time with enough ciprofloxacin (or an alternative antibiotic) for use at home. If you develop a fever, you should begin taking the antibiotic when you first record a temperature of about 38.5 °C (about 101°F) or if you feel you are developing a fever and a thermometer is not available. In addition, **if you develop a fever, you should notify your study doctor immediately or his/her team as soon as possible** and you may be asked to return to the study location for evaluation and possible treatment.

This drug combination has affected a few patients in other studies with interstitial pneumonitis, a very serious lung infection. Therefore, during dosing in this study, if you experience shortness of breath or develop a dry cough, **you should notify your study doctor immediately or his/her team as soon as possible** and you may be asked to return to the clinic for evaluation and possible treatment.

The following evaluations will be performed prior to dosing on Day 1 of each cycle:

- Physical examination, including weight
- Review of any medications you are taking or have taken since your last visit
- Review of any medical procedures you have had since your last visit
- Review of any side effects or other medical problems you have had since your last visit
- Assessment of your overall general health (performance status)
- Check of your sense of touch
- Serum (blood) pregnancy test will be performed within 72 hours prior to treatment on day 1 of each cycle if you are a woman of childbearing potential to make sure you are not pregnant. About 1-2 teaspoons of blood will be taken.
- Blood draw (approximately 3 teaspoons)for the following:
    - Routine safety tests to evaluate blood count, liver, and kidney function
    - CA 19-9, (or CA 125, or CEA if not expressers of CA 19-9), a test that measures the level of tumor-associated antigens (substances causing an immune response) found in the blood
- Blood pressure, heart rate, temperature and respiratory rate
- Collect urine sample for urinalysis
- Complete questionnaires regarding quality of life, pain, and symptoms related to your pancreatic cancer. It is expected that this will take you about 10 minutes to complete.
- Administration of study treatment as detailed in the above section.
- Day 2: IV hydration

The following evaluations will be performed weekly (Day 8 and Day 15):

- Physical examination (not required day 15 after cycle 2)
- Review of any medications you are taking or have taken since your last visit
- Review of any side effects or other medical problems you have had since your last visit
- Assessment of your overall general health (performance status) (not required day 15 after cycle 2)
- Blood draw (approximately 2 teaspoons) for the following:
    - Routine safety tests to evaluate blood count, liver, and kidney function
    - CA 19-9, (or CA 125, or CEA if not expressers of CA 19-9), a test that measures the level of tumor-associated antigens (substances causing an immune response) found in the blood (not required day 15)
- Blood pressure, heart rate, temperature, respiratory rate (not required day 15 after cycle 2)
- Assessment of weight (day 8 only)
- Administration of study treatment as detailed in the above section (not required day 15)
- Day 9: pegfilgrastim 6mg and IV hydration

Every 9 weeks:

- CT scans of the chest, abdomen, and pelvis or any other studies required for tumor imaging (such as MRI), will be done every 9 weeks while you are on treatment. This will be the same type of imaging that you had at the screening evaluation

End of Treatment Visit:

An End of Study Treatment office visit will be performed when your study drug treatment ends for any reason. The End of Study Treatment evaluations include the following:

- Review of any medications you are taking or have taken since your last visit
- Review of any medical procedures you have had since your last visit
- Review of any side effects or other medical problems you have had since your last visit
- Physical examination
- Blood pressure, heart rate, temperature, and respiratory rate
- Assessment of your overall general health (performance status)
- Check of your sense of touch
- Blood draw (approximately 3 teaspoons) for the following:
    - Routine safety tests to evaluate blood count, liver, and kidney function
    - CA 19-9, (or CA 125, or CEA if not expressers of CA 19-9), a test that measures the level of tumor-associated antigens (substances causing an immune response) found in the blood
- Collect urine sample for urinalysis
- Complete questionnaires regarding quality of life, pain, and symptoms related to your pancreatic cancer. It is expected that this will take you about 10 minutes to complete.
- CT scan of chest, abdomen, and pelvis and any other studies required for tumor imaging (only if your previous CT scan was 8 weeks ago)
- Serum (blood) pregnancy test if you are a woman of childbearing potential to make sure you are not pregnant. About 1-2 teaspoons of blood will be taken.

Note that there may be additional blood draws throughout this study required for safety purposes; these will be considered "standard of care", for medical care and evaluation, and not for research purposes.

Post Study Follow-up Visit(s):

All subjects (or their family member) will be contacted in person or by telephone monthly after study completion or withdrawal for up to 12 months from the date of enrollment.

If after your last dose of study drugs you have ongoing side effects or other medical problems that started during the study, the study personnel might need to follow those conditions for a certain time or until they reach an acceptable level.

Follow-up evaluations for side effects or other medical problems that started during the study may include the following:

- Physical examination, blood pressure, heart rate, and weight measurements
- Review of any medications you are taking or have taken since your last visit
- Review of any medical procedures you have had since your last visit

- Check of your sense of touch
- Assessment of your overall general health (performance status)
- Test of certain chemicals and cells in your blood (about 3 teaspoons of blood will be taken)

Other Study Requirements:
You must not use any prescription or over the counter medication or supplements during the study without first checking with the study doctor. You must agree to not participate in any other research study while participating in this study. You must have stopped taking any research medications at least 4 weeks prior to enrolling in this study. You must have also stopped all other anti-cancer medications for this research study. Your study doctor will inform you of how long you must be off those medications to participate in this research study.

How Long Will the Study Last?
The length of time that you participate in the trial will depend on whether your cancer gets better or worse in response to the study treatment. It is expected that you will stay on study treatment as long as your cancer improves or is stable or until your cancer gets worse, side effects become intolerable, or you or your study doctor decide to not continue in the study. Long term follow-up will take place for 24 months after you stop study treatment.

Future Research
As a part of this study, if any tumor samples are left over after the planned testing is done, they will be stored in a secure laboratory for possible additional tests. It is not known at this time what the additional tests might be. Your samples may be tested by the study sponsor or by companies, laboratories or other entities working with the study sponsor. Your samples will only be used for research and may help develop new treatments or diagnostic tests in the future. It may be used by researchers to learn more about the development of the type of cancer you have and predictors of why your cancer gets worse. This research may include analyses of DNA, RNA, or proteins. Your samples will not be used for genetic testing to determine or predict risk of diseases that you do not currently have. Your samples will not be used for research related to human cloning.

Your tumor tissue samples will not have your name on them. Your samples will be labeled with a code. Researchers who perform tests on these samples will only see the code and will not see any personal information that specifically identifies you. Your study doctor will make every effort to protect your identity, but complete privacy cannot be guaranteed.

You will not get the results of any research tests performed on your samples. The results from the research tests are for research only and will not be used to make decisions about your medical care. The results of the research tests will not be put into your medical record.

RISKS AND DISCOMFORTS
Participation in this research study may involve added risks and discomforts, including the possible side effects of the study treatments described in this form. There also may be other potentially serious side effects that are not yet known. Let your study doctor know about any side effects you are experiencing. Your study doctor may be able to give you other drugs to make side effects less serious or uncomfortable. Many side effects go away after the study treatment is stopped but, in some cases, these side effects may be serious and/or long lasting. Rarely, side effects could be fatal (causing death).

Risks from the Study Drug
You may have side effects while you are in the study, but you will be carefully checked by the study doctor for any problems. There may be risks or side effects of the study drug that are unknown at this time. You should tell the study doctor/staff about anything that is bothering you or any side effects you have, even if you do not think they are related to the study drug.

nab-Paclitaxel
The following is a list of the most medically significant or most common side effects reported in completed studies considered to be related to nab-paclitaxel albumin. In some cases, side effects can be serious, long-lasting, or can cause death. Some side effects go away soon after you stop the study drug/therapy, and some may never go away. The study doctor may alter the dosage regimen of nab-paclitaxel or give you medicines to help lessen the side effects. This is not a complete list of all side effects that may occur. For more information about risks and side effects, please ask the study doctor.

Very common (Out of 100 people who receive nab-paclitaxel more than 10 people may have the following):

- Low red blood cell count - which may cause you to feel tired, look pale, and have shortness of breath)
- Low white blood cell count - which may also be associated with fever and temporarily place you at risk for infections including oral thrush, respiratory infection, and pneumonia
- Low platelet count - which may lead to bruising or bleeding
- Constipation
- Diarrhea
- Nausea
- Vomiting
- Stomach pain (Abdominal pain)
- pain, swelling or sores on the inside of the mouth (Stomatitis, Mucosal inflammation)
- Inflammation of the mouth and lips
- Numbness, tingling or burning of hands and feet
- Dizziness
- Headache
- Tiredness and weakness
- Joint and muscle pain
- Fluid retention in the hands and feet
- Fever, chills
- Loss of appetite
- Loss of taste
- Weight loss
- Difficulty sleeping (Insomnia)
- Depression
- Cough
- Shortness of breath (Dyspnea)
- Hair loss (reversible)

- Rash
- Itchy skin
- Nail changes
- Increase in liver function tests (AST/ALT)
- Dehydration (loss of water and minerals in the body)
- nosebleed (Epistaxis)
- decreased potassium levels in blood, which may cause fatigue, muscle weakness or cramps and/or an irregular heartbeat (Hypokalemia)

Common (Out of 100 people who receive nab-paclitaxel, at least 1 but less than 10 people may have the following):

- Bone marrow failure (which results in decreased levels of red blood cells, white blood cells, and platelets)
- Infections including yeast infection, upper and lower respiratory infections, nail infections, pneumonia, urinary tract infection
- Low white blood cell count, which may also be associated with fever (which may temporarily place you at risk for infection
- Inflammation or an irritation of the lung passages (Bronchitis)
- Pneumonitis or inflammation of the walls of the lungs
- Inflammation of the bowel causing abdominal pain or diarrhea (Colitis)
- Difficulty swallowing
- Indigestion
- Increase in bilirubin
- Increase in alkaline phosphatase
- Increase in kidney function tests (creatinine)
- Kidney failure (sudden and severe in nature)
- Blood in the urine
- Loss of coordinated muscle control
- Muscle weakness
- Anxiety
- Nasal congestion
- Painful swallowing, sore throat, that may also include ear pain
- Dry mouth, dry throat, nasal dryness
- Coughing up blood
- Blood clot that travels to the lungs (pulmonary embolism) leading to shortness of breath, pain, and potentially coughing up blood
- Blood clot that forms in a deep vein in the body, most commonly the lower leg or thigh (deep vein thrombosis)
- Flushing, redness of the skin
- Dry skin
- Hand-foot syndrome causes redness, swelling, and pain on the palms of the hands and/or the soles of the feet
- Changes in blood pressure, high blood pressure, low blood pressure
- Congestive heart failure, heart palpitations, irregular or increase in heartbeat
- Increase in tears
- Blurred vision, disturbance in vision

- Irritation or bruising at the site of the infusion
- Swelling of the arms and legs that may be painful

Uncommon (Out of 100 people who receive nab-paclitaxel, less than 1 person may have the following):

- Heart arrhythmias
- Cardiac arrest
- Serious allergic reaction that may include symptoms such as shortness of breath, flushing, low blood pressures, chest pain, irregular or slow heart beats, trouble breathing
- A condition that affects the blood and blood vessels and results in the destruction of platelets, low red blood cells, and kidney failure (hemolytic uremic syndrome)
- Inflammation in different parts of the eye, including conjunctiva (conjunctivitis), cornea (keratitis), macula (maculopathy), or retina (cystoid macular edema)
- Fluid retention
- Pulmonary edema (fluid in lungs)
- Tiredness and weakness
- Skins changes including sloughing of dry skin, hives, itchiness, and rash
- Temporary paralysis of the facial muscles due to damage to the facial nerves

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.

Gemcitabine Side Effects:

Common (Out of 100 people who receive gemcitabine at least 5 but less than 20 people may have the following):

- Anemia (low red blood cell count – which may cause you to feel tired, look pale, and have shortness of breath)
- Constipation
- Diarrhea
- Fever
- Flu-like symptoms (fever, feeling tired, loss of appetite, chills and cough)
- Hair loss (reversible)
- Liver function tests abnormal
- Low platelet count (which can lead to bruising or bleeding)
- Low white blood cell count (which may temporarily place you at risk for infection)
- Nausea
- Rash
- Vomiting

Less Common (Out of 100 people who receive gemcitabine, at least 1 but less than 5 people may have the following):

- Edema (fluid retention)
- Fatigue
- Irritation or bruising at the site of the infusion
- Itching
- Mouth or lip sores
- Tingling, prickling of the skin

Uncommon (Out of 100 people who receive gemcitabine, less than 1 person may have the following):

- Serious allergic reaction that may include symptoms such as shortness of breath, flushing, low blood pressures, chest pain, irregular or slow heart beats, trouble breathing
- Blood and protein in the urine
- Difficulty breathing
- Abnormal kidney function or failure

Rare (Out of 1000 people who receive gemcitabine, less than 1 person may have the following):

- A condition that affects the blood and blood vessels and results in the destruction of platelets, low red blood cells, and kidney failure (hemolytic uremic syndrome)
- Serious lung toxicity including inflammation of the lungs, spasm of the lungs, swelling of the lungs and adults respiratory distress syndrome (ARDS)
- A very rare condition in which fluid and proteins leak out of tiny blood vessels into surrounding tissues, which can result in low blood pressure, low albumin and decrease in plasma volume (capillary leak syndrome)
- A very rare condition with a rapid onset of symptoms including headache, confusion, seizures and visual loss (posterior reversible encephalopathy syndrome)

Cisplatin

Very common (Out of 100 people who receive cisplatin more than 10 people may have the following):

- 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
- Hiccups
- Loss of appetite
- Dry skin

- Dry mouth
- Dehydration
- Hearing loss
- Hair loss (reversible)
- Tinnitus (ringing in the ears)

Common (Out of 100 people who receive cisplatin at least 5 but less than 20 people may have the following):

- 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 or burning of hands and feet
- Difficulty breathing, inflammation of the lungs, respiratory failure
- Sepsis (life threatening condition when body's response to infection causes organ damage)

Less Common (Out of 100 people who receive cisplatin, at least 1 but less than 5 people may have the following):

- Fatigue
- Irritation or bruising at the site of the infusion

Uncommon (Out of 100 people who receive cisplatin, less than 1 person may have the following):

- Serious allergic reaction that may include symptoms such as shortness of breath, flushing, low blood pressures, chest pain, irregular or slow heart beats, trouble breathing
- Myocardial infarction (heart attack)
- Heart block
- Heart failure
- Arterial vasospasm (constriction of the blood vessels)
- Low blood pressure
- Stroke
- Hemolytic anemia (destruction of red blood cells)
- Thrombotic thrombocytopenic purpura (syndrome of abnormal clotting and bleeding)
- Hemolytic uremic syndrome (abnormal clotting and kidney failure)
- Limb and mesenteric ischemia (decreased blood flow to limbs and gut)
- Pancreatitis (inflammation of the pancreas)
- Papilledema (swelling of blood vessels in the eyes)
- Neutropenic typhlitis (infection in the gut due to low white blood cells)
- Reversible posterior leukoencephalopathy syndrome (a syndrome characterized by headache, confusion, seizures and visual loss)
- Visual disturbances (temporary), (Flashing light or blurry vision)
- Mouth or lip sores
- Gynaecomastia (enlarged breasts in males)

Risks of G-CSF or Pegfilgrastim (Neulasta® or NeulastaOnpro®)
The most common side effect of G-CSF is aching in the bones and muscles. Depending on the type of G-CSF given, possible but rare side effects include the following:

- Serious allergic reactions that may be life-threatening (symptoms can include rash, shortness of breath, wheezing, dizziness from a drop in blood pressure, swelling around the mouth or eyes, fast pulse, and/or sweating)
- Enlarged or ruptured spleen
- Adult respiratory distress syndrome (a condition caused by fluid buildup in the lungs that prevents normal breathing)
- Sickle cell crisis in subjects with Sickle Cell disease.
- Swelling of the optic (eye) disc (symptoms include headache, blind spot, blurring of vision and/or loss of vision)

Side Effects of palonosetron (Aloxi®):
Palonosetron will be given by IV before the paclitaxel protein bound, cisplatin and gemcitabine to prevent nausea and vomiting that you may experience.

Less serious side effects that can occur include:

- headache
- constipation
- pain, redness swelling or a lump under your skin where the needle is placed

More serious side effects that can occur include:

- allergic reaction (symptoms include hives, swelling of the face or hands, trouble breathing, tingling in your mouth or throat and/or chest tightness)
- anxiety
- restlessness
- fever
- sweating
- muscle spasms
- nausea and/or vomiting
- diarrhea
- lightheadedness, dizziness, fainting
- chest pain and/or irregular heartbeat

Side Effects of fosaprepitant (Emend®):
Fosaprepitant will be given by IV before the paclitaxel protein bound, cisplatin and gemcitabine to prevent nausea and vomiting. In addition, you may receive fosaprepitant orally to take on your own to prevent any nausea and vomiting that you may experience at home.

Less serious side effects that can occur include:

- nausea and/or vomiting
- heartburn
- stomach pain
- diarrhea or constipation
- loss of appetite

- hiccups
- increased thirst or hot, dry skin
- weakness, dizziness, tired feeling
- headache
- ringing in your ears
- fever, chills, body aches, flu symptoms
- sleep problems (insomnia)
- pain or a hard lump where the medicine was injected.

More serious side effects that can occur include:

- feeling light-headed
- fainting
- slow heart rate
- pale skin, easy bruising or bleeding
- pain or burning when you urinate

Side Effects of dexamethasone:
Dexamethasone will be given by IV before the paclitaxel protein bound, cisplatin and gemcitabine to prevent nausea and vomiting that you may experience.

Less serious side effects that can occur include:

- upset stomach
- stomach irritation
- vomiting
- headache
- dizziness
- insomnia
- restlessness
- depression
- anxiety
- acne
- increased hair growth
- easy bruising
- irregular or absent menstrual periods

More serious side effects that can occur include:

- skin rash
- swollen face, lower legs, or ankles
- vision problems
- cold or infection that lasts a long time
- muscle weakness
- black or tarry stool

Side Effects of ondansetron (Zofran®):
Ondansetron may be given in lieu or in addition to fosaprepitant to prevent/treat nausea and vomiting. Your doctor will decide what the best course of treatment is to prevent/treat any nausea/vomiting that you may experience.

Less serious side effects that can occur include:

- headache
- constipation
- weakness
- tiredness
- chills
- drowsiness

More serious side effects that can occur include:

- blurred vision or vision loss
- rash
- hives
- itching
- swelling of the eyes, face, lips, tongue, throat, hands, feet, ankles, or lower legs
- hoarseness
- difficulty breathing or swallowing
- chest pain
- shortness of breath
- dizziness, light-headedness, or fainting
- fast, slow or irregular heartbeat
- agitation
- hallucinations (seeing things or hearing voices that do not exist)
- fever
- excessive sweating
- confusion
- nausea, vomiting, or diarrhea
- loss of coordination
- stiff or twitching muscles
- seizures
- coma (loss of consciousness)

Additional medications not listed may be given to help treat any side effects. Please talk to your study doctor regarding any questions or concerns you may have about any side effects you are experiencing.

Pregnancy Risk
Women who are pregnant or nursing a child may not take part in this study. Before entering the study, you and your doctor must agree on the method of birth control you will use during the entire study. You must have a negative serum (blood) pregnancy test before you start taking the study drugs. If you think that you have gotten pregnant during the study or for 6 months after your last dose of study drug, you must tell your study doctor immediately. Pregnant women will be taken out of the study.

The study drugs may affect an unborn child or nursing infant. The risks to an unborn child or nursing infant are not fully known. You must not breast feed at any time you are in this study since any drugs you are taking may also affect the child. These drugs may also cause changes to eggs in women.

The study drugs may have a harmful effect on sperm. This can lead to damage to a fetus or embryo (developing unborn baby). If you are a fertile male, you must not impregnate a female while in this study. You must agree to use a form of birth control, along with the method your partner is using, that is medically acceptable to your study doctor during the study. You should ask your study doctor how long to continue the use of your birth control methods following your last dose of study drugs.

Women of childbearing potential are women who are biologically capable of becoming pregnant. This includes women who are using contraceptives or whose sexual partner is either sterile or using contraceptives.

The study drugs may affect an unborn child or nursing infant. The risks to an unborn child or nursing infant are not fully known. These drugs may also cause changes to eggs in women.

The following information is for women who are able to become pregnant:

- It is important that you do not become pregnant while in this study. If you become pregnant, you will be taken off this study.
- You must have a negative serum (blood) pregnancy test before you start taking the study drugs.
- If you do become pregnant or suspect you are pregnant, while you are on this study or for 6 months after the last dose of study drug, you must notify your study doctor immediately.
- You must not breast feed at any time you are in this study since any drugs you are taking may also affect the child.

Birth Control Requirements for Female Participants:
If you are sexually active and able to become pregnant, you must agree to use two forms of highly effective birth control methods listed below:

- Hormonal methods, such as birth control pills, patches, injections, vaginal ring, or implants
- Barrier methods (such as a condom or diaphragm) used with a spermicide (a foam, cream, or gel that kills sperm)
- Intrauterine device (IUD)
- Abstinence (no sex)

NOTE: Hormonal contraceptives alone are not considered an acceptable method of birth control for this study.

You must use birth control for the entire study this includes the 28 days prior to starting study treatment and for at least 6 months after your last dose of study drug.

Birth Control Requirements for Male Participants:
The study drugs may have a harmful effect on sperm. This can lead to damage to a fetus or embryo (developing unborn baby). If you are a fertile male, you must not impregnate a female while in this study. If you are sexually active, and able to father a child, you must agree to use two forms of birth control methods listed below:

- Barrier methods (such as a condom or diaphragm) used with a spermicide (a foam, cream, or gel that kills sperm)
- Hormonal methods used by your partner, such as birth control pills, patches, injections, vaginal ring, or implants
- Intrauterine device (IUD) used by your partner
- Abstinence (no sex)

You must use birth control for the entire study and for at least 6 months after your last dose of study drug. If your partner becomes pregnant while you are on the study or within 6 months of receiving the last dose of study medication, you will need to report this to your study doctor.

Other Risks

- **Infection:** Subjects receiving the nab-paclitaxel, cisplatin, and gemcitabine combination treatment are at increased risk of infection. Subjects over the age of 80 years have a greater risk of developing this infection. **Subjects that develop a fever should notify their study doctor or his team as soon as possible** and may be asked to return to the study location for evaluation and possible treatment. If you develop a fever, you should begin taking the antibiotic provided to you at the first visit immediately.
- **Intravenous (IV) Drug Administration:** Nab-Paclitaxel, Cisplatin, and Gemcitabine are given as IV infusions. Temporary irritation and bruising may occur at the infusion site. There may also be discomfort, pain, or bruising from the needle puncture. In rare cases, an infection may also occur at the site of the needle stick.
- **Blood Draw:** The risk of having blood drawn from a vein or receiving drug to a vein is that it may cause a small amount of pain from the puncture and may cause bruising, bleeding, infection, or fainting.

- **CT Scan:** CT scans send x-rays through the body at many different angles. You will be exposed to a small dose of radiation. All radiation adds up over a lifetime and may increase the risk of new cancer forming. Some people may feel "closed in" while lying in the scanner. However, the scanner is open at both ends, and an intercom allows you to talk with doctors and staff. If you feel ill or anxious during scanning, doctors and/or radiology technicians will give comfort, or the scanning will be stopped. When a CT scan of the abdominal area is taken, material may be inserted into the rectum to better define the bowel. You will usually drink liquid to help define various abdominal organs. This may cause nausea and/or vomiting. Solution may also be given by vein to make the x-ray pictures more accurate. This may cause flushing, nausea, and/or severe allergic reactions. The solution injection may also cause pain, bleeding, bruising, hives, and/or itching.
- **MRI Scan:** During the MRI, you may feel mild vibrations throughout your body. The machine will produce a loud knocking noise. This is normal. You will be given earplugs or earphones to protect your ears. Some people, especially those who tend to feel uncomfortable in small or closed spaces, may feel "closed in" and become anxious while in the scanner. The scanner has an intercom, which will allow you to speak to the staff during the procedure. If you feel ill or anxious during scanning, tell the MRI staff and the scanning will be stopped if you wish. The MRI will require a catheter to be inserted into one of your veins in order to inject the MRI contrast agent. This may cause skin irritation, bleeding, and/or infection. You may have an allergic reaction to the contrast agent. The magnetic field used in MRI scanning may harm people who have metal in their bodies (pacemakers, neurostimulators, certain clips, or staples from surgery). It may cause problems with devices, such as pacemakers. If you have metal in your body or a pacemaker, you should not have an MRI.
- **Other Medications:** Before each dose of study drug(s), your study doctor may decide to administer certain medications to help control side effects. The lowered blood counts may temporarily place you at risk for infection or bleeding, although this is uncommon. If necessary, these events may require a reduction in the dose of the study drug(s) and/or you will be given medication to help relieve any pain or discomfort.
- **Psychological Stress:** Some of the questions we will ask you as part of this study regarding quality of life, pain, and symptoms related to your pancreatic cancer 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.

In addition to the risks already described, there may be other discomforts or risks from the study drugs or study procedures which are unknown. You will be observed carefully for signs and symptoms of possible side effects. If you experience any unusual symptoms, please inform your study doctor immediately.

If you have any questions about the risks of participating in this research study, you may ask the study doctor, another study team doctor, or your regular doctor. You may ask questions now or you may call the study doctor at the phone number on the first page of this form.

There may be side effects that are not known at this time. Your condition may not get better or may get worse during this study.

NEW INFORMATION
You will be told about anything new that might change your decision to be in this study. If there is new information, you may be asked to sign a new consent form.

BENEFITS
It cannot be promised that you will receive any medical benefits from being in this study.

There may be no direct medical benefit to you from participating in this study, except you may gain information about your health from the different tests that are done as part of the study. The expected benefit of taking part in the study may be similar to that of getting commonly used chemotherapy. Gemcitabine combined with nab-paclitaxel has been shown to be effective in patients with metastatic pancreatic cancer. However, it is unknown whether nab-paclitaxel and cisplatin given together with gemcitabine will be as effective, more effective, or less effective than other commonly used chemotherapies.

Information obtained from this study will benefit the sponsor. It might also lead to treatments that help others in the future.

WHAT ARE MY RESPONSIBILITIES 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.

COSTS
The sponsor, HonorHealth Research Institute will pay for all procedures and tests done specifically for this research study. Those treatments, procedures and tests that you would be likely to receive whether you were in the study or not, are not paid for by the study sponsor, and are considered "standard of care" for your medical condition. If you have health insurance, the cost of these "standard of care" services will be billed to your insurance company. Your health insurance may not cover these costs because of your participation in this research study. If it does not, the costs will be your responsibility. If you do not have health insurance, the cost of these "standard of care" services will be billed to you.

You may want to talk with your insurance company about its payment policy for standard medical care given during a research study. If your insurance company does not pay, you may be billed for those charges.

You might have unexpected expenses from being in this study. Ask your study doctor to discuss the costs that will or will not be covered by the sponsor. This discussion should include who will pay the costs of treating possible side effects.

PAYMENT FOR PARTICIPATION
You will not be paid for your participation in this research.

ALTERNATIVE TREATMENT
There are other treatment options for metastatic pancreatic cancer. These options include other chemotherapy regimens, radiation, or other experimental therapy. Your study doctor will explain the other options available to you. You do not have to participate in this study to receive treatment for your condition. You may also choose to receive no treatment for your cancer.

If you decide that you don't want any more active treatment, one of your options is called "comfort care." Comfort care includes pain medication and other support. It aims to maintain your comfort and dignity rather than cure disease. Usually this care can be provided at home. If you think you might prefer comfort care, please discuss this with your family, friends and your doctor.

CONFIDENTIALITY OF YOUR INFORMATION COLLECTED DURING THE STUDY
As required by the Federal Health Insurance Portability and Accountability Act (HIPAA), every effort will be made to safeguard the confidentiality of information that identifies you and relates to your past, present and future physical and mental health. We will do our best to make sure that the personal information obtained during the course of this research study will be kept private (such as using codes or keeping consent forms separate from data to ensure that the subject's name and identity will not become known or linked with any information they have provided). However, we cannot guarantee total privacy. Your personal information may be given out if required by law.

Unless required by law, you will not be identified on any electronic form by name, social security number, address and telephone number or any other information that can directly identify you. The information shared with the Sponsor is protected by the use of a code, which is a number specifically assigned to you. The study doctor is in control of the code needed to connect your data to you, but the study doctor will not send the list with the code to the Sponsor. However, the study forms may contain other information about you, such as your age, sex and medical history. It is possible that this other information could be used to identify you even though your name does not appear.

The results of this study may be published by the Sponsor, including in a medical journal and shown at medical meetings. You will not be identified (by name or any other means, e.g., photo) in any of these publications.

Because this research is regulated by the Food and Drug Administration (FDA), the FDA may inspect records related to this research, which may include your protected health information or other information about you derived or maintained as part of this study.

Information derived from this study may be used for research purposes that may include publication and teaching. However, information used for publication and teaching will not disclose your identity.

COMPENSATION FOR INJURY

We will make every effort to prevent study-related injuries and illness. If you are injured or become ill while you are in the study and the illness or injury is due to your participation in this study, you may go to any emergency room or urgent care facility to seek medical treatment. If it is determined that the injury or illness is not related to the research, the costs of this care may be charged to you or to your health insurer. No funds are available from HonorHealth to compensate you for a study-related injury or illness. This does not mean that you are giving up any of your legal rights.

The study doctor will provide you medical care if you need it, and will also treat you for any complications that may occur during your participation in the study. If you become ill or are injured as a direct result of your participation in this study, you will be provided the reasonable and necessary treatment for that injury or illness. The bills for the injury or illness not caused by study participation may be billed to your medical insurance or to your third party or governmental programs in which you participate.

The sponsor **may** reimburse costs for documented medical expenses for injury or illness caused by administration of study drug in accordance with the protocol or any properly performed procedures required by the protocol including if a deviation from the protocol is necessary to protect your rights, safety or welfare. The Sponsor will not reimburse costs for injury caused by your failure to follow your study doctor's or study staff's instructions for the study. The Sponsor will not offer to pay costs of medical care for such an injury or items such as lost wages, expenses, compensation for pain and suffering, discomfort and disability. Please speak with your study doctor to make sure you understand your options regarding compensation for injury.

VOLUNTARY PARTICIPATION AND WITHDRAWAL

Your participation in this study is voluntary. You may decide not to take part or you may leave the study at any time. Your decision will not cause any penalty or loss of benefits to which you are entitled.

Your participation in this study may be stopped at any time by the study doctor or the sponsor without your consent for any of the following reasons:

- Your cancer becomes worse
- Side effects arise which prevent further study treatment
- You decide to withdraw from the study
- Changes in your condition occur that lead your study doctor to believe that it would be harmful for you to receive further study treatment
- You become pregnant or fail to use adequate birth control (if you are of child-bearing potential)

- Another anticancer medication is started
- You cannot or will not follow the instructions for participation in the study
- The study doctor decides it is in your best interest not to continue in the study.
- You do not consent to continue in the study after being told of changes in the research that may affect you,
- or for any other reason.

If you leave the study before the planned final visit, you may be asked by the study doctor to have some tests or procedures done so that you leave the study safely.

SOURCE OF FUNDING FOR THE STUDY

HonorHealth has received funding from Celgene to conduct this study. Your study doctor and nurse practitioner receive a salary from HonorHealth as employees but will not receive any additional payments for conducting this study.

AUTHORIZATION TO USE AND DISCLOSE INFORMATION FOR RESEARCH PURPOSES

What information will be collected by the study doctor and his research staff for this study?
The study doctor will collect your personal and medical information. This may include:

- Past and present medical records,
- Research records,
- Records about phone calls made as part of this research,
- Records about your study visits.

Who may use and give out information about you?
The study doctor and his research staff conducting the research.

Who will receive your personal and medical information collected?
Information from this study will be given to the study sponsor. "Sponsor" is the person or entity that initiates, provides oversight of activities within the study, and includes any persons or companies that are contracted by the sponsor to have access to the research information during and after the study. Medical records which identify you and the consent form signed by you will be looked at and collected for research purposes by:

- HonorHealth Research Institute, the sponsor,
- HonorHealth Research Institute, the study site
- Triligent International, an agent for the Sponsor

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

- The U.S. Food and Drug Administration (FDA),
- Department of Health and Human Services (DHHS) agencies,
- Governmental agencies in other countries,
- Governmental agencies to whom certain diseases (reportable diseases) must be reported,
- WCG Institutional Review Board (WCG IRB)
- HonorHealth Institutional Review Board (HIRB)
- Celgene who is providing funding for this study
- Mayo Clinic Medical Genome Facility
- University of California San Diego

The HonorHealth IRB and the HonorHealth Research Institute have the authority to review and monitor all records related to this research.

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

- for research purposes as described in this consent form,
- for consideration by the FDA or any governmental agencies in other countries for drug approval,
- to make sure the study was conducted appropriately as approved by the IRB.
- to be used for future research purposes

What will happen if you decide not to give permission to use and give out your private health information?
You cannot be in this research study.

Will you have access to the information collected during the study?
To maintain the integrity of this research study, you will not have access to your personal health information related to this research until the study is complete. At the conclusion of the research and at your request, you may request access to your health information that HonorHealth maintains in a designated record set, which means a set of data that includes medical information or billing records used in whole or in part by your doctors or other health care providers at HonorHealth. If it is necessary for your care, your health information will be provided to you or your physician.

Does this authorization expire?
This authorization does not expire unless it is canceled by you in writing.

Can this authorization be withdrawn or canceled?
You may withdraw or take away your permission to use and disclose your health information at any time. You do this by sending written notice to the study doctor. If you withdraw your permission, you will not be able to stay in this study.

When you withdraw your permission, no new health information identifying you will be gathered after that date. Information that has already been gathered may still be used and given to others.

Is my health information protected after it has been given to others?
There is a risk that your information will be given to others without your permission. Absolute confidentiality cannot be guaranteed because of the need to give information to these parties.

QUESTIONS
Contact Gayle Jameson, MSN, ACNP-BC, AOCN at 480-323-1350 (24 hours) for any of the following reasons:

- if you have any questions about your participation in this study,
- if at any time you feel you have had a research-related injury or a reaction to the study drug, or
- if you have questions, concerns, or complaints about the research.

If you have questions about your rights as a research subject or if you have questions, concerns, input, or complaints about the research, you may contact:

WCG IRB
1019 39th Avenue SE, Suite 120
Puyallup, Washington 98374
Telephone: 855-818-2289
E-mail: researchquestions@wcgirb.com

WCG IRB is a group of people who independently review research.

WCG IRB will not be able to answer some study-specific questions, such as questions about appointment times. However, you may contact WCG IRB if the research staff cannot be reached or if you wish to talk to someone other than the research staff.

Do not sign this consent form unless you have had a chance to ask questions and have gotten satisfactory answers.

If you agree to be in this study, you will receive a signed and dated copy of this consent form for your records.

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.

CONSENT

I have read this consent form and understand what has been discussed. All my questions about the study and my part in it have been answered. I voluntarily consent to be in this research study.

I authorize the use and disclosure of my health information to the parties listed in the authorization section of this consent for the purposes described above.

By signing this consent form, I have not given up any of my legal rights.

_____
Subject Name (printed)

_____ _____
Signature of Subject Date

_____
Name of Person Conducting Informed Consent Discussion (printed)

_____ _____
Signature of Person Conducting Informed Consent Discussion Date