THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center

Informed Consent

INFORMED CONSENT/AUTHORIZATION FOR PARTICIPATION IN RESEARCH

Women's Triple-Negative First-Line Study: A Phase II Trial of Panitumumab, Carboplatin and Paclitaxel (PaCT) in Patients with Localized Triple-Negative Breast Cancer (TNBC) with Tumors Predicted Insensitive to Standard Neoadjuvant Chemotherapy
2015-0294

Subtitle: TNBC Moonshot with PaCT

Study Chair: Clinton Yam

_____ _____
Participant's Name Medical Record Number

This is an informed consent and authorization form for a research study. It includes a summary about the study. A more detailed description of procedures and risks is provided after the summary.

This research study has been reviewed and approved by an Institutional Review Board (IRB – a committee that reviews research studies).

STUDY SUMMARY

The goal of this clinical research study is to learn if receiving 4 cycles of an experimental chemotherapy combination before surgery can help to shrink or slow the growth of tumors before they are removed through surgery. The safety of this combination will also be studied.

This is an investigational study. Paclitaxel and carboplatin are FDA approved and commercially available for the treatment of breast cancer. Panitumumab is FDA approved and commercially available for the treatment of colorectal cancer. It is currently being used for research purposes only in the breast cancer setting. The study doctor can explain how the study drugs are designed to work.

The study drugs may help to shrink or slow the growth of the tumor(s) before surgery. Future patients may benefit from what is learned. There may be no benefits for you in this study.

Your participation is completely voluntary. Before choosing to take part in this study, you should discuss with the study team any concerns you may have, including side

effects, potential expenses, and time commitment. You may choose not to take part in this study because it is a first in human study and because there are other standard options.

You can read a list of potential side effects below in the Possible Risks section of this consent.

You may receive up to 4 cycles of chemotherapy.

Panitumumab will be provided at no cost to you while you are on study. You and/or your insurance provider will be responsible for the cost of paclitaxel, carboplatin, and surgery.

You may choose not to take part in this study. Instead of taking part in this study, you may choose to receive standard chemotherapy or surgery. You may choose to receive other investigational therapy, if available. The study doctor will discuss the options available to you, including their risks and benefits. You may choose not to have treatment for cancer at all. In all cases, you will receive appropriate medical care, including treatment for pain and other symptoms of cancer.

1. STUDY DETAILS

Screening Tests

Signing this consent form does not mean that you will be able to take part in this study. The following screening tests will help the doctor decide if you are eligible:

- You will have a physical exam.
- Blood (about 2 teaspoons) will be drawn for routine tests.
- You will have a mammogram, ultrasound, and/or magnetic resonance imaging (MRI) to measure the disease.
- You will have an echocardiogram (ECHO) or multi-gated acquisition (MUGA) scan to check your heart function.
- If you can become pregnant, blood (about 1-2 teaspoons) or urine will be collected for a pregnancy test. To take part in this study, you must not be pregnant or breastfeeding.

The study doctor will discuss the screening test results with you. If the screening tests show that you are not eligible to take part in the study, you will not be enrolled. Other options will be discussed with you.

Up to 47 participants will be enrolled in this study. All will take part at MD Anderson.

Study Drug Administration

About 1 week before Cycle 1, if you are found to be eligible to take part in this study, you will receive a single dose of panitumumab by vein over about 1 hour.

You will then receive the study drug combination for 4 cycles. Each cycle is 21 days.

On **Day 1 of each Cycle**, you will receive panitumumab, carboplatin, and paclitaxel by vein. Panitumumab will be given over 30-60 minutes, paclitaxel over about 2 hours, and carboplatin over about 2 hours.

On **Days 8** and **15 of each cycle**, you will receive panitumumab and paclitaxel by vein following the same timing as Day 1.

If you have side effects, the study doctor may decide to lower the study drug dose(s) or to have you stop taking the drug(s). You may be able to restart the study drug(s) later at the same or a lower dose. The study doctor will discuss this with you.

Study Visits

About 1 week before Cycle 1, the same day that you receive the single dose of Panitumumab, you will have blood drawn (about 2 teaspoons) for pharmacokinetic (PK) testing. PK testing measures the amount of study drug in the body at different time points.

About 1 week after the first panitumumab dose, you will have blood drawn (about 2 teaspoons) for PK testing.

On **Day 1 of each cycle**:

- You will have a physical exam.
- Blood (about 2 teaspoons) will be drawn for routine tests.

On **Days 8 and 15 of each cycle,** blood (about 2 teaspoons) will be drawn for routine tests.

On **Day 21 (+/- 1 day) of Cycle 2**, blood (about 2 teaspoons) will be drawn for PK testing.

Surgery

After you have received 4 cycles of chemotherapy, or at any time that the disease appears to get worse, you will have an MRI, mammogram, or ultrasound to check the status of the disease. Based on the scans, the doctor will decide the type of surgery that you will have to remove the tumors. You will be given a separate surgery consent form that describes the procedure and its risks. If you come off study, you may be offered chemotherapy, more surgery, or another option.

At the time of your surgery, blood (about 2 teaspoons) will be drawn for PK testing.

You will no longer be able to take the study drugs if the disease gets worse, if intolerable side effects occur, or if you are unable to follow study directions.

Your participation on the study will be over at least 2 years after surgery.

Follow-Up

Every 3-4 months, the study team will track your standard of care physical exam visits.

2. POSSIBLE RISKS

While on this study, you are at risk for side effects. These side effects will vary from person to person. The more commonly occurring side effects are listed in this form, as are rare but serious side effects. You should discuss these with the study doctor. You may also want to ask about uncommon side effects that have been observed in small numbers of patients but are not listed in this form. Many side effects go away shortly after treatment is stopped, but in some cases side effects may be serious, long-lasting or permanent, and may even result in hospitalization and/or death.

Tell the study staff about any side effects you may have, even if you do not think they are related to the study drug/procedures.

Carboplatin and paclitaxel may each cause low blood cell counts (red blood cells, platelets, and/or white blood cells):

- A low red blood cell count (anemia) may cause difficulty breathing and/or fatigue. You may need a blood transfusion.
- A low platelet count increases your risk of bleeding (such as nosebleeds, bruising, stroke, and/or digestive system bleeding). You may need a platelet transfusion.
- A low white blood cell count increases your risk of infection (such as pneumonia and/or severe blood infection). Infections may occur anywhere and become life-threatening. Symptoms of infection may include fever, pain, redness, and difficulty breathing.

Panitumumab Side Effects

Common (occurring in more than 20% of patients)

• fatigue • itching • acne-like rash	• skin problems (such as skin rash/dryness/ peeling/cracking/ redness)	• nausea • diarrhea

Panitumumab may commonly cause an increased risk of infection, such as pneumonia. This infection may occur anywhere. It may become life-threatening. Symptoms of infection may include fever, pain, redness, and difficulty breathing.

Occasional (occurring in 3-20% of patients)

• fever • chills • acne • nail changes • blistering skin rash • shedding and scaling of	• mouth blisters/sores (possible difficulty swallowing) • dry mouth • vomiting • dehydration	• cough • lung inflammation (possible difficulty breathing) • infusion reaction (possible chills and/or

the skin (possible fatal loss of bodily fluids) • skin sores • low blood levels of magnesium (possible weakness and/or seizure)	• painful, red, teary, itchy eyes • eyelash growth • eye inflammation (possible sore on the eye)	hives) • nosebleed • immune reaction

Rare but serious (occurring in fewer than 3% of patients)

• tissue swelling • very severe blistering skin disease (with ulcers of the skin and digestive tract) • very severe blistering skin disease (loss of large portion of skin) • death of skin	• kidney failure as a result of severe diarrhea and dehydration • blockage in the lung (possible pain, shortness of breath, and/or failure to breathe) • lung damage and/or inflammation (possible difficulty breathing)	• severe life-threatening infection (possible low blood pressure, kidney failure, and/or heart failure) • allergic reaction that may be life-threatening (such as difficulty breathing, low blood pressure, and/or organ failure)

Call your doctor right away if your skin becomes red, tender, swollen, hot to the touch, blistered, starts peeling, becomes scaly, or is discolored.

Other drugs similar to panitumumab may cause heart damage. It is unknown if panitumumab may cause heart damage. If you have any symptoms such as fatigue, shortness of breath, weight gain, leg swelling, irregular heartbeat, chest discomfort, or other symptoms that you believe are related to the heart, you should contact your local emergency number and your study doctor right away.

<u>Carboplatin Side Effects</u>

Common (occurring in more than 20% of patients)

• abnormal salts, minerals, and/or acids in the blood (possible weakness, swelling, fatigue, low blood pressure, organ failure, heart problems, changes in mental status, and/or seizure)	• vomiting • low blood counts (red/ white/platelets) • pain	• abnormal liver tests (possible liver damage) • abnormal kidney test (possible kidney damage)

Occasional (occurring in 3-20% of patients)

• nerve damage (possible	• abdominal pain	• abnormal liver tests

numbness, pain, and/or loss of motor function) • hair loss (partial or total)	• nausea • constipation • diarrhea • weakness	(possible yellowing of the skin and/or eyes) • allergic reaction • infection

Rare but serious (occurring in fewer than 3% of patients)

• high blood pressure • low blood pressure (possible dizziness/fainting) • heart failure • stroke • dehydration • blood vessel blockage	• destruction of red blood cells (possible anemia, kidney damage, and/or failure) • reduced blood supply to the arms and legs • blindness • hearing loss	• difficulty breathing due to narrowing of the airways • tissue death at the injection site caused by drug leakage • life-threatening allergic reaction (such as difficulty breathing, low blood pressure, and/or organ failure)

Carboplatin may rarely cause the cancer to spread.

It is not known how long how often the following side effects may occur:

• decreased bone marrow function

<u>Paclitaxel Side Effects</u>

Common (occurring in more than 20% of patients)

• abnormal EKG • swelling • flushing • hair loss (partial or total) • mouth blisters/sores (possible difficulty swallowing)	• nausea/vomiting • diarrhea • low blood cell counts (red/platelets/white) • abnormal liver tests (possible liver damage) • pain (muscle/joint)	• nerve damage (possible numbness, pain, and/or loss of motor function) • abnormal kidney test (possible kidney damage) • allergic reaction • infection

Occasional (occurring in 3-20% of patients)

• low blood pressure (possible dizziness/ fainting) • slow heartbeat	• skin rash • abdominal pain • abnormal liver tests (possible yellowing of the skin and/or eyes)	• weakness • injection site reaction (possible redness, swelling, skin discoloration)

Rare but serious (occurring in fewer than 3% of patients)

• fast/irregular heartbeat • blood clots in a vein (possible pain, swelling, and/or redness) • heart failure • heart attack • decreased blood supply to the heart • high blood pressure • fainting • decreased brain function (possible paralysis and/or coma) • decreased brain function due to liver damage • seizure • severe sunburn-like rash at site of previous radiation (called radiation recall) • death of skin • inflammation at the site of previous tissue death	• worsening of existing scleroderma (severe hardened skin, which can cause difficult movement) • very severe blistering skin disease (with ulcers of the skin and digestive tract) • very severe blistering skin disease (loss of large portion of skin) • inflammation of the pancreas (possible abdominal pain) • inflammation of the intestines • dehydration • paralysis of the intestines • intestinal blockage • hole in the intestines (possible leaking contents into the abdomen) • decreased blood flow to part of the bowel (possibly causing death of tissue)	• difficulty walking • liver damage and/or failure • blind spot • hearing loss • decreased kidney function • blockage in the lung (possible pain and/or shortness of breath) • lung inflammation and/or damage (possible difficulty breathing) • blood clots in the lung (possible failure to breathe) • difficulty breathing • life-threatening allergic reaction (such as difficulty breathing, low blood pressure, and/or organ failure) • tissue death at the injection site caused by drug leakage

Using the study drugs together may cause side effects that are not seen when each is given alone. The study drug combination may also increase the frequency and/or severity of the side effects listed above.

Other Risks

Blood draws may cause pain, bleeding, and/or bruising. You may faint and/or develop an infection with redness and irritation of the vein at the site where blood is drawn. Frequent blood collection may cause anemia (low red blood cell count), which may create a need for blood transfusions.

Having **biopsies** performed may cause pain, bruising, bleeding, redness, low blood pressure, swelling, and/or infection at the site of the biopsies. An allergic reaction to the anesthetic may occur. A scar may form at the biopsy site.

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 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 you if you have certain types of metal in your body (as might be found in pacemakers, neurostimulators, or certain clips). It may cause problems with devices, such as pacemakers. If you have metal in your body or devices such as a pacemaker, you should discuss this with the study doctor.

ECHOs may cause discomfort while lying on the exam table.

MUGA scans may cause allergic reactions to the radioactive tracer, injection site soreness, and/or swelling. They may cause damage to cells or tissue from being exposed to the radiation used in the scan. These side effects may occur in less than 10% of patients.

Although every effort will be made to keep study data safe, there is a chance that your personal health information could be lost or stolen, which may result in a **loss of confidentiality**. All study data will be stored in password-protected computers and/or locked file cabinets and will continue to be stored securely after the study.

This study may involve unpredictable risks to the participants.

Pregnancy Related Risks
Taking part in this study can result in risks to an unborn or breastfeeding baby, so you should not become pregnant or breastfeed a baby while on this study. You must use birth control during the study if you are sexually active.

Birth Control Specifications: If you or your partner can become pregnant, you and your partner must use an acceptable method of birth control while you are on study and for 8 weeks after the last dose of study drug.

Acceptable forms of birth control include:

- intrauterine devices (IUDs)
- barrier methods (such as condom or diaphragm with spermicide)
- surgical sterilization ("tubes tied" or vasectomy)

Hormonal methods (such as birth control pills, injections, or implants) are not approved for use on this study.

Females: If you are pregnant, you will not be enrolled on this study. If you become pregnant or suspect that you are pregnant, you must tell your doctor right away.

Getting pregnant may result in your removal from this study.

OPTIONAL PROCEDURES FOR THE STUDY

Optional Procedure #1: You may already be enrolled in another MD Anderson study, 2014-0185. If you are **NOT** enrolled in the 2014-0185 study and you agree, leftover tumor tissue taken from a recent biopsy or surgery (called archival tissue), if available, will be collected and banked (stored in a database) for future biomarker tests, including tests for genetic biomarkers. Biomarkers are found in the blood/tissue and may be related to your reaction to the study drugs.

Optional Procedure Risks:
Researchers can learn about cancer and other diseases from your banked samples. In the future, people who may do research with these samples may need to know more information about your health. This information may be collected from your medical record by researchers under the supervision of the study chair. Sometimes your samples may be used for genetic research about diseases that are passed on in families.

Genetic research may result in the development of beneficial treatments, devices, new drugs, or patentable procedures. There are no plans to provide you compensation from such developments. The results of any genetic tests will not be put in your health records. If this information were released, it could be misused. Such misuse could be distressing, and it could cause you or your family members to have difficulty obtaining insurance coverage and/or a job.

A federal law called the Genetic Information Nondiscrimination Act (GINA) makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. However, this legal protection still may not keep someone from trying to discriminate against you in this way.

CONSENT/PERMISSION/AUTHORIZATION FOR OPTIONAL PROCEDURES

Circle your choice of "yes" or "no" for each of the following optional procedures:

Optional Procedure #1: If you are not enrolled in 2014-0185 and have archival tissue available, do you agree to allow the study team to collect a sample of archival tissue for biomarker testing?

YES NO

3. COSTS AND COMPENSATION

If you suffer injury as a direct result of taking part in this study, MD Anderson health providers will provide medical care. However, this medical care will be billed to your insurance provider or you in the ordinary manner. You will not be reimbursed for expenses or compensated financially by MD Anderson or Amgen for this injury. You may also contact the Chair of MD Anderson's IRB at 713-792-6477 with questions about study-related injuries. By signing this consent form, you are not giving up any of your legal rights.

Certain tests, procedures, and/or drugs that you may receive as part of this study may be without cost to you because they are for research purposes only. However, your insurance provider and/or you may be financially responsible for the cost of care and treatment of any complications resulting from the research tests, procedures, and/or drugs. Standard medical care that you receive under this research study will be billed to your insurance provider and/or you in the ordinary manner. Before taking part in this study, you may ask about which parts of the research-related care may be provided without charge, which costs your insurance provider may pay for, and which costs may be your responsibility. You may ask that a financial counselor be made available to you to talk about the costs of this study.

Samples that are collected from you in this study may be used for the development of treatments, devices, new drugs, or patentable procedures that may result in commercial profit.

There are no plans to compensate you for any patents or discoveries that may result from your participation in this research.

You will receive no compensation for taking part in this study.

Additional Information

4. You may ask the study chair (Dr. Clinton Yam, at 713-792-2817) any questions you have about this study. You may also contact the Chair of MD Anderson's Institutional Review Board (IRB - a committee that reviews research studies) at 713-792-6477 with any questions that have to do with this study or your rights as a study participant.

5. You may choose not to take part in this study without any penalty or loss of benefits to which you are otherwise entitled. You may also withdraw from participation in this study at any time without any penalty or loss of benefits. If you decide you want to stop taking part in the study, it is recommended for your safety that you first talk to your doctor. If you withdraw from this study, you will be removed from the study drugs and the study doctor will ask you to come to the clinic for safety tests. If you withdraw from this study, you can still choose to be treated at MD Anderson.

   If you stop being in the research, already collected data may not be removed from the study database. You may be asked whether the study doctor can collect data

from your routine medical care. If you agree, this data will be handled the same as research data.

6. This study or your participation in it may be changed or stopped without your consent at any time by the study chair, Amgen, the U.S. Food and Drug Administration (FDA), the Office for Human Research Protections (OHRP), or the IRB of MD Anderson. Reasons may include non-compliance with the study procedures, notable changes in the standard of care, and/or other situations beyond the control of the study staff.

7. You will be informed of any new findings or information that might affect your willingness to continue taking part in the study, and you may be asked to sign another informed consent and authorization form stating your continued willingness to participate in this study.

8. MD Anderson may benefit from your participation and/or what is learned in this study.

9. This study is sponsored and/or supported by: Amgen.

10. In a medical emergency, you may be cared for by someone who has a financial interest with the study sponsor(s)/supporter. If you have any questions about this, you may call the IRB at 713-792-6477.

Future Research

Data

Your personal information is being collected as part of this study. These data may be used by researchers at MD Anderson and Amgen and/or shared with other researchers and/or institutions for use in future research.

Samples

Samples (such as blood and/or tissue) are being collected from you as part of this study. Researchers at MD Anderson may use any leftover samples that are stored at MD Anderson in future research.

Before being used or shared for future research, every effort will be made to remove your identifying information from any data and/or research samples. If all identifying information is removed, you will not be asked for additional permission before future research is performed.

In some cases, all of your identifying information may not be removed before your data or research samples are used for future research. If future research is performed at MD Anderson, the researchers must get approval from the Institutional Review Board (IRB) of MD Anderson before your data and/or research samples can be used. At that time, the IRB will decide whether or not further permission from you is required. The IRB is a committee of doctors, researchers, and community members

that is responsible for protecting study participants and making sure all research is safe and ethical.

If this research is not performed at MD Anderson, MD Anderson will not have oversight of any data and/or samples.

Future research with your data and samples is required for this study. You cannot take part in the main study without allowing your data and samples used for future research.

Genetic Research
Research samples collected from you as part of this study will be used for genetic research, which may include whole genome sequencing. Whole genome sequencing is a type of testing in which researchers study your entire genetic makeup (DNA). This may help researchers learn how changes in the ordering of genes may affect a disease or response to treatment. If genetic research is done with your samples, those who have access to those samples may be able to identify you. The results of this research may also be able to be linked to you.

The Genetic Information Nondiscrimination Act (GINA) prohibits health insurers or health plan administrators from requesting or requiring genetic information of you or your family members, or using such information for decisions regarding your eligibility for insurance or your premiums. However, this law does not provide the same protection for disability, life insurance, or long-term care insurance. GINA also prohibits most employers (with 15 employees or more) from using genetic information when making decisions on your employment, including decisions related to hiring, firing, promotion, pay, and job assignments. Please contact the study doctor if you would like more information about GINA and how it protects you from genetic discrimination.

Conflict of Interest

Dr. Naoto Ueno (Study Co-Chair) has received compensation from Amgen, Inc. as a Speaker. The financial interests are within the limits of the conflict of interest policy.

Authorization for Use and Disclosure of Protected Health Information (PHI):

A. During the course of this study, MD Anderson will be collecting and using your PHI, including identifying information, information from your medical record, and study results. For legal, ethical, research, and safety-related reasons, your doctor and the research team may share your PHI with:
   - Federal agencies that require reporting of clinical study data (such as the FDA, National Cancer Institute [NCI], and OHRP)
   - The IRB and officials of MD Anderson
   - Amgen, who is a sponsor or supporter of this study, and/or any future sponsors/supporters of the study
   - Amgen

- Study monitors and auditors who verify the accuracy of the information
- Individuals who put all the study information together in report form

Study sponsors and/or supporters receive limited amounts of PHI. They may also view additional PHI in study records during the monitoring process. MD Anderson's contracts require sponsors/supporters to protect this information and limit how they may use it.

If the results of this study are published, your identity will remain confidential.

B. Signing this consent and authorization form is optional but you cannot take part in this study or receive study-related treatment if you do not agree and sign.

C. MD Anderson will keep your PHI confidential when possible (according to state and federal law). However, in some situations, the FDA could be required to reveal the names of participants.

Once disclosed outside of MD Anderson, federal privacy laws may no longer protect your PHI.

D. The permission to use your PHI will continue indefinitely unless you withdraw your authorization in writing. Instructions on how to do this can be found in the MD Anderson Notice of Privacy Practices (NPP) or you may contact the Chief Privacy Officer at 713-745-6636. If you withdraw your authorization, you will be removed from the study and the data collected about you up to that point can be used and included in data analysis. However, no further information about you will be collected.

E. 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/AUTHORIZATION

I understand the information in this consent form. I have had a chance to read the consent form for this study, or have had it read to me. I have had a chance to think about it, ask questions, and talk about it with others as needed. I give the study chair permission to enroll me on this study. By signing this consent form, I am not giving up any of my legal rights. I will be given a signed copy of this consent document.

_____ _____
SIGNATURE OF PARTICIPANT DATE

_____
PRINTED NAME OF PARTICIPANT

WITNESS TO CONSENT

I was present during the explanation of the research to be performed under Protocol 2015-0294.

_____ _____
SIGNATURE OF WITNESS TO THE VERBAL CONSENT PRESENTATION (OTHER THAN PHYSICIAN OR STUDY CHAIR) DATE

A witness signature is only required for vulnerable adult participants. If witnessing the assent of a pediatric participant, leave this line blank and sign on the witness to assent page instead.

_____
PRINTED NAME OF WITNESS TO THE VERBAL CONSENT

PERSON OBTAINING CONSENT

I have discussed this research study with the participant and/or his or her authorized representative, using language that is understandable and appropriate. I believe that I have fully informed this participant of the nature of this study and its possible benefits and risks and that the participant understood this explanation.

_____ _____
PERSON OBTAINING CONSENT DATE

_____
PRINTED NAME OF PERSON OBTAINING CONSENT

TRANSLATOR

I have translated the above informed consent as written (without additions or subtractions) into_____and assisted the people
(Name of Language)
obtaining and providing consent by translating all questions and responses during the consent process for this participant.

_____ _____ _____

NAME OF TRANSLATOR SIGNATURE OF TRANSLATOR DATE

☐ Please check here if the translator was a member of the research team. (If checked, a witness, other than the translator, must sign the witness line below.)

_____ _____
SIGNATURE OF WITNESS TO THE VERBAL TRANSLATION (OTHER THAN TRANSLATOR, PARENT/GUARDIAN, OR STUDY CHAIR) DATE

_____
PRINTED NAME OF WITNESS TO THE VERBAL TRANSLATION