THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center

Informed Consent

INFORMED CONSENT/AUTHORIZATION FOR PARTICIPATION IN RESEARCH WITH OPTIONAL PROCEDURES

A Phase I Trial of Vemurafenib in Combination with Cetuximab and Irinotecan in Patients with BRAF V600 Mutant Advanced Solid Malignancies 2012-0748

Study Chair: David S. Hong

_____ _____
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.

STUDY SUMMARY

The goal of this clinical research study is to find the highest tolerable dose of vemurafenib that can be given in combination with cetuximab and irinotecan to patients with advanced cancer. The safety of this drug combination will also be studied.

Vemurafenib is designed to block BRAFV600 inside the cancer cells, which is involved in cancer cell growth.

Cetuximab is designed to block proteins inside the cancer cell, which may prevent or slow the growth of cancer cells and leads to cell death.

Irinotecan is designed to stop cancer cells from making new DNA (the genetic material of cells). If the cancer cells cannot make DNA, they cannot divide into new cells and may die.

This is an investigational study. Vemurafenib is FDA approved and commercially available for the treatment of certain types of melanoma in patients with BRAF mutation.

Cetuximab is FDA approved and commercially available for the treatment of KRAS wild type, EGFR expressing metastatic colorectal cancer and squamous cell carcinoma of the head and neck.

Irinotecan is FDA approved and commercially available for the treatment of metastatic colorectal cancer.

The use of these drugs together in advanced cancer is investigational.

Taking the study drugs may help to control the disease. 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. If you take part in this study, you may experience side effects, some of which may be severe or fatal.

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

You may continue taking the study drugs for as long as your doctor thinks it is in your best interest.

While you are on study, vemurafenib will be provided at no cost to you. You and/or your insurance provider will be responsible for the cost of cetuximab and irinotecan. You may choose not to take part in this study. Instead of taking part in this study, you may choose to receive a standard therapy, which may include chemotherapy, radiation therapy, and/or surgery. You may choose to receive other investigational therapy, if available. 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. You will have screening tests to help the doctor decide if you are eligible to take part in this study. If you have had some of these tests or procedures recently, they may not have to be repeated.

- Your medical history will be recorded.
- You will have a physical exam, including measurement of your weight and vital signs (blood pressure, heart rate, temperature, and breathing rate). Your skin will be checked. You will also have a head and neck exam.
- You will be asked about any drugs you may be taking.

- You will be asked how well you are able to perform the normal activities of daily living (performance status).
- Blood (about 2 teaspoons) and urine will be collected for routine tests.
- If you are able to become pregnant, you will have a blood (about 1 teaspoon) or urine pregnancy test. To take part in this study, you must not be pregnant.
- You will have an electrocardiogram (EKG) to check your heart function.
- You will have imaging to check the status of the disease. This imaging may include some or all of the following: a computed tomography (CT) scan, a magnetic resonance imaging (MRI) scan, a positron emission tomography (PET) scan, and/or a bone scan. You will also have a chest x-ray.
- Blood (about 2 teaspoons) will be drawn to measure biomarkers. Biomarkers are found in the blood/tissue and may be related to your reaction to the study drug.
- If you are assigned to a certain group in this study, blood (about 2 teaspoons) will be drawn for pharmacodynamic (PD) testing. PD testing measures how the level of study drug in your body may affect the disease.
- If you are enrolled in the colorectal cancer dose expansion group, you will have a biopsy for biomarker testing. The type of biopsy you have will be based on the type of disease you have. The procedure, and its risks, will be discussed with you in more detail. Biomarkers are found in the blood/tissue and may be related to your reaction to the study drug.

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.

Study Groups

If you are found to be eligible to take part in this study, your doctor will decide which dose level of vemurafenib you will receive. All participants will receive the standard dose of cetuximab and irinotecan.

Dose Escalation Group

Up to 3 dose levels of vemurafenib will be tested in combination with cetuximab and irinotecan. Up to 6 participants will be enrolled at each dose level.

The dose of any of the study drug combinations that you receive may be lowered if you have intolerable side effects.

Dose Expansion Group

After the highest tolerable dose of vemurafenib is found, additional participants will be enrolled in the expansion group and will receive the study drug combination at that dose. This group will have up to 15 participants with BRAF mutant, KRAS wild type colorectal cancer.

Up to 33 patients will be enrolled in this study. All will be enrolled at MD Anderson.

Study Drug Administration

You will take vemurafenib by mouth 2 times a day. If the doctor thinks it is needed, you may take it less often. Vemurafenib can be taken with or without food. Always take it with food or always take on an empty stomach. Take with full glass of water.

You will receive cetuximab and irinotecan by vein over 90 minutes on Day 1 of each cycle. You will be monitored for at least 1 hour after the end of drug infusion.

Study Visits

During **Week 1 of Cycles 2 and beyond**:

- You will have a physical exam and your skin will be checked.
- Your medical history will be recorded.
- Blood (about 4 teaspoons) will be collected for routine tests.
- You will be asked about any drugs you may be taking and side effects you may be having.

At Week 1 of Cycles 1-2, if you are in a certain group on study, blood (about 2 teaspoons each time) will be drawn before your dose of irinotecan and 8 more times over the next 24 hours for pharmacokinetic (PK) testing. PK testing measures the amount of study drug in the body at different time points.

If you are enrolled in the colorectal cancer dose expansion group, you will have a biopsy for biomarker testing on Day 14 of Cycle 2.

Beginning at Week 1 of Cycle 3, you will have EKG every other cycle (once monthly) for 3 months, and then once every 3 months until the end of the study.

Beginning at Week 1 of Cycle 3, blood (about 2 teaspoons) will be drawn for biomarker testing every other cycle (once monthly).

Beginning at Week 1 of Cycle 3, women who are able to become pregnant will have a blood (about 2 teaspoons) or urine pregnancy test every other cycle.

At Week 1 of Cycle 3 and Cycle 5, urine will be collected for routine tests.

At Week 1 of Cycle 3, if you are in a certain group on study, blood (about 2 teaspoons) will be drawn for PD testing.

Every 3 Cycles, you will have imaging to check the status of the disease. These tests can include some or all of the following: a CT scan, MRI scan, PET scan, and/or bone scan. You will also have a chest x-ray.

You will have an additional head and neck exam every 12 weeks while on study.

All patients will have a chest CT 6 months after their last dose of vemurafenib. SCC patients will have additional chest CTs at screening and every 6 months while on study.

You will be taken off study early if the disease gets worse, if you continue to have intolerable side effects, or if you are unable to follow study directions.

Your participation on the study will be over once you have completed the end-of-study visit.

End-of-Study Visit

Within 30 days after your last dose of study drugs, you will have an end-of-study visit. At this visit, the following tests and procedures will be performed:

- Your medical history will be recorded.
- You will have a physical exam, including measurement of your vital signs and weight. Your skin will be checked. You will also have a head and neck exam.
- You will be asked about any drugs you may be taking and side effects you may be having.
- Your performance status will be recorded.
- Blood (about 4 teaspoons) will be collected for routine tests.
- If the doctor thinks it is needed, blood (about 2 teaspoons) will be drawn to measure tumor markers.
- If you are in a certain group on study, blood (about 2 teaspoons) will be drawn for PK testing.
- You will have imaging to check the status of the disease. These tests can include some or all of the following: a chest x-ray, CT scan, MRI scan, PET scan, and/or bone scan.
- If you are in the Dose Expansion group and the disease got worse while you were on study, blood (about 2 teaspoons) will be drawn for biomarker testing.

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 drugs.

Cetuximab, irinotecan, and vemurafenib 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.

Cetuximab Side Effects

Common (occurring in more than 20% of patients)

• heart attack • fatigue/lack of energy • headache • difficulty sleeping • fever • skin rash (possibly acne-like), peeling, and/or itching • dry skin • nail changes • low blood levels of magnesium (possible weakness and/or seizures)	• weight loss • dehydration • abdominal pain • constipation • diarrhea • mouth blisters/sores (possible difficulty swallowing) • vomiting • nausea • loss of appetite • low white blood cell count	• abnormal liver tests (possible liver damage) • weakness • pain • nerve damage (loss of sensory function) • difficulty breathing • cough • sore throat • infection • severe rash at the site of previous radiation • life-threatening allergic reaction (such as difficulty breathing, low blood pressure, and/or organ failure)

Occasional (occurring in 3-20% of patients)

• confusion • depression • anxiety • chills/shivering • skin sores • hair loss (partial or total)	• low blood levels of calcium and/or potassium (possible weakness and/or cramping) • dry mouth • abnormal taste	• painful red eyes • immune reaction • infusion reaction (possible chills and/or hives) • severe life-threatening infection (possible low

• hand-foot syndrome (palms of hands/soles of feet having pain, swelling, and blistering)	• upset stomach	blood pressure, kidney failure, and/or heart failure)

Frequency unknown but occurring in 1-10% of patients

• hair growth

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

• heart attack • stoppage of heart and lung function • decreased blood supply to the heart • low blood pressure (possible dizziness/fainting) • irregular heartbeat • inflammation of the membranes around the spinal cord and brain (possible headache and/or coma)	• shock • loss of consciousness • large skin blisters • very severe blistering skin disease (with ulcers of the skin and digestive tract) • very severe blistering skin disease (loss of large portion of skin) • changes in body salts such as sodium and/or potassium (possible fatigue and/or weakness)	• eye ulcer • kidney failure • lung inflammation (possible difficulty breathing) • difficulty breathing due to narrowing of the airways • blockage in the lung (possible pain, shortness of breath, and/or failure to breathe)

<u>Irinotecan Side Effects</u>

Common (occurring in more than 20% of patients)

• flushing • dizziness • fever • sweating • hair loss (partial or total) • increased saliva • mouth blisters/sores (possible difficulty swallowing) • loss of appetite • weight loss	• nausea • food moving quickly through the digestive tract • vomiting • constipation • cramps • diarrhea • abdominal pain • low blood cell counts (red, white, platelets)	• abnormal liver tests (possible yellowing of the skin and/or eyes) • weakness • pain • eye pupils getting smaller • teary eyes • difficulty breathing • runny nose

Occasional (occurring in 3-20% of patients)

• low blood pressure (possible dizziness/fainting) • swelling • difficulty sleeping • sleepiness • headache	• confusion • chills • skin rash • dehydration • gas • feeling of fullness • fluid in the abdomen	• upset stomach • abnormal liver test (possible liver damage) • jaundice (yellowing of skin and/or eyes) • cough

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

• chest pain due to heart trouble • changes in heart rhythm (such as slow heartbeat) • heart failure • decreased blood circulation • decreased blood supply to the heart • sudden stopping of the heart • heart attack • blood clots in an artery (possible organ damage such as stroke and/or heart attack) • blood clots in a vein (possible pain, swelling, and/or redness) • blood vessel blockage in the arms, legs, and/or lungs • fainting • stroke • difficulty forming or speaking words	• sores • high blood sugar (possible diabetes) • low blood levels of sodium (possible headache, confusion, seizures, and/or coma) • paralysis of the intestines • hole in the intestines (possibly leaking contents into the abdomen) • digestive system bleeding • intestinal blockage • decreased blood flow to part of the bowel (possibly causing death of tissue) • enlarged bowel (possible abdominal pain) • inflammation of the colon (possible abdominal pain and/or diarrhea)	• inflammation of the pancreas (possible abdominal pain) • enlarged liver • abnormal sensation (such as pins and needles) • decreased kidney function • kidney failure • lung inflammation (possible difficulty breathing) • blood clots in the lung (possible failure to breathe) • abnormal chest x-ray (possible cough and/or shortness of breath) • allergic reaction, possibly life threatening (such as difficulty breathing, low blood pressure, and/or organ failure)

Vemurafenib Side Effects

Common (occurring in more than 20% of patients)

• swelling (arm/leg) • fatigue • headache • skin rash • skin sensitivity to sunlight or lamps	• hair loss (partial or total) • skin thickening • itching • non-cancerous or pre-cancerous skin lesions	• nausea • diarrhea • vomiting • loss of appetite • pain (joint and/or muscle)

Vemurafenib may commonly cause you to develop another type of cancer (such as skin cancer).

Occasional (occurring in 3-20% of patients)

• fever • dry skin • skin redness • constipation • abnormal taste • low white blood cell count	• spots on the skin (caused by low platelet count) • abnormal liver test (possible yellowing of the skin and/or eyes and/or liver damage)	• pain (arm/leg/back/bone) • weakness • cough • difficulty breathing

Exact frequency unknown but occurring in fewer than 10% of patients:

• irregular heartbeat • low blood pressure (possible dizziness/fainting) • abnormal EKG • blood vessel inflammation (possible bleeding and/or bruising) • dizziness • light-headedness • paralysis of nerves controlling the head • infection of hair follicles • hand-foot syndrome (palms of hands/soles of feet having pain, swelling, and blistering)	• very severe blistering skin disease (with ulcers of the mouth, skin and digestive tract) • painful skin bumps • inflammation of the pancreas (possible abdominal pain) • liver damage due to inflammation • weight loss • abnormal growth in the intestines • nerve damage (possible numbness,	• joint inflammation and swelling • abnormal kidney blood test results • blurry vision • eye sensitivity to light • blocked blood vessel in the retina of the eye (possible blindness) • inflammation of the eye and/or inside the eye • inflammation or damage to the kidney (swelling, difficulty urinating and fatigue)

• very severe blistering skin disease (loss of large portion of skin)	pain, and/or loss of motor function) • inflammation of nerves (possible pain and/or loss of motor or sensory function)	• life-threatening allergic reaction (such as difficulty breathing, low blood pressure, and/or organ failure)

You should avoid spending time in the sun while taking vemurafenib and for at least 5 days after your last dose of study drug. You should also use a broad-spectrum sunscreen and lip balm of at least SPF 30 to help prevent sunburn or sun damage.

Vemurafenib may rarely cause new tissue to form inside your hands and feet. This new tissue may cause the tissues in your palm to tighten so that your smaller fingers cannot extend fully. It may also cause a lump to form in the sole of your foot, at the top of the arch, which may be painful to walk on.

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.

The type of **genetic testing** being performed in this study will not provide you or your doctor information about diseases that are passed down in families. It will not tell the study researchers anything that will prevent you from getting health insurance, and it will not tell the study researchers anything about any diseases or conditions you may get in the future.

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, breastfeed a baby, or father a child while on this study. You must use birth control during the study if you are sexually active.

Birth Control Specifications: Acceptable forms of birth control include:

- Birth control pills plus a barrier method (such as a condom)

- Intrauterine devices (IUD) plus a barrier method (such as a condom)
- Implantable or injectable birth control (Norplant^{R} or Depo-Provera^{R} started at least 3 months before joining the study) plus a barrier method (such as a condom)
- Double-barrier methods (such as a condom and diaphragm)
- Surgical sterilization

Males: Tell the doctor right away if your partner becomes pregnant or suspects pregnancy.

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 will result in your removal from this study.

OPTIONAL PROCEDURES FOR THE STUDY

If you agree and you are in the dose expansion group, tumor tissue that is left over from an earlier biopsy will be used for PD testing.

If you are asked and agree, you will have a biopsy at screening and on Day 14 of Cycle 2 for PD testing. The type of biopsy you have will be based on the type of disease you have. The procedure, and its risks, will be discussed with you in more detail.

There will be no cost to you for taking part in the optional procedures.

There are no benefits to taking part in the optional procedures. You may stop taking part at any time.

Optional Procedure Risks:
Sending the **tissue for testing** will mean that the tissue may no longer be available to you for additional testing and you will not be able to get the tissue back.

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.

CONSENT/PERMISSION/AUTHORIZATION FOR OPTIONAL PROCEDURES

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

Do you agree to allow leftover tumor tissue to be used for PD testing?

YES NO

Do you agree to have a tumor biopsy performed for PD 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 Genentech 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. David S. Hong, at 713-593-1930) 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 can still choose to be treated at MD Anderson.

6. This study or your participation in it may be changed or stopped without your consent at any time by the study chair, Genentech, the U.S. Food and Drug Administration (FDA), the Office for Human Research Protections (OHRP), or the IRB of MD Anderson.

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: Genentech.

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

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

Before being shared for future research, every effort will be made to remove your identifying information from any data and/or 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 samples are used for future research. If this 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 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.

Genetic Research

Samples collected from you as part of this study may 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.

Conflict of Interest

Dr. Sarina Piha-Paul (Study Co-Chair) has received compensation from Genentech, Inc. as a Consultant. The financial interests are within the limits of the conflict of interest policy.

Outside Care

Part of your care may be provided outside of MD Anderson by your home doctor(s).

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
   - Genentech, who is a sponsor or supporter of this study, and/or any future sponsors/supporters of the study
   - Covance
   - 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.

   Genentech is supplying study drug. Both Genentech and Covance will receive blood samples and data for review.

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

LEGALLY AUTHORIZED REPRESENTATIVE (LAR)

The following signature line should only be filled out when the participant does not have the capacity to legally consent to take part in the study and/or sign this document on his or her own behalf.

SIGNATURE OF LAR DATE

RELATIONSHIP TO PARTICIPANT

WITNESS TO CONSENT

I was present during the explanation of the research to be performed under Protocol **2012-0748**.

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.

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

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