Approved
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Ochsner IRB

OCHSNER CLINIC FOUNDATION
RESEARCH INFORMED CONSENT

A pilot phase 2 study of albumin-bound sirolimus nanoparticles, ABI-009, in patients with metastatic, unresectable, low or intermediate grade neuroendocrine tumors of the lung or gastroenteropancreatic system

Principal Investigator: Robert Ramirez, DO
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504-842-3910

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504-842-3910 or 1-800-956-6247

Sponsor's Protocol # NET-001
Sponsor name: Robert Ramirez, DO funded by Aadi Bioscience, Inc.

You have been invited to participate in a research study. The doctors and staff at Ochsner study the nature of disease and attempt to improve methods of diagnosis and treatment. This is called clinical research. Understanding this study's risks and benefits will allow you to make an informed judgment about whether to be part of it. This process is called informed consent.

This consent form may contain words that you do not understand. Please ask the study doctor or the study staff to explain any words or information that you do not clearly understand. You may take home an unsigned copy of this consent form to think about or discuss with family or friends before making your decision.

Participating in a research study is not the same as getting regular medical care. The purpose of regular medical care is to improve your health. The purpose of a research study is to gather information. Being in this study does not replace your regular medical care.

PURPOSE

You are being asked to take part in this study because you have been diagnosed with an advanced, malignant neuroendocrine tumor of the lung, gastrointestinal tract and/or pancreas that cannot be removed by surgery.

The purpose of this study is to determine whether ABI-009 (study drug) will make your cancer smaller and slow the spread of your cancer.

ABI-009, human albumin-bound sirolimus, is an experimental drug. "Experimental" means that the drug has not been approved by the Food and Drug Administration (FDA).

Sirolimus, the active part of the drug, prevents a biological pathway that is out of control in neuroendocrine cancer cells. Sirolimus and similar types of drugs have been used in many other tumors, including advanced renal cell carcinoma. The human albumin component of ABI-009 may allow sirolimus to reach cancer cells more effectively.

ABI-009 has not been approved for the treatment of advanced, malignant neuroendocrine tumors of the lung, gastrointestinal tract and/or pancreas. There are no drugs currently approved for this. The information from this study might help us identify if ABI-009 is safe and effective in this disease.

LENGTH OF STUDY AND NUMBER OF PARTICIPANTS

You will remain on study drug until your disease gets worse or you or your doctor decide that the treatment is not right for you. After your last dose of study drug, you will be followed by phone every 3 months until you start a new treatment, withdraw consent, or the study closes. This study will only take place at Ochsner and will enroll 10 subjects.

PROCEDURE

Before you can receive study drug, the doctor will perform tests to find out whether you can participate in the study.

In this study, you will receive ABI-009 given through a vein (intravenous) once weekly for 2 weeks (on days 1 and 8) followed by a week of rest in a 21-day cycle.

If you are found to be eligible by your study doctor, you will receive therapy within 28 days. You will be given this study drug until your disease progresses or depending on how well you tolerate the therapy. After you are finished receiving the study drug, you will be followed by phone calls every 3 months, or more frequently if needed, to see how you are doing, and to collect information on any new anti-cancer treatment you may be taking. Your study doctor or staff will tell you when and where you will go for treatment, tests, exams, and procedures.

The study doctor or his/her staff will perform the following procedures during the study:

Screening (≤ 28 days prior to the first dose of study drug)

- Demographics (date of birth, sex, race, and ethnicity)
- Medical/cancer history, record medications you are taking, and record procedures you have had
- Physical examination, performance status assessment
- Vital signs (e.g., blood pressure, pulse, respiration rate, temperature, height, weight)
- Blood Tests: chemistry, complete blood count (CBC), differential, platelet count, pregnancy test for women of childbearing potential, fasting lipids and cholesterol
- CT scans (or MRI, if CT is not possible)
- Adverse events

Day 1 of every cycle (unless otherwise stated)

- Physical examination
- Vital signs (e.g., blood pressure, pulse, respiration rate, temperature, weight)
- Record medications you are taking and procedures you have had
- Blood samples including complete blood count (CBC), differential, and clinical chemistry panel
- Blood sample for fasting lipids and cholesterol *(every even cycle)*
- Blood sample for sirolimus levels which show the amount of study drug in your body *(cycle 2 only)*
- ECOG performance status – an assessment your doctor makes about your disease to help them treat your cancer
- Adverse events assessment

Day 8 of every cycle (unless otherwise stated)

- Physical evaluation
- Vital signs (e.g., blood pressure, pulse, respiration rate, temperature, weight)
- Record medications you are taking and procedures you have had
- Blood samples including complete blood count (CBC), differential, and clinical chemistry panel
- Blood sample for sirolimus levels which show the amount of study drug in your body *(cycle 1 and cycle 2 only)*
- Adverse event assessment

Day 15 of cycle 1 and cycle 2 (these may be performed as needed on Day 15 of other cycles after cycle 1 and cycle 2)

- Physical evaluation
- Vital signs (e.g., blood pressure, pulse, respiration rate, temperature, weight)
- Record medications you are taking and procedures you have had
- Blood samples including complete blood count (CBC), differential, and clinical chemistry panel
- Blood sample for sirolimus levels which show the amount of study drug in your body *(cycle 1 and cycle 2 only)*
- Adverse event assessment

End of Treatment Visit

The EOT Visit is a safety follow-up visit that is to be performed within 1 month after the last dose of ABI-009.

- Physical evaluation including performance status assessment
- Vital signs (e.g., blood pressure, pulse, respiration rate, temperature, weight)

- Record medications you are taking and procedures you have had
- Urine pregnancy test for women of childbearing potential
- Blood samples including complete blood count (CBC), differential, and clinical chemistry panel

Response Assessment

Tumor response will be assessed by CT (or MRI, if CT is not possible) scan of the chest, abdomen, and pelvis.

CT or MRI scans to be performed at the following frequency:

- screening
- followed by every 9 weeks after the first dose of study drug for the first year; then every 12 weeks until disease progression or unacceptable toxicity. End of Treatment Visit CT (or MRI) should be performed only for those subjects that discontinue treatment for a reason other than disease progression.

An unscheduled scan for suspected disease progression may be performed at any time.

Follow-up Period

Post-treatment survival time will be recorded about every 12 weeks (±3 weeks) from the end of treatment visit or more frequently as needed. This information will be recorded until death, withdrawal of consent, new anticancer therapy, or when the study closes, whichever is earliest. This evaluation may be by medical record review and/or telephone contact.

RISKS

Risks from ABI-009, 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.

The following is a list of the most medically significant or most common side effects reported in previous or ongoing studies and considered to be related to ABI-009. In some cases, side effects can be serious or long-lasting. Some side effects go away soon after you stop the study drug/therapy, and some may take time to resolve. The study doctor may alter the dosage regimen of ABI-009 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.

Based on ABI-009 Investigator Brochure v7.0, the most common to uncommon side effects as follows:

Very common (>10% or more chance that this will happen, based on a previous study with ABI-009):

- low blood platelets (thrombocytopenia)
- low blood hemoglobin (anemia)
- low white blood cell count (neutropenia)
- low potassium levels (hypokalemia)
- elevated lipid levels (hypertriglyceridemia)
- elevated cholesterol (hypercholesterolemia)
- elevated blood glucose (hyperglycemia)
- diarrhea
- nausea
- vomiting
- constipation
- inflammation of the mucus membrane (mucosal inflammation)
- fatigue
- decreased liver function (elevated AST)
- weight decrease
- rash
- dermatitis
- headache
- infection (including candidiasis, cellulitis, folliculitis, urinary tract)
- decreased appetite (anorexia)
- altered sense of taste (dysgeusia)
- edema

Common (between a 1% to less than 10% chance that this will happen):

- low blood phosphate levels (hypophosphatemia)
- increased amylase
- increased lipase
- low magnesium levels (hypomagnesemia)
- decreased liver function (elevated ALT)
- elevated creatinine levels
- low lymphocyte count
- cough
- labored breathing (dyspnea)
- pneumonitis
- insomnia
- epistaxis
- dry mouth
- hair loss (alopecia)
- nail disorder
- muscle pain (myalgia)

- hypertension
- fever
- acute kidney injury
- failure to thrive
- enteritis (including ileitis, colitis)
- weakness, numbness, or tingling in hand and feet (neuropathy)
- vertigo (dizziness)

Uncommon (between a 0.1 to less than 1% chance that this will happen):

- elevated potassium levels (hyperkalemia)
- low sodium levels (hyponatremia)
- low blood albumin levels
- pancytopenia
- alkalosis
- hypothyroidism
- dehydration
- odynophagia
- lip blister
- infusion site pain
- thirst
- suicidal ideas
- disorientations
- fast heart rate (tachycardia)
- transient chest pain (acute coronary syndrome)

ABI-009 contains human serum albumin. Human serum albumin presents a small risk of allergic or anaphylactic type reactions. Tell your doctor if you have ever had a reaction to human serum albumin.

Human serum albumin is a derivative of human blood. Based on effective donor screening and product manufacturing processes, it carries an extremely remote risk for transmission of viral diseases and variant Creutzfeldt-Jakob disease (vCJD). There is a theoretical risk for transmission of Creutzfeldt-Jakob disease (CJD), but if that risk actually exists, the risk of transmission would also be considered extremely remote. No cases of transmission of viral diseases, CJD, or vCJD have ever been identified for licensed albumin.

Sirolimus, also known as rapamycin, is known to be associated with the following potential risks after long term use:

- testicular toxicities
- pulmonary toxicities (pneumonitis)
- increased risk for cancer

Risks from the Study Procedures

Risk with Intravenous (IV) Drug Administration: 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 draws: Needle sticks carry some risks such as fainting, bleeding, bruising, discomfort, dizziness, infection and/or pain at the puncture site.

CT and MRI Scans: As part of this study, you will have CT and MRI scans. CT scans involve exposure to radiation. Some people may be worried about the amount of radiation they receive during a CT scan. The amount of radiation from this entire study is well below the levels that are thought to result in a significant risk of harmful effects. Radiation exposure from a CT scan can be higher than from a regular x-ray.

Some people experience mild itching or hives. Signs of a more serious allergic reaction include shortness of breath and swelling of the throat or other parts of the body, abdominal pain, or vomiting. You should tell the technologist immediately if you experience any of these symptoms, so you can be treated immediately. You may experience discomfort related to lying still in an enclosed space for a prolonged period of time while the CT scan or MRI is being taken.

General / Unforeseeable

There may be side effects and discomforts that are not yet known. You should tell your study doctor about any side effects you experience even if you think they are not related.

Louisiana law requires us to set forth the known risks of a medical treatment, including the risks, if any, of death, brain damage, quadriplegia (paralysis in all arms and legs), paraplegia (paralysis of both legs), the loss or loss of function of any organ or limb, and disfiguring scars, which might be associated with a necessary procedure. Any clinical study carries with it risks of which we may be unaware at this time, including those listed in this paragraph.

Reproductive Risks

No studies of ABI-009 have been conducted in pregnancy. It is not known if ABI-009 passes into milk during breast feeding

Females: If you decide to take part in this study, and are able to have children, you must agree to use medical doctor-approved contraception plus a barrier contraceptive throughout the study, and for 3 months after your last dose of study treatment. In addition, if you have had your tubes tied (tubal ligation) you must also agree to use a second form of birth control. If you become pregnant while receiving study treatment you must tell the study doctor right away. If this happens, your participation in this study treatment will be discontinued. If you become pregnant within 3 months after taking your last dose of study drug you must tell the study doctor right away. The study doctor will follow you and your pregnancy to birth.

Males: If you are a man, you will not be able to donate sperm for the length of the trial

and for 3 months following treatment. If you have a partner able to have children, you must agree to use a medical doctor-approved form of contraception plus a barrier contraceptive throughout the study and should avoid fathering a child for 3 months after your last dose of study treatment. In addition, if you have had a vasectomy you must also agree to use a second form of birth control. If your partner becomes pregnant during the study or within 3 months after you took your last dose of study treatment, you must tell the study doctor right away. Your study doctor and the sponsor will ask your partner to allow them to collect information about her pregnancy and the health of the baby in a separate consent form.

If you or your partner becomes pregnant while participating in this study, you MUST contact your study doctor immediately.

Radiation Risks

Although you will undergo some tests involving ionizing radiation in this protocol, they are the same you would undergo if you were not in this study, and at the same frequency. Therefore, this study does not involve any additional radiation risk for you.

POTENTIAL BENEFITS

You may not receive direct personal or health benefit from taking part in this study. However, the information gained from your participation in this study may be used to help others in the future.

COSTS

Although the Sponsor may pay for certain study-related items and services, any other tests, procedures, or medications that may be necessary for the treatment of your medical condition will be billed to your insurance in the normal way. You may be responsible for co-payments or deductibles. These costs are not covered by this research study. If you have any questions about treatment for which you may be responsible for paying, please discuss this with your physician or study staff.

PAYMENT FOR PARTICIPATION AND/OR REIMBURSEMENT OF EXPENSES

You will not be paid or offered any other compensation for participating in this study.

Ochsner Clinic Foundation is being funded by Aadi Bioscience, Inc. to conduct this research.

ALTERNATIVE METHODS/TREATMENTS

You do not have to join this study. If you do not join, your care at Ochsner will not be affected.

STUDY RELATED QUESTIONS AND COMPENSATION FOR INJURY

If you have any questions concerning your participation in this study or if at any time you feel you have experienced a research-related injury, contact the study doctor or their alternate contact listed on the front page of this consent form.

If you believe you are injured as a direct result of your participation in this study, you should seek appropriate medical attention and immediately contact your study doctor at the number provided above. Medical treatment and/or hospitalization, if necessary for such injuries, is available. This medical treatment and/or hospitalization is not free of charge. You, your insurance company or the Sponsor may be billed for the care you receive for the injury. We will try to get these costs paid for you, but you may be responsible for some or all of them. You may be responsible for all co-payments and deductibles required under your insurance. If injuries occur that are the result of a medication, device, procedure or test required for this study that is not part of your usual medical care, the Sponsor will reimburse the standard charges for the treatment of these injuries.

By signing this consent form you have not given up any legal rights.

QUESTIONS ABOUT YOUR RIGHTS

If you have questions about your rights as a research subject, you may contact:

Ochsner Clinic Foundation Institutional Review Board
1514 Jefferson Highway
New Orleans, LA 70121
Telephone: 1-504-842-3535
Email: IRB@ochsner.org

The Institutional Review Board (IRB) is a group of people who perform independent review of research for human subject protection. You may contact the IRB to discuss any problems, concerns or questions you have about research. The IRB can assist you in obtaining information about research and encourages input from research subjects.

VOLUNTARY PARTICIPATION

Participation in this study is voluntary. You may decide not to participate in this study or you may withdraw from this study at any time without penalty or loss of benefits to which you are otherwise entitled at this site. If you leave the study before the final regularly scheduled visit, you may be asked by the study doctor to make a final visit for some end of study procedures.

Your participation in this study will be entered in your electronic medical record here at Ochsner. You should tell your study doctor about all of your past and present health conditions and allergies of which you are aware, and all drugs and medications which you are presently using.

EMPLOYEES IN RESEARCH

If you are an employee of Ochsner Clinic Foundation (OCF), you are not required to participate in this research study to maintain employment nor will your employment status or performance evaluations be negatively affected in any way if you decide not to be a research subject. Should you decide to enroll yourself or your child in this study, you may withdraw your (or your child's) participation at any time, and this decision will not affect your employment or performance evaluations.

NEW FINDINGS

During the study you will be told about any important new information that may change your mind about staying in the study.

STUDY WITHDRAWAL

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

- You do not meet study criteria
- the study doctor thinks it necessary for your health or safety;
- you have not followed study instructions;
- the sponsor has stopped the study; or
- administrative reasons require your withdrawal.

UNEXPECTED FINDINGS

When your data/images are collected and studied, there is the chance of finding something unexpected. There may be benefits to learning such results (such as early detection and treatment of a medical condition), but there are risks as well (such as feeling worried about a finding for which no treatment is available or appropriate).

In this study, you will be told of any unexpected findings that may be discovered. The results from the data/images we collect in this research study are the same quality as what you would receive as part of your health care. The data/images will be reviewed by a physician who normally reads such results. You will be given this information so that you may discuss it with your primary care physician. However, if you believe you are having symptoms that may require care prior to receiving any information from this study, you should contact your primary care physician.

CONFIDENTIALITY

Your identity and your personal records will be kept confidential and, to the extent permitted by the applicable laws and/or regulations, will not be made publicly available.

Confidentiality will be maintained during and after your participation in this study.

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.

The results of this research may also be published in scientific journals or presented at medical meetings, but your identity will not be disclosed.

HIPAA AUTHORIZATION TO RELEASE INFORMATION FOR RESEARCH

Under federal law (the "Privacy Rule"), your Protected Health Information (PHI) that is created or obtained during this clinical research study cannot be "used" to conduct the research or "disclosed" (given to anyone) for research purposes without your permission. This permission is called an "Authorization". **Therefore, you may not take part in this study unless you agree to this authorization.**

Before you agree to take part in the study, we want to tell you:

- How study information may identify you
- Who may use or share your protected health information
- Why your protected health information will be used or shared
- Your rights concerning use and/or sharing of your protected health information

How may study information identify me?

Study information may identify you in the following ways:

- Name, address, telephone number
- Other details about you including your past medical records

Medical information that identifies you and relates to your participation will be created, and may be used and/or shared, including information obtained from:

- Study visits and phone calls
- Physical examinations, blood and urine tests, x-rays, and other procedures or tests
- Your response to any study treatments you receive
- Any other information that you may release to us, including information about your health history.

Who may use or share my protected health information?

The Investigator (study doctor) and research staff may give protected health information to others during and after the study, including:

- The study sponsor, including any people or companies working for or with the sponsor or owned by the sponsor.
- Doctors and healthcare professionals taking part in the study
- Government agencies in the United States and in other countries
- Ochsner Clinic Foundation

- Third party vendors as authorized by Ochsner Clinic Foundation

Why will this study information be used and/or shared?

- To carry out the research study
- To analyze and evaluate the results of the study
- To conduct internal research compliance reviews
- To comply with governmental reporting requirements
- To obtain marketing approval for new products

What are my rights regarding my health information?

- You have the right to review and copy your health information. However, as a participant in this research study, you would not be allowed to look at or copy your information until after the research is completed.
- You may withdraw or revoke (cancel) your permission to use and disclose your health information at any time. However, unless you revoke your permission by sending written notice to the study doctor, this authorization (permission) will not expire (end) until it is no longer required by the Sponsor.

When you withdraw your permission, no new health information that might identify you will be gathered after that date. Information that has already been gathered may still be used and given to others. This would be done if it were necessary for the research to be reliable. **If you withdraw your permission, you will not be able to continue being in this study.**

Are there possible limitations on the protection of my health information?

- If your health information is given to the parties listed above and/or to others who are not required to comply with federal privacy laws, your information may no longer be protected, and there is a risk that your information will be released to others without your permission.
- Your personal information may be disclosed if required by law.
- Your records for this study may be sent by facsimile transmission (FAX) or over the Internet. It is possible that your records could be sent to the wrong person.

How long is my information kept?

Ochsner Clinic Foundation policy requires that all files related to a research study are stored for ten (10) years after the research study has been closed at the Ochsner site.

Do not sign this consent form unless you have had a chance to ask questions and have received satisfactory answers to all of your questions.

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

CONSENT

I have been informed about this study's purpose, procedures, possible benefits and risks, and the use and disclosure of my health care information from this research. All my questions about the study and my participation in it have been answered. I freely consent to participate 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 waived any of the legal rights that I otherwise would have as a subject in a research study.

CONSENT SIGNATURE

Subject Signature	Printed Name	Date
Person Obtaining Consent - Signature	Printed Name	Date

---------- Use the following only if applicable ----------

IMPARTIAL WITNESS STATEMENT (IF APPLICABLE)

If this consent and authorization document is read to the subject because the subject is unable to read the document, an impartial witness (a person, who is independent of the trial, who cannot be unfairly influenced by people involved with the trial, who attends the informed consent process if the subject cannot read, and who reads the informed consent and any other written information supplied to the subject) must be present for the consent and sign the following statement:

I attest that the information in this consent and authorization was explained to and understood by the subject. I also attest that the subject agreed to participate in this research study.

_____
Printed Name of Impartial Witness

_____ _____
Signature of Impartial Witness Date

Note: This signature block cannot be used for translations into another language. A translated consent form, with the translation approved by the IRB, is necessary for enrolling subjects who do not speak English.

Ochsner Health System complies with applicable Federal civil rights laws and does not discriminate on the basis of race, color, national origin, age, disability, or sex.

ATENCIÓN: si habla español, tiene a su disposición servicios gratuitos de asistencia lingüística. Llame al 1-800-928-6247.

CHÚ Ý: Nếu bạn nói Tiếng Việt, có các dịch vụ hỗ trợ ngôn ngữ miễn phí dành cho bạn. Gọi số 1-800-928-6247.