The University of New Mexico

Consent to Participate in Research

A Dose-escalation Study to Detect Urease-producing Bacteria in Lungs of Healthy Volunteers and Subjects with Cystic Fibrosis Using Aerosolized ^{13}C-urea

11/29/2012

(H. Pylori patients)

Introduction

You are being asked to participate in a research study that is being done by Dr. Hengameh Raissy, PharmD, who is the Principal Investigator, Dr. Lea Davies, MD, from the Department of Department of Pediatrics and Dr. Michelle Harkins, MD, from the Department of Internal Medicine. This research is to investigate the use of the Urea Breath Test Kit to rapidly detect an infection in the lungs with a group of bacteria including Pseudomonas aeruginosa (P. aeruginosa). P. aeruginosa is one of the most prominent types of bacteria found in lungs of patients with Cystic Fibrosis (CF).

The Urea Breath Test Kit is very similar to a collection kit called BreathTek® which is used to detect Helicobacter pylori (H. pylori) bacteria. H. pylori can cause ulcer and the Unites States Food and Drug Administration (FDA) has approved use of BreathTek® in patients as young as three years. BreathTek® works with patients drinking the urea solution and then a breath sample is collected by blowing into a bag. If a patient has H. pylori bacteria in their stomach, the bacteria turns urea to CO2 gas which can be measured from the exhaled breath in the bag by connecting the bag to an analyzer. In this study, we will have urea inhaled, instead of swallowed, to detect P. aeruginosa in the lungs of CF patients. We will use a nebulizer which transforms the liquid form of urea to a mist that can be inhaled. The use of inhaled urea via a nebulizer in this study is investigational, meaning that nebulizing urea solution is not approved by the FDA and this is the first study in human using nebulized urea to detect P. aeruginosa in CF patients. However, nebulized urea has been studied before as an agent for “airway clearance” (just like hypersaline solution) in CF and patients with Chronic Obstructive Pulmonary Disease (COPD) but it was not effective. Urea has also been used intravenously (given through a vein) for patients with brain injury.

Patients with CF have a high rate of long term infection in the lungs predominately due to P. aeruginosa. In order to find out if someone has P. aeruginosa, a culture of the mucus that the patient spits out needs to be done. Mucus that has been spit out is also called sputum. Spitting out mucus, or sputum, is not easy for all the patients especially

for children. In this research study, we are using a "noninvasive" and "easy" method to find out if a CF patient has P. aeruginosa in their lungs. It is important to detect P. aeruginosa in the lungs of patients with CF so treatment can be started as needed.

There are three phases to this study. Phase I: we will look at safety of using the Urea Breath Test Kit in approximately 6 healthy volunteers. Phase II: we will look at how approximately 3 patients with ulcer cause by H. Pylori respond to the nebulized urea. Phase III: we will look at the use of nebulized urea to detect P. aeruginosa in approximately 6 patients with CF.

Food and Drug Administration may inspect the records.

You are being asked to participate in this study because you have recently been diagnosed with H. pylori. All the patients will be enrolled by the University of New Mexico Health Sciences Center.

Avisa Company is funding this study. Avisa Company is interested in marketing this kit.

This form will explain the research study, and will also explain the possible risks as well as the possible benefits to you. We encourage you to talk with your family and friends before you decide to take part in this research 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.

What will happen if I decide to participate?

If you agree to participate, the following things will happen:
All study visits will take place at the University of New Mexico Hospital

Pediatric/Adult Pulmonary Clinic, Ambulatory Care Center, 2211 Lomas Blvd NE

Albuquerque NM, 87106.

All samples that are collected during study visits will be sent to the following lab for the processing:

Quest Diagnostics Nichols Institute
33608 Ortega Highway
San Juan Capistrano, CA 92690

Screening Visit

Before any study-related procedures are performed, you will be asked to read and sign this informed consent form if you wish to participate in this study. The Screening Visit will take approximately 1 hour to complete. The following tests and procedures will be performed to determine if you qualify to participate in this study:

- Review of your medical history, including the medications you currently use or have used in the last 48 hours before the administration of study drug.
- Introduce and review the criteria for participation in the study.
- Measurement of your vital signs. (blood pressure, heart rate, temperature, height and weight)
- Electrocardiogram (ECG - measures the electrical activity of the heart)
- Collection of blood sample (approximately 1 teaspoon) for detection of H.pylori in the blood.
- Pulmonary Function Tests (PFTs). PFTs are the measurement of air inhaled and exhaled from the lungs. When PFTs are performed, you will wear a nose clip and be asked to blow as hard and as fast as you can into a tube three or more separate times.

All above procedures are part of a standard of care for patients with CF except the ECG.

If, based upon the results of the Screening tests and procedures, you qualify to participate in the study; you will be scheduled to return to the study center for The Study Visit.

The Study (Visit 1)

Visit 1 will occur within 4-7 days of the screening visit and will take approximately 3 hours to complete. All the procedures in this visit are part of the research.

During this visit, the following tests and procedures will be performed:

Pre-Dosing Procedures

- You will be asked about any changes in your health or any new medicines you have taken since your screening visit.
- Review the criteria for participation in the study.

- Collection of a urine sample for a pregnancy test for females who are able to get pregnant. The result of the pregnancy test must be negative for you to continue to participate in this study.
- Measurement of your vital signs. (blood pressure, heart rate, and temperature)
- Focused physical examination of your breathing and lung-related symptoms. (breathing rate, breath sounds, pulse oximetry, and cough)
- Pulmonary function tests. (PFTs)
- Air from your exhaled breaths will be collected into a breath collection bag.

Dose of Urea:

If you qualify to participate in this study, you will receive one dose of urea. The dose will be 50 mg of urea mixed with 3 mL of sterile water prepared for inhalation. The solution of urea will be administered using a nebulized in a PARI LC Sprint Star nebulizer cup that transforms the liquid form to a mist that can be inhaled.

Post-Dosing Procedures

- Air from your exhaled breaths will be collected into a breath collection bag at three different times during the 15 minutes following the end of the nebulization of the urea.
- Pulmonary function tests (PFTs) will be performed after the last breath collection.

Follow-up

Twenty-four hours after the administration of the study drug the research coordinator will call to ask how you are feeling after participating in the study. The second question will be about what medications, if any have been taken since receiving study drug. If you have experienced any problems since taking the study drug you will be asked to return to the clinic for a follow up assessment.

How long will I be in this study?

Participation in this study will take a total of 5 hours over a period of 9 days.

What are the risks or side effects of being in this study?

There are risks of stress, emotional distress, inconvenience and possible loss of privacy and confidentiality associated with participating in a research study. Everyone taking part in the study will be followed carefully for any side effects. However, doctors do not know all the side effects that may happen. Side effects may be mild or very serious. Your study doctor may give you medicines to help lessen the side effects. In some cases, side effects can be serious, long lasting, or may never go away.

You should report to your study doctor any side effect you experience while taking part in the study.

Nebulized urea may cause bronchoconstriction (tightness of airways), coughing and wheezing in patients with asthma. If that occurs, you will receive albuterol to open up your airways followed by a spirometry to assure your lung function is back to baseline.

There is also risk of coughing a feeling light-headed when you do spirometry.

Albuterol can cause increased heart rate and blood pressure, nausea, headache, and a jittery or nervous feeling. These symptoms usually go away in less than an hour.

Reproductive Risks: You should not become pregnant or father a baby while on this study because the drugs in this study can affect an unborn baby. Women should not breastfeed a baby while on this study. If you are of child bearing potential, it is important to understand that you need to use birth control while on this study. Check with the investigator about what kind of birth control methods to use and how long to use them. Some methods might not be approved for use in this study. If you were to become pregnant while on this study, the sponsor may want to obtain information from you even after the study has ended.

Allergic reaction: With any drug there is a risk of allergic reaction. Symptoms may include but not be limited to trouble breathing, fast heart rate, rash, dizziness, and swelling. If you experience any of these symptoms, you should contact the investigator immediately.

For more information about risks and side effects, ask the investigator.

What are the benefits to being in this study?

We do not anticipate you will experience any direct benefit from your participation in this study. However, it is hoped that information gained from this study will help in the treatment of future patients with CF and P. aeruginosa infection.

What other choices do I have if I do not want to be in this study?

You do not have to participate in this study to receive treatment for your condition.

How will my information be kept confidential?

We will take measures to protect the security of all your personal information, but we cannot guarantee confidentiality of all study data.

Information contained in your study records is used by study staff and, in some cases it will be shared with the sponsor of the study. The University of New Mexico Health

Sciences Center Human Research Review Committee (HRRC) that oversees human subject research, and the Food and Drug Administration and/or other entities may be permitted to access your records. There may be times when we are required by law to share your information. However, your name will not be used in any published reports about this study. A copy of this consent form will be kept in your medical record.

Information and/or specimens collected as part of the study will be labeled with your study ID number. Study data and information (without your name) will be entered into a secure computer database that only the study team has access to. Study files will be kept in locked file cabinet in the Principal Investigator's office. Dr. Raissy and her associates will have access to your study information. Data will be stored for 5 years, and then will be destroyed.

What are the costs of taking part in this study?

You will not be charged for any study procedures or treatments. The costs of the Urea Breath Test Kit, sputum culture, spirometry and office visits required by the research will be covered by the study. You or your third party payer will be responsible for the costs of your standard medical care and birth control.

You will be reimbursed by the University of New Mexico for reasonable medical expenses for treatment of any adverse reaction to the study drug if both the study doctor and the University of New Mexico agree that the adverse reaction was caused from proper use of the investigational product as outlined in the protocol for the study. The University of New Mexico will not provide any other compensation.

Will I be paid for taking part in this study?

If you complete all study visits, you will be paid up to $150 for taking part in this study. You will be paid as follows:

- Screening Visit: $50
- Study Visit 1: $100

How will I know if you learn something new that may change my mind about participating?

You will be informed of any significant new findings that become available during the course of the study, such as changes in the risks or benefits resulting from participating in the research or new alternatives to participation that might change your mind about participating.

Can I stop being in the study once I begin?

Your participation in this study is completely voluntary. You have the right to choose not to participate or to withdraw your participation at any point in this study without affecting your future health care or other services to which you are entitled.

Whom can I call with questions or complaints about this study?

If you have any questions, concerns or complaints at any time about the research study, Dr. Raissy, or her associates will be glad to answer them at 505-272-5484.

If you need to contact someone after business hours or on weekends, please call 505-272-5551 and ask for the pulmonologist on call.

If you would like to speak with someone other than the research team, you may call the UNMHSC HRPO at (505) 272-1129.

Whom can I call with questions about my rights as a research participant?

If you have questions regarding your rights as a research participant, you may call the UNMHSC HRPO at (505) 272-1129. The HRPO is a group of people from UNM and the community who provide independent oversight of safety and ethical issues related to research involving human participants. For more information, you may also access the IRB website at http://hsc.unm.edu/som/research/hrrc/irbhome.shtml.

CONSENT

You are making a decision whether to participate (or to have your child participate) in this study. Your signature below indicates that you/your child read the information provided (or the information was read to you/your child). By signing this consent form, you are not waiving any of your (your child's) legal rights as a research participant.

I have had an opportunity to ask questions and all questions have been answered to my satisfaction. By signing this consent form, I agree to participate (or let my child participate) in this study. A copy of this consent form will be provided to you.

_____	_____	_____
Name of Adult Subject (print)	Signature of Adult Subject	Date

INVESTIGATOR SIGNATURE

I have explained the research to the participant and answered all of his/her questions. I believe that he/she understands the information described in this consent form and freely consents to participate.

_____

Name of Investigator/ Research Team Member (type or print)

_____ _____

(Signature of Investigator/ Research Team Member) Date