

A Randomized, Double Blind, Placebo Controlled Study of the Effectiveness of Chronic Incretin-Based Therapy on Insulin Secretion in Cystic Fibrosis (Aim 2)

Sponsor: Cooperative study between CHOP and Upenn, The study is being conducted with general research funds from National Institute for Diabetes, Digestive & Kidney Diseases at the National Institute of Health

Brief Description:

- The purpose of this research study is to examine and understand the various mechanisms that contribute to Cystic Fibrosis Related Diabetes (CFRD) and gain a better understanding of potential means to treat it.
- **Type 1 and Type 2 diabetes** - result when either the body does not make enough insulin or the body does not respond correctly to this insulin.
- Insulin-a hormone which is made by cells in the pancreas and helps carry glucose (sugar) from the food we eat to the cells of the body for energy.
- In recent years, diabetes has emerged as one of the most significant co-diseases that many cystic fibrosis (CF) patients develop. While CFRD has many features similar to both Type 1 and Type 2 diabetes, it is very different; therefore, treatment and care of CFRD should not be the same.
- Your participation in this study will include 6-7 study visits (between 4-6 hours) to the Clinical & Translational Research Center (CTRC) at the Hospital of The University of Pennsylvania (UPenn).
- Your participation in this study will be conducted over 6 months and you can be compensated up to \$950 (on a Visa gift card) for completion of all study procedures.

Eligibility:

Currently recruiting patients:

- With cystic fibrosis
- Who have been diagnosed with pancreatic insufficiency (take enzymes with meals)
- Who are ≥ 18 years of age

Key Exclusion Criteria:

- If you are a woman who is pregnant or plans to become pregnant within the next year
- Have had acute pancreatitis within the past year
- Have had a prior lung or liver transplant
- Have been diagnosed with severe CF liver disease (defined by portal hypertension)
- Have been diagnosed with fundoplication-related dumping syndrome

Contact Information:

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Study Procedures:

Oral Glucose Tolerance Test*:

- We will test your body's response to glucose by taking some of your blood from a blood drawing intravenous (IV) catheter.
- You will then be given a large dose of sugar to drink.
- We will then take blood samples at 60 and 120 minutes after drinking the sugar drink.
- A total of 6 mL (or less than one tablespoon) of blood will be drawn for this test.
- This test is recommended annually for most patients with Cystic Fibrosis in order to screen for CFRD
- If you qualify to participate, you can continue with the study procedures.

*If an oral glucose tolerance test was completed within 6 months prior to study procedures, this visit is not required

Mixed Meal Tolerance Test (MMTT):

- 2 total MMTT tests (baseline and 6 months after drug or placebo therapy)
- This test will look at your body's response to food.
- Prior to this visit, you will work with the study team to decide on a breakfast that is appealing to you but is comprised of a specific combination of calories, protein and carbohydrates.
- After you eat, you will have blood drawn from your IV multiple times over a 4 hour period.
- The total amount of blood for this test is about 4½ tablespoons.
- Compensation for this part of the study is \$150 for each meal test

Glucose Potentiated Arginine (GPA) test with incretin infusion:

- 3 total GPA tests (baseline, 1 month, and six months)
- **Arginine**- a naturally occurring amino acid in your body. In this study it is given in your IV to make the cells in your pancreas secrete the hormone insulin.
- The GPA test will measure the insulin and other glucose controlling hormones which will assist in measuring pancreas cell function.
- Infusion of an incretin hormone one visit and placebo during the other: You will be randomized to receive one of two incretin hormones, GLP-1 or GIP.
- **Incretin Hormones**- are produced by the cells in your small intestine and help to make your body more sensitive to glucose.
- You will receive your assigned incretin hormone during one time at visit 2 or 3, and a placebo infusion at the other visit. (These 2 visits will occur 1 –4 weeks apart)
- After baseline blood levels are drawn, the study team will follow a schedule of administering arginine, glucose, and checking your blood levels over approximately an hour.
- You will be allowed to eat lunch and your blood sugar will continue to be monitored over at least the next hour.
- You may be discharged once we confirm that your blood sugar level has normalized.
- The study team will monitor you closely during this testing, checking your blood glucose levels approximately every 5 minutes.
- The total amount of blood for this test is approximately 9 tablespoons.
- Compensation for this part of the study is \$150 for each GPA test.

Continuous Glucose Monitoring System (CGMS) (Optional):

- CGMS is a way to measure blood sugar continuously for 3 days.
- You will be taught how to use CGMS during a GPA visit.
- CGMS requires the placement of a thin tube under the surface of the skin.
- After you complete 72 hours of CGMS at home, you will send the equipment back to CHOP with an envelope that we will provide.
- Compensation for this part of the study is \$100.

Randomization to study drug:

- At the end of your 1-month GPA test, you will be assigned by chance, like the flip of a coin, to get sitagliptin (Januvia ®) 100mg tablet or a matching placebo daily.
- The pill is to be taken every day for 6 months.
- Sitagliptin is a drug that helps the pancreas respond to insulin to lower your blood sugar levels after a meal.
- 2 scheduled office visits are required (at 1 month and 3 months) after starting medication.
- You will be compensated \$50 for each office visit

What are the possible risks or discomforts?

- **Blood sample collections and IV catheter:** The process for collecting blood samples requires a needle to be inserted into a vein. Possible side effects from blood drawing include faintness, inflammation of the vein, pain, bruising, or bleeding at the site of puncture. There is also a slight possibility of infection.
- **Hypoglycemia/Fasting:** Most people do not have medical problems associated with fasting; however, some people have medical conditions that limit their ability to tolerate a fast. If your doctor has told you not to fast, we ask that you not participate in this study.
- **GPA test:** There is the possibility of experiencing a burning or stinging sensation as a result of the glucose infusion. Administration of arginine may briefly cause a metallic taste in your mouth. Rarely, arginine may also cause nausea, vomiting, headache, flushing, numbness, allergy or rash, and irritation of the vein.
- **Sitagliptin therapy:** Rare cases (<1%) of pancreatitis which is severe abdominal pain with or without nausea have been reported with sitagliptin therapy. If you experience any abdominal pain that is persistent or radiating to your back while taking the study medication, please stop the medication and call the study team immediately. Hypersensitivity reactions have also been rarely reported with sitagliptin use.