A Two-Part, Randomized, Placebo and Active-Controlled, Double-Blind, Thorough QT Study Evaluating the Effects of Intravenous Exenatide on Cardiac Repolarization in Healthy Male and Female Volunteers.

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Part A Pilot:The purpose of Part A is to investigate how quickly and to what extent exenatide is absorbed and eliminated from the body and whether the plasma levels of exenatide will reach the levels seen in patients with renal impairment. It will...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON43489

Source
ToetsingOnline

Brief title
Exenatide Thorough QT study

Condition

- Other condition

Synonym
Cardiac repolarization

Health condition

repolarisatie van het hart

Research involving
Human

Sponsors and support

Primary sponsor: Intarcia Therapeutics, Inc.
Source(s) of monetary or material Support: Farmaceutische industrie

Intervention

Keyword: Cardiac Repolarization, Intravenous Exenatide, Investigate amount & effect exenatide, Pilot and Core Part

Outcome measures

Primary outcome

Part A pilot:

To determine if the infusion regimen of a 6-h continuous IV infusion of

exenatide could lead to mean plasma concentration of 500 pg/mL at the end of

the infusion.

Part B:

To evaluate whether exenatide at therapeutic and supra-therapeutic

concentrations has a pharmacological effect on cardiac repolarization, as

detected by changes in the QTc interval, that reaches the ICH E14 threshold.

Secondary outcome

Part A Pilot:

-To evaluate the safety, tolerability and PK of a 6 h continuous IV infusion of

exenatide

Part B:

-To evaluate the relationship between plasma concentrations of exenatide and

QTc interval.

-To evaluate the effects of exenatide on other cardiac intervals such as PR,

RR, QRS, QT, T- and U- wave morphology.

-To assess the assay sensitivity to detect a change in the QTc interval, using

400 mg moxifloxacin as the active control.

-To evaluate the safety, tolerability and PK of a 6 h continuous IV infusion of

exenatide.

Study description

Background summary

Part A Pilot:
ITCA 650 is a new device, developed by Intracia, to administer exenatide. Exenatide is a drug that is used for the treatment of type 2 diabetes mellitus (T2DM). Exenatide is a compound that is similar to a human hormone (glucagon-like peptide-1, GLP-1). This hormone works by increasing insulin production with increasing glucose levels in blood and delays the gastric emptying of the stomach and decreases appetite. Exenatide is no new drug; it is already available in the market under several dosages and formulations. In this study the new device will not be used, but it is necessary for the further development of the device.

Part B:
ITCA 650 is a new device, developed by Intracia, to administer exenatide continuously over a period of up to 12 months. Exenatide is a drug that is used for the treatment of diabetes mellitus type 2. Exenatide is a compound that is similar to a human hormone (glucagon-like peptide-1, GLP-1). This hormone works by increasing insulin production of the body with increasing glucose levels in blood and delays the gastric emptying of the stomach and decreases appetite. Exenatide is no new drug; it is already available in the market under several dosages and formulations. In this study the new device will not be used, but it is necessary for the further development of the device.

Study objective

Part A Pilot:
The purpose of Part A is to investigate how quickly and to what extent exenatide is absorbed and eliminated from the body and whether the plasma levels of exenatide will reach the levels seen in patients with renal impairment. It will also be investigated how safe the administration of exenatide, when administered as a continuous IV infusion of 6 hours, is and how well it is tolerated.

Part B:
The prupose of Part B is to evaluate if there is a prolongation of the so-called QT interval; the QT interval is an ECG variable. When the QT interval is prolonged, repolarization is delayed. This means that cardiac cells need more time to prepare for the next beat. When a new heartbeat is about to start and not all cardiac cells are prepared for that, arrhythmias may develop.

Study design

Part A Pilot:
The actual study will consist of 1 period during which you will stay in the clinical research center in Groningen for 4 days (3 nights).
During the study you the volunteer will receive exenatide as a continuous 6-hour IV infusion. 30 minutes before the start of the IV infusion, you will receive an IV administration of palonosetron.

Initially 2 volunteers will receive the study compound with the start time of the infusion for the second volunteer 2 hours after the start of the first infusion, if deemed safe by the research physician. If the infusion was well tolerated and safe a similar process will be followed on the second day with 2 hours between the start of the administration to the third and fourth volunteer. If the infusion was tolerated well by the third volunteer further volunteers will receive the study compound with shorter intervals.

Part B:
The actual study will consist of 3 periods during which the volunteer will stay in the clinical research center in Groningen for 4 days (3 nights) during the first period and for 3 days (2 nights) during the second and third period. The time interval between the different periods is 7 days between 2 study compound administrations.
During the study the volunteer will receive exenatide or placebo as a continuous 6-hour IV infusion. 30 minutes before the start of the IV infusion, the volunteer will receive an IV administration of palonosetron.

Intervention

Part A:
The study will consist of 1 period during which 0.406 µg/kg exenatide will be given as a continuous IV infusion of 6 hours. For the second group the dose can be adjusted if the target exposure has not been reached.

Part B:
The study will consist of 3 periods during which the subject will receive exenatide once and placebo twice. Exenatide and placebo will be given as a continuous IV infusion of 6 hours during each period.

During 1 of the placebo periods the subject will also receive moxifloxacin. Moxifloxacin will be given as a 400 mg oral tablet. The subject will also receive a single IV injection of palonosetron 30 minutes before the start of the infusion of the study compound in each study period.

Study burden and risks

Pain, minor bleeding, bruises and possible infection.

Contacts

Public
Intarcia Therapeutics, Inc.

Industrial Blvd. 24650
Hayward CA 94545
US
Scientific
Intarcia Therapeutics, Inc.

Industrial Blvd. 24650
Hayward CA 94545
US

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

-Healthy males and females
-18 - 65 years old;
-Body mass index (BMI) >=19.0 and <=35.0 kg/m2;

Exclusion criteria

Suffering from hepatitis B, hepatitis C, cancer or HIV/AIDS. In case of participation in another drug study within 90 days before the start of this study or being a blood donor within 60 days from the start of the study. In case of donating more than 1.5 liters of blood in the 10 months prior the start of this study.

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	18-01-2016
Enrollment:	82
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Aloxi
Generic name:	n/a
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Avelox
Generic name:	n/a
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Bydureon
Generic name:	n/a
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	07-01-2016
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	14-01-2016
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2015-003041-26-NL
CCMO	NL55758.056.15