OPEN-LABEL, RANDOMIZED STUDY TO ASSESS THE SAFETY AS WELL AS THE PHARMACOKINETIC PROFILE AND TO INVESTIGATE THE EFFICACY TRENDS ON BIOMARKERS IN TYPE 2 DIABETES MELLITUS PATIENTS OF A SUSTAINED RELEASE FORMULATION OF EXENATIDE BASED ON MEDUSA* TECHNOLOGY

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Glucose metabolism disorders (incl diabetes mellitus)
Study type	Interventional

Summary

ID

NL-OMON44056

Source
ToetsingOnline

Brief title
Exenatide MPF SAD and MAD study

Condition

- Glucose metabolism disorders (incl diabetes mellitus)

Synonym
Diabetes Mellitus Type 2

Research involving
Human

Sponsors and support

Primary sponsor: FLAMEL TECHNOLOGIES
Source(s) of monetary or material Support: farmaceutische industrie

Intervention

Keyword: Diabetes Mellitus Type 2, Exenatide, T2DM

Outcome measures

Primary outcome

To assess the safety and tolerability of Exenatide MPF *Sustained Release* formulation following two subsequent rising doses in healthy volunteers versus a reference treatment in healthy volunteers

To assess the safety and tolerability of a repeated dosing regimen of Exenatide MPF *Sustained Release* formulation in type 2 diabetes mellitus (T2DM) patients

Secondary outcome

To assess the pharmacokinetic (PK) profile and PK parameters variability of Exenatide MPF *Sustained Release* formulation following two sequential dose escalations in healthy volunteers versus a reference treatment in healthy volunteers

To investigate the effect of Exenatide MPF *Sustained Release* formulation following a 4 week repeated dosing regimen on selected biomarkers and surrogate endpoints in T2DM patients

To assess the PK profile and PK parameters variability of Exenatide MPF

Sustained Release formulation following a repeated dosing regimen in T2DM

patients

Study description

Background summary

Exenatide is a registered medication that has been developed for the treatment of Diabetes Mellitus Type 2. It concerns a synthetic form of a naturally occurring gut hormone, GLP-1 (Glucagon-Like Peptide 1), a protein that is administered by a subcutaneous injection. Exenatide is used to lower the blood sugar level in patients with Diabetes Mellitus Type 2 where the conventional oral medication does not provide sufficient reduction of the blood sugar level. It stimulates the production of insulin in response to increased levels of glucose in the blood.

Exenatide MPF (MicroParticles Formulation) is a new formulation of Exenatide that will aim for a sustained and prolonged release of the original drug substance, allowing patients themselves less frequent injections to administer and to experience fewer side effects.

Study objective

The purpose of the study is to investigate to what extent Exenatide MPF is tolerated.
It will also be investigated how quickly and to what extent Exenatide, when administered as Exenatide MPF, is absorbed and eliminated from the body (this is called pharmacokinetics). In addition, the effect of the compound on blood levels and body weight will be investigated (this is called pharmacodynamics).

Study design

Part A:
The actual study will consist of 2 periods. During Period 1, you will stay in the clinical research center in Groningen for 5 days (4 nights) followed by 3 ambulant visits during which you will visit the clinical research center in Groningen, or you will stay in the clinical research center in Groningen for 3 days (2 nights), depending on the treatment sequence (see *How much of the study compound will I receive?*). If you will receive Byetta® during Period 1, your stay will be shorter as the clearance of the product is significantly shorter than that of Exenatide MPF. During Period 2, you will stay in the clinical research center in Groningen for 5 days (4 nights) followed by 5 ambulant visits.

During the study you will receive Exenatide MPF or Byetta® within 60 minutes prior to a standardized breakfast, and in case of Byetta®, you will receive a second dose within 60 minutes prior to a standardized dinner. Exenatide MPF and Byetta® will be given as a subcutaneous injection in the abdominal wall.

Part B:
Visit schedule:
Week 1: from Day 2 to Day 4, followed by 2 ambulant visits on Day 5 and Day 6
Week 2: from Day 7 to Day 8, followed by 2 ambulant visits on Days 10 and 12
Week 3: from Day 14 to Day 15
Week 4: from Day 21 to Day 25, followed by 1 ambulant visit on Day 26
from Day 27 to Day 28, followed by 5 ambulant visits on Days 29, 31, 33, 36 and 39, and a post study screening on Day 43
During the study you will receive Exenatide MPF within 60 minutes prior to a breakfast. Exenatide MPF will be given as a subcutaneous injection.

Intervention

Part A of the study will consist of 2 periods. During Period 1, you will receive a single dose of Exenatide MPF or two doses of Byetta® at a 12-hour interval. Byetta® is the existing and registered formulary of Exenatide that acts shorter. It will be administered in order to compare the pharmacokinetics and tolerability of the new agent to that of the existing compound. During Period 2, you will receive a single dose of Exenatide MPF. Exenatide MPF and Byetta® will be given in the form of a subcutaneous injection.

The following treatment sequences are planned:

Sequence 1 (n=10) Period 1: two subcutaneous doses of 5 µg Byetta® at 12-hour interval
Period 2: a single subcutaneous dose of 70 µg Exenatide MPF

Sequence 2 (n=10) Period 1: two subcutaneous doses of 5 µg Byetta® at 12-hour interval
Period 2: a single subcutaneous dose of 140 µg Exenatide MPF

Sequence 3 (n=10) Period 1: a single subcutaneous dose of 10 µg Exenatide MPF
Period 2: a single subcutaneous dose of 70 µg Exenatide MPF

Sequence 4 (n=10) Period 1: a single subcutaneous dose of 10 µg Exenatide MPF
Period 2: a single subcutaneous dose of 140 µg Exenatide MPF

Whether you will receive treatment sequence 1, 2, 3 or 4 will be determined by chance.

Part B of the study will consist of 1 period during which you will receive Exenatide MPF once-a-week for 4 weeks. Exenatide MPF will be given in the form of a subcutaneous injection in the abdominal wall.

Subjects will receive:
140 µg or 180 µg Exenatide MPF once-a-week for 4 weeks

Study burden and risks

Procedures: pain, light bleeding, heamatoma, possibly an infection.

As Exenatide MPF will be administered to man for the first time in this study, adverse effects of Exenatide MPF in man have not been reported to date. However, the most important possible adverse effects of the current formulation of Exenatide (Byetta®) are nausea and vomiting; in addition, diarrhea, constipation, reactions at the injection site, loss of appetite and weight loss. A rare complication is pancreatitis.

Contacts

Public
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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Part A;
Gender: healthy male or female
Age: 18 - 65 years, inclusive
Body Mass Index: >22.0 - <35.0 kg/m2 ;Part B:
Gender: male or female T2DM patients
Age: 18 - 75 years, inclusive
Body Mass Index: >25.0 - <40.0 kg/m2

Exclusion criteria

Suffering from hepatitis B, hepatitis C, cancer or HIV/AIDS. In case of participation in another drug study within 60 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:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL
Recruitment status: Recruitment stopped

Start date (anticipated):	15-07-2015
Enrollment:	64
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Byetta
Generic name:	Exenatide
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	na
Generic name:	Exenatide MPF

Ethics review

Approved WMO Date:	08-07-2015
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	10-07-2015
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	11-01-2016
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	15-01-2016
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO	

Date:	15-02-2016
Application type:	Amendment
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	EUCTR2015-002390-38-NL
CCMO	NL54120.056.15