A bridging trial to compare the pharmacokinetics of Glepaglutide (ZP1848) after a single subcutaneous administration by vial/syringe and by autoinjector in healthy subjects: a phase 1, randomized, open-label, three-way, reference-replicated crossover trial

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- To compare the pharmacokinetics (PK) of glepaglutide after a single subcutaneous (SC) administration by vial/syringe and by autoinjector.- To evaluate the safety and tolerability of glepaglutide following SC dosing in healthy subjects.

Ethical review	Approved WMO
Status	Completed
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON49360

Source
ToetsingOnline

Brief title
Glepaglutide BE study: subcutaneous and autoinjector administration

Condition

- Other condition

Synonym
Healthy volunteers

Health condition

Bioequivalence

Research involving
Human

Sponsors and support

Primary sponsor: Zealand Pharma A/S
Source(s) of monetary or material Support: Biotech

Intervention

Keyword: Glepaglutide (ZP1848), Pharmacokinetic, randomized

Outcome measures

Primary outcome

• Cmax = maximum concentration of ZP1848total in plasma

• AUC0-t = area under the plasma ZP1848total concentration-time curve (AUC)

from time zero to the last time point with a measurable concentration both for

the conceptual analyte ZP1848total (glepaglutide + ZP18481-34 + ZP18481-35) in

plasma

Secondary outcome

• AUC0-inf = AUC from time 0 extrapolated to infinity

• AUC0-t = AUC from time 0 to the last time point with a measurable

concentration in plasma for ZP1848 and main metabolite ZP18481-34

• Cmax = maximum concentration of ZP1848 and ZP18481 34 in plasma

• Tmax = time to attain Cmax

• *z = terminal elimination phase rate constant

• t1/2 = terminal elimination half-life all for the conceptual analyte

ZP1848total and main metabolite ZP18481 34 in plasma

• Adverse events

Safety:

• Change from baseline in:

o Clinical laboratory values (hematology, clinical chemistry, and urinalysis)

o Standard 12-lead electrocardiogram (ECG) evaluation

o Vital signs (diastolic and systolic blood pressure, heart rate, and body temperature)

o Physical examination evaluation

Immunogenicity

• Overall anti-glepaglutide antibody incidences (treatment-induced and treatment-boosted) and titers

• Antibodies reacting to the main metabolite (ZP18481-34)

• Antibodies cross-reacting to endogenous GLP-2

• Glepaglutide neutralizing antibodies

Study description

Background summary

Glepaglutide is a new compound that may be used for the treatment of short bowel syndrome. Short bowel syndrome is a disease where there is a shortage of functional small intestine, for example due to disease or surgery. As patients that suffer from this syndrome cannot effectively absorb fluid and nutrients from food, it often results in symptoms such as feeling tired, weight loss, dehydration, and malnutrition.

A compound that is present in the intestines (GLP-2) has been found to be able to improve the functioning of the intestines and could increase the absorption of nutrients. The downside of GLP-2 is that it is quickly degraded in the body. Glepaglutide is a new compound that looks the same as GLP-2, but works for a longer period.

Study objective

- To compare the pharmacokinetics (PK) of glepaglutide after a single subcutaneous (SC) administration by vial/syringe and by autoinjector.
- To evaluate the safety and tolerability of glepaglutide following SC dosing in healthy subjects.

Study design

The actual study will consist of 3 periods during each of which the subject will stay in the research center for 5 days (4 nights) or optionally 3 days (2 nights). In each period, this will be followed by short visits to the research center on Days 5, 6, 7, 8, and 14. Optionally, when the subject decides to stay for 3 days (2 nights) in the clinic this will be followed by short visits on Days 2 (evening), 3, 4, 5, 6, 7, 8, and 14. These short visits take approximately half an hour. There will be 7 weeks in between administration of the study compound in each period.
Day 1 is the day of administration of the study compound. In each period, the subject is expected at the research center at 14:00 h in the afternoon prior to the day of administration of the study compound. They will leave the research center on Day 4 (or optionally Day 2) of each period.

Intervention

Glepaglutide will be administered as an injection under the skin (subcutaneous) with either a syringe or an autoinjector.

There are two different treatments:
• 10 mg glepaglutide administered with a syringe
• 10 mg glepaglutide administered with an autoinjector

The subject will receive 1 treatment per period, so 3 treatments in total. The order in which these treatments are given are shown in the table below. The subject will be randomly assigned to sequence 1, 2 or 3:

	Period 1	Period 2	Period 3
Sequence 1	Autoinjector	Syringe	Syringe
Sequence 2	Syringe	Autoinjector	Syringe
Sequence 3	Syringe	Syringe	Autoinjector

Study burden and risks

In a previous study, 45 healthy volunteers received a single injection of between 1.6 mg and 96 mg glepaglutide
The most common side effect that were reported included:
• Mild injection site reactions: Reddening of the skin, especially at the higher doses

Furthermore, doses of up to 96 mg glepaglutide did not result in significant findings in physical, neurological, respiratory or laboratory examinations. Glepaglutide was considered safe.

Glepaglutide is currently is being assessed in a study in patients with short bowel syndrome, where they are dosed with glepaglutide 10mg once weekly or 10mg twice weekly for over 2 years.

Administration of glepaglutide may trigger the production by the immune system of antibodies directed against glepaglutide. In rare cases, these antibodies could cross-react to GLP-2 and reduce the action of the normal production of GLP-2 in the body. This risk is considered very small.

Administration of glepaglutide may be associated with a risk of allergic reactions similar to those observed for other therapeutic peptides or proteins. Subjects with known or suspected allergies to the trial products or related products are excluded from participation in trials with glepaglutide. Mild or moderate allergic reactions may include symptoms of rash, fever, flu-like symptoms, nausea, headache and myalgia. Acute generalized hypersensitivity reactions are usually very rare but may include symptoms of rash, flushing, itching, sneezing or runny nose, abdominal pain, diarrhea, swelling of face, tongue or throat, dizziness, lightheadedness or fainting, trouble breathing, irregular or racing heart rate, and seizures.

Possible discomforts due to procedures
Drawing blood and/or insertion of the indwelling cannula may be painful or cause some bruising.

In total, we will take about 340 milliliters of blood from the volunteer over the 3 periods (21 weeks). This amount does not cause any problems in adults. To compare: a blood donation involves 500 mL of blood being taken each time.

To make a heart tracing, electrodes will be pasted at specific locations on your arms, chest and legs. Prolonged use of these electrodes can cause skin irritation.

A sample for the coronavirus test will be taken from the back of the nose and throat using a swab. Taking the sample only takes a few seconds, but can cause

discomfort and can give an unpleasant feeling. Taking a sample from the back of the throat may cause the volunteer to gag. When the sample is taken from the back of the nose, the volunteer may experience a stinging sensation and the eyes may become watery.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1. Informed consent of the subject has to e obtained before any trial-related activities are performed (trial-related activities are any procedures that would not have been performed during normal management of the subject).
2. Subject has to be a healthy male or female aged between 18 years and 54 years, both inclusive, at screening.
3. Body mass index (BMI)of the subject has to be >20.0 kg/m2 and <29.9 kg/m2,

both inclusive, at screening.
4. Subject is willing to maintain a stable weight for the duration of the trial.
5. Subject is in overall good health according to age (medical history, physical examination, vital signs, and laboratory assessments), as judged by the Investigator at screening.

Exclusion criteria

1. Subject cannot have a significant medical history or clinical manifestation of any metabolic, allergic, dermatological, hepatic, renal, hematological, pulmonary, cardiovascular, gastrointestinal, neurological, respiratory, endocrine, or psychiatric disorder, as determined by the Investigator.
2. Subject with a history of colon cancer or a history of other cancers within the last 5 years.
3. The physical examination of the subject should not show clinically significant abnormalities in the standard 12-lead ECG, or vital signs measurements as determined by the Investigator.
4. Clinically significant abnormality in hematology, clinical chemistry, or urinalysis as determined by the Investigator (congenital nonhemolytic hyperbilirubinemia [eg, Gilbert*s syndrome] is acceptable).
5. Subject cannot have a history of significant hypersensitivity, intolerance, suspected hypersensitivity to glepaglutide or related products, or allergy to any drug compound, food, or other substance, unless approved by the Investigator.

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	04-03-2020

Enrollment:	72
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	N/A
Generic name:	Glepaglutide

Ethics review

Approved WMO Date:	21-01-2020
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	15-02-2020
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	09-03-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	16-03-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	10-07-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	16-07-2020

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	EUCTR2019-004517-14-NL
CCMO	NL72557.056.20

Study results

Date completed:	10-06-2021
Results posted:	17-02-2022

First publication
13-01-2022