Pharmacokintetics, safety and tolerability study of subcutaneous Rizatriptan (DFN-10) in healthy subjects

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The purpose of Part A is to investigate how quickly and to what extent Rizatriptan in DFN-10 is absorbed and eliminated from the body (this is called pharmacokinetics). In addition, it will be investigated to what extent DFN-10 is tolerated.In Part...

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

Summary

ID

NL-OMON42170

Source
ToetsingOnline

Brief title
DFN-10 SAD and bioavailability study

Condition

- Headaches

Synonym
headache, migraine

Research involving
Human

Sponsors and support

Primary sponsor: Dr. Reddy's Laboratories Ltd.
Source(s) of monetary or material Support: Farmaceutische industrie

Intervention

Keyword: DFN-10, migraine, Rizatriptan

Outcome measures

Primary outcome

- To assess the pharmacokinetics (PK), safety and tolerability of a single subcutaneous (sc) injection of DFN-10 (0.5, 1.0, 2.0 and 3.0 mg) in healthy adult subjects under fasting conditions

- To evaluate and compare the PK parameters of rizatriptan following sc injection of DFN-10 and oral administration of 10 mg Maxalt® (rizatriptan benzoate) tablets in healthy adult subjects under fasting conditions

Secondary outcome

To evaluate and compare the safety and tolerability of DFN-10 and Maxalt® in healthy adult male and female volunteers

Study description

Background summary

DFN-10 is a new investigational formulation of the registered compound rizatriptan and may eventually be used for the treatment of acute migraine with or without aura. Migraine is a severe, painful headache that is often accompanied by nausea, vomiting and increased sensitivity to light and sound. Auras are perceptual disturbances, often manifesting as the perception of a strange light, an unpleasant smell or confusing thoughts or experiences.

Rizatriptan is an activator of the serotonin receptors called 5 HT1B and 5 HT1D. A receptor is a protein on the surface of a cell to which a molecule (e.g., serotonin) can bind, causing a change in the activity of the cell. 5 HT1B/1D receptors are found on blood vessels and nerve tissue in the brain. People who suffer from migraine tend to have low levels of serotonin. Because

Rizatriptan, like serotonin, activates serotonin receptors, DFN-10 is in development for the treatment of acute migraine. This is the first time this new formulation of Rizatriptan via this dosing route (injection under the skin) is being given to humans. The expected advantages of a formulation that is administered per injection are that it can be effective in case of vomiting (which is a rather common symptom of migraine), and that the effect of the medication may start sooner after dosing.

In Part B of the study the volunteer will also receive Maxalt®, which is drug that is already available in the market under several dosages and formulations. The active ingredient of Maxalt® is the same as the active ingredient of DFN-10 (Rizatriptan, an activator of the 5 HT1B/1D receptors), so the working mechanism is comparable.

Study objective

The purpose of Part A is to investigate how quickly and to what extent Rizatriptan in DFN-10 is absorbed and eliminated from the body (this is called pharmacokinetics). In addition, it will be investigated to what extent DFN-10 is tolerated.

In Part B of the study it will be investigated whether the pharmacokinetic properties of DFN-10 are comparable to the pharmacokinetic properties of Maxalt®.

Study design

Part A:
The actual study will consist of 1 period during which the volunteer will stay in the clinical research center in Zuidlaren for 3 days (2 nights).

Part B:
The actual study will consist of 2 periods. In each period the volunteer will stay in the clinical research center in Zuidlaren for 3 days (2 nights). The time interval between the different periods is 4 days.

Intervention

Part A:
The study will consist of 1 period during which you will receive a single dose of DFN-10 or a single dose of placebo. A placebo is the same formulation without the active ingredient. DFN-10 and placebo will be given as an injection under the skin (subcutaneous injection).

Group Day Treatment How often
1 1 DFN-10 0.5 mg or placebo Once

2 1 DFN-10 1.0 mg or placebo Once
3 1 DFN-10 2.0 mg or placebo Once

Part B:
The study will consist of 2 periods. In the first period you will receive a single dose of DFN-10 or a single dose of placebo. A placebo is the same formulation without the active ingredient. In the second period you will receive a single dose of 10 mg Maxalt® or a single dose of placebo. DFN-10 will be given as an injection under the skin (subcutaneous injection). Maxalt® will be given as a tablet.

The order in which the volunteer will be administered DFN-10 and Maxalt® will be determined by chance.

The dose DFN 10 that will be administered to the volunteer is 3 mg. This dose is based on the results of Part A of the study. Should, in the opinion of the investigators, unacceptable adverse effects appear, the study will be discontinued..

Study burden and risks

All potential drugs cause adverse events; the extent to which this occurs differs. As DFN-10 will be administered to man for the first time in this study, adverse effects of DFN-10 in man have not been reported to date. However, DFN-10 has been studied in animals. The most frequently observed adverse effect in animals was: tremors. Because the active ingredient of DFN-10 is the same as the active ingredient of the registered drug Maxalt®, similar adverse effects, and possibly other, still unknown adverse effects, may occur.

Maxalt® is a drug that is already available in the market since 1998 under several dosages and formulations. Maxalt® has been evaluated in 8630 adult patients and is now being used by many patients suffering from migraine. The most frequently observed adverse effects are: tingling sensation, headache, decreased sensitivity of skin, decreased mental sharpness, insomnia, fast or irregular heartbeat, flushing (redness of the face lasting a short time), throat discomfort, nausea, dry mouth, vomiting, diarrhea, indigestion, feeling of heaviness in parts of the body, neck pain, stiffness, pain in abdomen or chest.

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

healthy male and female subjects (female only for Part B)
18 - 45 yrs, inclusive
20.0 - 29.0 kg/m2, inclusive

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:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-12-2014
Enrollment:	40
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Maxalt®
Generic name:	rizatriptan benzoate

Ethics review

Approved WMO Date:	20-10-2014
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	28-10-2014
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	19-03-2015
Application type:	Amendment

Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	25-03-2015
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	EUCTR2014-003864-19-NL
CCMO	NL51080.056.14