A phase 1, randomized, double-blind, placebo-controlled, single-site study to assess the safety, tolerability, pharmacokinetics and food effect of MIN-102 following oral administration of single and multiple ascending doses in healthy male volunteers

Published: 17-05-2016
Last updated: 16-04-2024

The purpose of the study is to investigate to what extent MIN-102 is tolerated.It will also be investigated how quickly and to what extent MIN-102 is absorbed and eliminated from the body (this is called pharmacokinetics). In addition, the effect of...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Metabolism disorders NEC
Study type	Interventional

Summary

ID

NL-OMON42947

Source
ToetsingOnline

Brief title
MIN-102 SAD/FE/MAD Study

Condition

- Metabolism disorders NEC

Synonym
metabolic disorder, X-linked adrenoleukodystrophy

Research involving
Human

Sponsors and support

Primary sponsor: Minoryx Therapeutics S.L.
Source(s) of monetary or material Support: Ministerie van OC&W,Farmaceutische industrie

Intervention

Keyword: metabolic disorder, MIN-102, X-ALD

Outcome measures

Primary outcome

Part A:

To evaluate the safety and tolerability of MIN-102 administered orally as a

single dose in healthy male volunteers.

Part B:

To evaluate the safety and tolerability of MIN-102 administered orally as a

multiple dose in healthy male volunteers.

Part C:

To evaluate the safety and tolerability of MIN-102 administered orally as a

multiple dose in healthy male volunteers.

Secondary outcome

Part A:

- To evaluate the PK parameters in plasma and urine of MIN-102 and M3 after a

single oral administration of MIN-102 in healthy male volunteers.

- To evaluate the food effect (FE) in the PK of MIN-102 and M3 after a single oral administration of MIN-102 in healthy male volunteers.
- To evaluate the enantiomer proportionality of MIN-102 in plasma.
- To evaluate the adiponectin and fatty acid binding protein 4 (FABP4) levels in plasma before and after a single dose of MIN-102

Part B:

- To evaluate the PK parameters in plasma and CSF of MIN-102 and M3 after single and multiple oral administrations of MIN-102 in healthy male volunteers.
- To evaluate the levels in plasma and CSF of biomarkers (adiponectin, FABP4, cytokines [interleukin 6 (IL-6), interleukin 1 receptor agonist (IL-1ra), interleukin-8 (IL-8)] chemokines [monocyte chemotactic protein 1 (MCP-1), C-X-C motif chemokine 10-Interferon gamma-induced protein 10 (CXCL10*IP10)], and adhesion molecules [soluble intercellular adhesion molecules (sICAM) and soluble vascular cellular adhesion molecule-1 (sVCAM1)]) after multiple oral administrations of MIN-102.

Part C:

- To evaluate the PK parameters in plasma and cerebrospinal fluid (CSF) of MIN-102 and M3 after single and multiple oral administrations of MIN-102 in healthy male volunteers.
- To evaluate the levels of biomarkers (adiponectin, FABP4, CRP, cytokines [IL-6, IL- 1ra, IL-8] chemokines [MCP-1, CXCL10*IP10], and adhesion molecules [sICAM and sVCAM1]) in plasma and CSF after multiple oral administrations of

MIN-102.

Study description

Background summary

MIN-102 is a new investigational compound that may eventually be used for the treatment of X-linked adrenoleukodystrophy (X-ALD). X-ALD is a relatively rare inherited metabolic disorder affecting the metabolism of very long-chain fatty acids (VLCFA). This results in high levels of VLCFA primarily in brain cells and adrenocortical cells. These high levels of VLCFA cause damage to the nervous system (degradation of myelin, an isolating layer around the axon of nervous cells) and the steroid producing adrenocortical and testes cells. MIN-102 interacts with a receptor regulating the fatty acid storage and glucose metabolism. MIN-102 is a differentiated peroxisome proliferator-activated receptor * (PPAR*) agonist. This is the first time that this study compound is being given to humans.

MIN 102 is an active metabolite of the marketed drug Pioglitazone which is used in the treatment of type 2 diabetes (T2D). Approximately 25% of Pioglitazone is transferred to M4 (MIN-102) in the body.

Study objective

The purpose of the study is to investigate to what extent MIN-102 is tolerated.

It will also be investigated how quickly and to what extent MIN-102 is absorbed and eliminated from the body (this is called pharmacokinetics). In addition, the effect of MIN-102 on enzymes related to X-ALD will be investigated (this is called pharmacodynamics).

Study design

Part A:
The study will consist of 4 periods during which the volunteer will stay in the clinical research center in Groningen for 7 days (6 nights). The time interval between the different periods is approximately 7 days.

Part B:
The study will consist of 1 period during which the volunteer will stay in the clinical research center in Groningen for 15 days (14 nights).

Part C:
The study will consist of 1 period during which the volunteer will stay in the

clinical research center in Groningen for 15 days (14 nights).

Intervention

Part A:
The study will consist of 4 periods during which the volunteer will receive MIN-102 or placebo once in each period. MIN-102 and placebo will be given as oral suspension of 20 mL.

Part B:
The study will consist of 1 period during which the volunteer will receive MIN-102 or placebo once daily for 8 days. MIN-102 and placebo will be given as an oral suspension of 20 mL.

Part C:
The study will consist of 1 period during which the volunteer will receive MIN-102 once daily for 8 days. MIN-102 will be given as an oral suspension of not more than 20 mL. The dose levels used in Part C of the study are not known yet: The dose for the first group of
Part B will be determined based on the results of Part A where 3 doses are tested (planned doses 30, 60 and 120 mg). The dose level for the second group of Part C will be determined based on the results of Part A of the study and the results of the first groups of Part B and Part C.

Study burden and risks

All potential drugs cause adverse effects; the extent to which this occurs differs. As MIN-102 will be administered to man for the first time in this study, adverse effects of MIN-102 in man have not been reported to date. However, MIN-102 has been studied in animals. The following adverse effects were observed, only at the highest dose given, in animals: decreased bodyweight, goose bumps, rough coat, and hunched posture. Excess saliva production and abnormal blood values were also observed.

MIN-102 is a natural active metabolite of Pioglitazone, a drug that has been on the market for several years and has been prescribed to many T2D patients. In effect, many people have been exposed to the study compound, though in lower doses. For Pioglitazone the most frequently described adverse effects in man were: common (may affect up to 1 in 10 people): respiratory infection, abnormal vision, weight gain, general numbness, broken bones in women; uncommon (may affect up to 1 in 100 people): inflammation of the sinuses (sinusitis), difficulty sleeping (insomnia) and bladder cancer; not known (frequency cannot be estimated from the available data): increase in liver enzymes, allergic reactions and eye diseases. It is not known whether these adverse effects were the result of the metabolite MIN-102 or one of its metabolites.

Procedures: pain, minor bleeding, bruising, possible infection

Contacts

Public
Minoryx Therapeutics S.L.

Av. Ernest Lluch 32
Mataró (Barcelona) 08302
ES
Scientific
Minoryx Therapeutics S.L.

Av. Ernest Lluch 32
Mataró (Barcelona) 08302
ES

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

healthy male volunteers
18 - 55 yrs, inclusive
BMI: 18.0 - 28.0 kg/m2, inclusive
non-smoking

Exclusion criteria

Suffering from hepatitis B, hepatitis C, cancer or HIV/AIDS.
Participation in a drug study within 90 days prior to the first drug administration in the current study. Participation in more than 3 other drug studies (for male subjects) in the 10 months prior to (the first) drug administration in the current study.
Donation or loss of more than 100 mL of blood within 60 days prior to the first drug administration. Donation or loss of more than 1.5 liters of blood (for male subjects) in the 10 months prior to (the first) drug administration in the current 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):	08-06-2016
Enrollment:	33
Type:	Actual

Ethics review

Approved WMO Date:	17-05-2016
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	07-06-2016
Application type:	First submission

Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	24-06-2016
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	EUCTR2016-000607-82-NL
CCMO	NL57650.056.16