A single-center, randomized, double-blind, placebo-controlled, parallel-group studie investigating the safety, tolerability and pharmacokinetics of single- and multiple-ascending subcutaneous doses of TA-46 in healthy volunteers

Published: 09-01-2018
Last updated: 12-04-2024

The study will be conducted in 94 healthy male and female volunteers. The study consists of 3 parts: Part A, Part B and Part C.Part A will be conducted in 40 healthy male and female volunteers divided into 5 groups with 8 volunteers each.Part B will...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Chromosomal abnormalities, gene alterations and gene variants
Study type	Interventional

Summary

ID

NL-OMON48911

Source
ToetsingOnline

Brief title
TA-46 SAD and MAD dose study to investigate safety and PK

Condition

- Chromosomal abnormalities, gene alterations and gene variants

Synonym
Achondroplasia, dwarfism

Research involving
Human

Sponsors and support

Primary sponsor: Therachon SAS
Source(s) of monetary or material Support: Farmaceutische industrie

Intervention

Keyword: MAD, SAD, TA-46

Outcome measures

Primary outcome

To evaluate the safety and tolerability of single and multiple ascending doses

of TA-46 administered to healthy male and female subjects.

Secondary outcome

To evaluate the pharmacokinetics (PK) of TA-46 following single and multiple

ascending doses

To compare the safety, tolerability, and pharmacokinetics of single doses of 2

formulations of TA-46.

Study description

Background summary

TA-46 is a new compound that may eventually be used for the treatment of achondroplasia. People with achondroplasia have a short stature and achondroplasia is a common cause of dwarfism. Achondroplasia is caused by an alteration in the gene (hereditary predisposition) for a protein called Fibroblast Growth Factor Receptor 3 (FGFR3). FGFR3 plays an important role in bone growth and FGFR3 causes shorter bones. In achondroplasia the altered form of FGFR3 is overly active and this leads to very short bones. FGFR3 is activated by binding specific proteins called fibroblast growth factors. TA-46 is constructed to resemble FGFR3. TA-46 is a decoy protein. When TA-46 is to be administered to humans a large part of the fibroblast growth factors will bind

to the decoy protein TA-46 instead of FGFR3 whereby FGFR3 will be less activated. It is hoped for that the overly active FGFR3 will be inhibited in achondroplasia, thus increasing bone growth and thereby increasing height. In this way, TA-46 may be used as a treatment of dwarfism from achondroplasia.

Study objective

The study will be conducted in 94 healthy male and female volunteers. The study consists of 3 parts: Part A, Part B and Part C.
Part A will be conducted in 40 healthy male and female volunteers divided into 5 groups with 8 volunteers each.
Part B will be conducted in 32 healthy male and female volunteers divided into 6 groups with 8 volunteers each.
Part C will be conducted in 6 healthy male and female volunteers.
Part D will be conducted in 24 healthy male and female volunteers.

The aim of this research is to find out how safe TA-46 is and how well it is tolerated when given to healthy volunteers. TA-46 has not been administered to people before. It has been tested in the laboratory and also on animals. TA-46 is tested in various strengths.

It will also be investigated how quickly and to what extent TA-46 is absorbed and excreted in the body (this is called pharmacokinetics).

TA-46 will be compared with a placebo (part A and part B). A placebo is a substance with no active ingredient, a 'fake' medicine.

Study design

This is a single-center, randomized, double-blind, placebo-controlled, parallel-group study in 70 healthy male and female volunteers.
The duration of the study for an individual volunteer is 8, 12, or 10 weeks respectively for Part A, Part B, or Part C.

For Part A, the study consists of 1 period in which the volunteer will stay in the PRA research center at the location of the Martini Hospital for 5 days (4 nights) . This is followed by 6 short visits to the research center. These short visits take place on Day 5 and 8, 10, 12, 14 and 22 (Day 22 is applicable for Group A5 only and only if the volunteers of this group agree upon attending the additional visit)

For Part B the study consists of 7 periods: in period 1 and 7 the volunteer will stay for 6 days (5 nights) in the PRA research center at the location of the Martini Hospital. This is followed by 5 short periods during which the volunteer will stay in the research center for 1 night. This is followed by 4

short visits to the research center. These short visits take place on Day 31, 33, 35 and 39.
For Group B3: the volunteers will stay 5 days (4 nights) for period 7 and period 7 is followed by 5 short visits to the research center. These short visits take place on Day 30, 33, 36, 38 and 46.

For Part B3-B6 the study consists of 2 periods of 5 days (4 nights). Furthermore there will be 2 short periods during which the volunteer will stay in the research center for 1 night.

For Part C the study will consist of 2 periods during which the volunteers will stay in the PRA research center at the Martini Hospital location for 5 days (4 nights). In each period this will be followed by 5 days during which you will visit the research center for a short visit. These short visits will take place on Days 6, 9, 12, 16, and 22.

For Part D the study will consist of 1 period during which the volunteers will stay in the research center for 5 days (4 nights). This will be followed by short visits on 6 days. These will take place on Days 5, 8, 10, 12, 14 and 22.

Intervention

Part A: Each group consists of 8 volunteers with 6 subjects receiving TA-46 as a subcutaneous injection / infusion and the 2 subjects receiving a single dose placebo.
Part B: Each group consists of 8 volunteers with 6 subjects receiving TA-46 as multiple doses (1 time per week for 4 weeks) as a subcutaneous injection / infusion and 2 subjects receiving placebo as multiple doses.
Part C: The study will consist of 2 periods during which the volunteers will receive TA-46 once per period. TA-46 will be administered as 2 different preparations with the same dose of TA-46 and these preparations will be given under the skin (subcutaneous) in the abdomen as 1-2 injection(s) for one preparation and an infusion for the other preparation. The duration of the infusion will depend on the volume to be administered, but will not exceed a period of 1 hour.
Part D: The study will consist of 1 period during the volunteers will receive which TA-46 (as the 120 mg/ml formulation) as a single dose. TA-46 will be given under the skin (subcutaneous) in the abdomen as an infusion.

Study burden and risks

As TA-46 will be administered to humans for the first time in this study, side effects of TA-46 in humans have not been reported to date. However, TA-46 is specifically developed for children with abnormal growth as result of an alteration in cartilage cells accountable for the growth of long bones. These cells have disappeared in adulthood hence we expect no effect on the volunteers

growth. TA-46 has been studied in mice and monkeys and a proportion of the animals developed antibodies. It is possible that the volunteer may develop antibodies against TA-46. Based on experience with TA-46 it is not expected that the presence of these antibodies will have consequences for the volunteers health. In mice TA-46 often caused an allergic reaction. Allergic reactions are seen often in mice, when human proteins like TA-46 are recognized as foreign by their immune system. Since TA-46 has the potential to induce immune reactions, the volunteer will be monitored for this, though such reactions are not expected. In some monkeys receiving 30 and 100 mg/kg TA-46, transiently swollen eyelids were seen. Because of the important role of FGFR3 in wound healing of the skin, in phosphate levels and in vitamin D levels, you will be monitored for changes in these as well.

Infection, pain, minor bleedings, possibly an infection.

Contacts

Public
Therachon SAS

Route des Lucioles 2000
Biot 06410
FR
Scientific
Therachon SAS

Route des Lucioles 2000
Biot 06410
FR

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Elderly (65 years and older)

Inclusion criteria

- healthy male or female subjects
- female volunteers sterilized or post-memopausal
- 21-55 yrs, inclusive
- BMI: 18.0-28.0 kg/m2, inclusive
- non-smoking or light smokers (smoking not allowed in clinic)

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:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	19-01-2018
Enrollment:	102
Type:	Actual

Ethics review

Approved WMO Date:	09-01-2018
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	18-01-2018
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	05-03-2018
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	30-05-2018
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	28-06-2018
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	06-08-2018
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	15-08-2018
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO	

Date:	13-09-2018
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	20-09-2018
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	10-01-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	11-01-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	15-05-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	22-05-2019
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	EUCTR2017-003596-55-NL
CCMO	NL64225.056.17