A phase I randomized, double-blind, placebo-controlled, multiple ascending dose study to evaluate the safety, tolerability and pharmacokinetics of NPT189 in healthy subjects

Published: 05-02-2019
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Ethical review	Approved WMO
Status	Completed
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON48151

Source
ToetsingOnline

Brief title
Study to evaluate the safety, tolerability and PK of NPT189

Condition

- Other condition

Synonym
Amyloidosis

Health condition

Amyloïdose

Research involving
Human

Sponsors and support

Primary sponsor: Proclara Biosciences, Inc.
Source(s) of monetary or material Support: Farmaceutische industrie

Intervention

Keyword: NPT189, PK

Outcome measures

Primary outcome

- To evaluate the safety and tolerability of repeated IV infusions of NPT189

Secondary outcome

- To evaluate the PK profile of NPT189 after repeated IV infusions

Study description

Background summary

NPT189 is a new compound that may eventually be used for the treatment of amyloidosis. Amyloidosis is a group of rare diseases characterized by a buildup of abnormal proteins, called amyloids, in different organs. These proteins have a somewhat different structure which allows them to stick together and makes it difficult for the body to remove them. This often causes problems in the organs in which these proteins are deposited. There are different types of amyloidosis, depending on the type of amyloid and where in the body the buildup occurs. General symptoms include changes in skin color, severe fatigue, joint pain, shortness of breath, severe weakness and tingling and numbness in legs and feet. There is currently no cure for amyloidosis, and treatments only slow the development of the disease and manage the symptoms. Especially when amyloidosis affects the heart and kidneys it can be deadly. NPT189 binds to these amyloid proteins and is being studied to understand whether it can suppress the buildup of amyloid in organs and break up these amyloid proteins so they can be cleared from the body.

Study objective

The purpose of this study is to investigate how safe the new compound NPT189 is and how well it is tolerated when it is administered to healthy volunteers. NPT189 has been administered to humans before. It has also been previously tested in the laboratory and on animals. NPT189 will be tested at various dose levels.

The study will also investigate how quickly and to what extent NPT189 is metabolized and eliminated from the body. In addition, the effect of NPT189 on the body will be investigated.

The effects of NPT189 will be compared to the effects of a placebo.

Study design

The study will consist of 5 periods in the research center during which the volunteer will stay in the research center for 4 days (3 nights). After the 5th period the volunteer will return to the research center for 4 short visits. These short visits will take place on approximately Day 35, 42, 56 and 84.

Day 1, 8, 15, 22 and 29 are the days of administration of the study compound. The volunteer is expected at the research center at 10:00 h in the morning prior to the day of each administration of the study compound. The volunteer will leave the research center on the 3rd day after drug administration.

NPT189 or placebo will be given as an intravenous infusion (solution of the compound that will be administered directly in a blood vessel), once per period. The infusion will take about an hour.

Whether the volunteer will receive NPT189 or placebo will be determined by chance. Per group, 6 volunteers will receive NPT189 and 2 volunteers will receive placebo. Neither the volunteer, nor the responsible doctor knows if NPT189 or placebo will be administered; we call this a double-blinded study. However, if it is important for the volunteers health, for example in case of a serious side effect, this information can be looked up during the study.

For safety reasons, in each group initially 2 volunteers will receive the study compound. One volunteer will receive NPT189, and 1 volunteer will receive placebo. After administration, the safety and tolerability of the study compound in these 2 volunteers will be closely monitored. If there are no concerns about the safety and tolerability 48 hours after administration, then the remaining 6 volunteers (5 will receive NPT189 and 1 will receive placebo) will receive the study compound.

Please refer to the table below to see the planned dose levels for each group. The doses of Groups 2 and 3 can be adjusted based on the results of the previous group(s). However, the dose will not be lower than 2.0 mg/kg and not higher than 12.5 mg/kg. The dose for the next group will only be increased if

the lower dose of the previous group was found to be well tolerated and in case of no objection by the Medical Research Ethics Committee. The study will be discontinued if, in the opinion of the investigators, unacceptable side effects appear.

Group Dose
1 NPT189 2.0 mg/kg or placebo
2 NPT189 5.0 mg/kg or placebo*
3 NPT189 12.5 mg/kg or placebo*
* In case the dose level will be lower or higher than planned, you will be informed verbally.

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Study burden and risks

As multiple doses of NPT189 have not been administered to humans there could be unknown side effects. In humans who received a single dose of NPT189 up to 25 mg, NPT189 was well-tolerated.

Monkeys who received multiple doses of NPT189 showed no adverse effects with respect to, for example body weight, appetite and clinical blood tests. Some skin irritations have been observed in monkeys at the site of the infusion after repeated infusions, but these resolved without the need for treatment.

It is possible that the volunteer has a reaction to NPT189 during or after its administration, such as nausea, decreased blood pressure, difficulty breathing or a rash. The volunteer should immediately contact the investigator if you develop nausea, vomiting, skin reactions, or breathing difficulties.

The study compound may also have side effects that are still unknown.

Possible discomforts due to procedures

Drawing blood and/or insertion of the indwelling cannula (tube in an arm vein) may be painful or cause some bruising.

In total, we will take about 400 milliliters (mL) of blood from the volunteer.

To make a heart tracing, electrodes (small, plastic patches) will be pasted at specific locations on the volunteer arms, chest and legs.

Contacts

Public
Proclara Biosciences, Inc.

Bolton Street 85
Cambridge 02140
US
Scientific
Proclara Biosciences, Inc.

Bolton Street 85
Cambridge 02140
US

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

- healthy males and females
- 18-65 years, inclusive
- Weight >= 45 kg and <= 120 kg with a BMI of 18.0-32.0 inclusive

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:	Completed
Start date (anticipated):	12-02-2019
Enrollment:	24
Type:	Actual

Ethics review

Approved WMO Date:	05-02-2019
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	11-02-2019
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	13-09-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	01-10-2019
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	EUCTR2019-000323-41-NL
CCMO	NL68923.056.19

Study results

Date completed: 27-06-2019

Results posted: 26-10-2021

Summary results
Trial ended prematurely

First publication
04-11-2019