A Phase 1 Randomized, Double-Blind, Placebo-Controlled, Single Ascending Dose Study to Evaluate the Safety, Tolerability and Pharmacokinetics of NPT189 in Healthy Subjects

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

Summary

ID

NL-OMON46311

Source
ToetsingOnline

Brief title
Phase 1 Single Ascending Dose Study Evaluating NPT189 in Healthy Volunteers

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 a single IV infusion of NPT189.

Secondary outcome

To evaluate the pharmacokinetics (PK) of a single IV infusion of NPT189.

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 prevents the body from removing these proteins. 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 your heart and kidneys it can be deadly. NPT189 binds to these amyloid proteins and is thought to suppress the buildup of amyloid in organs and is thought to 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

when it is administered to healthy subjects. NPT189 has not been administered to humans before. It has been previously tested in the laboratory and on animals. NPT189 will be tested at various dose levels.

It will also be investigated how quickly and to what extent NPT189 is absorbed and eliminated from the body (pharmacokinetics).

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

Study design

The study will consist of 1 period during which the volunteer will stay in the research center in Groningen, location Martini Hospital for 4 days (3 nights). This will be followed by 3 days during which the volunteer will visit the research center for a short visit. These short visits will take place on Day 7, 14 and 28.

Day 1 is the day of administration of the study compound. The volunteer is expected at the research center at 14:00 h in the afternoon prior to the day of administration of the study compound (Day -1). The volunteer will leave the research center on Day 3 of the study.

During the short visits on Day 7, 14 and 28 of the study a physical examination will be done including measurement of blood pressure, heart rate, number of breath per minute and body temperature, a heart trace (on Day 7 only) and a number of blood tests. The volunteer will also be asked about any possible adverse effects and medication use.

On Day 49 of the study volunteers health will be checked for the last time.

Intervention

NPT189 and placebo will be given as an intravenous infusion (solution of the compound that will be administered directly in a blood vessel). 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, meaning that the volunteer will have 75% chance to receive NPT189 and 25% chance to receive placebo. Neither the volunteer, nor the responsible doctor knows if NPT189 or placebo will be dosed; *the study is blinded*. However, if it is important for volunteers health, for example in case of a serious adverse event, this information can be looked up during the study.

Please refer to the table below to see the planned dose levels for the groups. The dose for the groups 2 to 5 will only be increased if the lower dose of the previous group was found to be well tolerated and in the case of no objection by the Medical Research Ethics Committee. The investigation will be discontinued if, in the opinion of the investigators, unacceptable adverse effects appear. The doses of Groups 2 to 5 can be adjusted based on the results of the previous group(s). The planned starting dose is 2.0 mg and the dose will not be higher than 30.0 mg.

Verblijf (Dag -1 tot 3)

Group 1
Day 1 (Infusion): NPT189 0.2 mg/kg or placebo
Day 7, 14, en 28: Follow-up visit
Day 49: Last follow-up visit

Group 2
Day 1 (Infusion): NPT189 0.5 mg/kg or placebo
Day 7, 14, en 28: Follow-up visit
Day 49: Last follow-up visit

Group 3
Day 1 (Infusion): NPT189 1.5 mg/kg or placebo
Day 7, 14, en 28: Follow-up visit
Day 49: Last follow-up visit

Group 4
Day 1 (Infusion): NPT189 4.5 mg/kg or placebo
Day 7, 14, en 28: Follow-up visit
Day 49: Last follow-up visit

Group 5
Day 1 (Infusion): NPT189 12.0 mg/kg or placebo
Day 7, 14, en 28: Follow-up visit
Day 49: Last follow-up visit

Group 5
Day 1 (Infusion): NPT189 25.0 mg/kg or placebo
Day 7, 14, en 28: Follow-up visit
Day 49: Last follow-up visit

Each group will have 3 separate dosing groups. In the first dosing group only 2 volunteers will be dosed first. One volunteer will receive NPT189 and one volunteer will receive placebo. In Group 1 and 2 these volunteers will be continuously monitored during the first 8 hours following dosing for safety and tolerability (presence of side effects). If there are no medical concerns in the first 24-48 hours, the remaining volunteers will be dosed in 2 separate

dosing groups of 3 volunteers each approximately 24 hours apart. The volunteers of each of the following dosing group will be closely monitored for safety and tolerability during the first 24 hours following dosing. If there are no medical concerns, the volunteers in the next dosing group will be dosed.

Study burden and risks

The study compound may cause side effects.

As NPT189 will be administered to humans for the first time in this study, therefore, side effects of NPT189 in humans have not been reported to date. However, NPT189 has been studied in animals.

Monkeys who received multiple doses of NPT218 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 volunteer develop nausea, vomiting, skin reactions, or breathing difficulties.

Other, as yet unknown risks, are also possible as NPT-189 has not previously been administered to humans.

Tests
Drawing blood and/or insertion of the indwelling cannula may be painful or cause some bruising.

In total, we will take about 122 milliliters of blood from the volunteer. This amount does not cause any problems in adults. To compare: a blood donation involves 500 ml of blood being taken each time.

To monitor the heart rate, electrodes (small, plastic patches) will be pasted at specific locations on the chest and abdomen. Prolonged use of these electrodes can cause skin irritation (rash and itching).

Procedures: pain, minor bleeding, bruising, possible infection.

Contacts

Public
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Scientific
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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 or female subjects
-18-65 yrs, inclusive
-BMI: 18-32 kg/m2, inclusive
-Weight >= 45kg and <= 120kg
-Non-smoking

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):	02-07-2018
Enrollment:	48
Type:	Actual

Ethics review

Approved WMO

Date:	21-06-2018
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Approved WMO

Date:	29-06-2018
Application type:	First submission
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	EUCTR2018-001713-33-NL
CCMO	NL66251.056.18