First-in-human, randomized, double-blind, placebo-controlled, single ascending dose study to evaluate the safety, tolerability, pharmacokinetic and pharmacodynamic effects of Apta-1.

Published: 29-09-2022
Last updated: 25-03-2025

Part ATo evaluate the safety and tolerability of single and split intravenous doses of Apta-1 in healthy volunteers.Part BTo evaluate the safety and tolerability of split intravenous doses of Apta-1 after LPS infusion in healthy volunteers.

Ethical review	Approved WMO
Status	Completed
Health condition type	Immune disorders NEC
Study type	Interventional

Summary

ID

NL-OMON51837

Source
ToetsingOnline

Brief title
First in human study of Apta-1

Condition

- Immune disorders NEC

Synonym
blood poisoning, Sepsis

Research involving
Human

Sponsors and support

Primary sponsor: Aptahem AB
Source(s) of monetary or material Support: Biotechnology company Aptahem AB

Intervention

Keyword: Aptamer, FIH, LPS, Sepsis

Outcome measures

Primary outcome

Parts A+B

• Treatment-related (serious) adverse events ([S]AEs).

• Concomitant medication.

• Vital signs: Systolic blood pressure (mmHg), diastolic blood pressure (mmHg),

heart rate (bpm), respiratory rate (bpm), body temperature (°C).

• Clinical laboratory tests: hematology, coagulation, blood chemistry and

urinalysis as listed in section 6.1.5.

• Electrocardiogram (ECG) parameters (Heart Rate (HR) (bpm), PR, QRS, QT,

QTcF).

Secondary outcome

Part A

Single intravenous dose administration (cohort 1):

o AUCinf, AUCinf(%extrap), AUClast, AUC0-1h, CL, Cmax, t1/2, tmax, tlast, Vz.

o Dose-normalized PK parameters: AUCinf, AUClast, Cmax.

Single intravenous dose with split (two equal doses) administration (cohort

2-6):

o AUC0-1h, AUCinf, AUCinf(%extrap), AUClast, CL, Cmax-dose1, Cmax-dose2,

t1/2, tmax, tlast, Vz.

o Dose-normalized PK parameters on total dose: Cmax, AUCinf, AUClast

o Dose-normalized PK parameters on separate dose: AUC0-1h, Cmax-dose1,

Cmax-dose2

Part B

Single intravenous dose with split (two equal doses) administration:

o AUC0-1h, AUCinf, AUCinf(%extrap), AUClast, CL, Cmax-dose1, Cmax-dose2, t1/2,

tmax, tlast, Vz.

o Dose-normalized PK parameters on total dose: AUCinf, AUClast

o Dose-normalized PK parameters on separate dose: AUC0-1h, Cmax-dose1,

Cmax-dose2

Study description

Background summary

Sepsis, including septic shock, is a dysregulated immunological host response to infection leading to life-threatening organ dysfunction. It is a worldwide leading cause of critical illness and mortality and, with its increasing incidence, a major public health concern accounting for more than $20 billion (5.2%) of total United States hospital costs in 2011. Despite decades of clinical experience and research, we still lack approved treatments specifically targeting sepsis or septic shock. This condition remains a significant challenge as it frequently results in high morbidity and mortality. Currently applied treatments exist of supportive care, for instance fluid resuscitation, antibiotics, vasopressors, and organ replacement therapy. Apta-1, an aptamer which is a mixture of single-stranded ribonucleic acid (RNA)-oligonucleotides, is proposed as a new treatment for sepsis and septic shock. This first-in-human study will primarily assess the safety and tolerability and pharmacodynamic activity of Apta-1 in healthy volunteers. As

additional objective, its effects on systemic LPS challenges, resulting in a systemic inflammatory response, will be evaluated.

Study objective

Part A
To evaluate the safety and tolerability of single and split intravenous doses of Apta-1 in healthy volunteers.

Part B
To evaluate the safety and tolerability of split intravenous doses of Apta-1 after LPS infusion in healthy volunteers.

Study design

This is a first-in-human, randomized, double-blind, placebo-controlled, single, and split ascending dose study, consisting of two parts (part A and part B).

Part A - Safety, tolerability, pharmacokinetics and pharmacodynamic effects of a single dose of Apta-1
Part B - Exploration of safety, tolerability, pharmacokinetics and pharmacodynamic effects of a single dose of Apta-1 with LPS as a challenge agent.

Intervention

Apta-1 or placebo

Study burden and risks

This is a study in healthy volunteers, so no direct benefit is expected for participants. For a structured risk assessment see Section 10 of the protocol. Healthy males and female, women of childbearing potential (WOCBP) and women of non-childbearing potential (WONCBP) volunteers are recruited for this study, which is deemed an appropriate population for this first-in-human study. The in- and exclusion criteria (see section 4.2 and 4.3 of the protocol) have been defined to minimize associated risks to the mechanism of action of the IMP and/or study procedures.

Contacts

Public
Aptahem AB

Norra Vallgatan 58
Malmo 211 22
SE
Scientific
Aptahem AB

Norra Vallgatan 58
Malmo 211 22
SE

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

1. Has the ability to communicate well with the Investigator in the Dutch language and is willing and able to comply with all study procedures and give written informed consent prior to any study-mandated procedure.
2. Healthy male and female subjects,18 to 55 years of age, inclusive, at screening.
3. Body mass index (BMI) between 18 and 30 kg/m2 and with a weight between 50 and 100 kg, both inclusive, at screening.
4. Female subjects of childbearing potential and male subjects who have sexual intercourse with a woman of childbearing potential must be willing to practice effective contraception (see paragraph 4.5.1.) during the study and be willing and able to continue contraception for respectively at least 180 days (females) and 90 days (males) after their last dose of study treatment.
Women of childbearing potential are defined as all women physiologically capable of becoming pregnant, unless they meet one of the following conditions:
• Post-menopausal: 12 months of natural (spontaneous) amenorrhea or 6 weeks after surgical bilateral oophorectomy with or without hysterectomy;
• Post-hysterectomy.

Exclusion criteria

1. Evidence of any active or chronic disease or condition (e.g. history of sepsis, cardiovascular disease, syncope or malignancy) that could interfere with, or for which the treatment of might interfere with, the conduct of the study, or that would pose an unacceptable risk to the subject in the opinion of the investigator (following a detailed medical history, physical examination, vital signs (systolic and diastolic blood pressure, pulse rate, body temperature) and 12-lead electrocardiogram (ECG)). Minor deviations from the normal range may be accepted, if judged by the Investigator to have no clinical relevance.
2. Clinically significant abnormalities, as judged by the investigator, in laboratory test results (including hepatic and renal panels, complete blood count, chemistry panel and urinalysis). In the case of uncertain or questionable results, tests performed during screening may be repeated before randomization to confirm eligibility or judged to be clinically irrelevant for healthy subjects.
3. Hemorrhagic diathesis (e.g. nose bleeds, mucosal bleedings, easy bruising, gastrointestinal bleeding, menorrhagia), as judged by the investigator.
4. Use of any prescription or OTC medications, antibiotics, NSAIDs (such as ibuprofen), aspirin, anti-platelet therapy, anti-coagulation therapy, prophylactic and therapeutic LMWH or un-fractioned heparin within 4 weeks, or 5 half-lives (whichever is longer), prior to first IMP administration. Exception for prescription contraceptives.
5. Any active or ongoing chronic inflammatory or infectious disease including periodontitis except for common viral or fungal skin infections such as plantar warts or athlete*s foot.

Additional criteria for part B:
1. Previous participation in a systemic (i.v./inhaled) LPS challenge trial or prior exposure to systemic endotoxin within a year before LPS administration in this study.
2. Significant risk or history of cardiac failure, overfilling and/or developing edema.
3. Estimated glomerular filtration rate (eGFR) of <90mL/min/1.73m2.

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):	01-12-2022
Enrollment:	72
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Apta-1
Generic name:	Not appicable

Ethics review

Approved WMO Date:	29-09-2022
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Approved WMO Date:	10-11-2022
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Approved WMO Date:	19-07-2023
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	EUCTR2022-002473-28-NL
CCMO	NL81960.056.22

Study results

Date completed: 04-03-2024

Results posted: 09-07-2024

Summary results
Trial ended prematurely

First publication
08-07-2024

URL result
URL
Type
int
Naam
M2.2 Samenvatting voor de leek
URL

Internal documents
File