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First in human study of Apta-1

Submission date 23/11/2022	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol
Registration date 25/11/2022	**Overall study status** Completed	[_] Statistical analysis plan [_] Results
Last Edited 27/08/2025	**Condition category** Other	[_] Individual participant data [_] Record updated in last year

Plain English summary of protocol

Background and study aims
Under normal circumstances, the immune system fights off pathogens and prevents inflammation. In sepsis (the body's extreme response to an infection), for reasons still unknown, the immune system has an overwhelming and overactive response to a pathogen. This reaction is so violent that it can lead to tissue and organ damage and it can be so severe that it can kill patients.
Sepsis is also known as blood poisoning. Typical symptoms of sepsis are fever, altered mental status, increased heart rate and low blood pressure. In severe cases, this can lead to life-threatening low blood pressure. This condition is called septic shock.

Apta-1 is an investigational drug being developed for the treatment of sepsis and septic shock. It binds to thrombin through the heparin binding sites with a high affinity and specificity. Thrombin plays a role in the immune response and in the blood clotting system. Once bound to thrombin, Apta-1 is supposed to inhibit the overwhelming, overactive immune response seen in sepsis. Apta-1 has not been administered to humans before.

This first-in-human study will primarily evaluate the safety and tolerability, pharmacokinetics, and pharmacodynamic activity of Apta-1 in healthy volunteers. As an additional exploratory objective, its effects on systemic LPS challenges, resulting in a systemic inflammatory response, will be evaluated.

Who can participate?
Healthy male and female subjects, 18 to 55 years of age.

What does the study involve?
Part A:
• Screening: 42 days prior day of dosing (Day 1)
• Day -1 up to day 2 (IMP administration on Day 1. In cohort 1, Apta-1 will be administered as a single intravenous infusion. In cohorts 2-6, Apta-1 will be administered as a split dose infusion).
• FU: day 6-10

Part B:
• Screening: 42 days prior day of dosing (Day 1)
• Day -1 up to 2 (LPS administration and Apta-1 administration on Day 1. Apta-1 will be

administered as intended in a clinic setting, i.e. using the split dose infusion).
• FU: day 6-10

What are the possible benefits and risks of participating?
Subjects do not benefit from taking part in this study. But they do help in the search for a better treatment for sepsis and septic shock. The risks consist of experiencing possible side effects of Apta-1 (including laboratory changes such as prolonged bleeding times), LPS (including fever, shivering, headache), and the study measurements (for example: taking a blood sample and inserting the intravenous cannulas can be a little painful or you could get a bruise as a result.).

Where is the study run from?
Centre for Human Drug Research (the Netherlands)

When is the study starting and how long is it expected to run for?
January 2022 to December 2023

Who is funding the study?
Aptahem AB (Sweden)

Who is the main contact?
Matthijs Moerland, PI, clintrials@chdr.nl

Contact information

Type(s)
Principal investigator

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Additional identifiers

Clinical Trials Information System (CTIS)
2022-002473-28

Protocol serial number
CHDR2201

Study information

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

Acronym
Apta-1

Study objectives
Apta-1 is proposed as new treatment for sepsis and septic shock. This first-in-human study will primarily evaluate the safety and tolerability, pharmacokinetics, and pharmacodynamic activity of Apta-1 in healthy volunteers. As additional exploratory objective, its effects on systemic LPS challenges, resulting in a systemic inflammatory response, will be evaluated.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 10/11/2022, Stichting Beoordeling Ethiek Biomedisch Onderzoek (stichting BEBO, Dr. Nassaulaan 109401 HK ASSEN, The Netherlands; +31 592405871; info@stbebo.nl), ref: NL81960.056.22

Primary study design
Interventional

Study design
A first-in-human randomized double-blind placebo-controlled single and split ascending dose study

Study type(s)
Treatment

Health condition(s) or problem(s) studied
First in human study, with healthy volunteers, for a compound targeting the treatment of sepsis and septic shock.

Interventions
Part A focusses on the safety, tolerability, pharmacokinetics and pharmacodynamic effects of Apta-1.
Part B (exploratory study part) explores the safety, tolerability, pharmacokinetics and pharmacodynamic effects of Apta-1 in a systemic LPS-challenged background.

Part A: Six dose levels of Apta-1 solutions for infusion 10mg/mL and corresponding matching placebo will be prepared. Apta-1/placebo will be administered intravenously to healthy volunteers.
Part A cohort 1: 15-minute intravenous infusion
Part A cohort 2-6: 2 x 15-minute intravenous infusion, 1 hour apart (thus total dose in 75 minutes)

LPS challenge:
LPS 2-minute intravenous infusion 30 minutes before Apta-1/placebo dosing.
NaCl 0.45%/Glucose 2.5% intravenous infusion 2 hours (750mL/h-IMP volume) prior to LPS dosing until 6 hours (150mL/h) after LPS dosing.

Part B: Two dose levels of Apta-1 solutions for infusion 10mg/mL and corresponding matching placebo will be prepared. The dose will be based on data from part A and will not exceed the highest administered dose in part A. The dose will be administered as split intravenous infusions. In part B, healthy subjects will be administered intravenous LPS 60 minutes before the start of the first infusion of IMP (on Day 1).
2 x 15-minute intravenous infusion, 1 hour apart (thus total dose in 75 minutes)

Duration of the follow-up for all study arms:
In-clinic period: Study Day -1 until Day 2 (dosing occurs on Day 1)
Follow-up visit: Study Day 6-10

Randomisation process:
The randomization code will be generated by a study independent unblinded statistician. The code will be kept strictly confidential. Sealed individual randomization codes, per subject and per treatment, will be placed in a sealed envelope with the label 'emergency decoding envelopes' in a safe cabinet at CHDR. The code will be broken after study closure for data analysis or if required for subject safety

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
Apta-1

Primary outcome(s)
1. Treatment-related (serious) adverse events measured by inquiry to the subjects throughout the study (at screening, continuous during in-clinic period and follow-up). If abnormalities are indicated by the subjects, the details (including complaints, starttime, stoptime, diagnose, seriousness, relatedness) of the event will be stored in the database.
2. Concomitant medication measured by inquiry to the subjects throughout the study (at screening, continuous during in-clinic period and follow-up). Concomitant medications initiated, stopped, up-titrated or down-titrated for an AE will be recorded with all details (including used drug, starttime, stoptime, indication, route of administration, dose) and will be stored in the database.
3. Vital signs measured by valuations of systolic and diastolic blood pressure, pulse rate, respiratory rate, and temperature will be performed throughout the study using a Dash 3000, Dash 4000, Dynamap 400 or Dynamap ProCare 400. Timepoints:
3.1. Part A cohort 1: at screening, on day -1, on day 1 pre-dose and at +15m, +30m, +45m, +1h, +2h, +4h, +8h, +24h, +30h after dosing, and follow-up.
3.2. Part A cohort 2-6 and part B: at screening, on day -1, on day 1 pre-dose and at +15m, +30m, +45m, +1h, +1h15m, +1h30m, +1h45m, +2h, +4h, +8h, +24h, +30h after dosing, and follow-up.
4. Clinical laboratory tests measured by haematology, coagulation, chemistry (including glucose), serology and urinalysis will be conducted by an external laboratory; the laboratory of the Leiden

University Medical Centre, using validated routine methodology. Timepoints:
4.1. Part A cohort 1: at screening, on day -1, on day 1 pre-dose and at +1h, +4h, +8h, +24h after dosing, and follow-up.
4.2. Part A cohort 2-6 and part B: at screening, on day -1, on day 1 pre-dose and at +1h, +2h, +4h, +8h, +24h after dosing, and follow-up.
5. Electrocardiogram parameters measured by ECGs will be obtained during the study using Marquette 2000/5500 and stored using the MUSE Cardiology Information System. The investigator will assess the ECG recording as 'normal', 'abnormal -not clinically significant', or 'abnormal -clinically significant' and include a description of the abnormality as required. The ECG parameters assessed will include heart rate, PR, QRS, QT, and QTcF (calculated using Fredericia's method). Timepoints:
5.1. Part A cohort 1: at screening, on day -1, on day 1 pre-dose and at +30m, +1h, +2h, +4h, +8h, +24h after dosing, and follow-up.
5.2. Part A cohort 2-6 and part B: at screening, on day -1, on day 1 pre-dose and at +30m, +1h, +1h30m, +2h, +4h, +8h, +24h after dosing, and follow-up.

Key secondary outcome(s)
PK-parameters (AUC0-1h, AUCinf, AUCinf(%extrap), AUClast, CL, Cmax-dose1, Cmax-dose2, t1/2, tmax, tlast, Vz) will be analysed by an external laboratory, the laboratory of Axolabs, using a validated AEX-HPLC method and dose-normalized PK parameters on total dose (AUCinf, AUClast, dose-normalizedPK parameters on separate dose: AUC0-1h, Cmax-dose1, Cmax-dose2) will be calculated by a pharmacometrician using non-compartmental analyses. Timepoints at which the blood samples for analysis are being drawn:
Part A cohort 1: on day 1 pre-dose and at +15m, +30m, +45m, +1h, +1h30m, +2h, +4h, +8h, +24h, +30h after dosing.
Part A cohort 2-6 and part B: on day 1 pre-dose and at +15m, +30m, +45m, +1h, +1h15m, +1h30m, +1h45m, +2h, +3h, +4h, +6h, +8h, +24h, +30h after dosing.

Completion date
31/12/2023

Eligibility

Key inclusion criteria
Applicable to part A and part B:
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 during the study and be willing and able to continue contraception for respectively at least 180 days (females) or 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:
4.1. Post-menopausal: 12 months of natural (spontaneous) amenorrhea or 6 weeks after surgical bilateral oophorectomy with or without hysterectomy;
4.2. Post-hysterectomy.

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Upper age limit
55 Years

Sex
All

Key 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/1.73m^2.

Date of first enrolment
01/12/2022

Date of final enrolment
31/10/2023

Locations

Countries of recruitment
Netherlands

Study participating centre
Centre for Human Drug Research
Zernikedreef 8
Leiden
Netherlands
2333 CL

Sponsor information

Organisation
Aptahem AB

Funder(s)

Funder type
Industry

Funder Name
Aptahem AB

Results and Publications

Individual participant data (IPD) sharing plan
This will only be made available upon reasonable request, since the data is personal subject data and confidential. Matthijs Moerland, PI, clintrials@chdr.nl

IPD sharing plan summary
Available on request