A Partially Double-Blinded Phase 1 Study to Assess the Safety, Tolerability and Pharmacokinetics of AST-004 as a Short Loading Intravenous infusion Followed by AST-004 as a Continuous Infusion in Healthy Adult Subjects.

Published: 21-02-2023
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Primary objective:• To evaluate the safety and tolerability profile of single intravenous doses of AST-004 given as a short loading intravenous infusion followed by a 6-hour continuous intravenous (IV) infusion in healthy adult subjects.Secondary...

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

Summary

ID

NL-OMON53360

Source
ToetsingOnline

Brief title
CS0398-230004 Astrocyte

Condition

- Other condition

Synonym
acute ischemic stroke

Health condition

cerebral infarction and traumatic brain injury

Research involving
Human

Sponsors and support

Primary sponsor: Astrocyte Pharmaceuticals Inc.
Source(s) of monetary or material Support: United States of America Department of Defense (DoD)

Intervention

Keyword: Pharmacokinetics, Safety, Tolerability

Outcome measures

Primary outcome

Efficacy is not being assessed in this study. The primary endpoints are the

safe and well tolerated administration of the study medication.

Secondary outcome

PK of AST-004 in plasma and CSF will be important in determining the dose of

the study medication to be used in Phase 2 trials and to be used in any future

Phase 1 studies. PK of AST-004 as well as identification of any major

metabolites in urine and plasma will be obtained.

Mechanistic and pharmacodynamic biomarkers of AST-004 will also be assessed in

the plasma and CSF including changes in cytokine levels.

Study description

Background summary

Astrocyte Pharmaceuticals Inc. is developing the small molecule, AST-004, as a

cerebroprotectant for treating patients with acute ischemic stroke (AIS), and other brain injuries including traumatic brain injury (TBI), concussion, and neurodegenerative disease. The proprietary, novel approach at Astrocyte Pharmaceuticals differs significantly from historical neuron-centric cerebroprotective attempts by focusing on a non-neuronal cell type, the astrocyte. Astrocytes have only recently received broader attention as an important cellular target for successful therapeutic research. AST-004 acts via a novel cerebroprotective mechanism, namely the activation of adenosine A3 receptors (A3R) expressed on astrocytes, leading to enhanced mitochondrial energy production, and the promotion of multiple intrinsic healing mechanisms. The small molecule AST-004 is blood-brain barrier (BBB) penetrant.
AST-004 is a promising cerebroprotectant therapeutic demonstrating significant efficacy in multiple preclinical models of AIS and with a favorable TI that warrants further investigation in human subjects.
See the IB for further information.

Study objective

Primary objective:
• To evaluate the safety and tolerability profile of single intravenous doses of AST-004 given as a short loading intravenous infusion followed by a 6-hour continuous intravenous (IV) infusion in healthy adult subjects.
Secondary objective:
• To characterize the PK profile of AST-004 in plasma, CSF and urine when given as a short loading intravenous infusion followed by a 6-hour continuous IV infusion.

Study design

This is an adaptive-design, Phase 1 safety-tolerability, and pharmacokinetic study, conducted in two study parts:
• Part 1: Single Partially Double-blinded Dose (SD) IV Load infusion followed by a 6-hour continuous infusion (CI)
• Part 2: Single Dose (SD) IV Load infusion followed by a 6-hour continuous infusion (CI) with periodic Cerebrospinal Fluid collection (CSF)

Intervention

AST-004 or matching placebo

Study burden and risks

Since the study is being executed in healthy volunteers, there are no anticipated benefits of the IMP.
There has been one study completed in healthy individuals. Up to now, 42 persons have been administered AST-004. The study drug was well tolerated and

there were no serious side effects identified. Side effects that were reported during this study are:
• Headache
• Neck and back stiffness
• Increase in liver blood test values. These values returned to normal when administration of the study drug was stopped.
• Increase in inflammatory marker values that returned to normal when administration of the study drug was stopped.
• Abnormalities in the heart tracing (ECG).
• Chills without fever
AST-004 can also have side effects that we do not yet know, and these could also be serious side effects.

Please see the overall benefit risk analysis in the CSP for further information.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age

Adults (18-64 years)

Inclusion criteria

1. Male or female subjects aged >= 18 to <= 65 years at the time of signing the informed consent form (ICF).
2. Body mass index (BMI) >= 18.0 and <= 30.0 kg/m2.
3. Weight of 50.0 kg - 100.0 kg.
4. Women of childbearing potential who agree to use a highly effective method of contraception for 3 months after the last dose of study drug or as per the local regulation.

Exclusion criteria

1. Presence of any contraindication to pharmacokinetic sampling, with particular attention to lumbar punction in Part 2 (e.g., possible raised intracranial pressure, thrombocytopenia or other bleeding diathesis, suspected spinal epidural abscess)
2. History of seizures other than clearly documented febrile seizure prior to 2 years of age, myoclonus or other movement disorders, periodic paralysis, unexplained loss of consciousness, structural neurological abnormalities, traumatic brain injury including concussion within the last three years, history of epilepsy, depression or suicidal ideation
3. Any clinically significant abnormality identified during pre-study (prior to dosing) on full physical examination, vital signs, laboratory tests, and ECG
4. Any laboratory value noted here: Hgb Neutrophils <1.5 x 10 9/L, Platelets ULN, Total Bilirubin >ULN,
may be up to 1.5x ULN if Direct Bilirubin is repeated x1 during the screening period.

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):	05-04-2023
Enrollment:	44
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Nap.
Generic name:	Nap.

Ethics review

Approved WMO Date:	21-02-2023
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	23-03-2023
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	EUCTR2023-000028-12-NL
CCMO	NL83655.056.23

Study results

Results posted: 29-12-2023

First publication
01-12-2023