A two-part, single dose, randomized, single-blinded, placebo controlled, phase I study to assess the safety and pharmacokinetics of oral MT1980 in healthy volunteers when dosed in the fasted state

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Ethical review	Approved WMO
Status	Completed
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON51342

Source
ToetsingOnline

Brief title
Safety and CSF sampling PK study of MT1980 vs placebo

Condition

- Other condition
- Neurological disorders NEC

Synonym
preventative treatment of a decline in brain functions after surgery

Health condition

preventative treatment of a decline in brain functions after surgery

Research involving
Human

Sponsors and support

Primary sponsor: Monument Therapeutics Limited
Source(s) of monetary or material Support: Pharmaceutical Industry

Intervention

Keyword: MT1980, pharmacokinetics, safety

Outcome measures

Primary outcome

To characterize the safety and tolerability of MT1980 in humans

Secondary outcome

- To provide information on the systemic bioavailability of study drug from a

single oral dose of MT1980

- To provide information on the amount of study drug in cerebrospinal fluid

(CSF) from a single oral dose of MT1980

- To provide information on the amount of study drug in CSF from a single oral

dose of MT1980

Study description

Background summary

MT1980 is being developed as a treatment for neuroinflammation (an inflammatory response in the brain and/or spinal cord). Much research has focused on the central role of neuroinflammation in the pathogenesis of many conditions relating to the CNS, including eg, traumatic brain injury, stroke, Alzheimer's

disease, post-operative cognitive decline (POCD)/perioperative neurocognitive disorder, and now even long-term cognitive side effects from severe acute respiratory syndrome corona virus 2 (SARS-CoV-2). Current anti-inflammatories do not easily cross the blood-brain barrier from the systemic circulation to the brain, making neuroinflammation a difficult condition to treat.

Study objective

In this study we will investigate how safe the new compound MT1980 is and how well it is tolerated when it is used by healthy participants.

We also investigate how quickly and to what extent MT1980 is absorbed, transported, and eliminated from the body. In addition, we look at the amount of drug in cerebrospinal fluid (CSF, the liquid surrounding the brain and the spinal cord) and in blood plasma after MT1980 intake.

We compare the effects and safety of MT1980 with the effects of a placebo.

Study design

The study will take a maximum of about 4.5 weeks from the screening until the follow-up visit.

Screening -> Between Day -21 and Day -1

Treatment Part 1 and 2 - Arrival -> Day -1
Treatment Part 1 and 2 - In-house stay -> Day -1 up to Day 4
Treatment Part 1 and 2 - Departure -> Day 4

Follow-up call -> Between Day 7 and Day 9

Either MT1980 or placebo as oral capsules with 240 milliliters (mL) of (tap) water.

Intervention

Part 1: once 140 mg MT1980 or placebo

Part 2: once between 25 mg and 250 mg MT1980 based on the results from Part 1 or placebo

Study burden and risks

Blood draw
Drawing blood may be painful or cause some bruising. The use of the indwelling cannula (a tube in a vein in the arm) can sometimes lead to inflammation,

swelling, hardening of the vein, blood clotting, and bleeding in the environment (bruising) of the puncture site. In some individuals, a blood draw can sometimes cause pallor, nausea, sweating, low heart rate, or drop in blood pressure with dizziness or fainting.

In total, we will take about 82 milliliters (mL) of blood from screening to follow-up. This amount does not cause any problems in adults. To compare: a blood donation involves 500 mL of blood being taken each time. If the investigator thinks it is necessary for the safety of a participant, extra samples might be taken for possible additional testing. If this happens, the total amount of blood drawn may be more than the amount indicated above.

Heart tracing
To make a heart tracing, electrodes (small, plastic patches) will be placed on arms, chest and legs. Prolonged use of these electrodes can cause skin irritation (rash and itching).

Collection of CSF via lumbar puncture

Procedure
The collection of up to 2 mL CSF is done via lumbar puncture by placing a needle into the lower back, where there is the CSF. CSF will be collected at 2 timepoints (Part 1) or 1 timepoint (Part 2), after administration of the study compound. The anesthesiologist will apply numbing medication to minimize any pain or discomfort from the needle. If needed, a syringe may be used to gently aspirate CSF.

Risks during the procedure
CSF collection via lumbar puncture may cause pain (particularly in the back), nausea (feeling sick), headache, discomfort, bruising, stiffness, fainting, allergic reactions, and, rarely, an infection at the site of the needle insertion. Occasionally, during needle insertion, a nerve in the spinal cord (spinal nerve) might be touched, causing pain to spread to the buttock or leg. This usually lasts only a short time. Rarely, participants may experience bleeding into the spinal canal, or a spinal canal nerve damage.

Meningitis (an acute inflammation of the protective membranes covering the brain and spinal cord, known collectively as the meninges) is a rare potential side effect of CSF collection. This could cause headache, photophobia (abnormal intolerance to light), neck stiffness, and pyrexia (increase in body temperature). If this happens, routine standard of care for the management of suspected bacterial meningitis must be implemented (for example, antibiotic treatment).

What is allowed during the procedure
Subjects will be asked to lie down on their back with limited movement for approximately 1 hour after the lumbar puncture. If they develop a headache,

they will be encouraged to lie in a comfortable position.

Risks after the procedure
Headache after lumbar puncture often occurs, especially in younger people, and can be accompanied by dizziness, nausea, and ringing in the ears (tinnitus). The symptoms can persist for several days up to 2 weeks after removal of the needle. The cause of the headache is probably the leakage of CSF. The headache is usually in the front and back of the head and is less when one lies down. The headache usually goes away on its own within 7 days and can be reduced with rehydration, paracetamol, and caffeine. In severe cases, it may be decided to close the hole with an injection of their own blood at the site where the needle was inserted in the back. This treatment is called *blood patch*.

Coronavirus test
Samples for the coronavirus test will be taken from the back of the nose and throat using swabs. Taking the samples only takes a few seconds, but can cause discomfort and can give an unpleasant feeling. Taking a sample from the back of the throat may cause them to gag. When the sample is taken from the back of the nose, they may experience a stinging sensation and the eyes may become watery.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1. Sex: male or female; females may be of childbearing potential, of nonchildbearing potential, or postmenopausal.
2. Age: 18 to 65 years, inclusive, at screening.
3. Body mass index: 18.0 to 30.0 kg/m2, inclusive, at screening.
4. Weight: >=50 kg and <=100 kg, inclusive, at screening.
5. At screening, females must not be pregnant or lactating, or must be of nonchildbearing potential (either surgically sterilized or physiologically incapable of becoming pregnant, or at least 1 year postmenopausal [follicle stimulating hormone testing]); nonpregnancy will be confirmed for all females by a negative serum pregnancy test at screening, and admission.

Exclusion criteria

1. Previous randomization in the current study.
2. Participation in a drug study within 30 days prior to drug administration in the current study. Participation in 4 or more other drug studies in the 12 months prior to drug administration in the current study.
3. Subjects who are contract research organization (CRO) employees, or immediate family members of a clinical research center or Sponsor employee.
4. History of drug or alcohol dependency or abuse (including soft drugs like cannabis products) within the 2 years prior to screening.
5. Average intake of more than 24 units of alcohol per week (1 unit of alcohol equals approximately 250 mL of beer, 100 mL of wine, or 35 mL of spirits).

Study design

Design

Study type:	Interventional
Intervention model:	Other
Allocation:	Randomized controlled trial

Masking:	Single blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	31-05-2022
Enrollment:	26
Type:	Actual

Ethics review

Approved WMO Date:	26-04-2022
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Approved WMO Date:	27-05-2022
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Approved WMO Date:	29-07-2022
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	EUCTR2022-000252-11-NL
ClinicalTrials.gov	NCT05429840
CCMO	NL81302.056.22

Study results

Date completed: 04-10-2022

Results posted: 20-03-2023

First publication
07-02-2023