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Study to evaluate the concentrations and safety /tolerability of IV DM199 when administered in a PVC bag

Submission date 07/03/2023	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [_] Record updated in last year
Registration date 17/03/2023	**Overall study status** Completed	
Last Edited 11/07/2023	**Condition category** Other	

Plain English summary of protocol

Background and study aims
DiaMedica Therapeutics Inc. is conducting this study to test how a new type of intravenous (IV) bag material may affect the amount of an investigational drug called DM199 participants may receive, and to measure any side effects they may experience. DM199 is an investigational drug, or experimental treatment, being researched to potentially treat patients with acute ischemic stroke (when the blood supply to part of the brain is interrupted or reduced, preventing brain tissue from getting oxygen and nutrients), kidney disease patients, and potentially patients with other conditions in the future.
The main aims of this study are:
1. To measure the amount of DM199 a study participant receives by taking small blood samples to measure how much drug is present in their blood at different times as the drug is being given to them and after it's been given. This is also known as pharmacokinetics (PKs).
2. To measure whether a study participant's body has an immune response (this is also known as immunogenicity - like when the body fights off a cold) to DM199
3. To measure any side effects that are seen

Who can participate?
Part A: Healthy volunteers over the age of 18 years
Part B: Patients over the age of 18 years who have recently taken a drug called an ACE inhibitor

What does the study involve?
Participants will come to the hospital to undergo tests to see if they may qualify for this study. If a participant qualifies, they will be required to stay at a clinical research unit/hospital for 3 consecutive nights and 4 days. During their stay, participants will receive a single dose of DM199 into a vein. In addition, participants will be monitored for side effects, and this includes having their vital signs checked, electrocardiograms (ECGs) to check their heart rhythm, and their blood drawn for lab testing at various points during their stay.

What are the possible benefits and risks of participating?
There are no direct medical benefits to those taking part. The information gathered in this study

may help to ensure that the appropriate dose of DM199 is administered to patients with varying diseases in the future.
DM199 is an investigational drug in research, and not all side effects are known at this time. Participants may have none, some, or all of the effects listed below, and they may be mild, moderate or severe. The likely side effects could be headache, constipation, and oral candidiasis (yeast infection in the mouth and throat). Other frequent side effects could include dizziness, feeling faint or lightheaded, orthostatic hypotension (which means a drop in blood pressure that may make someone feel faint when they stand up), fever, pain, low potassium levels in the blood, weight loss, depression, rash, eye disorders, nausea, vomiting, and/or diarrhoea.

Where is the study run from?
Scientia Clinical Research Limited (Australia)

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

Who is funding the study?
DiaMedica Therapeutics, Inc. (USA)

Who is the main contact?
Sandra Kisor, skisor@diamedica.com

Contact information

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Principal investigator

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Additional identifiers

Protocol serial number
DM199-2023-001

Study information

Scientific Title
A Phase 1C, open-label, single ascending dose study to evaluate the safety, tolerability, and pharmacokinetics of DM199 administered IV with PVC bag in adult healthy participants and adults recently taking ACE inhibitors

Study objectives
The objective of this study is to evaluate the safety, tolerability, and pharmacokinetics (PK) of a single dose of DM199 administered intravenously (IV) with a polyvinyl chloride (PVC) bag in healthy adult participants and adults recently taking angiotensin-converting enzyme (ACE) inhibitors.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 03/02/2023, The Bellberry Human Research Ethics Committee South Australia (123 Glen Osmond Road, Eastwood, SA 5063, Australia; +61 (0)8 8361 3222; bellberry@bellberry.com.au), ref: 2022-12-1417

Primary study design
Interventional

Study design
Single-centre Phase 1C open-label single ascending dose study

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Adult healthy participants (Part A) and adults recently taking ACE inhibitors (Part B)

Interventions
Part A: DM199 will be given as a single intravenous dose diluted into 50 ml of normal saline in a PVC bag and controlled IV kit materials. A minimum of three participant cohorts will be dosed. The first cohort dose will be 0.1 µg/kg DM199 and doses will be escalated in the subsequent cohorts until a maximum tolerated dose with PK levels in a projected therapeutic range is reached.

Part B: Once the maximum tolerated dose (MTD) level is determined in the healthy participants then at least one additional cohort of three non-healthy participants (who have been on recent ACE inhibitor medications) will receive a single intravenous dose of DM199 at the MTD as determined in healthy participants.

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
DM199

Primary outcome(s)
The safety of a single dose of DM199 administered by IV in a PVC bag will be assessed as follows:
1. Safety is measured by the incidence, frequency, severity, and causality of adverse events (AEs), serious adverse events (SAEs), and adverse events of special interest (AESIs) evaluated continuously while in the Phase 1 unit from Screening to Day 3
2. Tolerability of DM199 is measured by the incidence and severity of infusion-related reactions during the infusion on Day 1 and after the infusion up to Day 3
3. Safety is measured by change in physical examination (PE) findings from the initial baseline physical exam on day minus 1, to a PE at 24 hours post-infusion start, to a PE at 48 hours post-infusion start
4. Safety is measured by change in vital sign measurements (resting heart rate, systolic blood pressure [SBP], diastolic blood pressure [DBP], respiratory rate, and body temperature) from the initial baseline vital signs on day one (pre-dose), and blood pressure and heart rate at 5, 10,15,

20, 30, 40, 50,60, 90 minutes post the start of the study drug infusion, and also at 2, 3, 4, 8, 12 hours, and full vital signs again at 24 and 48 hours post-infusion start
5. Safety is measured by change in hematology and chemistry parameters from baseline (day 1 pre-dose) and 24 hours post-dose
6. Safety is measured by change in 12-lead electrocardiogram (ECG) from baseline, at infusion end (approximately 60 minutes post-dose on Day 1), and 24 hours post-dose

Key secondary outcome(s)
Current secondary outcome measures as of 05/06/2023:

1. Pharmacokinetics of DM199 will be measured by the plasma concentrations of DM199/KLK1 at baseline (day 1 pre-dose), and at 5, 10 ,15, 20, 30, 40, 50, 60, 90 minutes post the start of the study drug infusion, and also at 2, 3, 4, 8, and 12, 24 and 48 hours post infusion start for Part A participants. For Part B participants, pharmacokinetics of DM199 will be measured by the plasma concentrations of DM199/KLK1 at screening, baseline (day 1 pre-dose), and at 5, 15, 30, 50, 90 minutes post the start of the study drug infusion, and also at 4, 12, 24 and 48 hours post infusion start.
2. Immunogenicity of DM199 will be measured by the plasma DM199 antidrug antibodies (ADA) at baseline (day 1 pre-dose), and at 48 hours post infusion start for all participants.

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Previous secondary outcome measures:

1. Pharmacokinetics of DM199 will be measured by the plasma concentrations of DM199/KLK1 at baseline (day 1 pre-dose), and at 5, 10 ,15, 20, 30, 40, 50, 60, 90 minutes post the start of the study drug infusion, and also at 2, 3, 4, 8, and 12, 24 and 48 hours post infusion start
2. Immunogenicity of DM199 will be measured by the plasma DM199 antidrug antibodies (ADA) at baseline (day 1 pre-dose), and at 48 hours post infusion start

Completion date
07/07/2023

Eligibility

Key inclusion criteria
1. ≥18 years of age
2. Part A only: healthy participants with no clinically significant medical problems and taking no medications for a chronic medical condition (oral supplements and vitamins as well as oral contraception medications are allowed)
3. Part B only: non-healthy participants recently taking ACE inhibitor medications:
3.1. Non-healthy participants taking ACE inhibitor medications for chronic medical conditions including hypertension, diabetes, or mild congestive heart failure with the last dose of medication taken >24 hours prior to the start of the IV infusion
3.2. Participant is willing to forego taking prescribed ACE inhibitor medication through the duration of the study or at minimum do not restart ACE inhibitor until 24 hours after completion of the IV infusion (i.e., half-life of DM199 given IV is approximately 4 hours
and 24 hours is greater than 5 half-lives)
3.3. All other chronic medications may be allowed if taking stable doses for at least 3 months with no new recent medications, and with pre-approval from the Sponsor Medical Monitor
4. Weight between 50 and 130 kg

5. No history of alcohol or drug abuse (barbiturates, benzodiazepines, cocaine, methadone, amphetamines, methamphetamines, opiates, tetrahydrocannabinol [cannabis])
6. Non-smokers or light smokers (<5 cigarettes per day or approximately equivalent nicotine amount) by history and planned during the study; smoking includes tobacco and nicotine only vaping
7. No history of significant allergic diathesis such as urticaria, angioedema or anaphylaxis
8. Willing and able to sign written, informed consent
9. Participant is willing and able to comply with the study protocol, in the PI's opinion

Participant type(s)
Mixed

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Sex
All

Total final enrolment
12

Key exclusion criteria
1. Participant has a positive drug test and/or a positive alcohol breath test
2. Any significant past or current cardiac, pulmonary, hepatic, renal or other medical condition which in the opinion of the investigator would make the participation of the participant in this study medically unsafe or compromise the accuracy of assessment of safety, and PK data of the study
3. Participants who have abnormal safety labs outside the local lab ranges will be excluded at the PI’s discretion based on his/her assessment of clinical significance (can be repeated once at Screening at the PI’s discretion)
4. Participants with a past medical history of malignancy except for basal cell or squamous cell carcinoma of the skin who have had curative surgical treatment and at least 6 months have elapsed since the procedure
5. A value below the specified range of 100 mmHg for SBP OR 60 mmHg for DBP at Screening (can be repeated once at Screening as per PI’s discretion)
6. History of clinically significant acute bacterial, viral, or fungal systemic infections in the last 4 weeks prior to Screening
7. Clinical or laboratory evidence of an active infection at the time of Screening
8. Known alpha 1-antitrypsin deficiency (α1-antitrypsin deficiency)
9. Serological evidence of HIV, HBsAg, or anti-HCV at Screening
10. Females who are pregnant or nursing
11. Females of childbearing potential (i.e., any woman who is not surgically sterile e.g., hysterectomy, bilateral oophorectomy or >1-year postmenopausal status confirmed by FSH levels as defined by established lab ranges) and all men who, if participating in heterosexual sexual activity that could lead to pregnancy are unable or unwilling to practice medically

effective contraception during the study. They should agree to use two reliable methods of contraception (eg, double-barrier condom plus diaphragm, condom or diaphragm plus a stable dose of hormonal contraception) throughout the study period and until 1 month after receiving the study drug. Women of childbearing potential (WOCBP) will require compulsory pregnancy testing. A negative pregnancy test (urine) will be documented during Screening and on Day -1 respectively
12. Participation in any other drug study within 8 weeks or 5 half-lives of the study drug, whichever is longer
13. Unable or unwilling to comply with the protocol requirements for study visits and procedures
14. Participants who do not have good venous access for infusion of study drug or for blood sampling

Date of first enrolment
22/03/2023

Date of final enrolment
07/07/2023

Locations

Countries of recruitment
Australia

Study participating centre
Scientia Clinical Research Limited
Bright Building, Level 5 Corner High & Avoca Street
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Sponsor information

Organisation
DiaMedica Therapuetics, Inc.

Funder(s)

Funder type
Industry

Funder Name
DiaMedica Therapeutics, Inc.

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analyzed during the current study will be available upon request from Julie Daves (jdaves@diamedica.com). Consent is required and will be obtained. Study participant research data, which is for purposes of statistical analysis and scientific reporting, will be transmitted via the web-based data system to the Sponsor. This transmission will identify subjects by a unique study participant identification number. All procedures were approved by an Ethics Committee (Bellberry Limited) and reported to the Therapeutic Goods Administration (TGA) prior to eligibility screening.

IPD sharing plan summary
Available on request