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A phase I, single-dose, double-blind, randomised, dose escalation study to assess the safety, tolerability and pharmacokinetics of NNZ-2566 when administered as a 10-minute infusion

Submission date	Recruitment status	[ ] Prospectively registered
10/05/2006	No longer recruiting	[ ] Protocol
Registration date	**Overall study status**	[ ] Statistical analysis plan
24/05/2006	Completed	[ ] Results
Last Edited	**Condition category**	[ ] Individual participant data
20/09/2007	Injury, Occupational Diseases, Poisoning	[ ] Record updated in last year

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

Protocol serial number
Neu-2566-HV-001

Study information

Scientific Title

Study objectives
Based on pre-clinical studies, NNZ-2566 is shown to have the potential to prevent the neurological damage that can occur as a result of the traumatic brain injury. Objectives of this study are:
1. To determine the safety and tolerability of a single intravenous dose of NNZ 2566 in healthy volunteers when administered as a 10-minute infusion
2. To determine the single dose pharmacokinetics of NNZ-2566 after a 10-minute infusion

Ethics approval required
Old ethics approval format

Ethics approval(s)
Ethics approval received from the Alfred Ethics Committee on the 13th February 2006 (ref: 7/06).

Study design
Placebo-controlled, double-blind, randomised, single-dose, dose escalation, phase I study in healthy volunteers

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Traumatic brain injury

Interventions
Subjects will undergo screening to confirm eligibility. Subsequently, subjects will be admitted to the clinical facility for administration of either placebo or the active drug in a 2:5 fashion in each of the five cohorts. This in-house stay will involve collection of blood samples for pharmacokinetic (PK) analysis. Subjects will stay for a minimum of 24 hours after initial dosing. A dose-escalation schema has been chosen to maximise safety for participants based on preclinical toxicology studies. The pre-defined dose levels are: 0.1 mg/kg, 1.0 mg/kg, 10.0 mg/kg, 20.0 mg /kg, 30.0 mg/kg. The dosing scheme will consist of a single fixed-dose intravenous infusion of NNZ-2566 over 10 minutes. Dose escalation is subject to the Data Safety Monitoring Committee's (DSMC's) recommendation. A review time period of two to three weeks from end of dosing of each cohort is estimated to enable PK analysis prior to starting the next cohort. The study design precludes intra-subject dose-escalation.

Subjects will then return to the unit on day 7 for an exit evaluation, which will include collection of additional blood samples for safety laboratory testing and safety monitoring.

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
NNZ-2566

Primary outcome(s)
To determine the safety and tolerability of a single intravenous dose of NNZ 2566 when administered as a 10-minute infusion.

Key secondary outcome(s))
To determine the single dose pharmacokinetics of NNZ 2566 after a 10-minute infusion.

Completion date
15/10/2006

Eligibility

Key inclusion criteria
1. Aged between 18 years and 50 years (inclusive)
2. Male only: males must also agree to use adequate contraceptive precautions (unless the subject is surgically sterilised) for the duration of the study and for at least 30 days thereafter
3. Body mass index (BMI) of 18 to 30 kg/m^2
4. Healthy - this will be determined by a medical history with particular attention to:
4.1. A drug history identifying any known drug allergies and the presence of drug abuse
4.2. Any chronic use of medication
4.3. A thorough review of body systems. This will also be determined by having no clinically significant abnormal findings on physical examination, which includes an electrocardiogram (ECG), which in the opinion of the investigator would jeopardise the safety of the subject or impact on the validity of the study results
5. Volunteers with adequate venous access in their left and right arm to allow collection of blood samples and drug administration
6. Fluency in the English language
7. Have voluntarily given written informed consent to participate in this study

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
Male

Key exclusion criteria

1. History of allergy and/or hypersensitivity to any of the stated ingredients of the formulations (including lactose intolerance). A known hypersensitivity to lidocaine or any surgical dressing which may be used in the study procedures.
2. Medical conditions:
2.1. History of clinically significant gastrointestinal, hepatic, renal, cardiovascular, dermatological, immunological, respiratory, endocrine, oncological, neurological, metabolic, psychiatric disease or haematological disorders
2.2. Any history of asthma during the last 10 years
2.3. A creatinine clearance of less than 75 ml/min calculated using Cockroft and Gault Formula
2.4. Any predisposing condition that might interfere with the absorption, distribution, metabolism, and/or excretion of drugs
2.5. History of abnormal bleeding tendencies or thrombophlebitis unrelated to venepuncture or intravenous cannulation
2.6. History of hepatitis B, a positive test for hepatitis B surface antigen, a history of hepatitis C, a positive test for hepatitis C antibody, a history of human immunodeficiency virus (HIV) infection or demonstration of HIV antibodies
3. Any evidence of organ dysfunction, or any clinically significant clinical laboratory value which, in the opinion of the investigator would jeopardise the safety of the subject or impact on the validity of the study results, including a liver function test (LFT) greater than 1.5 x upper limit of normal (ULN)
4. Those who may have difficulty abstaining from alcohol during the 48 hours prior to dose administration and until completion of blood sampling on day 7
5. History of, or current evidence of, abuse of alcohol or any drug substance, licit or illicit, or positive urine drug screen for drugs of abuse
6. Medication:
6.1. Difficulty in abstaining from any prescription medications for 14 days prior to dose administration and for the duration of the study
6.2. Difficulty in abstaining from over-the-counter (OTC) medications or herbal supplements for 14 days prior to dose administration and for the duration of the study, (with the exception of occasional analgesia, vitamin and other nutrient supplement use, at the discretion of the investigator)
7. Difficulty in abstaining from food and/or beverages that contain caffeine or other xanthines (e. g., coffee, tea, cola and chocolate) during the 24 hours prior to dose administration and whilst confined at the clinical facility
8. History of any psychiatric illness which may impair the ability to provide written informed consent
9. Poor compliers or those unlikely to attend
10. Receipt of any drug as part of a research study within 30 days of initial dose administration in this study
11. Standard blood donation (usually 550 ml) within the 12-week period before dose administration
12. Unusual dietary habits, including vegetarian diets and excessive or unusual vitamin intakes
13. Vaccination or immunisation within 30 days of initial dose administration

Date of first enrolment

15/05/2006

Date of final enrolment

15/10/2006

Locations

Countries of recruitment
Australia

New Zealand

Study participating centre
Center for Clinical Studies
Melbourne
Australia
3004

Sponsor information

Organisation
Neuren Pharmaceuticals (New Zealand)

ROR
https://ror.org/0503fq502

Funder(s)

Funder type
Industry

Funder Name
Technology New Zealand (TechNZ) (New Zealand) - grant

Funder Name
Foundation for Research Science and Technology (FoRST) (New Zealand) - grant (grant ref: NRNZ0301, NRNZ0402, NRNZ0502)

Funder Name
Neuren Pharmaceuticals Limited (New Zealand) - internally funded

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration