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A randomised, double-blind, placebo-controlled study of Glypromate® in patients undergoing cardiopulmonary bypass surgery: Studying Neurons Using Glypromate® - second study

Submission date 27/06/2007	**Recruitment status** No longer recruiting	[_] Prospectively registered [_] Protocol
Registration date 05/07/2007	**Overall study status** Completed	[_] Statistical analysis plan [_] Results
Last Edited 09/08/2011	**Condition category** Circulatory System	[_] Individual participant data [_] 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

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
Neu-GPE-CPB-001

Study information

Scientific Title

Acronym
SNUG-2

Study objectives
In 2004, the American College of Cardiology/American Heart Association (ACC/AHA) Task Force described the occurrence of adverse neurological outcomes as either Type 1 or Type 2 injuries. Type 1 injuries are predominantly focal stroke, transient ischaemic attack and fatal cerebral injuries. Type 2 events reflect a more global/diffuse injury with disorientation or immediate or intellectual decline. The Task Force reports that 53% of Cardiopulmonary Bypass (CPB) - Coronary Artery Bypass Graft (CABG) patients experience Type 2 abnormal neurocognitive function at the time of hospital discharge. Six months after surgery, abnormalities could still be identified in 24% of patients.

Hypothesis:
To determine whether Glypromate® may provide neurocognitive preservation and reduction of memory loss.

This new phase 3 trial is a follow-on from the earlier phase 2 study registered under ISRCTN67437862.

Please note that, as of 13/08/2008, the number of participants on this ISRCTN record has been amended from 672 to 350. On 30/06/2008, the target number of participants was reduced to 350, due to high quality of data and fewer drop outs than expected. Recruitment has been completed as the new target number has been achieved. They were recruited from 11 sites in Australia, 6 sites in New Zealand and 7 sites in the USA. The trial is now in follow-up phase.

Ethics approval required
Old ethics approval format

Ethics approval(s)
The study was approved at 6 New Zealand sites. Lead site, Mercy Ascot Hospital, was approved by the Multi-Region Ethics Committee on 5 July 2007 (ref: MEC/07/02/025).

The study was approved at 11 Australian sites. Lead site, Ashford Hospital, was approved by Bellberry Human Research Ethics Committee on 16 July 2007 (ref: 60/07).

The study was approved at 7 US sites. Lead site, Union Memorial Hospital, was approved by MedStar Research Institute on 18 October 2007 (ref: 2007-238).

Study design
International, randomised, double-blind, placebo-controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet

Health condition(s) or problem(s) studied
Cardiopulmonary bypass surgery

Interventions
A four-hour continuous intravenous (i.v.) infusion of Glypromate® 1 mg/kg/hr or placebo will be commenced on completion of protamine administration following cardiopulmonary bypass.

Intervention Type
Drug

Phase
Phase III

Drug/device/biological/vaccine name(s)
Glypromate®

Primary outcome measure
This study has co-primary endpoints measured by the composite Z score for cognition and the composite score for the ADL assessment. The primary analyses will compare effects of Glypromate® and placebo-based on the standardised composite cognitive change scores and the ADL scores. The total composite cognitive change score is calculated as the corrected directional sum of the changes in the five individual domain components plus three ancillary tests, i.e. the Pegboard Test, Stroop Test and Trail Making Test (adjusted for direction). The test battery comprises 12 tests, 9 from the Cognitive Drug Research's (CDR) computerised cognitive assessment system plus Trail Making Test (parts A & B), Stroop Test (congruent and incongruent), and Lafayette Grooved Regboard Test.

The co-primary instrumental and physical ADL assessments used in this study are from the Older Americans Resources and Services (OARS) Multidimensional Functional Assessment Questionnaire, Centre for the Study of Aging and Human Development, Duke University.

Primary outcome measures are collected at baseline (pre-surgery), 4 - 6 weeks post surgery and 12 - 14 weeks post surgery.

Secondary outcome measures
1. Global evaluation of the patient's ability to perform activities of daily living (question 101 from the OARS Multidimensional Functional Questionnaire)

2. The incidence of stroke and Transient Ischaemic Attack (TIA) after CPB surgery
3. The change in cognitive domain (power of attention, continuity of attention, quality of working memory, quality of episodic memory, speed of memory) and individual cognitive test performance

Secondary outcome measures are assessed at the same timepoints as per the primary measures and in addition an assessment is made on Day 2 post surgery for stroke and TIA.

Overall study start date
01/06/2007

Completion date
31/12/2008

Eligibility

Key inclusion criteria
1. Scheduled for non-emergency CABG surgery and/or valve replacement/repair, with CPB
2. Willing to provide written informed consent
3. Able and agreeable to undergo all cognitive and Activities of Daily Living (ADL) testing (i.e. understands English, able to read, write, have sufficient motor dexterity and be available for follow-up visit at 4 - 6 weeks and 12 - 14 weeks post surgery)
4. Greater than or equal to 50 years old

Participant type(s)
Patient

Age group
Senior

Sex
Both

Target number of participants
350

Key exclusion criteria
1. Pre-operative mechanical assist device or intra-aortic balloon pump inserted for shock or low output syndrome
2. Women of child-bearing potential or breastfeeding women
3. History of or any current condition that in the Investigator's opinion would interfere with study participation or evaluation of results
4. Congenital heart disease with a risk of polycythaemia, circulatory problems, or need for a shunt
5. Renal insufficiency (serum creatinine greater than 180 umol/L [greater than 2 mg/dL])
6. Past or present bleeding disorder
7. History of organic brain syndrome
8. Currently receiving treatment for alcohol or drug abuse
9. Currently participating in another investigational drug or device study
10. Prior enrolment in this study

Date of first enrolment
01/06/2007

Date of final enrolment
31/12/2008

Locations

Countries of recruitment
Australia

New Zealand

United States of America

Study participating centre
Director of Coronary Care & Green Lane Cardiovascular Research Unit
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Sponsor information

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Neuren Pharmaceuticals Limited (New Zealand)

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Sponsor type
Industry

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Funder(s)

Funder type
Industry

Funder Name
Neuren Pharmaceuticals Limited (New Zealand)

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration