Clinical trial results:
Vascular Augmentation of Late-life Unremitted Depression

Summary

EudraCT number	2010-023969-21
Trial protocol	GB
Global end of trial date	15 April 2014

Results information

Result version number	v1 (current)
This version publication date	11 July 2019
First version publication date	11 July 2019
Summary attachment (see zip file)	VALUeD Final Report (VALUeD Final Report_15jun2015_Final.pdf)

Trial information

Trial identification

Sponsor protocol code	724

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Gateshead Health NHS Foundation Trust
Sponsor organisation address	Sheriff Hill, Gateshead, United Kingdom, NE9 6SX
Public contact	Professor Alan J Thomas, Institute of Ageing & Health Campus for Ageing & Vitality Newcastle upon Tyne NE4 5PL, 0191 4455212, alan.thomas@newcastle.ac.uk
Scientific contact	Professor Alan J Thomas, Institute of Ageing & Health Campus for Ageing & Vitality Newcastle upon Tyne NE4 5P, 0191 4455212, alan.thomas@newcastle.ac.uk

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	17 April 2014
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	15 April 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To provide estimates of the effectiveness of the study medication, amlodipine, to inform a calculation for a larger more definitive study. We hypothesise that the amlodipine addition (augmentation) to a patients routine treatment will lead to significantly more people achieving remission (a lessening of their symptoms) at 16 weeks when compared with those patients who have the placebo augmentation. This is however a pilot study and as such is not expected to have sufficient numbers of participants to provide definitive proof of this.

Protection of trial subjects:

The questionnaires and instruments used for this study asked questions of the patient that could be upsetting by their very nature of asking questions about the patient's mental state, feelings of guilt, cognition, hallucinations, thoughts of suicide, sexual performance and the impact of the patient's depression and its possible affects on their daily lives. While all of this information is requested to permit a full understanding of the disease and to permit a measure if there are differences between the arms of this study, it is possible that the patient could become upset by the questions and their answers. The staff working on the study are experienced members of the research team with a great understanding of the disease and how it affects the patients'. Every care was taken to explain the requirements of the questionnaires and their importance while being sensitive and supportive to the patient and the carer. Support was provided through routine care in line with local policy to manage any particular concern that could be raised during the course of the study.

Background therapy: -
Evidence for comparator: -

Actual start date of recruitment	09 February 2012
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 8
Worldwide total number of subjects	8
EEA total number of subjects	8

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37	0

wk	
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	8
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects were identified by searching Quality Outcome Framework long term illness databases for people over 50 who were on antidepressant medication, which shows that patients have been assessed as having a depressive illness which needs more than watchful waiting or counselling.

Pre-assignment

Screening details:

Potential participants were identified by screening computerised records in primary care, and secondary care. Local primary care practices were identified in Newcastle and Gateshead through the PCRN and NTW CLRN. Staff at these practices conducted computerised screening and sent out letters to potential study subjects using support from the PCRN/CL

Period 1

Period 1 title	overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Assessor

Blinding implementation details:

Randomisation was conducted by the Newcastle Clinical Trials Unit (NCTU) web-based system in a 1:1 ratio stratified by severity (defined by a dichotomous variable indicating whether baseline HAM-D was less than or greater than or equal to 15) and the treatment allocation was kept blind from the subjects and the study assessors and investigators until study completion.

Arms

Are arms mutually exclusive?	Yes
Arm title	Amlodipine

Arm description:

This was a pilot and feasibility study to assess whether a large scale randomised controlled trial of augmentation treatment with the calcium channel blocker amlodipine would be feasible and acceptable in vascular depression.

Arm type	Experimental
Investigational medicinal product name	Amlodipine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Ocular use

Dosage and administration details:

Active and placebo study medication was provided as a 4 week initial supply of 5mg capsules followed by total of 12 week’s supply of 10mg, dispensed at week 4 and week 8.

Arm title	Placebo

Arm description:

This was a pilot and feasibility study to assess whether a large scale randomised controlled trial of augmentation treatment with the calcium channel blocker amlodipine would be feasible and acceptable in vascular depression.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Active and placebo study medication was provided as a 4 week initial supply of 5mg capsules followed by total of 12 week's supply of 10mg, dispensed at week 4 and week 8.

Number of subjects in period 1	Amlodipine	Placebo
Started	4	4
Completed	4	4

Baseline characteristics

End points

End points reporting groups

Reporting group title	Amlodipine

Reporting group description:

This was a pilot and feasibility study to assess whether a large scale randomised controlled trial of augmentation treatment with the calcium channel blocker amlodipine would be feasible and acceptable in vascular depression.

Reporting group title	Placebo

Reporting group description:

This was a pilot and feasibility study to assess whether a large scale randomised controlled trial of augmentation treatment with the calcium channel blocker amlodipine would be feasible and acceptable in vascular depression.

Primary: Determine response rates to study invitation to GP practices and patients

End point title	Determine response rates to study invitation to GP practices and patients

End point description:

End point type	Primary

End point timeframe:

Measure remission (Hamilton Rating Scale for Depression (HAM-D)<10 for 2 consecutive assessments) by 16 weeks of augmentation

End point values	Amlodipine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	4		
Units: Measure remission (Hamilton Rating Scale				
number (not applicable)	4	4		

Statistical analyses

Statistical analysis title	Summary Statistics

Statistical analysis description:

In total, of the 206 invited patients, 8 were recruited into the study. Rate = 8/206 = 3.9% (95% CI: 1.7 to 7.5%). As a result of this small sample size the analysis plan was altered from that described in the protocol. There was no comparative hypothesis testing and instead summary statistics were calculated for pre-specified outcome variables by arm.

Study compliance was assessed in both group as well as remission rates. None of the patients achieved remission at any point in the study.

Comparison groups	Amlodipine v Placebo

Number of subjects included in analysis	8
Analysis specification	Post-hoc
Analysis type	other[1]
P-value	> 0 [2]
Method	N/A
Parameter estimate	Confidence Intervals
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.92
upper limit	11.58
Variability estimate	Standard deviation

Notes:

[1] - This analysis is descriptive only. As a result of the achieved sample size no statistical comparison has been made between the trial arms.
[2] - No P value obtained due to small sample size

Adverse events

Adverse events information[1]	
Timeframe for reporting adverse events:	
Any serious adverse events will be recorded throughout the duration of the trial until 1 week after trial therapy is stopped	
Adverse event reporting additional description:	
No serious adverse events were reported	
Assessment type	Systematic

Dictionary used	
Dictionary name	None
Dictionary version	0

Frequency threshold for reporting non-serious adverse events: 0 %

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: Only small sample size achieved.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
06 March 2013	Extra exclusion criteria
04 July 2013	Amendment 10 was a change to the exit strategy. Following a meeting of the DMEC, the committee agreed that unblinding the patients prior to study completion and data analysis may cause bias within the study due to associated unblinding of study staff. Unfortunately an internal error within CSP caused a delay in this amendment being approved by the Newcastle upon Tyne Hospitals NHS Foundation Trust. By the time that the approval came through, all patients had completed the trial and therefore consented to the earlier version of the PIS. 5 of the 8 participants requested to be unblinded in total.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported