EU Clinical Trials Register

Clinical trial results:
Towards Onset Prevention of COGnitive decline in adults with Down syndrome (the TOP-COG study)

Summary

EudraCT number	2011-001564-21
Trial protocol	GB
Global end of trial date	14 September 2014

Results information

Result version number	v1 (current)
This version publication date	18 December 2019
First version publication date	18 December 2019
Summary attachment (see zip file)	2011-001564-21 summary (2011-001564-21 summary.pdf)

Trial information

Trial identification

Sponsor protocol code	GN09CP301

Additional study identifiers

ISRCTN number	ISRCTN67338640
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-
Other trial identifiers	NRS reference: NRS11/CG06, IRAS project code: 77898, Portfolio ID: 11619, MREC reference: 11/AL/0200, Sponsor reference: GN09CP301

Notes:

Sponsors

Sponsor organisation name	NHS Greater Glasgow and Clyde
Sponsor organisation address	J B Russell House, Gartnavel Royal Hospital, 1055 Great Western Road, Glasgow, United Kingdom, G12 0XH
Public contact	Joanne McGarry Academic Research Coordinator, NHS Greater Glasgow & Clyde, +44 (0)141 314 4011, Joanne.McGarry@ggc.scot.nhs.uk
Scientific contact	Joanne McGarry Academic Research Coordinator, NHS Greater Glasgow & Clyde, +44 (0)141 314 4011, Joanne.McGarry@ggc.scot.nhs.uk
Sponsor organisation name	University of Glasgow
Sponsor organisation address	University Avenue, Glasgow, United Kingdom, G12 8QQ
Public contact	Dr Debra Stuart, University of Glasgow, debra.stuart@glasgow.ac.uk
Scientific contact	Dr Debra Stuart, University of Glasgow, debra.stuart@glasgow.ac.uk

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric	No

investigation plan (PIP)	
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	18 December 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	31 August 2014
Global end of trial reached?	Yes
Global end of trial date	14 September 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The aims of the study are to gather the data needed to design a full-scale multi-centred RCT of oral simvastatin 40mg a day.

The principal research questions are:

What are the:
(1) trial recruitment/retention rates and recruitment sources,
(2) rates of tolerability/safety of oral simvastatin 40mg a day,
(3) most sensitive instruments to detect early cognitive decline in adults with Down syndrome, and
(4) perceptions of adults with Down syndrome and their carers on deciding whether to participate, on randomisation, and their experience of the assessments?

Protection of trial subjects:

Participants were fully informed of the time required to participate before making a decision.
The primary study researcher was experienced in working with adults with intellectual disabilities.
Interviews were conducted in participants' homes where requested.
Capillary blood tests and saliva collection were offered in place of venous blood sampling.
Participants underwent baseline measurements followed by a comprehensive check at 6-12 weeks after starting treatment to identify any initial adverse events.

Background therapy:

Not applicable

Evidence for comparator: -

Actual start date of recruitment	27 February 2012
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 21

Worldwide total number of subjects	21
EEA total number of subjects	21

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
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)	21
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The setting was the general community of Scotland, UK; specifically, the health board areas of Greater Glasgow and Clyde, Lothian, Tayside, Lanarkshire and Borders. Recruitment was from multiple sources within the general community, Down Syndrome Scotland, Local Authorities and National Health Service clinical services.

Pre-assignment

Screening details:

Inclusion: Down syndrome; aged ≥ 50 yrs/Exclusion: no consent; unable to comply with protocol, including tissue samples; dementia; diabetes; clinically evident atherosclerotic disease; at risk of cardiovascular disease; liver disease; chronic renal insufficiency; statin therapy; previous statin SAE; unable to avoid grapefruit juice; excess alcohol

Period 1

Period 1 title	Baseline
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

One capsule of placebo at night for 12 months

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

Dosage and administration details:

One oral placebo capsule at night by mouth

Arm title	Simvastatin

Arm description:

Simvastatin 40mg at night by oral administration

Arm type	Experimental
Investigational medicinal product name	Simvastatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Simvastatin 40mg at night by oral administration.
Swallowed whole, not chewed.

Number of subjects in period 1	Placebo	Simvastatin
Started	11	10
Completed	11	10

Period 2

Period 2 title	12 month follow-up
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Carer, Subject

Blinding implementation details:

Randomisation conducted by the Robertson Centre for Biostatistics and information communicated directly with the Pharmacy Production Unit. On receipt of a prescription, the study drugs were posted directly to participants.
The active drug and placebo were over-encapsulated, identical in appearance and similar in weight

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

One capsule of placebo at night for 12 months

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

Dosage and administration details:

One oral placebo capsule at night by mouth

Arm title	Simvastatin

Arm description:

Simvastatin 40mg at night by oral administration

Arm type	Experimental
Investigational medicinal product name	Simvastatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Simvastatin 40mg at night by oral administration.
Swallowed whole, not chewed.

Number of subjects in period 2	Placebo	Simvastatin
Started	11	10
Completed	5	3
Not completed	6	7
Carer concerned about drug	-	3
Consent withdrawn by subject	1	1
Adverse event, non-fatal	2	-
Lost to follow-up	2	3
Protocol deviation	1	-

Baseline characteristics

Reporting groups

Reporting group title	Placebo
Reporting group description:	
One capsule of placebo at night for 12 months	
Reporting group title	Simvastatin
Reporting group description:	
Simvastatin 40mg at night by oral administration	

Reporting group values	Placebo	Simvastatin	Total
Number of subjects	11	10	21
Age categorical			
Units: Subjects			
In utero			0
Preterm newborn infants (gestational age < 37 wks)			0
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)			0
From 65-84 years			0
85 years and over			0
Age continuous			
Age			
Units: years			
arithmetic mean	53.67	54.68	
standard deviation	± 3.16	± 3.10	-
Gender categorical			
Units: Subjects			
Female	5	5	10
Male	6	5	11
Intellectual disability			
Units: Subjects			
Mild ID	4	0	4
Moderate ID	3	4	7
Severe ID	4	5	9
Profound ID	0	1	1
Apolipoprotein E gene			
Apolipoprotein E (APOE)			
Units: Subjects			
APOE ε3/2	1	1	2
APOE ε3/3	7	6	13
APOE ε4/3	3	3	6
Cholesterol			
Units: mmol/l			
arithmetic mean	5.3	5.1	

standard deviation	± 0.8	± 0.5	-

Quality of Life

EuroQol 5 Dimension Questionnaire (EQ-5D) health utility

Units: Score			
arithmetic mean	0.81	0.54	
standard deviation	± 0.29	± 0.38	-

Adaptive Behaviour Scale total score

Units: Score			
arithmetic mean	224	177	
standard deviation	± 39	± 50	-

Townsend Scale total score

Units: Score			
arithmetic mean	8.2	9.3	
standard deviation	± 3.0	± 4.3	-

Neuropsychological Assessement of Dementia in Individuals with Intellectual Disabilities (NADIID)

Memory for Objects test

Units: Score			
arithmetic mean	5.7	4.0	
standard deviation	± 2.3	± 2.4	-

Selective Attention Cancellation Test

Overall score

Units: Score			
arithmetic mean	17.0	25.3	
standard deviation	± 9.3	± 25.0	-

Cambridge Neuropsychological Test Automated Battery (CANTAB) pattern recognition memory

Units: % correct			
arithmetic mean	61.5	56.6	
standard deviation	± 23.5	± 12.3	-

Cats and Dogs switching condition

Time taken

Units: Time			
arithmetic mean	58.8	40.5	
standard deviation	± 36.3	± 22.0	-

Cats and Dogs switching condition

Number of errors

Units: Number of errors			
arithmetic mean	4.1	11.0	
standard deviation	± 5.3	± 7.6	-

Tower of London test

Revised for learning disabilities

Units: Total score			
arithmetic mean	21.7	20.7	
standard deviation	± 8.5	± 8.0	-

Cued Recall Test

Units: Total score			
arithmetic mean	34.1	21.2	
standard deviation	± 4.5	± 12.7	-

Category Fluency Test

Number correct

Units: Number			
arithmetic mean	12.1	8.0	
standard deviation	± 4.2	± 4.2	-
Category Fluency Test			
Number repeated			
Units: Number			
arithmetic mean	0.7	2.6	
standard deviation	± 1.1	± 1.7	-
Category Fluency Test			
Number of errors			
Units: Number			
arithmetic mean	0.3	0.0	
standard deviation	± 0.5	± 0.0	-
Story Recall Test			
Free recall			
Units: Score			
arithmetic mean	5.8	5.0	
standard deviation	± 3.7	± 6.3	-
Story Recall Test			
Cued recall			
Units: Score			
arithmetic mean	4.4	2.4	
standard deviation	± 2.7	± 4.3	-

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
One capsule of placebo at night for 12 months	
Reporting group title	Simvastatin
Reporting group description:	
Simvastatin 40mg at night by oral administration	
Reporting group title	Placebo
Reporting group description:	
One capsule of placebo at night for 12 months	
Reporting group title	Simvastatin
Reporting group description:	
Simvastatin 40mg at night by oral administration	

Primary: Recruitment

End point title	Recruitment[1]
End point description:	
Monthly numbers screened and recruited	

End point type	Primary
End point timeframe:	
12 months	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Between-group analyses were not conducted for this end point. Instead, descriptive statistics were used to describe the total study cohort.

End point values	Placebo	Simvastatin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	10		
Units: Number of patients				
Month 1	2	1		
Month 2	2	1		
Month 3	0	0		
Month 4	0	0		
Month 5	0	0		
Month 6	1	1		
Month 7	0	0		
Month 8	3	2		
Month 9	0	0		
Month 10	1	2		
Month 11	0	2		
Month 12	2	1		

Statistical analyses

No statistical analyses for this end point

Primary: Retention

End point title	Retention[2]

End point description:

End point type	Primary

End point timeframe:

Baseline to 12 months

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Between-group analyses were not conducted for this end point. Instead, descriptive statistics were used to describe the total study cohort.

End point values	Placebo	Simvastatin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	10		
Units: Proportion of participants				
Included in analysis	9	7		
Lost to follow-up	2	3		

Statistical analyses

No statistical analyses for this end point

Primary: Recruitment and retention

End point title	Recruitment and retention[3]

End point description:

Number of participants recruited per base general population size

End point type	Primary

End point timeframe:

12 months

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Between-group analyses were not conducted for this end point. Instead, descriptive statistics were used to describe the total study cohort.

End point values	Placebo	Simvastatin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	10		
Units: Number of participants	9	7		

Statistical analyses

No statistical analyses for this end point

Secondary: Neuropsychological Assessment of Dementia in Individuals with Intellectual Disabilities

End point title	Neuropsychological Assessment of Dementia in Individuals with Intellectual Disabilities
End point description:	
Memory for Objects test	
End point type	Secondary
End point timeframe:	
12 months	

End point values	Placebo	Simvastatin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	6		
Units: Score				
arithmetic mean (standard deviation)	4.9 (± 2.6)	5.3 (± 2.7)		

Statistical analyses

Statistical analysis title	Memory for Objects test
Comparison groups	Placebo v Simvastatin
Number of subjects included in analysis	15
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.047
Method	Regression, Linear
Parameter estimate	Mean difference (final values)
Point estimate	2.2
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.45
upper limit	3.96
Variability estimate	Standard error of the mean

Secondary: Selective Attention Cancellation Test

End point title	Selective Attention Cancellation Test
End point description:	
Overall score	
End point type	Secondary
End point timeframe:	
12 months	

End point values	Placebo	Simvastatin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	3		
Units: Score				
arithmetic mean (standard deviation)	18.8 (± 11.6)	21.7 (± 8.4)		

Statistical analyses

Statistical analysis title	Selective Attention Cancellation Test
Comparison groups	Placebo v Simvastatin
Number of subjects included in analysis	12
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.669
Method	Regression, Linear
Parameter estimate	Mean difference (final values)
Point estimate	-5.36
Confidence interval	
level	90 %
sides	2-sided
lower limit	-29.2
upper limit	18.45
Variability estimate	Standard error of the mean

Secondary: Cambridge Neuropsychological Test Automated Battery (CANTAB)

End point title	Cambridge Neuropsychological Test Automated Battery (CANTAB)
End point description:	
% correct	
End point type	Secondary
End point timeframe:	
12 months	

End point values	Placebo	Simvastatin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	5		
Units: Score				
arithmetic mean (standard deviation)	67.3 (± 17.4)	57.0 (± 12.2)		

Statistical analyses

Statistical analysis title	CANTAB pattern recognition memory
Comparison groups	Placebo v Simvastatin
Number of subjects included in analysis	9
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.118
Method	Regression, Linear
Parameter estimate	Mean difference (final values)
Point estimate	-15.7
Confidence interval	
level	90 %
sides	2-sided
lower limit	-32.6
upper limit	1.31
Variability estimate	Standard error of the mean

Secondary: Cats and Dogs switching condition

End point title	Cats and Dogs switching condition
End point description:	
Time taken	
End point type	Secondary
End point timeframe:	
12 months	

End point values	Placebo	Simvastatin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	5		
Units: Time				
arithmetic mean (standard deviation)	47.0 (± 31.5)	44.0 (± 10.9)		

Statistical analyses

Statistical analysis title	Cats & Dogs switching condition (time taken)
Comparison groups	Placebo v Simvastatin
Number of subjects included in analysis	13
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.94
Method	Regression, Linear
Parameter estimate	Mean difference (final values)
Point estimate	-1.74
Confidence interval	
level	90 %
sides	2-sided
lower limit	-44.5
upper limit	41
Variability estimate	Standard error of the mean

Secondary: Cats and Dogs switching condition

End point title	Cats and Dogs switching condition
End point description:	
Number of errors	
End point type	Secondary
End point timeframe:	
12 months	

End point values	Placebo	Simvastatin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	7		
Units: Number				
arithmetic mean (standard deviation)	7.0 (± 8.2)	7.8 (± 7.5)		

Statistical analyses

Statistical analysis title	Cats & Dogs switching condition (number of errors)
Comparison groups	Simvastatin v Placebo

Number of subjects included in analysis	15
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.417
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.33
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.04
upper limit	3.09

Secondary: Tower of London test

End point title	Tower of London test
End point description:	
Revised for learning disabilities	
End point type	Secondary
End point timeframe:	
12 months	

End point values	Placebo	Simvastatin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	6		
Units: Score				
arithmetic mean (standard deviation)	24.8 (± 13.6)	20.3 (± 11.7)		

Statistical analyses

Statistical analysis title	Tower of London test
Comparison groups	Placebo v Simvastatin
Number of subjects included in analysis	15
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.429
Method	Regression, Linear
Parameter estimate	Mean difference (final values)
Point estimate	-5.71
Confidence interval	
level	90 %
sides	2-sided
lower limit	-18.4
upper limit	6.9

Variability estimate	Standard error of the mean

Secondary: Cued Recall Test

End point title	Cued Recall Test
End point description:	
Total score	
End point type	Secondary
End point timeframe:	
12 months	

End point values	Placebo	Simvastatin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	5		
Units: Score				
arithmetic mean (standard deviation)	28.7 (± 13.0)	12.8 (± 14.2)		

Statistical analyses

Statistical analysis title	Cued Recall Test
Comparison groups	Placebo v Simvastatin
Number of subjects included in analysis	12
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.451
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	3.33
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.26
upper limit	46.07
Variability estimate	Standard error of the mean

Secondary: Category Fluency Test

End point title	Category Fluency Test
End point description:	
Number correct	
End point type	Secondary
End point timeframe:	
12 months	

End point values	Placebo	Simvastatin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	6		
Units: Number				
arithmetic mean (standard deviation)	9.2 (± 3.9)	8.2 (± 6.1)		

Statistical analyses

Statistical analysis title	Category Fluency Test (number correct)
Comparison groups	Placebo v Simvastatin
Number of subjects included in analysis	15
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.685
Method	Regression, Linear
Parameter estimate	Mean difference (final values)
Point estimate	1.46
Confidence interval	
level	90 %
sides	2-sided
lower limit	-4.92
upper limit	7.84
Variability estimate	Standard error of the mean

Secondary: Category Fluency Test

End point title	Category Fluency Test
End point description:	
Number repeated	
End point type	Secondary
End point timeframe:	
12 months	

End point values	Placebo	Simvastatin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	5		
Units: Number				
arithmetic mean (standard deviation)	1.0 (± 1.1)	1.6 (± 1.1)		

Statistical analyses

Statistical analysis title	Category Fluency Test (number repeated)
Comparison groups	Placebo v Simvastatin
Number of subjects included in analysis	14
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.189
Method	Regression, Linear
Parameter estimate	Mean difference (final values)
Point estimate	-0.87
Confidence interval	
level	90 %
sides	2-sided
lower limit	-2
upper limit	0.26
Variability estimate	Standard error of the mean

Secondary: Category Fluency Test

End point title	Category Fluency Test
End point description:	
Number of errors	
End point type	Secondary
End point timeframe:	
12 months	

End point values	Placebo	Simvastatin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	5		
Units: Number				
arithmetic mean (standard deviation)	0.1 (± 0.3)	0.2 (± 0.5)		

Statistical analyses

Statistical analysis title	Category Fluency Test (number of errors)
Comparison groups	Placebo v Simvastatin

Number of subjects included in analysis	14
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.653
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.16
upper limit	25.23
Variability estimate	Standard error of the mean

Secondary: Story Recall Test

End point title	Story Recall Test
End point description:	
Free recall	
End point type	Secondary
End point timeframe:	
12 months	

End point values	Placebo	Simvastatin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	5		
Units: Number				
arithmetic mean (standard deviation)	3.6 (± 3.3)	3.0 (± 4.2)		

Statistical analyses

Statistical analysis title	Story Recall Test (Free recall)
Comparison groups	Placebo v Simvastatin
Number of subjects included in analysis	13
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.488
Method	Regression, Linear
Parameter estimate	Mean difference (final values)
Point estimate	-1.72

Confidence interval	
level	90 %
sides	2-sided
lower limit	-5.39
upper limit	1.94
Variability estimate	Standard error of the mean

Secondary: Story Recall Test

End point title	Story Recall Test
End point description:	
Cued recall	
End point type	Secondary
End point timeframe:	
12 months	

End point values	Placebo	Simvastatin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	5		
Units: Number				
arithmetic mean (standard deviation)	3.9 (± 3.0)	2.6 (± 3.7)		

Statistical analyses

Statistical analysis title	Story Recall Test (cued recall)
Comparison groups	Placebo v Simvastatin
Number of subjects included in analysis	13
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.413
Method	Regression, Linear
Parameter estimate	Mean difference (final values)
Point estimate	-1.9
Confidence interval	
level	90 %
sides	2-sided
lower limit	-6.03
upper limit	2.24
Variability estimate	Standard error of the mean

Secondary: Change in Aβ40

End point title	Change in Aβ40

End point description:
Change over 12 months: simvastatin group compared to placebo group

End point type	Secondary

End point timeframe:

12 months

End point values	Simvastatin			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: pmol/L				
number (not applicable)	-24.4			

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Aβ42

End point title	Change in Aβ42

End point description:

Change over 12 months: simvastatin group compared to placebo group

End point type	Secondary

End point timeframe:

12 months

End point values	Simvastatin			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: pmol/l				
number (not applicable)	-0.26			

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Aβ42/Aβ40 ratio

End point title	Change in Aβ42/Aβ40 ratio

End point description:

Change over 12 months: simvastatin group compared to placebo group

End point type	Secondary

End point timeframe:

12 months

End point values	Simvastatin			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: ratio				
number (not applicable)	-0.02			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Cholesterol

End point title	Cholesterol
End point description:	

End point type	Other pre-specified
End point timeframe:	

12 months

End point values	Placebo	Simvastatin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	7		
Units: mmol/l				
arithmetic mean (standard deviation)	5.4 (± 0.7)	4.7 (± 0.7)		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: EuroQoL 5 Dimension Questionnaire (EQ-5D)

End point title	EuroQoL 5 Dimension Questionnaire (EQ-5D)
End point description:	
EQ-5D health utility	
End point type	Other pre-specified
End point timeframe:	

12 months

End point values	Placebo	Simvastatin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	7		
Units: Score				
arithmetic mean (standard deviation)	0.75 (± 0.29)	0.68 (± 0.25)		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Adaptive Behaviour Scale (ABS)

End point title	Adaptive Behaviour Scale (ABS)
End point description:	
Total score	
End point type	Other pre-specified
End point timeframe:	
12 months	

End point values	Placebo	Simvastatin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	7		
Units: Score				
arithmetic mean (standard deviation)	214 (± 38)	170 (± 56)		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Townsend Scale

End point title	Townsend Scale
End point description:	
Total score	
End point type	Other pre-specified
End point timeframe:	
12 months	

End point values	Placebo	Simvastatin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	7		
Units: Score				
arithmetic mean (standard deviation)	8.1 (± 3.4)	11.3 (± 3.3)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:	
12 month treatment period	
Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	15.1

Reporting groups

Reporting group title	Placebo
Reporting group description:	
One capsule of placebo at night for 12 months	
Reporting group title	Simvastatin
Reporting group description:	
Simvastatin 40mg at night by oral administration	

Serious adverse events	Placebo	Simvastatin	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			

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

Non-serious adverse events	Placebo	Simvastatin	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 11 (9.09%)	3 / 10 (30.00%)	
Injury, poisoning and procedural complications			
Leg injury			
subjects affected / exposed	0 / 11 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	1	1	
Gastrointestinal disorders			
Episodic diarrhoea			
subjects affected / exposed	0 / 11 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	1	1	
Skin and subcutaneous tissue disorders			

Rash			
subjects affected / exposed	0 / 11 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	1	1	
Endocrine disorders			
Thyroid dysfunction			
subjects affected / exposed	1 / 11 (9.09%)	0 / 10 (0.00%)	
occurrences (all)	1	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
26 September 2011	Protocol amendment, addressing points raised by the MHRA during its review. Within NHS GG&C, the amended protocol (version 3) was approved as part of Health Board management approval.
05 April 2012	Protocol version 4 Replacement of outcome measure instrument - 'Cats and Dogs test' in place of 'Delayed Matching to Sample test' No baseline interviews conducted yet so no participant recall required.
16 May 2012	Protocol v5 - Revised medication supply process - Revised unblinding process - Clarification of data sharing, to facilitate drug supply - Additional exclusion criterion
03 December 2013	Protocol version 7 Revised exclusion criteria and expected Adverse Reactions, following a change to the Summary of Product Characteristics and subsequently updated Reference Safety Information.
21 January 2014	Protocol version 8 Inclusion of sub-study assessing cognitive performance tools, for patients otherwise ineligible for the full study. No drug therapy involved.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Recruitment was challenging. However, valuable feasibility data was obtained, allowing the possibility of designing a full-scale Randomised Controlled Trial, with a realistic recruitment strategy & seeking an appropriate level of funding to implement

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/27473843