Clinical trial results:
Simvastatin in aneurysmal subarchnoid haemorrhage (STASH): a multicentre randomised controlled clinical phase III study

Summary

EudraCT number	2006-000277-30
Trial protocol	GB SE
Global end of trial date	10 January 2014

Results information

Result version number	v1 (current)
This version publication date	08 July 2016
First version publication date	30 July 2015
Summary attachment (see zip file)	AEs & SAEs for STASH (AE and SAE report for EudraCT STASH.xlsx)

Trial information

Trial identification

Sponsor protocol code	STASH01

Additional study identifiers

ISRCTN number	ISRCTN75948817
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Cambridge University NHS Foundation Trust
Sponsor organisation address	Hills Road, Cambridge University Hospitals NHS Foundation Trus, United Kingdom, CB2 0QQ
Public contact	Carole Turner, Dept of Neurosurgery , +44 1223 217205, clt29@medschl.cam.ac.uk
Scientific contact	Peter Kirkpatrick, Dept of Neurosurgery, +44 1223 217205, pjk21@medschl.cam.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	10 January 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	15 August 2013
Global end of trial reached?	Yes
Global end of trial date	10 January 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine if up to a 3 week treatment period of simvastatin can improve the long-term outcome in subjects who have had an aneurysmal subarachnoid haemorrhage.

Protection of trial subjects:

All subjects were monitored whilst in hospital as part of clinical care. Biochemical papameters were recorded at baseline and between days 9-12, in addition subjects were reviewed regularly by the research team.

Background therapy:

Subjects received either simvastatin 40mg or a matched placebo, in tablet form, once a day for up to 14 days. The study medication stopped at discharge from the acute Neurosurgical Units.

Evidence for comparator:

Matched placebo

Actual start date of recruitment	02 January 2007
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	Singapore: 25
Country: Number of subjects enrolled	Uruguay: 23
Country: Number of subjects enrolled	United States: 6
Country: Number of subjects enrolled	Colombia: 10
Country: Number of subjects enrolled	Canada: 26
Country: Number of subjects enrolled	Russian Federation: 11
Country: Number of subjects enrolled	Sweden: 20
Country: Number of subjects enrolled	United Kingdom: 676
Country: Number of subjects enrolled	Italy: 6
Worldwide total number of subjects	803
EEA total number of subjects	702

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)	803
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Recruitment period was Jan 2006 to Feb 2013. All patients were recruited in on an acute Neurosurgical ward in a tertiary referral centre

Pre-assignment

Screening details:

Patients were screened for eligiblitiy by the clinical team, on admission to the acute neurosurgical centre.

Pre-assignment period milestones

Number of subjects started	803
Number of subjects completed	803

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, Monitor, Data analyst

Blinding implementation details:

n/a

Arms

Are arms mutually exclusive?	Yes
Arm title	Statin

Arm description:

Subjects precribed to statin arm

Arm type	Active comparator
Investigational medicinal product name	Simvastatin
Investigational medicinal product code	C10A A01
Other name	Ritechol
Pharmaceutical forms	Tablet
Routes of administration	Nasogastric use , Oral use

Dosage and administration details:

40mg once a day

Arm title	Placebo

Arm description:

Subjects prescribed to placebo

Arm type	No intervention

No investigational medicinal product assigned in this arm

Number of subjects in period 1	Statin	Placebo
Started	391	412
Completed	379	403
Not completed	12	9
Lost to follow-up	12	9

Baseline characteristics

Reporting groups	
Reporting group title	Statin
Reporting group description:	
Subjects precribed to statin arm	
Reporting group title	Placebo
Reporting group description:	
Subjects prescribed to placebo	

Reporting group values	Statin	Placebo	Total
Number of subjects	391	412	803
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	391	412	803
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous			
Units: years			
arithmetic mean	51	49	
standard deviation	± 9.5	± 9.8	-
Gender categorical			
Units: Subjects			
Female	260	291	551
Male	131	121	252
UK subject			
Units: Subjects			
UK subject	332	344	676
non-UK subjects	59	68	127

End points

End points reporting groups

Reporting group title	Statin
Reporting group description: Subjects precribed to statin arm	
Reporting group title	Placebo
Reporting group description: Subjects prescribed to placebo	

Primary: Modified Rankin Scale (mRS)

End point title	Modified Rankin Scale (mRS)
End point description: Clinical outcome as measured by the mRS	
End point type	Primary
End point timeframe: 6 months	

End point values	Statin	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	379	403		
Units: subjects				
mRS 0-2	271	289		
mRS 3-6	108	114		

Statistical analyses

Statistical analysis title	analysis of outcome measures

Statistical analysis description:

intention to treat population. Primary outcome based on ordinal analysis of 6 month mRS assuming treatment effect followed a proportional odds model

Comparison groups	Placebo v Statin
Number of subjects included in analysis	782
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.809
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.97

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.75
upper limit	1.25
Variability estimate	Standard deviation

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

consent to discharge

Adverse event reporting additional description:

Adverse events reported are given in the attachment. They are not coded .

Assessment type	Systematic

Dictionary used

Dictionary name	Not coded
Dictionary version	na

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: The adverse events are given in the attachment

AEs break down for the Statin Arm:
subjects exposed 391
subjects affected by SAE 71
subject affected by non-AE 63
of deaths (all causes) 37
# of deaths resulting from AEs 37

AE break down for the Placebo Arm:
# of subjects exposed 412
# of subjects affected by SAEs 74
# of subject affected by non-AEs 73
# of deaths (all causes) 35
# of deaths resulting from AEs 35

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
29 July 2010	Request to reduce the cohort from 1600 to 800 based on statistical analysis of the primary outcome measures

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
03 June 2009	Request by Sponsor to suspend recruitment as a result of a commissioned audit. It was noted that IMP was being supplied to sites in other contries with the label in English only. REC and MHRA were notified	29 July 2010

Notes:

Limitations and caveats

None reported