Clinical trial results:
A study of very low dose twice-daily compared to standard low dose once-daily aspirin following acute coronary syndromes - WILL lOWer dose aspirin be more effective following ACS?

Summary

EudraCT number	2016-000920-25
Trial protocol	GB
Global end of trial date	30 March 2017

Results information

Result version number	v1 (current)
This version publication date	07 November 2018
First version publication date	07 November 2018

Trial information

Trial identification

Sponsor protocol code	STH19177

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02741817
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Sheffield Teaching Hospitals NHS FT
Sponsor organisation address	Glossop ROad, Sheffield, United Kingdom, S10 2JF
Public contact	Clinical Research Office, Sheffield Teaching Hospitals NHS Foundation Trust, 0114 2712763, ResearchAdministration@sth.nhs.uk
Scientific contact	Prof Rob Storey, Sheffield Teaching Hospitals NHS Foundation Trust, r.f.storey@sheffield.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	30 April 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	30 March 2017
Global end of trial reached?	Yes
Global end of trial date	30 March 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The principal objective of this study is to assess the effects of two aspirin regimens (very low dose twice daily or standard low dose once daily) on the levels of thromboxane and prostacyclin, substances relevant to platelet activity, measured as their breakdown products in blood and urine, in patients on dual antiplatelet therapy for acute coronary syndromes (heart attacks and severe 'unstable' angina).

Protection of trial subjects:

Study participants were asked to take a lower dose of aspirin than usual for 14 days within the study. The patients to be studied were already on established on standard doses of aspirin and ticagrelor for acute coronary syndromes (ACS), and enough into the treatment period to be in a stable phase and therefore to minimise any additional risk.
The REC approved protocol was followed as well as local SOPs.
The IMP dose and bleeding times were kept to the mininum to answer the outcome measure.

Background therapy:

Not applicable as there was no requirements for the patient to be on any other drugs.

Evidence for comparator:

Aspirin 75mg once daily represents guideline directed standard therapy.

Actual start date of recruitment	28 June 2016
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: 20
Worldwide total number of subjects	20
EEA total number of subjects	20

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)	10
From 65 to 84 years	10
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Recruitment period: 20/06/2016 to 01/12/2016.
Participants were recruited from England at one site in Sheffield.

Pre-assignment

Screening details:

Number of subjects screened: 216

Screening enrollment criteria
Male or female aged over 18 years
Diagnosis of acute coronary syndrome greater than 30 days and less than 10 months
Receiving dual antiplatelet therapy with aspirin 75 mg once daily and ticagrelor 90 mg twice daily

Pre-assignment period milestones

Number of subjects started	20
Number of subjects completed	20

Period 1

Period 1 title	Study medication period (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

Not applicable

Arms

Are arms mutually exclusive?	Yes
Arm title	Sequence 1

Arm description:

Aspirin 20mg twice daily for 14 days and Ticagrelor 90mg twice daily for 14 days
Followed by Aspirin 75mg once daily for 14 days and Ticagrelor 90mg twice daily for 14 days

Arm type	Experimental
Investigational medicinal product name	Aspirine lysine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for oral solution in sachet
Routes of administration	Oral use

Dosage and administration details:

20mg twice daily or 75mg twice daily

Arm title	Sequence 2

Arm description:

Aspirin 75mg twice daily for 14 days and Ticagrelor 90mg twice daily for 14 days
Followed by Aspirin 20mg once daily for 14 days and Ticagrelor 90mg twice daily for 14 days

Arm type	Experimental

Investigational medicinal product name	Aspirine lysine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for oral solution in sachet
Routes of administration	Oral use

Dosage and administration details:

20mg twice daily or 75mg twice daily

Number of subjects in period 1	Sequence 1	Sequence 2
Started	10	10
Visit 1 -14 days	10	10
Visit 2 - 28 days	10	10
Visit 3 - 42 days	10	10
Completed	10	10

Baseline characteristics

Reporting groups

Reporting group title	Study medication period

Reporting group description: -

Reporting group values	Study medication period	Total	
Number of subjects	20	20	
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 Units: years			
arithmetic mean	64.3		
standard deviation	± 11.9	-	
Gender categorical Units: Subjects			
Female	4	4	
Male	16	16	

Subject analysis sets

Subject analysis set title	Pharmacodynamic analysis set Aspririn 20mg
Subject analysis set type	Full analysis

Subject analysis set description:

All patients randomised to receive study medication when receiving Aspirin 20mg

Subject analysis set title	Pharmacodynamic analysis set Aspirin 75mg
Subject analysis set type	Full analysis

Subject analysis set description:

All patients that received Aspirin 75mg

Reporting group values	Pharmacodynamic analysis set Aspririn 20mg	Pharmacodynamic analysis set Aspirin 75mg	
Number of subjects	20	20	
Age categorical Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			

Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous Units: years			
arithmetic mean	64.3	64.3	
standard deviation	± 11.9	± 11.9	
Gender categorical Units: Subjects			
Female	4		
Male	16		

End points

End points reporting groups

Reporting group title	Sequence 1
Reporting group description:	
Aspirin 20mg twice daily for 14 days and Ticagrelor 90mg twice daily for 14 days Followed by Aspirin 75mg once daily for 14 days and Ticagrelor 90mg twice daily for 14 days	
Reporting group title	Sequence 2
Reporting group description:	
Aspirin 75mg twice daily for 14 days and Ticagrelor 90mg twice daily for 14 days Followed by Aspirin 20mg once daily for 14 days and Ticagrelor 90mg twice daily for 14 days	
Subject analysis set title	Pharmacodynamic analysis set Aspririn 20mg
Subject analysis set type	Full analysis
Subject analysis set description:	
All patients randomised to receive study medication when receiving Aspirin 20mg	
Subject analysis set title	Pharmacodynamic analysis set Aspirin 75mg
Subject analysis set type	Full analysis
Subject analysis set description:	
All patients that received Aspirin 75mg	

Primary: Serum thromboxane

End point title	Serum thromboxane
End point description:	
End point type	Primary
End point timeframe:	
In steady state after 14 days of treatment after two hours following the last dose of the period	

End point values	Pharmacodynamic analysis set Aspririn 20mg	Pharmacodynamic analysis set Aspirin 75mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	20	20		
Units: nanogram(s)				
arithmetic mean (standard deviation)	3.03 (± 3.64)	0.83 (± 1.93)		

Statistical analyses

Statistical analysis title	Overall analysis
Statistical analysis description:	
Post-dose serum TXB2 results for participants when receiving aspirin 20 mg twice daily vs. 75 mg once daily were analysed using a two-tailed paired t-test (3.03 ± 3.64 ng/ml vs. 0.83 ± 1.93 ng/ml, p=0.018).	
Comparison groups	Pharmacodynamic analysis set Aspririn 20mg v Pharmacodynamic analysis set Aspirin 75mg

Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.018
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)

Secondary: Bleeding time

End point title	Bleeding time

End point description:

End point type	Secondary

End point timeframe:

After each 14 day treatment period. Two hours after last dose

End point values	Pharmacodynamic analysis set Aspririn 20mg	Pharmacodynamic analysis set Aspirin 75mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	20	20		
Units: second				
arithmetic mean (standard deviation)	679.5 (± 305.5)	833.9 (± 385.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Pre-dose serum thomboxane serum 2

End point title	Pre-dose serum thomboxane serum 2

End point description:

End point type	Secondary

End point timeframe:

After 14 days of treatment and before the last dose

End point values	Pharmacodynamic analysis set Aspririn 20mg	Pharmacodynamic analysis set Aspirin 75mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	20	20		
Units: nanogram(s)				
arithmetic mean (standard deviation)	3.51 (± 4.07)	2.48 (± 3.14)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: From enrollment to day 42 phone call	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	19
Reporting groups	
Reporting group title	Aspiring 20mg regime
Reporting group description: -	
Reporting group title	Aspiring 75mg regime
Reporting group description: -	

Serious adverse events	Aspiring 20mg regime	Aspiring 75mg regime	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

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

Non-serious adverse events	Aspiring 20mg regime	Aspiring 75mg regime	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 20 (5.00%)	4 / 20 (20.00%)	
General disorders and administration site conditions			
Epistaxis			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Respiratory tract infection			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			

Haematoma			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Oedema peripheral			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
Chest discomfort			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported