Clinical trial results:
Study of two regimens of TicagrElor compared to clopidogrel in patients undergoing ELective Percutaneous Coronary Intervention (STEEL PCI)

Summary

EudraCT number	2014-004783-38
Trial protocol	GB
Global end of trial date	31 May 2018

Results information

Result version number	v1 (current)
This version publication date	04 August 2021
First version publication date	04 August 2021

Trial information

Trial identification

Sponsor protocol code	STH18423

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02327624
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Sheffield Teaching Hospitals NHS Foundation Trust
Sponsor organisation address	Trust Headquarters, 8 Beech Hill Road, Sheffield, United Kingdom, S10 2SB
Public contact	Dr Dipak Patel, Sheffield Teaching Hospitals NHS Foundation Trust, sth.ResearchAdministration@nhs.net
Scientific contact	Dr Dipak Patel, Sheffield Teaching Hospitals NHS Foundation Trust, sth.ResearchAdministration@nhs.net

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	31 May 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	22 March 2017
Global end of trial reached?	Yes
Global end of trial date	31 May 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is to assess the effects of a single loading regimen and two different maintenance regimens of ticagrelor on erythrocyte adenosine reuptake compared with standard regimens of clopidogrel.

Protection of trial subjects:

Participants were regularly monitored by research staff post - procedure in appointments at the research facility and phone calls. An SOP was designed to aid the transition from ticagrelor to clopidogrel where necessary and follow up phonecalls confirmed that the patients were able to get repeat prescriptions from their GP.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	09 June 2015
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: 180
Worldwide total number of subjects	180
EEA total number of subjects	180

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)	87
From 65 to 84 years	93
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

180 patients were recruited from the PCI pre assessment clinic.

Pre-assignment

Screening details:

Patients over the age of 18 were considered if listed for a PCI. Exclusion criteria such as no previous MI, no medication issues, no extreme bleeding events and fitness to participate were assessed prior to enrolment.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Ticagrelor 60 mg

Arm description:

Patients randomised to ticagrelor 180 mg loading dose 2 hours prior to PCI then 60 mg BD of ticagrelor for 1 month.

Arm type	Experimental
Investigational medicinal product name	Ticagrelor 60 mg
Investigational medicinal product code	274693-27-5
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

180 mg loading dose 2 hours prior to PCI then 60 mg BD for one month

Arm title	Ticagrelor 90 mg

Arm description:

Patients randomised to 180 mg ticagrelor loading dose 2 hours prior to PCI then 90 mg ticagrelor BD for 1 month.

Arm type	Experimental
Investigational medicinal product name	Ticagrelor 90 mg
Investigational medicinal product code	274693-27-5
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

180 mg ticagrelor given as loading dose a minimum of 2 hours prior to PCI then ticagrelor 90 mg BD for 1 month

Arm title	Clopidogrel

Arm description:

Standard of care- patients randomised to this arm received a standard loading dose of clopidogrel prior to PCI followed by 1 month clopidogrel 75 md OD.

Arm type	Active comparator

Investigational medicinal product name	Clopidogrel 75 mg
Investigational medicinal product code	113665-84-2
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Standard of care- patients randomised to this arm received a standard loading dose of clopidogrel prior to PCI followed by 1 month clopidogrel 75 md OD.

Number of subjects in period 1	Ticagrelor 60 mg	Ticagrelor 90 mg	Clopidogrel
Started	60	60	60
Enrolment	60	60	60
Randomisation	60	60	60
Visits 3 to 5	55	51	56
Visit 6	54	48	53
Completed	54	48	53
Not completed	6	12	7
Adverse event, serious fatal	-	1	-
Consent withdrawn by subject	5	2	3
Physician decision	-	-	1
Adverse event, non-fatal	-	1	1
Did not proceed to PCI	1	8	2

Baseline characteristics

Reporting groups	
Reporting group title	Ticagrelor 60 mg
Reporting group description:	
Patients randomised to ticagrelor 180 mg loading dose 2 hours prior to PCI then 60 mg BD of ticagrelor for 1 month.	
Reporting group title	Ticagrelor 90 mg
Reporting group description:	
Patients randomised to 180 mg ticagrelor loading dose 2 hours prior to PCI then 90 mg ticagrelor BD for 1 month.	
Reporting group title	Clopidogrel
Reporting group description:	
Standard of care- patients randomised to this arm received a standard loading dose of clopidogrel prior to PCI followed by 1 month clopidogrel 75 md OD.	

Reporting group values	Ticagrelor 60 mg	Ticagrelor 90 mg	Clopidogrel
Number of subjects	60	60	60
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	66.9	66.0	64.6
standard deviation	± 8.6	± 7.7	± 8.5
Gender categorical Units: Subjects			
Female	11	9	14
Male	49	51	46

Reporting group values	Total		
Number of subjects	180		
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			
standard deviation	-		
Gender categorical			
Units: Subjects			
Female	34		
Male	146		

Subject analysis sets

Subject analysis set title	Efficacy Analysis Set
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

All randomised patients who attended hospital for their planned PCI procedure and received a loading dose of study medication (unless randomised to clopidogrel and having received more than 5 days maintenance therapy and/or a loading dose prior to admission in which case hospital attendance for the PCI procedure will be the criterion for inclusion).

Reporting group values	Efficacy Analysis Set		
Number of subjects	162		
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	66		
standard deviation	± 8		
Gender categorical			
Units: Subjects			
Female	30		
Male	132		

End points

End points reporting groups

Reporting group title	Ticagrelor 60 mg
Reporting group description:	
Patients randomised to ticagrelor 180 mg loading dose 2 hours prior to PCI then 60 mg BD of ticagrelor for 1 month.	
Reporting group title	Ticagrelor 90 mg
Reporting group description:	
Patients randomised to 180 mg ticagrelor loading dose 2 hours prior to PCI then 90 mg ticagrelor BD for 1 month.	
Reporting group title	Clopidogrel
Reporting group description:	
Standard of care- patients randomised to this arm received a standard loading dose of clopidogrel prior to PCI followed by 1 month clopidogrel 75 md OD.	
Subject analysis set title	Efficacy Analysis Set
Subject analysis set type	Modified intention-to-treat
Subject analysis set description:	
All randomised patients who attended hospital for their planned PCI procedure and received a loading dose of study medication (unless randomised to clopidogrel and having received more than 5 days maintenance therapy and/or a loading dose prior to admission in which case hospital attendance for the PCI procedure will be the criterion for inclusion).	

Primary: In vitro adenosine uptake at PCI

End point title	In vitro adenosine uptake at PCI
End point description:	
End point type	Primary
End point timeframe:	
At PCI	

End point values	Ticagrelor 60 mg	Ticagrelor 90 mg	Clopidogrel	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	54	51	57	
Units: micromole(s)/litre				
arithmetic mean (standard deviation)	0.288 (± 0.10)	0.278 (± 0.15)	0.274 (± 0.133)	

Statistical analyses

Statistical analysis title	T Test
Comparison groups	Ticagrelor 90 mg v Clopidogrel

Number of subjects included in analysis	108
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.28
Method	t-test, 2-sided

Secondary: Proportion of non-responders defined as PRU greater than 208.

End point title	Proportion of non-responders defined as PRU greater than 208.
End point description:	

End point type	Secondary
End point timeframe:	
Post loading dose.	

End point values	Ticagrelor 60 mg	Ticagrelor 90 mg	Clopidogrel	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	53	57	59	
Units: Patients	1	0	18	

Statistical analyses

Statistical analysis title	T Test
Comparison groups	Clopidogrel v Ticagrelor 60 mg
Number of subjects included in analysis	112
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	t-test, 2-sided

Statistical analysis title	T Test
Comparison groups	Clopidogrel v Ticagrelor 90 mg
Number of subjects included in analysis	116
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	t-test, 2-sided

Secondary: PRU (CYP2C19 loss of function carrier)

End point title	PRU (CYP2C19 loss of function carrier)

End point description:

End point type	Secondary

End point timeframe:

1 month post dose.

End point values	Ticagrelor 60 mg	Ticagrelor 90 mg	Clopidogrel	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	16	8	16	
Units: PRU				
arithmetic mean (standard deviation)	35 (± 25)	8 (± 3)	176 (± 60)	

Statistical analyses

No statistical analyses for this end point

Secondary: PRU (CYP2C19 no loss of function)

End point title	PRU (CYP2C19 no loss of function)

End point description:

End point type	Secondary

End point timeframe:

1 month post dose.

End point values	Ticagrelor 60 mg	Ticagrelor 90 mg	Clopidogrel	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	35	39	36	
Units: PRU				
arithmetic mean (standard deviation)	32 (± 32)	27 (± 22)	155 (± 49)	

Statistical analyses

No statistical analyses for this end point

Secondary: Periprocedural Myocardial Infarction

End point title	Periprocedural Myocardial Infarction

End point description:

End point type	Secondary

End point timeframe:

24 hours post procedure.

End point values	Ticagrelor 60 mg	Ticagrelor 90 mg	Clopidogrel	Efficacy Analysis Set
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	54	51	57	162
Units: Patients	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: 1 month.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	18.0

Reporting groups	
Reporting group title	Ticagrelor 60
Reporting group description: -	
Reporting group title	Ticagrelor 90
Reporting group description: -	
Reporting group title	Clopidogrel
Reporting group description: -	

Serious adverse events	Ticagrelor 60	Ticagrelor 90	Clopidogrel
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 56 (12.50%)	6 / 58 (10.34%)	5 / 60 (8.33%)
number of deaths (all causes)	0	1	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Radial artery injury			
subjects affected / exposed	0 / 56 (0.00%)	1 / 58 (1.72%)	0 / 60 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Haematoma			
subjects affected / exposed	1 / 56 (1.79%)	1 / 58 (1.72%)	0 / 60 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute massive pulmonary embolism			
subjects affected / exposed	0 / 56 (0.00%)	0 / 58 (0.00%)	1 / 60 (1.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Heart racing			

subjects affected / exposed	0 / 56 (0.00%)	1 / 58 (1.72%)	0 / 60 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina			
subjects affected / exposed	0 / 56 (0.00%)	0 / 58 (0.00%)	1 / 60 (1.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chest pain - cardiac			
subjects affected / exposed	0 / 56 (0.00%)	0 / 58 (0.00%)	1 / 60 (1.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chest pain exertional			
subjects affected / exposed	1 / 56 (1.79%)	0 / 58 (0.00%)	0 / 60 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericardial effusion			
subjects affected / exposed	1 / 56 (1.79%)	0 / 58 (0.00%)	0 / 60 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Loss of consciousness			
subjects affected / exposed	1 / 56 (1.79%)	0 / 58 (0.00%)	0 / 60 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vasovagal symptoms			
subjects affected / exposed	0 / 56 (0.00%)	1 / 58 (1.72%)	0 / 60 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Vessel puncture site haemorrhage			
subjects affected / exposed	1 / 56 (1.79%)	1 / 58 (1.72%)	2 / 60 (3.33%)
occurrences causally related to treatment / all	1 / 1	1 / 1	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Chest pain (non-cardiac)			
subjects affected / exposed	0 / 56 (0.00%)	1 / 58 (1.72%)	0 / 60 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Swelling arm			
subjects affected / exposed	1 / 56 (1.79%)	0 / 58 (0.00%)	0 / 60 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Bowel ischaemia			
subjects affected / exposed	0 / 56 (0.00%)	1 / 58 (1.72%)	0 / 60 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0

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

Non-serious adverse events	Ticagrelor 60	Ticagrelor 90	Clopidogrel
Total subjects affected by non-serious adverse events			
subjects affected / exposed	21 / 56 (37.50%)	27 / 58 (46.55%)	9 / 60 (15.00%)
Injury, poisoning and procedural complications			
Bruising			
subjects affected / exposed	1 / 56 (1.79%)	1 / 58 (1.72%)	2 / 60 (3.33%)
occurrences (all)	1	1	2
Vascular disorders			
Haematoma			
subjects affected / exposed	1 / 56 (1.79%)	0 / 58 (0.00%)	0 / 60 (0.00%)
occurrences (all)	1	0	0
Hypertension			
subjects affected / exposed	0 / 56 (0.00%)	1 / 58 (1.72%)	0 / 60 (0.00%)
occurrences (all)	0	1	0
Cardiac disorders			
Palpitations			
subjects affected / exposed	1 / 56 (1.79%)	0 / 58 (0.00%)	0 / 60 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			

Syncope			
subjects affected / exposed	1 / 56 (1.79%)	1 / 58 (1.72%)	0 / 60 (0.00%)
occurrences (all)	1	1	0
Pre-syncope			
subjects affected / exposed	1 / 56 (1.79%)	0 / 58 (0.00%)	0 / 60 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			
Oedema			
subjects affected / exposed	1 / 56 (1.79%)	0 / 58 (0.00%)	0 / 60 (0.00%)
occurrences (all)	1	0	0
Fatigue			
subjects affected / exposed	2 / 56 (3.57%)	0 / 58 (0.00%)	0 / 60 (0.00%)
occurrences (all)	2	0	0
Non-cardiac chest pain			
subjects affected / exposed	3 / 56 (5.36%)	6 / 58 (10.34%)	2 / 60 (3.33%)
occurrences (all)	3	6	2
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 56 (1.79%)	0 / 58 (0.00%)	0 / 60 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
Gastrointestinal discomfort			
subjects affected / exposed	3 / 56 (5.36%)	2 / 58 (3.45%)	3 / 60 (5.00%)
occurrences (all)	3	2	3
Reproductive system and breast disorders			
Haematospermia			
subjects affected / exposed	0 / 56 (0.00%)	2 / 58 (3.45%)	0 / 60 (0.00%)
occurrences (all)	0	2	0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	4 / 56 (7.14%)	11 / 58 (18.97%)	0 / 60 (0.00%)
occurrences (all)	4	11	0
Epistaxis			
subjects affected / exposed	0 / 56 (0.00%)	1 / 58 (1.72%)	0 / 60 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders			

Rash			
subjects affected / exposed	1 / 56 (1.79%)	1 / 58 (1.72%)	0 / 60 (0.00%)
occurrences (all)	1	1	0
Shingles			
subjects affected / exposed	0 / 56 (0.00%)	1 / 58 (1.72%)	1 / 60 (1.67%)
occurrences (all)	0	1	1
Metabolism and nutrition disorders			
Gout			
subjects affected / exposed	1 / 56 (1.79%)	0 / 58 (0.00%)	1 / 60 (1.67%)
occurrences (all)	1	0	1

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

Online references

http://www.ncbi.nlm.nih.gov/pubmed/29930021