



## Clinical trial results:

### Study of two regimens of TicagrElor compared to clopidogrel in patients undergoing ELection 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
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##### 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
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<b>Arm title</b>	Ticagrelor 60 mg
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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

<b>Arm title</b>	Ticagrelor 90 mg
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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

<b>Arm title</b>	Clopidogrel
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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 mg OD.

Arm type	Active comparator
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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.

<b>Number of subjects in period 1</b>	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 Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years)	0 0 0 0 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

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### 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

<b>Statistical analysis title</b>	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

<b>Statistical analysis title</b>	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

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### 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
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	18.0
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### Reporting groups

Reporting group title	Ticagrelor 60
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Reporting group description: -

Reporting group title	Ticagrelor 90
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Reporting group description: -

Reporting group title	Clopidogrel
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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 %

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

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported

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### Online references

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