Clinical trial results:
The Effect of Intravenous Cangrelor and Oral Ticagrelor on Platelets, the Microcirculation and Myocardial Damage in Patients admitted with STEMI Treated by Primary Percutaneous Coronary Intervention
A randomized controlled pilot trial

Summary

EudraCT number	2016-000195-19
Trial protocol	GB
Global end of trial date	31 October 2017

Results information

Result version number	v1 (current)
This version publication date	18 April 2022
First version publication date	18 April 2022

Trial information

Trial identification

Sponsor protocol code	2015CAR77

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02733341
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	The Royal Wolverhampton NHS Trust
Sponsor organisation address	Research & Development Directorate, The Chestnuts, Wolverhampton, United Kingdom, WV10 0QP
Public contact	Lorraine Jacques, The Royal Wolverhampton NHS Trust, 01902 695065, lorraine.jacques@nhs.net
Scientific contact	Sarah Glover, The Royal Wolverhampton NHS Trust, 1902 695065, sarah.glover7@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 October 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	28 January 2017
Global end of trial reached?	Yes
Global end of trial date	31 October 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine the degree and time-course of platelet inhibition in patients admitted with STEMI treated with IV Cangrelor vs oral Ticagrelor. To assess the impact of Cangrelor vs Ticagrelor on the index of myocardial microcirculatory resistance using IMR.
To investigate the impact of Cangrelor vs Ticagrelor on markers of PPCI success (TIMI flow grade assessment to evaluate coronary blood flow after PPCI).
To assess ST segment resolution post PPCI.
To investigate the impact of Cangrelor vs Ticagrelor on initial myocardial infarct size based on Peak Troponin.
To investigate the impact of Cangrelor vs Ticagrelor on final myocardial infarct size by CMR at three months post PPCI.

Protection of trial subjects:

Trial management group utilised.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	21 July 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: 100
Worldwide total number of subjects	100
EEA total number of subjects	0

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)	58
From 65 to 84 years	37
85 years and over	5

Subject disposition

Recruitment

Recruitment details:

Recruitment of subjects start: 21/07/16, end 28/01/17 in a single centre, UK

Pre-assignment

Screening details:

Patients treated with GP IIb/IIIa receptor antagonist therapy during the primary PCI were withdrawn from the analysis.

Pre-assignment period milestones

Number of subjects started	117[1]
Number of subjects completed	100

Pre-assignment subject non-completion reasons

Reason: Number of subjects	the use of GPIIb/IIIa inhibitors: 11
Reason: Number of subjects	extreme clinical instability: 2
Reason: Number of subjects	presence of an alternative diagnosis: 4

Notes:

[1] - The number of subjects reported to have started the pre-assignment period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: Seventeen subjects were withdrawn from the study after randomization

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	Cangrelor

Arm description:

IV cangrelor drug arm

Arm type	Experimental
Investigational medicinal product name	Cangrelor
Investigational medicinal product code	B01AC25
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Cangrelor was administered at a rate of 30 micrograms/kg intravenous bolus followed immediately by 4 micrograms/kg/min intravenous infusion. The bolus and infusion will be initiated in the cardiac catheter lab prior to the PCI procedure and continued for at least two hours or for the duration of the procedure (to increase up to three hours), whichever is longer.

Arm title	Ticagrelor

Arm description:

Patients allocated to ticagrelor received a loading dose of 180mg of the drug orally immediately following randomization and prior to admission to the catheter suite. They then continued a maintenance dose of 90mg twice daily for 12 months as per standard clinical practice.

Arm type	Active comparator

Investigational medicinal product name	ticagrelor
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Patients allocated to ticagrelor received a loading dose of 180mg of the drug orally immediately following randomization and prior to admission to the catheter suite. They then continued a maintenance dose of 90mg twice daily for 12 months as per standard clinical practice.

Number of subjects in period 1	Cangrelor	Ticagrelor
Started	50	50
Completed	50	50

Baseline characteristics

Reporting groups	
Reporting group title	Cangrelor
Reporting group description:	
IV cangrelor drug arm	
Reporting group title	Ticagrelor
Reporting group description:	
Patients allocated to ticagrelor received a loading dose of 180mg of the drug orally immediately following randomization and prior to admission to the catheter suite. They then continued a maintenance dose of 90mg twice daily for 12 months as per standard clinical practice.	

Reporting group values	Cangrelor	Ticagrelor	Total
Number of subjects	50	50	100
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)	27	31	58
From 65-84 years	22	15	37
85 years and over	1	4	5
Age continuous Units: years			
arithmetic mean	61.2	63.4	
standard deviation	± 13.9	± 12.9	-
Gender categorical Units: Subjects			
Female	11	17	28
Male	39	33	72

End points

End points reporting groups

Reporting group title	Cangrelor
Reporting group description: IV cangrelor drug arm	
Reporting group title	Ticagrelor
Reporting group description: Patients allocated to ticagrelor received a loading dose of 180mg of the drug orally immediately following randomization and prior to admission to the catheter suite. They then continued a maintenance dose of 90mg twice daily for 12 months as per standard clinical practice.	

Primary: P2Y12 reaction units at balloon inflation time

End point title	P2Y12 reaction units at balloon inflation time
End point description:	
End point type	Primary
End point timeframe: At balloon inflation time	

End point values	Cangrelor	Ticagrelor		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	50		
Units: P2Y12 reaction units				
arithmetic mean (standard deviation)	145.2 (± 50.6)	248.3 (± 55.1)		

Statistical analyses

Statistical analysis title	PRU at balloon inflation time
Comparison groups	Cangrelor v Ticagrelor
Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	t-test, 2-sided

Primary: platelet inhibition at 4 hours

End point title	platelet inhibition at 4 hours
End point description:	
End point type	Primary

End point timeframe:
4 hours after balloon inflation

End point values	Cangrelor	Ticagrelor		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	50		
Units: P2Y12 reaction units				
arithmetic mean (standard deviation)	158.1 (± 92.1)	131.2 (± 92.9)		

Statistical analyses

Statistical analysis title	PRU 4 hours after balloon inflation time
Comparison groups	Cangrelor v Ticagrelor
Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.15
Method	t-test, 2-sided

Primary: Platelet inhibition at at 24-36 hours

End point title	Platelet inhibition at at 24-36 hours

End point description:

End point type	Primary

End point timeframe:
24-36 hours after balloon inflation

End point values	Cangrelor	Ticagrelor		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	50		
Units: P2Y12 reaction units				
arithmetic mean (standard deviation)	61.0 (± 50.0)	60.1 (± 56.3)		

Statistical analyses

Statistical analysis title	PRU 24-36 hours after balloon inflation time
Comparison groups	Cangrelor v Ticagrelor

Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.93
Method	t-test, 2-sided

Adverse events

Adverse events information	
Timeframe for reporting adverse events: FROM RECRUITMENT UNTIL PATIENTS DISCHARGE FROM HOSPITAL	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	10

Reporting groups	
Reporting group title	Cangrelor
Reporting group description: IV cangrelor drug arm	
Reporting group title	Ticagrelor
Reporting group description: Patients allocated to ticagrelor received a loading dose of 180mg of the drug orally immediately following randomization and prior to admission to the catheter suite. They then continued a maintenance dose of 90mg twice daily for 12 months as per standard clinical practice.	

Serious adverse events	Cangrelor	Ticagrelor	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 50 (2.00%)	0 / 50 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Respiratory, thoracic and mediastinal disorders			
acute pulmonary oedema	Additional description: Acute Pulmonary Oedema, needed CPAP/Intubation and Acute Ischemic MVR led to MVR Prosthetic + single graft to OM.		
subjects affected / exposed	1 / 50 (2.00%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Cangrelor	Ticagrelor	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 50 (4.00%)	4 / 50 (8.00%)	
General disorders and administration site conditions			
hematoma			

subjects affected / exposed	2 / 50 (4.00%)	3 / 50 (6.00%)	
occurrences (all)	2	3	
Respiratory, thoracic and mediastinal disorders			
shortness of breath			
subjects affected / exposed	0 / 50 (0.00%)	1 / 50 (2.00%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 January 2016	Addition of a poster

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.

The principal limitation of this study is its sample size. While adequately powered for the P2Y12 related endpoints, the results of surrogate endpoints do not provide convincing data and should be interpreted as hypothesis generating

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/31129911