Clinical trial results:
A Single Center, Phase II, Assessor-Blinded, RaNdomized, Active Controlled, Parallel-Group Trial to COmpare Ticagrelor Versus Clopidogrel on the REduction of ArteriaL STiffness and Wave Reflections in Patients with CoronarY Artery Disease. The 'NOVELTY' Study

Summary

EudraCT number	2013-004376-35
Trial protocol	GR
Global end of trial date	20 October 2017

Results information

Result version number	v1 (current)
This version publication date	13 December 2021
First version publication date	13 December 2021

Trial information

Trial identification

Sponsor protocol code	ISSBRILO176

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Hellenic Cardiovascular Research Society
Sponsor organisation address	Ethnikis Antistaseos 61, Halandri, Greece, 15231
Public contact	Charalambos Vlachopoulos, 1st Department of Cardiology, University of Athens Medical School, Hippokration Hospital, 0030 2132088099, cvlachop@otenet.gr
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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	11 March 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	20 October 2017
Global end of trial reached?	Yes
Global end of trial date	20 October 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To compare ticagrelor versus clopidogrel regarding their effect on arterial stiffness as assessed by PWV, at 3 hours after the loading dose of each regimen, in eligible subjects with CAD.

Protection of trial subjects:

Treated in routine care.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	03 February 2013
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	Greece: 60
Worldwide total number of subjects	60
EEA total number of subjects	60

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)	20
From 65 to 84 years	40
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

60 subjects fulfilling all study-specific eligibility criteria were initially recruited for the ‘acute’ study period of 24-hour duration. Subjects that underwent ad hoc PCI continued in the subsequent ‘chronic’ study period of 30-day duration.

Pre-assignment

Screening details:

Inclusion criteria: Provision of informed consent prior to any study specific procedures, Male and female subjects > 18 and < 79 years of age, Indication for elective coronary angiography with or without PCI for inclusion in the ‘acute’ study period, Indication for ad hoc or elective PCI for inclusion in the ‘chronic’ study period.

Period 1

Period 1 title	Acute period
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Single blind
Roles blinded	Assessor[1]

Arms

Are arms mutually exclusive?	Yes
Arm title	Ticagrelor

Arm description: -

Arm type	Active comparator
Investigational medicinal product name	Ticagrelor
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

A single 180 mg oral loading dose (two tablets of 90 mg) plus one additional oral dose (first maintenance dose) of 90 mg, 12 hours after randomisation.

Arm title	Clopidogrel

Arm description: -

Arm type	Active comparator
Investigational medicinal product name	Clopidogrel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

A single 600 mg loading dose (two tablets of 300 mg or 8 tablets of 75 mg).

Notes:

[1] - The roles blinded appear inconsistent with a simple blinded trial.

Justification: Patients, Principal Investigator, study personnel and safety assessors will not be blinded to treatment allocation. Blinding participants would be difficult, as there is an obvious difference in the frequency of administration between clopidogrel and ticagrelor. It was decided that an assessor-blinded RCT design represents the most cost-efficient approach to better accommodating the purposes of this study.

Number of subjects in period 1	Ticagrelor	Clopidogrel
Started	30	30
Completed	29	29
Not completed	1	1
Consent withdrawn by subject	1	1

Period 2

Period 2 title	Chronic period
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Single blind
Roles blinded	Assessor[2]

Arms

Are arms mutually exclusive?	Yes
Arm title	Clopidogrel

Arm description: -

Arm type	Active comparator
Investigational medicinal product name	Clopidogrel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

The subjects of the 'acute' period population that will eventually undergo ad hoc PCI, will continue with clopidogrel maintenance oral dose of 75 mg QD, starting with the administration of the first maintenance dose 24 hours after randomisation (administration of the loading dose).
Subjects planned for elective PCI that will be recruited for the 'chronic' period, will be initiated on a single 600 mg oral loading dose (two tablets of 300 mg or 8 tablets of 75 mg) and continue on maintenance dosing of 75 mg QD.

Arm title	Ticagrelor

Arm description: -

Arm type	Active comparator
Investigational medicinal product name	Ticagrelor
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

• The subjects of the 'acute' period population that will eventually undergo ad hoc PCI, will continue with ticagrelor maintenance oral dose of 90 mg BID, starting with the administration of the second maintenance dose 24 hours after randomisation (12 hours after the administration of the first loading dose during the 'acute' period).
• Subjects planned for elective PCI that will be recruited for the 'chronic' period, will be initiated on a single 180 mg oral loading dose (two tablets of 90 mg) and continue on maintenance dosing of 90 mg BID.

Notes:

[2] - The roles blinded appear inconsistent with a simple blinded trial.

Justification: Patients, Principal Investigator, study personnel and safety assessors will not be blinded to treatment allocation. Blinding participants would be difficult, as there is an obvious difference in the frequency of administration between clopidogrel and ticagrelor. It was decided that an assessor-blinded RCT design represents the most cost-efficient approach to better accommodating the purposes of this study.

Number of subjects in period 2	Clopidogrel	Ticagrelor
Started	29	29
Completed	28	31
Not completed	2	1
Lost to follow-up	2	1
Joined	1	3
to reach at least 30 subjects at randomization	1	3

Baseline characteristics

Reporting groups	
Reporting group title	Acute period
Reporting group description: 58	

Reporting group values	Acute period	Total	
Number of subjects	60	60	
Age categorical Units: Subjects			
18-79 yo	60	60	
Gender categorical Units: Subjects			
Female	22	22	
Male	38	38	

End points

End points reporting groups

Reporting group title	Ticagrelor
Reporting group description: -	
Reporting group title	Clopidogrel
Reporting group description: -	
Reporting group title	Clopidogrel
Reporting group description: -	
Reporting group title	Ticagrelor
Reporting group description: -	

Primary: difference in the mean change in the cfPWV

End point title	difference in the mean change in the cfPWV

End point description:

End point type	Primary

End point timeframe:

The primary outcome is the between treatment difference in the mean change in the cfPWV from baseline (0 hours) at 3 hours after the loading dose of each regimen, in ticagrelor and clopidogrel acute period populations.

End point values	Ticagrelor	Clopidogrel	Clopidogrel	Ticagrelor
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	29	29	28	31
Units: m/s				
arithmetic mean (standard deviation)	8.3 (± 1.2)	8.3 (± 1.8)	9.1 (± 1.3)	9.6 (± 1.6)

Statistical analyses

Statistical analysis title	Acute phase analysis

Statistical analysis description:

Ticagrelor and clopidogrel had no statistically significant effect adjusted for age and BP level cfPWV at baseline (9.61.6 versus 9.11.3 m/s, P=0.19).

Comparison groups	Clopidogrel v Ticagrelor
Number of subjects included in analysis	58
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.27
Method	ANCOVA

Statistical analysis title	Chronic phase
Comparison groups	Clopidogrel v Ticagrelor
Number of subjects included in analysis	59
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.05 [1]
Method	ANCOVA

Notes:

[1] - At 30-day follow-up,
cfPWV decreased significantly in the ticagrelor group (by 0.430.57 m/s, P<0.001, by paired t test), whereas treatment with clopidogrel was associated with a mild, nonsignificant (by 0.120.14 m/s, P=0.47) increase in cfPWV.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse Events will be collected from the time of signature of informed consent throughout the treatment period and including the 30-day follow-up period.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20

Reporting groups

Reporting group title	Ticagrelor randomized

Reporting group description: -

Serious adverse events	Ticagrelor randomized		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 30 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	Ticagrelor randomized		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 30 (10.00%)		
Respiratory, thoracic and mediastinal disorders			
mild dyspnea			
subjects affected / exposed	3 / 30 (10.00%)		
occurrences (all)	3		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 December 2014	change of timetable
11 March 2016	change of timetable

Notes:

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/31165663