Clinical trial results:
Cost-effectiveness of CYP2C19 guided treatment with antiplatelet drugs in patients with ST-segment-elevation myocardial infarction undergoing immediate percutaneous coronary intervention with stent implantation

Summary

EudraCT number	2010-024667-40
Trial protocol	NL
Global end of trial date	04 April 2019

Results information

Result version number	v1 (current)
This version publication date	06 May 2021
First version publication date	06 May 2021
Summary attachment (see zip file)	Trial results (Claassens et al..pdf)

Trial information

Trial identification

Sponsor protocol code	PGxSTEMI08

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01761786
WHO universal trial number (UTN)	-
Other trial identifiers	NTR: NTR3017

Notes:

Sponsors

Sponsor organisation name	St Antonius hospital
Sponsor organisation address	Koekoekslaan 1, Nieuwegein, Netherlands,
Public contact	Jurrien M ten Berg, St. Antonius Hospital, 31 883201232, j.ten.berg@antoniusziekenhuis.nl
Scientific contact	Jurrien M ten Berg, St. Antonius Hospital, 31 883201232, j.ten.berg@antoniusziekenhuis.nl

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	04 April 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	04 April 2019
Global end of trial reached?	Yes
Global end of trial date	04 April 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine whether the CYP2C19 genotype guided antiplatelet treatment strategy is not inferior to a treatment strategy with the newer antiplatelet drugs i.e. ticagrelor and prasugrel (control group) in terms of the composite of death, recurrent MI, definite stent thrombosis, stroke and PLATO major bleeding at 1 year, in patients undergoing primary PCI for STEMI. If non-inferiority is proven, analysis will be performed for superiority.

To determine whether the genotype guided treatment strategy is superior to a treatment of the control group in terms of a composite endpoint of PLATO major and minor bleeding.

To assess the quality of life of patients and health-care resource use in both treatment groups to calculate Quality Adjusted Life Years (QALY's) and net costs per life-year and QALY.

Protection of trial subjects:

Blood samples were collected at the same time as other blood samples. Thus not requiring additional vena punctures.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 June 2011
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	Belgium: 84
Country: Number of subjects enrolled	Netherlands: 2523
Country: Number of subjects enrolled	Italy: 144
Worldwide total number of subjects	2751
EEA total number of subjects	2751

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)	1627
From 65 to 84 years	1074
85 years and over	50

Subject disposition

Recruitment

Recruitment details:

Inclusion between june 2011 and april 2018

Pre-assignment

Screening details:

Inclusion criteria
1) more than 21 years of age with symptoms of acute myocardial infarction of more than 30 minutes but less than 12 hours
2) performed primary PCI with stenting for STEMI

Period 1

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

Blinding implementation details:

Outcome assessor was blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Genotype-guided

Arm description:

Carriers of CYP2C19*2 or *3 loss-of-function alleles were treated with ticagrelor/prasugrel while noncarriers were treated with clopidogrel

Arm type	Experimental
Investigational medicinal product name	Clopidogrel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

75mg once daily

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

Dosage and administration details:

90mg twice daily

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

Dosage and administration details:

10mg once daily or 5mg once daily according to the guideline

Arm title	Standard treatment

Arm description:

Ticagrelor or prasugrel according to guideline instructions

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:

90mg twice daily

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

Dosage and administration details:

10mg once daily or 5mg once daily according to the guideline

Notes:

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

Justification: The members of the clinical event committee were blinded for the treatment allocation of the trial subjects.

Number of subjects in period 1	Genotype-guided	Standard treatment
Started	1370	1381
Completed	1240	1245
Not completed	130	136
Consent withdrawn by subject	33	38
Duplicate randomization	6	7
Included under older protocol	89	90
Lost to follow-up	2	1

Baseline characteristics

Reporting groups	
Reporting group title	Genotype-guided
Reporting group description:	
Carriers of CYP2C19*2 or *3 loss-of-function alleles were treated with ticagrelor/prasugrel while noncarriers were treated with clopidogrel	
Reporting group title	Standard treatment
Reporting group description:	
Ticagrelor or prasugrel according to guideline instructions	

Reporting group values	Genotype-guided	Standard treatment	Total
Number of subjects	1370	1381	2751
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	61.9	61.4	
standard deviation	± 11.1	± 11.5	-
Gender categorical			
Units: Subjects			
Female	317	309	626
Male	1053	1072	2125

End points

End points reporting groups	
Reporting group title	Genotype-guided
Reporting group description:	
Carriers of CYP2C19*2 or *3 loss-of-function alleles were treated with ticagrelor/prasugrel while noncarriers were treated with clopidogrel	
Reporting group title	Standard treatment
Reporting group description:	
Ticagrelor or prasugrel according to guideline instructions	

Primary: Primary outcome	
End point title	Primary outcome
End point description:	
All-cause death, recurrent myocardial infarction, stent thrombosis, stroke, PLATO major bleeding	
End point type	Primary
End point timeframe:	
12 months after primary PCI	

End point values	Genotype-guided	Standard treatment		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1242	1246		
Units: 136				
number (not applicable)	63	73		

Statistical analyses

Statistical analysis title	Primary outcome non-inferiority
Comparison groups	Genotype-guided v Standard treatment
Number of subjects included in analysis	2488
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.001
Method	Logrank

Statistical analysis title	Primary outcome superiority analysis
Comparison groups	Genotype-guided v Standard treatment

Number of subjects included in analysis	2488
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4
Method	Logrank
Parameter estimate	Cox proportional hazard
Point estimate	0.87
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.62
upper limit	1.21

Primary: Primary bleeding outcome

End point title	Primary bleeding outcome
End point description:	

End point type	Primary
End point timeframe:	
12 months after primary PCI	

End point values	Genotype-guided	Standard treatment		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1242	1248		
Units: 278				
number (not applicable)	122	156		

Statistical analyses

Statistical analysis title	Primary bleeding outcome
Comparison groups	Genotype-guided v Standard treatment
Number of subjects included in analysis	2490
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.04
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.78
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.61
upper limit	0.98

Adverse events

Adverse events information[1]	
Timeframe for reporting adverse events: 12 months	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	No dictionary
Dictionary version	0

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

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: As per the trial protocol non-serious adverse events were not systematically collected, since the trial included only approved drugs.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
16 February 2012	The standard treatment group switched from using clopidogrel as standard treatment to using ticagrelor or prasugrel as standard treatment due to a change in the guidelines.

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/31479209

http://www.ncbi.nlm.nih.gov/pubmed/32139231

http://www.ncbi.nlm.nih.gov/pubmed/33722066