Clinical trial results:
GLOBAL LEADERS: Comparative effectiveness of 1 month of ticagrelor plus aspirin followed by ticagrelor monotherapy versus a current-day intensive dual antiplatelet therapy in all-comers patients undergoing percutaneous coronary intervention with bivalirudin and BioMatrix family drug-eluting stent use.

Summary

EudraCT number	2012-003515-58
Trial protocol	IT DE GB AT ES BE NL DK HU PT BG
Global end of trial date	16 February 2018
Results information	
Result version number	v1 (current)
This version publication date	17 February 2019
First version publication date	17 February 2019
Summary attachment (see zip file)	Global Leaders main paper (Global Leaders main paper_Lancet August 2018.pdf) Global leaders supplementary appendix (supplementary appendix.pdf)

Trial information

Trial identification	
Sponsor protocol code	ECRI-12-001
Additional study identifiers	
ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01813435
WHO universal trial number (UTN)	-

Notes:

Sponsors	
Sponsor organisation name	ECRI b.v.
Sponsor organisation address	Westblaak 98, Rotterdam, Netherlands,
Public contact	Managing Director, ECRI b.v., 0031 0102062850, GA.vEs@ecri-trials.com
Scientific contact	Managing Director, ECRI b.v., 0031 0102062850, GA.vEs@ecri-trials.com

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	16 February 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	16 February 2018
Global end of trial reached?	Yes
Global end of trial date	16 February 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine in all-comers patients undergoing PCI under standardised treatment (including the BioMatrix family of drug-eluting stents and bivalirudin), whether treatment with 1 month of ticagrelor and aspirin followed by 23 months of ticagrelor monotherapy is superior with respect to the composite of all-cause mortality or non-fatal new Q-wave MI compared to treatment with 12 months of standard dual anti platelet therapy (DAPT) followed by aspirin monotherapy.

Protection of trial subjects:

NA, phase IV trial

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 May 2013
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	Netherlands: 1159
Country: Number of subjects enrolled	Poland: 1532
Country: Number of subjects enrolled	Portugal: 113
Country: Number of subjects enrolled	Spain: 951
Country: Number of subjects enrolled	United Kingdom: 1713
Country: Number of subjects enrolled	Austria: 672
Country: Number of subjects enrolled	Belgium: 2185
Country: Number of subjects enrolled	Bulgaria: 943
Country: Number of subjects enrolled	Denmark: 131
Country: Number of subjects enrolled	France: 849
Country: Number of subjects enrolled	Germany: 2267
Country: Number of subjects enrolled	Hungary: 527
Country: Number of subjects enrolled	Italy: 1578
Country: Number of subjects enrolled	Switzerland: 705
Country: Number of subjects enrolled	Australia: 83
Country: Number of subjects enrolled	Brazil: 248
Country: Number of subjects enrolled	Singapore: 142

Country: Number of subjects enrolled	Canada: 170
Worldwide total number of subjects	15968
EEA total number of subjects	14620

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)	7877
From 65 to 84 years	7854
85 years and over	237

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

please refer to the manuscript for screening details

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	experimental intervention group

Arm description: -

Arm type	Experimental
Investigational medicinal product name	dual antiplatelet regimen for 30 days after revasc
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

NA

Arm title	control group

Arm description: -

Arm type	control
Investigational medicinal product name	dual antiplatelet regimen for 365 days after revasc
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

NA

Number of subjects in period 1	experimental intervention group	control group
Started	7980	7988
Completed	7980	7988

Baseline characteristics

Reporting groups	
Reporting group title	overall trail

Reporting group description: -

Reporting group values	overall trail	Total	
Number of subjects	15968	15968	
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	64.5		
standard deviation	± 10.3	-	
Gender categorical Units: Subjects			
Female	3714	3714	
Male	12254	12254	

End points

End points reporting groups

Reporting group title	experimental intervention group
Reporting group description: -	
Reporting group title	control group
Reporting group description: -	

Primary: all-casue mortality or new Q-wave myocardial infarction

End point title	all-casue mortality or new Q-wave myocardial infarction
End point description:	
End point type	Primary
End point timeframe:	
up to 2 years post randomisation	

End point values	experimental intervention group	control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7980	7988		
Units: %	304	349		

Statistical analyses

Statistical analysis title	primary endpoint
Comparison groups	experimental intervention group v control group
Number of subjects included in analysis	15968
Analysis specification	Pre-specified
Analysis type	other[1]
P-value	< 0.001
Method	Mantel-Cox

Notes:

[1] - Mantel-Cox method

Adverse events

Adverse events information[1]	
Timeframe for reporting adverse events:	
AE needed to be reported from ICF signature until last follow-up visit	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	20.0

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

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: see results in manuscript

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