Clinical trial results:
A Randomized, Parallel Group, Double-Blind Study of Ticagrelor Compared with Aspirin for Prevention of Vascular Events in Patients Undergoing Coronary Artery Bypass Graft Operation
TiCAB– Ticagrelor in CABG

Summary

EudraCT number	2012-003630-16
Trial protocol	DE AT
Global end of trial date	16 May 2018
Results information	
Result version number	v1 (current)
This version publication date	08 March 2019
First version publication date	08 March 2019
Summary attachment (see zip file)	Synopsis of Clinical Study Report (TiCAB_EudraCT 2012-003630-16_Synopsis of Final Study Report_20181122_final_geschwärzte Namen.pdf)

Trial information

Trial identification	
Sponsor protocol code	GEIDENo.D00112
Additional study identifiers	
ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

Sponsors	
Sponsor organisation name	Deutsches Herzzentrum München
Sponsor organisation address	Lazarettstraße 36, München, Germany, 80636
Public contact	Project Manager, ISAResearch Center, 49 8912182774, ticab@dhm.mhn.de
Scientific contact	Project Manager, ISAResearch Center, 49 8912182774, ticab@dhm.mhn.de

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	20 September 2018
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	16 May 2018
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is to test the hypothesis that Ticagrelor is superior to Aspirin (ASA) for the prevention of major cardiovascular and cerebrovascular events (MACCE; cardiovascular death, myocardial infarction, recurrent revascularization or stroke) in patients undergoing coronary artery bypass graft operation (CABG).
The primary efficacy MACCE-endpoint is the composite of cardiovascular death, myocardial infarction, recurrent revascularization, and stroke at twelve month after coronary artery bypass operation.

Protection of trial subjects:

not applicable

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	29 March 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	Austria: 258
Country: Number of subjects enrolled	Germany: 1614
Country: Number of subjects enrolled	Switzerland: 21
Worldwide total number of subjects	1893
EEA total number of subjects	1872

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)	721

From 65 to 84 years	1161
85 years and over	11

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

For inclusion in the study patients must fulfill the following criteria (1-3):
1. Patients 18 years of age or older
2. Informed, written consent by the patient
3. Indication for CABG surgery: - coronary three vessel disease, or - left main stenosis, or - two vessel disease with impaired left ventricular function (<50%)

Period 1

Period 1 title	Overall period (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor

Arms

Are arms mutually exclusive?	Yes
Arm title	Ticagrelor

Arm description:

Patrients randomised to Ticagrelor

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:

90 mg twice daily

Arm title	Acetylsalicyl acid

Arm description:

Patients randomised to ASA

Arm type	Active comparator
Investigational medicinal product name	ASA
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

100 mg once daily

Number of subjects in period 1	Ticagrelor	Acetylsalicyl acid
Started	946	947
Completed	931	928
Not completed	15	19
Lost to follow-up	15	19

Baseline characteristics

End points

End points reporting groups	
Reporting group title	Ticagrelor
Reporting group description: Patrients randomised to Ticagrelor	
Reporting group title	Acetylsalicyl acid
Reporting group description: Patients randomised to ASA	

Primary: Death	
End point title	Death
End point description: All documented deaths	
End point type	Primary
End point timeframe: at 12 months after coronary artery bypass operation	

End point values	Ticagrelor	Acetylsalicyl acid		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	931	928		
Units: 1	24	23		

Statistical analyses

Statistical analysis title	Full analysis set (FAS)

Statistical analysis description:

All patients who have been randomized to study treatment will be included irrespective of their protocol adherence and continued participation in the study. If a patient prematurely discontinues study medication, every effort will be made to determine the patient's status regarding MI, stroke, coronary revascularization procedures and mortality at the end of their scheduled study duration. Patients will be analyzed according to their randomized study medication irrespective of whether the event

Comparison groups	Ticagrelor v Acetylsalicyl acid
Number of subjects included in analysis	1859
Analysis specification	Pre-specified
Analysis type	other
P-value	= 1 [1]
Method	Cox Model

Notes:

[1] - The p-values for the subgroup analyses will not be adjusted for multiple comparisons as the tests are exploratory and will be interpreted descriptively.

Primary: Death CV	
End point title	Death CV[2]

End point description:

End point type	Primary

End point timeframe:

at 12 months after CABG

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Several analyses to be performed

End point values	Ticagrelor	Acetylsalicyl acid		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	946	947		
Units: 1	17	19		

Statistical analyses

No statistical analyses for this end point

Primary: Myocard Infarction

End point title	Myocard Infarction[3]

End point description:

End point type	Primary

End point timeframe:

12 months after CABG

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Several analyses to be performed

End point values	Ticagrelor	Acetylsalicyl acid		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	946	947		
Units: 1	17	31		

Statistical analyses

No statistical analyses for this end point

Primary: Stroke

End point title	Stroke

End point description:

End point type	Primary

End point timeframe:

12 months after CABG

End point values	Ticagrelor	Acetylsalicyl acid		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	946	947		
Units: 1	30	24		

Statistical analyses

Statistical analysis title	Full analysis set

Statistical analysis description:

All patients who have been randomized to study treatment will be included irrespective of their protocol adherence and continued participation in the study. If a patient prematurely discontinues study medication, every effort will be made to determine the patient's status regarding MI, stroke, coronary revascularization procedures and mortality at the end of their scheduled study duration. Patients will be analyzed according to their randomized study medication irrespective of whether the event

Comparison groups	Ticagrelor v Acetylsalicyl acid
Number of subjects included in analysis	1893
Analysis specification	Pre-specified
Analysis type	other[4]
P-value	= 0.5 [5]
Method	t-test, 2-sided
Parameter estimate	Odds ratio (OR)
Point estimate	0.775
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.1
upper limit	0.9

Notes:

[4] - several analyses to be performed

[5] - The p-values for the subgroup analyses will not be adjusted for multiple comparisons as the tests are exploratory and will be interpreted descriptively.

Primary: Revascularisation

End point title	Revascularisation[6]

End point description:

End point type	Primary

End point timeframe:

12 months after CABG

Notes:

[6] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Several analyses to be performed

End point values	Ticagrelor	Acetylsalicyl acid		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	946	947		
Units: 1	41	36		

Statistical analyses

No statistical analyses for this end point

Primary: Bleeding

End point title	Bleeding[7]

End point description:

End point type	Primary

End point timeframe:

12 months after CABG

Notes:

[7] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Several analyses to be performed

End point values	Ticagrelor	Acetylsalicyl acid		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	946	947		
Units: 1	30	29		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
12 months after coronary artery bypass operation	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	Internal
Dictionary version	1

Reporting groups	
Reporting group title	All patients
Reporting group description:	
All patients	

Serious adverse events	All patients		
Total subjects affected by serious adverse events			
subjects affected / exposed	377 / 1893 (19.92%)		
number of deaths (all causes)	59		
number of deaths resulting from adverse events	58		
Cardiac disorders			
Several SAEs reported			
subjects affected / exposed	377 / 1893 (19.92%)		
occurrences causally related to treatment / all	85 / 1052		
deaths causally related to treatment / all	8 / 58		

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

Non-serious adverse events	All patients		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	783 / 1893 (41.36%)		
Vascular disorders			
Several different AEs documented			
subjects affected / exposed	783 / 1893 (41.36%)		
occurrences (all)	1950		

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