Clinical trial results:
Evaluating the benefit of additional platelet inhibition in acute coronary syndrome patients with high platelet reactivity undergoing PCI

Summary

EudraCT number	2010-020219-35
Trial protocol	GB DE
Global end of trial date	17 October 2013

Results information

Result version number	v1 (current)
This version publication date	16 October 2019
First version publication date	16 October 2019
Summary attachment (see zip file)	APACS publication (APACS Publication.pdf)

Trial information

Trial identification

Sponsor protocol code	2011CI007H

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Royal Brompton & Harefield NHS Trust
Sponsor organisation address	Sydney Street, London, United Kingdom, SW3 6NP
Public contact	Dr. Tobias Geisler Medizinische Klinik III, Department of Cardiology and Cardiovascular disease, , Dr. Tobias Geisler Medizinische Klinik III, Department of Cardiology and Cardiovascular disease, , 0049 70712983688, tobias.geisler@med.uni-tuebingen.de
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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	16 April 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	17 October 2013
Global end of trial reached?	Yes
Global end of trial date	17 October 2013
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

Main objective of the trial:
OBSERVATIONAL REGISTRY OF SCREENED PATIENTS
To identify the proportion of patients who are good responders to routine doses of Clopidogrel and compare the events of death at 30 days.
RANDOMISED PATIENTS
To evaluate if reloading with Prasugrel compared to a high dose regimen of Clopidogrel results in more patients having a low platelet reactivity. Patients will be identified who have poor platelet response to previous Clopidogrel and have undergone an invasive procedure (PCI) to treat their narrowed or blocked heart vessels.
SUBSTUDIES
1. Title: APACS-HPR genetic substudy
To determine the relevant influence of genetic heritage on response variability to the Clopidogrel and Prasugrel antiplatelet treatment.
2) Title: APACS-HPR biomarker substudy
To determine the variability of platelet inhibition to Clopidogrel or Prasugrel treatment if this is influenced by the inflammatory condition and the extent of platelet activation and blood flow to the

Protection of trial subjects:

The APACS trial included patients with known coronary artery anatomy pre-planned PCI clinically. Therefore, the prasugrel loading and maintenance dosing regimen was consistent with standard prescribing guidelines.
At the time there was no evidence and no consistent recommendation on how to treat ACS patients who have been pretreated
with clopidogrel and who are poor responders. It was belived at the time that these patients may have been exposed to increased bleeding risk by re-loading them with prasugrel, however these patients benefited from preselection of patients with high platelet reactivity (i.e. poor responders) by reduction of ischemic rather than increase in bleeding risk.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 February 2012
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	Germany: 38
Country: Number of subjects enrolled	United Kingdom: 6
Worldwide total number of subjects	44
EEA total number of subjects	44

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)	30
From 65 to 84 years	14
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study started enrolment in 15 February 2012 and recruitment terminated on the 31st July 2013 well before the predicted recruiting time, so that only 44 patients could be recruited.

Pre-assignment

Screening details:

Screening details:
Patients admitted to the hospital with suspected ACS (unstable angina, NSTEMI or STEMI) requiring PCI were screened. A study blood sample was required at least 2 hours after prior loading with clopidogrel to evaluate platelet activity. If this was not achievable for clinical reasons then this patient would not be eligible for

Period 1

Period 1 title	TP 0
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Arm title	Clopidogrel

Arm description:

Group 1: Clopidogrel (Plavix)
• Day 1 Loading 600mg
• Day 2 to 7 day: 150mg o.d.
• Day 8 to 30 days: 75mg o.d.

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

Dosage and administration details:

Day 1 loading 60mg
Day 2 to 7 10mg o.d.
Day 8 to 30 days 10mg od

Number of subjects in period 1	Clopidogrel
Started	44
Completed	44

Period 2

Period 2 title	TP 1 to TP 6
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Prasugrel

Arm description:

Day 1 loading 60mg
Day 2 to 7 10mg o.d.
Day 8 to 30 days 10mg od

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

Dosage and administration details:

Day 1 loading 60mg
• Day 2 to 7 10mg o.d.
• Day 8 to 30 days 10mg od

Arm title	Clopidogrel (Plavix)

Arm description:

Day 1 Loading 600mg
Day 2 to 7 day: 150mg o.d.
Day 8 to 30 days: 75mg o.d.

Arm type	Active comparator
Investigational medicinal product name	Clopidogrel (Plavix)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Day 1 Loading 600mg
Day 2 to 7 day: 150mg o.d.
Day 8 to 30 days: 75mg o.d.

Number of subjects in period 2	Prasugrel	Clopidogrel (Plavix)
Started	22	22
Completed	22	22

Baseline characteristics

End points

End points reporting groups

Reporting group title	Clopidogrel
Reporting group description:	
Group 1: Clopidogrel (Plavix) • Day 1 Loading 600mg • Day 2 to 7 day: 150mg o.d. • Day 8 to 30 days: 75mg o.d.	
Reporting group title	Prasugrel
Reporting group description:	
Day 1 loading 60mg Day 2 to 7 10mg o.d. Day 8 to 30 days 10mg od	
Reporting group title	Clopidogrel (Plavix)
Reporting group description:	
Day 1 Loading 600mg Day 2 to 7 day: 150mg o.d. Day 8 to 30 days: 75mg o.d.	

Primary: decreased platelet reactivity under the cut-off value of 400 Au.min

End point title	decreased platelet reactivity under the cut-off value of 400 Au.min
End point description:	
End point type	Primary
End point timeframe:	
decreased platelet reactivity under the cut-off value of 400 Au.min in the prasugrel re-loading arm compared to the clopidogrel re-loading arm at 4 hours after loading with study drug in patients with initial high platelet reactivity	

End point values	Prasugrel	Clopidogrel (Plavix)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	22		
Units: 400 Au.min				
number (not applicable)	22	22		

Statistical analyses

Statistical analysis title	Statistical Analysis
Statistical analysis description:	
Baseline variables were compared with the use of chi-square tests for categorical variables; t-tests or the Wilcoxon rank-sum were used for continuous variables depending on the distributions of the variables. Comparison of the primary endpoint and secondary endpoints was carried out using a chi squared or Fishers exact test. The confidence intervals were two-sided with a 95% confidence level, and all hypothesis tests were two-sided carried out at a significance level $p < 0.05$.	
Comparison groups	Clopidogrel (Plavix) v Prasugrel

Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.05
Method	Chi-squared corrected
Parameter estimate	difference in proportions
Point estimate	0.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.48
upper limit	0.66

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Adverse Events reported on CRF and hospital notes in timely manner	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	15

Reporting groups	
Reporting group title	Prasugrel

Reporting group description: -

Serious adverse events	Prasugrel		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 1 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	Prasugrel		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 1 (100.00%)		
Cardiac disorders			
Hypotension			
subjects affected / exposed	1 / 1 (100.00%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
30 June 2011	Protocol Version 6, 23rd May; Changes to the study protocol as requested by BPharm.
29 February 2012	NOSA 2 – addition of 3 new sites. Data Custodianship changed. Non-substantial amendment 01 – change to sponsor contact person from Wendy Butcher to Angela Cooper. NOSA02 also includes delayed submission of NOSA01 to the MHRA (this is dated 24th January 2012)
29 October 2012	Protocol version 7/16 October 2012 PIS Version 5/16 October 2012; This amendment was never implemented. The REC was informed that this amendment was 'voided' due to new safety information in relation to Prasugrel. PIS V5.0 was approved as part of this amendment. However the CI decided that the amendment of the PIS was not required due to the changes subsequently made and implemented with SA04. Version 4.0 is the latest version of the PIS as approved with SA01.
09 January 2013	Protocol 8/09 January 2013; To 'void' SA03 – Protocol V7.0 was not in use all changes transferred to Protocol V8.0 submitted with this amendment as detailed

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
31 July 2013	The study was terminated early as clopidogrel use decreased sharply due to introduction of newer P2Y12 inhibitors	-

Notes:

Limitations and caveats

None reported