Clinical trial results:
Relative Bioavailability Study Between 75 Mg Tablet And 75 Mg Solution Of Clopidogrel (SR25990C) After Single Oral Administration To Young Healthy Men. Open, Crossover, Randomized And Monocenter Study

Summary

EudraCT number	2015-001245-89
Trial protocol	Outside EU/EEA
Global end of trial date	15 May 2002

Results information

Result version number	v1 (current)
This version publication date	23 May 2016
First version publication date	12 June 2015

Trial information

Trial identification

Sponsor protocol code	BDR4580

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Sanofi aventis recherche & développement
Sponsor organisation address	1 avenue Pierre Brossolette, Chilly, Mazarin, France, 91380
Public contact	Trial Transparency Team, Sanofi Aventis Recherche & Developpement, Contact-US@sanofi.com
Scientific contact	Trial Transparency Team, Sanofi Aventis Recherche & Developpement, Contact-US@sanofi.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-000049-PIP01-07
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	03 November 2002
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	15 May 2002
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To compare the bioavailabilty of clopidogrel administered as 75 mg Plavix® tablet to that of 75 mg of clopidogrel in drinkable solution, after single oral administration, in fasting state, in normal healthy subjects

Protection of trial subjects:

Subjects were fully informed of all pertinent aspects of the clinical trial as well as the possibility to discontinue at any time in language and terms appropriate for the subject and considering the local culture. During the course of the trial, subjects were provided with individual subject cards indicating the nature of the trial the subject is participating, contact details and any information needed in the event of a medical emergency.
Collected personal data and human biological samples were processed in compliance with the Sanofi-Aventis Group Personal Data Protection Charter ensuring that the Group abides by the laws governing personal data protection in force in all countries in which it operates.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	25 March 2002
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	France: 24
Worldwide total number of subjects	24
EEA total number of subjects	24

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)	24
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at a single centre in France. A total of 24 subjects were screened between 25 March 2002 and 17 April 2002.

Pre-assignment

Screening details:

All 24 screened subjects were randomized.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	No
Arm title	Clopidogrel 75 mg Solution

Arm description:

Single dose of clopidogrel solution.

Arm type	Experimental
Investigational medicinal product name	Clopidogrel
Investigational medicinal product code	SR25990C
Other name	
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:

Clopidogrel solution 75 mg.

Arm title	Clopidogrel 75 mg Tablet

Arm description:

Single dose of clopidogrel tablet.

Arm type	Active comparator
Investigational medicinal product name	Clopidogrel
Investigational medicinal product code	SR25990C
Other name	Plavix®
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Clopidogrel tablet 75 mg.

Number of subjects in period 1	Clopidogrel 75 mg Solution	Clopidogrel 75 mg Tablet
Started	24	24
Treated	24	24
Completed	24	24

Baseline characteristics

Reporting groups	
Reporting group title	Overall Study

Reporting group description: -

Reporting group values	Overall Study	Total	
Number of subjects	24	24	
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	26		
standard deviation	± 5.4	-	
Gender categorical Units: Subjects			
Female	0	0	
Male	24	24	

End points

End points reporting groups

Reporting group title	Clopidogrel 75 mg Solution
Reporting group description: Single dose of clopidogrel solution.	
Reporting group title	Clopidogrel 75 mg Tablet
Reporting group description: Single dose of clopidogrel tablet.	

Primary: Clopidogrel Metabolite (SR26334) Pharmacokinetics: AUC, AUClast, and Cmax

End point title	Clopidogrel Metabolite (SR26334) Pharmacokinetics: AUC, AUClast, and Cmax

End point description:

AUC was defined as area under the plasma concentration versus time curve extrapolated to infinity. AUClast was defined as area under the plasma concentration versus time curve calculated using the trapezoidal method from time zero to the real time tlast (time corresponding to the last concentration above the limit of quantification). Cmax was defined as maximum plasma concentration observed. A validated liquid chromatography mass spectrometry method (LCMS/MS) was used to quantify SR26334 concentrations.

End point type	Primary

End point timeframe:

t (0h-48h)

End point values	Clopidogrel 75 mg Solution	Clopidogrel 75 mg Tablet		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	24		
Units: Specified in each category				
arithmetic mean (standard deviation)				
AUC (ng.h/mL) (n= 24, 23)	8185.86 (± 1713.36)	7918.95 (± 1327.54)		
AUClast (ng.h/mL) (n= 24, 24)	8061.33 (± 1700)	7723.35 (± 1356.37)		
Cmax (ng/mL) (n= 24, 24)	3252 (± 835)	2762 (± 599)		

Attachments (see zip file)	Mean±SD SR26334 plasma conc. (n=24) - Linear scale/graph.

Statistical analyses

Statistical analysis title	AUC - Ratio Estimate

Statistical analysis description:

Actual number of subjects included in analysis were 24

Comparison groups	Clopidogrel 75 mg Solution v Clopidogrel 75 mg Tablet

Number of subjects included in analysis	48
Analysis specification	Pre-specified
Analysis type	equivalence
Parameter estimate	Geometric Mean Ratio
Point estimate	1.04
Confidence interval	
level	90 %
sides	2-sided
lower limit	1.01
upper limit	1.07

Statistical analysis title	AUClast - Ratio Estimate
Statistical analysis description:	
Actual number of subjects included in analysis were 24.	
Comparison groups	Clopidogrel 75 mg Solution v Clopidogrel 75 mg Tablet
Number of subjects included in analysis	48
Analysis specification	Pre-specified
Analysis type	equivalence
Parameter estimate	Geometric Mean Ratio
Point estimate	1.04
Confidence interval	
level	90 %
sides	2-sided
lower limit	1.01
upper limit	1.07

Statistical analysis title	Cmax - Ratio Estimate
Statistical analysis description:	
Actual number of subjects included in analysis were 24.	
Comparison groups	Clopidogrel 75 mg Solution v Clopidogrel 75 mg Tablet
Number of subjects included in analysis	48
Analysis specification	Pre-specified
Analysis type	equivalence
Parameter estimate	Geometric Mean Ratio
Point estimate	1.15
Confidence interval	
level	90 %
sides	2-sided
lower limit	1.02
upper limit	1.3

Primary: Clopidogrel Metabolite (SR26334) Pharmacokinetics: Tmax	
End point title	Clopidogrel Metabolite (SR26334) Pharmacokinetics: Tmax

End point description:

tmax was defined as time to reach maximum plasma concentration (Cmax).

End point type	Primary

End point timeframe:

t (0h-48h)

End point values	Clopidogrel 75 mg Solution	Clopidogrel 75 mg Tablet		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	24		
Units: Hours				
median (full range (min-max))	0.5 (0.33 to 2)	0.75 (0.5 to 1.5)		

Statistical analyses

Statistical analysis title	tmax - Ratio Estimate

Statistical analysis description:

Actual number of subjects included in analysis were 24.

Comparison groups	Clopidogrel 75 mg Solution v Clopidogrel 75 mg Tablet
Number of subjects included in analysis	48
Analysis specification	Pre-specified
Analysis type	equivalence
Parameter estimate	Ratio estimate
Point estimate	-0.14
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.25
upper limit	-0.09

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

All Adverse Events (AE) were collected from signature of the informed consent form up to the final visit (Day 24) regardless of seriousness or relationship to investigational product.

Adverse event reporting additional description:

Reported adverse events are treatment-emergent adverse events that is AEs that developed/worsened during the 'on treatment period' (from study drug administration up to 24 hours post dose).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	5.1

Reporting groups

Reporting group title	Clopidogrel Solution

Reporting group description:

Single dose of clopidogrel solution.

Reporting group title	Clopidogrel Tablet

Reporting group description:

Clopidogrel tablet 75 mg.

Serious adverse events	Clopidogrel Solution	Clopidogrel Tablet	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			

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

Non-serious adverse events	Clopidogrel Solution	Clopidogrel Tablet	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (0.00%)	

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: No subject experienced any adverse event.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
02 April 2002	Change of the principal Investigator for administrative reasons.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported