Clinical trial results:
An Open-Label, Dose-Ranging Study of Prasugrel in Pediatric Patients with Sickle Cell Disease

Summary

EudraCT number	2017-001243-12
Trial protocol	Outside EU/EEA
Global end of trial date	02 November 2012

Results information

Result version number	v1 (current)
This version publication date	08 June 2017
First version publication date	08 June 2017

Trial information

Trial identification

Sponsor protocol code	H7T-MC-TACX

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01476696
WHO universal trial number (UTN)	-
Other trial identifiers	Trial ID: 12324

Notes:

Sponsors

Sponsor organisation name	Eli Lilly and Company
Sponsor organisation address	Lilly Corporate Center, Indianapolis, IN, United States, 46285
Public contact	Available Mon Fri 9 AM 5 PM EST, Eli Lilly and Company, 1 877CTLilly,
Scientific contact	Available Mon Fri 9 AM 5 PM EST, Eli Lilly and Company, 1 8772854559,

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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	02 November 2012
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	02 November 2012
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study is to determine the correct prasugrel dosage to be given to children with sickle cell disease (SCD).

Protection of trial subjects:

This study was conducted in accordance with International Conference on Harmonization (ICH) Good Clinical Practice, and the principles of the Declaration of Helsinki, in addition to following the laws and regulations of the country or countries in which a study is conducted.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	30 November 2011
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	United States: 33
Worldwide total number of subjects	33
EEA total number of subjects	0

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)	21
Adolescents (12-17 years)	12
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

The study was conducted in 2 parts: Part A (single-dose range finding phase) then Part B (once-daily repeated dosing phase). Participants completing Part A could, but were not required to, participate in Part B. There were 2 dosing periods during Part B of the study.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Part A: Prasugrel Single Dose

Arm description:

Participants who only enrolled in Part A of the study.

Part A: 0.03 milligrams per kilogram (mg/kg) up to 0.60 mg/kg Prasugrel, each dose titrated up or down for each participant in order to achieve desired platelet inhibition (20% to 50%). Single dose administered orally [oral-disintegrating tablet (ODT)] up to 3 times, at different mg/kg doses, with up to 18 days between doses.

Arm type	Experimental
Investigational medicinal product name	Prasugrel Single Dose (Part A)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Prasugrel 0.03 milligrams per kilogram (mg/kg) to 0.60 mg/kg dosage to be titrated up or down based on desired platelet inhibition, administered orally [oral-disintegrating tablet (ODT)], single dose given up to 3 occasions, at different strengths, with up to 18 days between doses.

Arm title	Part B: Prasugrel Once-Daily Dose

Arm description:

Participants who only enrolled in Part B of the study.

Part B: Daily Prasugrel dose (mg/kg) expected to achieve mean platelet activation inhibition of 30%, administered orally, ODT, once daily for 14 ± 4 days (first dosing period during Part B). Initial dose, 0.08 mg/kg Prasugrel, administered then pharmacodynamic (PD) response measured 4 hours later. Based on 4-hour PD response, each participant assigned to either 0.08 or 0.06 mg/kg Prasugrel, administered orally, once daily for the remainder of the first dosing period in Part B. For the second continuous 14 ± 4-day period, participants were administered 1 of 3 possible doses: 0.06, 0.08, or 0.12 mg/kg depending on their steady-state PD response at the end of the first dosing period, such that the second dose would be unlikely to exceed 50% platelet inhibition. Participants received study drug for a total of 28 ± 8 days during Part B of the study.

Arm type	Experimental
Investigational medicinal product name	Prasugrel Once-Daily Dose (Part B)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Daily prasugrel dose (mg/kg) that is expected to achieve mean platelet activation inhibition of 30% administered orally, once daily for 10-18 days and then followed by prasugrel dose (mg/kg) that is expected to achieve mean platelet activation inhibition of 50% administered orally, once daily for 10-18 days, for a total of 20-36 days.

Arm title	Part A then Part B: Prasugrel Single Dose Then Once-Daily Dose

Arm description:

Participants who enrolled in Part A and B of study.
Part A: 0.03 up to 0.60 mg/kg Prasugrel, each dose titrated up or down for each participant to achieve desired platelet inhibition (20% to 50%). Single dose administered orally, ODT, up to 3 times, at different mg/kg doses, with up to 18 days between doses.
Part B: Daily Prasugrel dose (mg/kg) expected to achieve mean platelet activation inhibition of 30%, administered orally, ODT, once daily for 14 ± 4 days (first dosing period in Part B). Initial dose, 0.08 mg/kg Prasugrel, administered then PD response measured 4 hours later. Based on 4-hour PD response, each participant assigned to 0.08 or 0.06 mg/kg Prasugrel once daily for remainder of first dosing period. For second 14 ± 4-day period, participants assigned to 1 of 3 possible doses: 0.06, 0.08, or 0.12 mg/kg depending on steady-state PD response at end of first dosing period, such that the second dose would be unlikely to exceed 50% platelet inhibition.

Arm type	Experimental
Investigational medicinal product name	Prasugrel Single Dose (Part A)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Prasugrel 0.03 milligrams per kilogram (mg/kg) to 0.60 mg/kg dosage to be titrated up or down based on desired platelet inhibition, administered orally [oral-disintegrating tablet (ODT)], single dose given up to 3 occasions, at different strengths, with up to 18 days between doses.

Investigational medicinal product name	Prasugrel Once-Daily Dose (Part B)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Daily prasugrel dose (mg/kg) that is expected to achieve mean platelet activation inhibition of 30% administered orally, once daily for 10-18 days and then followed by prasugrel dose (mg/kg) that is expected to achieve mean platelet activation inhibition of 50% administered orally, once daily for 10-18 days, for a total of 20-36 days.

Number of subjects in period 1	Part A: Prasugrel Single Dose	Part B: Prasugrel Once-Daily Dose	Part A then Part B: Prasugrel Single Dose Then Once-Daily Dose
Started	15	9	9
Received at least 1 dose of study drug	15	9	9
Completed	12	8	9
Not completed	3	1	0
Consent withdrawn by subject	1	-	-
Sponsor decision	2	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Overall Study

Reporting group description: -

Reporting group values	Overall Study	Total	
Number of subjects	33	33	
Age, Customized Units: participants			
≥2 and ≤5 years	7	7	
≥6 and ≤11 years	14	14	
≥12 and ≤17 years	12	12	
Gender, Male/Female Units: Participants			
Female	19	19	
Male	14	14	
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	1	1	
Not Hispanic or Latino	32	32	
Unknown or Not Reported	0	0	
Race/Ethnicity, Customized Units: Subjects			
Native Hawaiian or Other Pacific Islander	1	1	
Black or African American	32	32	
Region of Enrollment Units: Subjects			
United States	33	33	
Genotype			
The number of participants who have the homozygous sickle cell (HbSS) or hemoglobin S beta^0 thalassemia (HbS β^0 thalassemia)] sickle cell genotype.			
Units: Subjects			
HbSS	30	30	
HbS Beta^0 Thalassemia	3	3	
Height Units: centimeters (cm)			
arithmetic mean	139.21		
standard deviation	± 22.663	-	
Weight Units: kilograms (kg)			
arithmetic mean	38.55		
standard deviation	± 18.785	-	
Body Mass Index			
Body mass index is an estimate of body fat based on body weight divided by height squared.			
Units: kilograms per square meter (kg/m^2)			
arithmetic mean	18.64		
standard deviation	± 4.091	-	

End points

End points reporting groups

Reporting group title	Part A: Prasugrel Single Dose

Reporting group description:

Participants who only enrolled in Part A of the study.

Part A: 0.03 milligrams per kilogram (mg/kg) up to 0.60 mg/kg Prasugrel, each dose titrated up or down for each participant in order to achieve desired platelet inhibition (20% to 50%). Single dose administered orally [oral-disintegrating tablet (ODT)] up to 3 times, at different mg/kg doses, with up to 18 days between doses.

Reporting group title	Part B: Prasugrel Once-Daily Dose

Reporting group description:

Participants who only enrolled in Part B of the study.

Part B: Daily Prasugrel dose (mg/kg) expected to achieve mean platelet activation inhibition of 30%, administered orally, ODT, once daily for 14 ± 4 days (first dosing period during Part B). Initial dose, 0.08 mg/kg Prasugrel, administered then pharmacodynamic (PD) response measured 4 hours later. Based on 4-hour PD response, each participant assigned to either 0.08 or 0.06 mg/kg Prasugrel, administered orally, once daily for the remainder of the first dosing period in Part B. For the second continuous 14 ± 4-day period, participants were administered 1 of 3 possible doses: 0.06, 0.08, or 0.12 mg/kg depending on their steady-state PD response at the end of the first dosing period, such that the second dose would be unlikely to exceed 50% platelet inhibition. Participants received study drug for a total of 28 ± 8 days during Part B of the study.

Reporting group title	Part A then Part B: Prasugrel Single Dose Then Once-Daily Dose

Reporting group description:

Participants who enrolled in Part A and B of study.
Part A: 0.03 up to 0.60 mg/kg Prasugrel, each dose titrated up or down for each participant to achieve desired platelet inhibition (20% to 50%). Single dose administered orally, ODT, up to 3 times, at different mg/kg doses, with up to 18 days between doses.
Part B: Daily Prasugrel dose (mg/kg) expected to achieve mean platelet activation inhibition of 30%, administered orally, ODT, once daily for 14 ± 4 days (first dosing period in Part B). Initial dose, 0.08 mg/kg Prasugrel, administered then PD response measured 4 hours later. Based on 4-hour PD response, each participant assigned to 0.08 or 0.06 mg/kg Prasugrel once daily for remainder of first dosing period. For second 14 ± 4-day period, participants assigned to 1 of 3 possible doses: 0.06, 0.08, or 0.12 mg/kg depending on steady-state PD response at end of first dosing period, such that the second dose would be unlikely to exceed 50% platelet inhibition.

Subject analysis set title	Entire Study Population
Subject analysis set type	Full analysis

Subject analysis set description:

Participants enrolled in Part A, Part A and B, or only Part B of study.
Part A: 0.03 up to 0.60 mg/kg Prasugrel, each dose titrated up or down for each participant to achieve desired platelet inhibition (20% to 50%). Single dose administered orally, ODT, up to 3 times, at different mg/kg doses, with up to 18 days between doses.
Part B: Daily Prasugrel dose (mg/kg) expected to achieve mean platelet activation inhibition of 30%, administered orally, ODT, once daily for 14 ± 4 days (first dosing period in Part B). Initial dose, 0.08 mg/kg Prasugrel, administered then PD response measured 4 hours later. Based on 4-hour PD response, each participant assigned to 0.08 or 0.06 mg/kg Prasugrel once daily for remainder of first dosing period. For second 14 ± 4-day period, participants assigned to 1 of 3 possible doses: 0.06, 0.08, or 0.12 mg/kg depending on steady-state PD response at end of first dosing period, so that the second dose would be unlikely to exceed 50% platelet inhibition.

Subject analysis set title	Part B: Baseline
Subject analysis set type	Full analysis

Subject analysis set description:

Participants in Part B of the study, prior to receiving treatment (Prasugrel once-daily doses).

Subject analysis set title	Part B: Prasugrel Once-Daily Dose (0.06 mg/kg)
Subject analysis set type	Full analysis

Subject analysis set description:

Participants who received 0.06 mg/kg Prasugrel administered orally, ODT, once daily, anytime (first or second dosing period) during Part B of the study, for a total of up to 36 days.

Subject analysis set title	Part B: Prasugrel Once-Daily Dose (0.08 mg/kg)
Subject analysis set type	Full analysis

Subject analysis set description:

Participants who received 0.08 mg/kg Prasugrel administered orally, ODT, once daily, anytime (first or second dosing period) during Part B of the study, for a total of up to 36 days.

Subject analysis set title	Part B: Prasugrel Once-Daily Dose (0.12 mg/kg)
Subject analysis set type	Full analysis

Subject analysis set description:

Participants who received 0.12 mg/kg Prasugrel administered orally, ODT, once daily, anytime (first or second dosing period) during Part B of the study, for a total of up to 36 days.

Primary: Pharmacokinetics: Area Under the Concentration-Time Curve (AUC) of Prasugrel active metabolite (Pras-AM)

End point title	Pharmacokinetics: Area Under the Concentration-Time Curve (AUC) of Prasugrel active metabolite (Pras-AM)[1]

End point description:

AUC of Pras-AM from time 0 up to the last sampling time of 4 hours postdose [AUC(0-tlast)] is reported by dose administered [0.03, 0.05, 0.07, 0.09, 0.11, 0.13, 0.15, 0.2, 0.25, 0.3, 0.35, 0.4, 0.45, 0.5, 0.55, and 0.6 milligrams per kilogram (mg/kg)] during Part A (single-dose range finding phase) and is reported for doses administered on site (0.06, 0.08, and 0.12 mg/kg) during Part B (once-daily repeated dosing phase) of the study. Four participants received the same dose at multiple visits where pharmacokinetic samples were collected.

99999 = NA: The geometric coefficient of variation could not be determined because data for only 1 profile were analyzed.

End point type	Primary

End point timeframe:

Parts A and B: 0.5, 1, 1.5, 2, 4 hours postdose

Notes:

[1] - 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: Data for Primary Outcome Measures 2 were collected for presentation of results in a scatter plot and were not intended to be summarized due to the limited number of participants per treatment.

End point values	Entire Study Population			
Subject group type	Subject analysis set			
Number of subjects analysed	33[2]			
Units: nanograms*hour per milliliter (ng*hr/mL)				
geometric mean (geometric coefficient of variation)				
Part A: 0.03 mg/kg (n=2)	8.68 (± 36)			
Part A: 0.05 mg/kg (n=2)	14.5 (± 44)			
Part A: 0.07 mg/kg (n=2)	20.8 (± 31)			
Part A: 0.09 mg/kg (n=2)	31.3 (± 25)			
Part A: 0.11 mg/kg (n=1)	22.2 (± 99999)			
Part A: 0.13 mg/kg (n=2)	50.3 (± 20)			
Part A: 0.15 mg/kg (n=2)	35.2 (± 86)			
Part A: 0.2 mg/kg (n=2)	43.7 (± 48)			
Part A: 0.25 mg/kg (n=3)	60.7 (± 88)			
Part A: 0.3 mg/kg (n=6)	87.9 (± 52)			
Part A: 0.35 mg/kg (n=11)	111 (± 59)			
Part A: 0.4 mg/kg (n=14)	108 (± 55)			
Part A: 0.45 mg/kg (n=8)	136 (± 53)			
Part A: 0.5 mg/kg (n=7)	186 (± 36)			

Part A: 0.55 mg/kg (n=1)	87 (± 99999)			
Part A: 0.6 mg/kg (n=3)	299 (± 4)			
Part B: 0.06 mg/kg (n=7)	16.3 (± 50)			
Part B: 0.08 mg/kg (n=17)	27.1 (± 20)			
Part B: 0.12 mg/kg (n=8)	38.5 (± 15)			

Notes:

[2] - 99999=NA

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Platelet Inhibition as Measured by VerifyNow™P2Y12 (VN)

End point title	Percentage of Platelet Inhibition as Measured by VerifyNow™P2Y12 (VN)[3]

End point description:

Accumetrics VN assay: A point-of-care device that measures platelet aggregation. Percentage of platelet inhibition is reported by dose administered [0.03, 0.05, 0.07, 0.09, 0.11, 0.13, 0.15, 0.2, 0.25, 0.3, 0.35, 0.4, 0.45, 0.5, 0.55, and 0.6 milligrams per kilogram (mg/kg)] during Part A (single-dose range finding phase) and also during the once-daily repeated dosing phase in Part B, at steady state, 14 ± 4 days after each new dose (0.06, 0.08, and 0.12 mg/kg) is administered. One participant received the same dose at multiple visits (Part A) and one participant received the same daily dose during both dosing periods in Part B.

End point type	Primary

End point timeframe:

Part A: 4 hours postdose and Part B: at steady state (14 ± 4 days after the start of each new dosage)

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: Data for Primary Outcome Measures 1 were collected for presentation of results in a scatter plot and were not intended to be summarized due to the limited number of participants per treatment.

End point values	Entire Study Population			
Subject group type	Subject analysis set			
Number of subjects analysed	33[4]			
Units: percentage of platelet inhibition				
arithmetic mean (standard deviation)				
Part A: 0.03 mg/kg (n=2)	2 (± 2.83)			
Part A: 0.05 mg/kg (n=2)	0 (± 0)			
Part A: 0.07 mg/kg (n=2)	0 (± 0)			
Part A: 0.08 mg/kg (n=18)	7.7 (± 9.35)			
Part A: 0.09 mg/kg (n=2)	2.5 (± 3.54)			
Part A: 0.11 mg/kg (n=1)	0 (± 9999)			
Part A: 0.13 mg/kg (n=2)	9.5 (± 13.44)			
Part A: 0.15 mg/kg (n=2)	4 (± 0)			
Part A: 0.2 mg/kg (n=2)	0 (± 0)			
Part A: 0.25 mg/kg (n=3)	18 (± 18.52)			
Part A: 0.3 mg/kg (n=6)	42.3 (± 27.21)			
Part A: 0.35 mg/kg (n=11)	38 (± 28.46)			
Part A: 0.4 mg/kg (n=14)	39.1 (± 26.77)			
Part A: 0.45 mg/kg (n=8)	35.3 (± 27.16)			
Part A: 0.5 mg/kg (n=7)	55.9 (± 27.85)			
Part A: 0.55 mg/kg (n=1)	31 (± 9999)			

Part A: 0.6 mg/kg (n=3)	70.3 (± 19.22)			
Part B: 0.06 mg/kg (n=8)	38.6 (± 21.07)			
Part B: 0.08 mg/kg (n=18)	37.8 (± 25.86)			
Part B: 0.12 mg/kg (n=8)	48.1 (± 11.29)			

Notes:

[4] - 9999=NA

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetics: Area Under the Concentration-Time Curve (AUC) of Prasugrel Inactive Metabolite

End point title	Pharmacokinetics: Area Under the Concentration-Time Curve (AUC) of Prasugrel Inactive Metabolite[5]

End point description:

AUC of prasugrel inactive metabolite(s) from time 0 up to the last sampling time of 4 hours postdose [AUC(0-tlast)]. Improvements in bioanalytical methodology enabled direct measurement of Pras-AM from plasma, obviating the need to estimate its concentration from inactive downstream metabolite(s). Thus, the AUC of prasugrel inactive metabolite(s) was not analyzed.

End point type	Secondary

End point timeframe:

Part A: 0.5, 1, 1.5, 2, 4 hours postdose

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Analysis was only planned for Part A: AUC of prasugrel inactive metabolite(s) from time 0 up to the last sampling time of 4 hours postdose [AUC(0-tlast)].

End point values	Part A: Prasugrel Single Dose			
Subject group type	Reporting group			
Number of subjects analysed	0[6]			
Units: nanograms*hour per milliliter (ng*hr/mL)				
median (full range (min-max))	(to)			

Notes:

[6] - No participants were analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Pain

End point title	Number of Participants with Pain

End point description:

The number of participants who answered "yes" to the first question in the Sickle Cell Disease Pain (SCD) Questionnaire is reported. Question 1: In the past 2 weeks, did you experience any sickle cell pain?

End point type	Secondary

End point timeframe:

Part B: Baseline and Day14 ± 4 days postdose in each dosing period

End point values	Part B: Baseline	Part B: Prasugrel Once-Daily Dose (0.06 mg/kg)	Part B: Prasugrel Once-Daily Dose (0.08 mg/kg)	Part B: Prasugrel Once-Daily Dose (0.12 mg/kg)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	18	9	17	8
Units: participants				
number (not applicable)	6	4	1	2

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Hemorrhagic Events Requiring Medical Intervention

End point title	Number of Participants with Hemorrhagic Events Requiring Medical Intervention

End point description:

Hemorrhagic events were determined by the study investigator. Medical intervention was defined as any medical attention resulting in therapy or further investigation, as determined by a trained medical professional.

End point type	Secondary

End point timeframe:

Part B: Baseline up to Day 36

End point values	Part B: Baseline			
Subject group type	Subject analysis set			
Number of subjects analysed	18[7]			
Units: participants				
number (not applicable)	0			

Notes:

[7] - Participants who received at least 1 dose of prasugrel.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Part A and B	
Adverse event reporting additional description: H7T-MC-TACX	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	15.1

Reporting groups	
Reporting group title	Prasugrel_Part A
Reporting group description: -	
Reporting group title	Prasugrel_Part B
Reporting group description: -	
Reporting group title	Prasugrel_Part A/B during Part A
Reporting group description: -	
Reporting group title	Prasugrel_Part A/B during Part B
Reporting group description: -	

Serious adverse events	Prasugrel_Part A	Prasugrel_Part B	Prasugrel_Part A/B during Part A
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 15 (13.33%)	2 / 9 (22.22%)	0 / 9 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Congenital, familial and genetic disorders			
sickle cell anaemia with crisis			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	2 / 15 (13.33%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
hypersplenism			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	0 / 15 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal			

disorders			
acute chest syndrome			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	1 / 15 (6.67%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Prasugrel_Part A/B during Part B		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 9 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Congenital, familial and genetic disorders			
sickle cell anaemia with crisis			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
hypersplenism			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
acute chest syndrome			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Prasugrel_Part A	Prasugrel_Part B	Prasugrel_Part A/B during Part A
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 15 (33.33%)	4 / 9 (44.44%)	6 / 9 (66.67%)
Injury, poisoning and procedural complications			
animal bite			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	0 / 15 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
contusion			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
excoriation			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	0 / 15 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
fall			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	0 / 15 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
muscle strain			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	1 / 15 (6.67%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
wound haemorrhage			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	0 / 15 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Congenital, familial and genetic disorders			
sickle cell anaemia			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	1 / 15 (6.67%)	0 / 9 (0.00%)	2 / 9 (22.22%)
occurrences (all)	1	0	2
sickle cell anaemia with crisis			
alternative dictionary used:			

MedDRA 15.1			
subjects affected / exposed	2 / 15 (13.33%)	1 / 9 (11.11%)	2 / 9 (22.22%)
occurrences (all)	3	1	2
General disorders and administration site conditions			
chest pain			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
pyrexia			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	0 / 15 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
vessel puncture site pain			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Ear and labyrinth disorders			
middle ear effusion			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
eyelid bleeding			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	0 / 15 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			
constipation			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	0 / 15 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
tooth loss			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	0 / 15 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	1	0

Reproductive system and breast disorders			
erectile dysfunction			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed[1]	0 / 6 (0.00%)	1 / 4 (25.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
penis disorder			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed[2]	0 / 6 (0.00%)	0 / 4 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			
asthma			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	2 / 9 (22.22%)
occurrences (all)	0	0	2
cough			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	2 / 15 (13.33%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	2	1	0
epistaxis			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
nasal congestion			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	0 / 15 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
oropharyngeal pain			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
rhinorrhoea			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	1 / 15 (6.67%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0

wheezing			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	1 / 15 (6.67%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Skin and subcutaneous tissue disorders			
rash			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
rash papular			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
skin swelling			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
arthralgia			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
back pain			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
pain in extremity			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	1 / 15 (6.67%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
hordeolum			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	0 / 15 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	1	0

otitis media			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	1 / 15 (6.67%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	1	0	1
viral infection			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	0 / 15 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	1	0

Non-serious adverse events	Prasugrel_Part A/B during Part B		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 9 (66.67%)		
Injury, poisoning and procedural complications			
animal bite			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
contusion			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
excoriation			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
fall			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
muscle strain			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
wound haemorrhage			
alternative dictionary used: MedDRA 15.1			

subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Congenital, familial and genetic disorders			
sickle cell anaemia			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	3 / 9 (33.33%)		
occurrences (all)	4		
sickle cell anaemia with crisis			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
General disorders and administration site conditions			
chest pain			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
pyrexia			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
vessel puncture site pain			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Ear and labyrinth disorders			
middle ear effusion			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Eye disorders			
eyelid bleeding			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			

constipation				
alternative dictionary used: MedDRA 15.1				
subjects affected / exposed	0 / 9 (0.00%)			
occurrences (all)	0			
tooth loss				
alternative dictionary used: MedDRA 15.1				
subjects affected / exposed	0 / 9 (0.00%)			
occurrences (all)	0			
Reproductive system and breast disorders				
erectile dysfunction				
alternative dictionary used: MedDRA 15.1				
subjects affected / exposed[1]	0 / 4 (0.00%)			
occurrences (all)	0			
penis disorder				
alternative dictionary used: MedDRA 15.1				
subjects affected / exposed[2]	0 / 4 (0.00%)			
occurrences (all)	0			
Respiratory, thoracic and mediastinal disorders				
asthma				
alternative dictionary used: MedDRA 15.1				
subjects affected / exposed	0 / 9 (0.00%)			
occurrences (all)	0			
cough				
alternative dictionary used: MedDRA 15.1				
subjects affected / exposed	0 / 9 (0.00%)			
occurrences (all)	0			
epistaxis				
alternative dictionary used: MedDRA 15.1				
subjects affected / exposed	1 / 9 (11.11%)			
occurrences (all)	1			
nasal congestion				
alternative dictionary used: MedDRA 15.1				
subjects affected / exposed	1 / 9 (11.11%)			
occurrences (all)	1			

oropharyngeal pain			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
rhinorrhoea			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	2 / 9 (22.22%)		
occurrences (all)	2		
wheezing			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Skin and subcutaneous tissue disorders			
rash			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
rash papular			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
skin swelling			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			
arthralgia			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
back pain			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
pain in extremity			

alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Infections and infestations			
hordeolum			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
otitis media			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
viral infection			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This event is gender specific, only occurring in male or female subjects. The number of subjects exposed has been adjusted accordingly.
[2] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This event is gender specific, only occurring in male or female subjects. The number of subjects exposed has been adjusted accordingly.

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

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Data for the Primary Outcome Measures 1 and 2 were collected for presentation of results in a scatter plot and were not intended to be summarized due to the limited number of participants per treatment.

Notes: