EU Clinical Trials Register

Clinical trial results:
A Phase 2, Multicenter, Randomized, Double-Blind, Placebo-Controlled Study to Assess the Safety, Tolerability, and Effect on Microvascular Obstruction of Temanogrel in Subjects Undergoing Percutaneous Coronary Intervention

Summary

EudraCT number	2020-000238-16
Trial protocol	NL SE
Global end of trial date	31 August 2022

Results information

Result version number	v1 (current)
This version publication date	03 September 2023
First version publication date	03 September 2023

Trial information

Trial identification

Sponsor protocol code	C5071002

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04848220
WHO universal trial number (UTN)	-
Other trial identifiers	APD791-202: Other study ID

Notes:

Sponsors

Sponsor organisation name	Pfizer Inc.
Sponsor organisation address	66 Hudson Blvd, New York, United States, NY 10018
Public contact	Pfizer ClinicalTrials.gov Call Center, Pfizer Inc., 001 800-718-1021, ClinicalTrials.gov_Inquiries@pfizer.com
Scientific contact	Pfizer ClinicalTrials.gov Call Center, Pfizer Inc., 001 800-718-1021, ClinicalTrials.gov_Inquires@pfizer.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	19 January 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	31 August 2022
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To assess the effect of temanogrel on microvascular obstruction (MVO) following percutaneous coronary intervention (PCI).

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Council for Harmonization (ICH) Good Clinical Practice (GCP) Guidelines. All the local regulatory requirements pertinent to safety of trials subjects were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	20 May 2021
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	Australia: 12
Country: Number of subjects enrolled	Netherlands: 10
Country: Number of subjects enrolled	United Kingdom: 3
Country: Number of subjects enrolled	United States: 2
Worldwide total number of subjects	27
EEA total number of subjects	10

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)	13
From 65 to 84 years	14

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study was conducted in two stages: Stage A (an ascending single dose study consisting of 2 cohorts of 20 and 40 milligram [mg] doses of temanogrel or placebo) and Stage B: parallel group study (consisting of 3 treatment groups of temanogrel 20 mg, temanogrel 40 mg and placebo). The study was terminated early due to business decision.

Pre-assignment

Screening details:

A total of 29 subjects were enrolled and randomized in the study of which only 27 subjects received the study treatment and were included in the safety population.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Temanogrel 20 mg

Arm description:

Subjects received a single intravenous (IV) dose of temanogrel 20 mg on Day 1 following which the subjects underwent percutaneous coronary intervention (PCI). Subjects had a follow-up phone call 7 days after administration of study treatment.

Arm type	Experimental
Investigational medicinal product name	Temanogrel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

20 mg single dose

Arm title	Temanogrel 40 mg

Arm description:

Subjects received a single IV dose of temanogrel 40 mg on Day 1 following which the subjects underwent PCI. Subjects had a follow-up phone call 7 days after administration of study treatment.

Arm type	Experimental
Investigational medicinal product name	Temanogrel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

40 mg single dose

Arm title	Placebo

Arm description:

Subjects received a single IV dose of placebo on Day 1 following which the subjects underwent PCI. Subjects had a follow-up phone call 7 days after administration of study treatment.

Arm type	Placebo

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Single dose

Number of subjects in period 1	Temanogrel 20 mg	Temanogrel 40 mg	Placebo
Started	10	8	9
Completed	10	8	9

Baseline characteristics

Reporting groups

Reporting group title	Temanogrel 20 mg
Reporting group description:	

Subjects received a single intravenous (IV) dose of temanogrel 20 mg on Day 1 following which the subjects underwent percutaneous coronary intervention (PCI). Subjects had a follow-up phone call 7 days after administration of study treatment.

Reporting group title	Temanogrel 40 mg
Reporting group description:	

Subjects received a single IV dose of temanogrel 40 mg on Day 1 following which the subjects underwent PCI. Subjects had a follow-up phone call 7 days after administration of study treatment.

Reporting group title	Placebo
Reporting group description:	

Subjects received a single IV dose of placebo on Day 1 following which the subjects underwent PCI. Subjects had a follow-up phone call 7 days after administration of study treatment.

Reporting group values	Temanogrel 20 mg	Temanogrel 40 mg	Placebo
Number of subjects	10	8	9
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	4	4	5
From 65-84 years	6	4	4
85 years and over	0	0	0
Age Continuous			
Units: Years			
arithmetic mean	65.9	64.5	63.3
standard deviation	± 7.81	± 3.27	± 9.63
Sex: Female, Male			
Units: Subjects			
Female	1	0	3
Male	9	8	6
Race			
Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	2	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	7	7	9
More than one race	0	0	0
Unknown	1	1	0
Ethnicity			

Units: Subjects			
Hispanic or Latino	0	1	0
Not Hispanic or Latino	10	7	9
Unknown or Not Reported	0	0	0

Reporting group values	Total		
Number of subjects	27		
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)	13		
From 65-84 years	14		
85 years and over	0		
Age Continuous			
Units: Years			
arithmetic mean			
standard deviation	-		
Sex: Female, Male			
Units: Subjects			
Female	4		
Male	23		
Race			
Units: Subjects			
American Indian or Alaska Native	0		
Asian	2		
Native Hawaiian or Other Pacific Islander	0		
Black or African American	0		
White	23		
More than one race	0		
Unknown	2		
Ethnicity			
Units: Subjects			
Hispanic or Latino	1		
Not Hispanic or Latino	26		
Unknown or Not Reported	0		

End points

End points reporting groups

Reporting group title	Temanogrel 20 mg
Reporting group description:	

Subjects received a single intravenous (IV) dose of temanogrel 20 mg on Day 1 following which the subjects underwent percutaneous coronary intervention (PCI). Subjects had a follow-up phone call 7 days after administration of study treatment.

Reporting group title	Temanogrel 40 mg
Reporting group description:	

Subjects received a single IV dose of temanogrel 40 mg on Day 1 following which the subjects underwent PCI. Subjects had a follow-up phone call 7 days after administration of study treatment.

Reporting group title	Placebo
Reporting group description:	

Subjects received a single IV dose of placebo on Day 1 following which the subjects underwent PCI. Subjects had a follow-up phone call 7 days after administration of study treatment.

Primary: Change in Index of Microcirculatory Resistance (IMR) From Baseline to Post Percutaneous Coronary Intervention (PCI)

End point title	Change in Index of Microcirculatory Resistance (IMR) From Baseline to Post Percutaneous Coronary Intervention (PCI)[1]

End point description:

IMR was defined as the mean distal pressure at maximum hyperemia multiplied by the mean hyperemic transit time. IMRcorr (IMR corrected for the influence from collateral supply) was calculated using the following equation, to account for the presence of significant epicardial stenosis without the need for balloon dilation to measure the coronary wedge pressure (Pw), IMRcorr=mean aortic pressure at maximum hyperemia (Pa)* mean transit time at maximal hyperemia (Tmn)*[1.34*mean distal coronary pressure at maximum hyperemia (Pd)/Pa minus 0.32]. Full analysis set(FAS) included all randomised subjects, irrespective of whether they received any study treatment. Here, 'Number of Subjects Analysed' signifies subjects evaluable for this endpoint. Combined data for Stage A and Stage B was presented as pre-specified in protocol.

End point type	Primary

End point timeframe:

From Baseline (prior to administration of study treatment) to 15 minutes post-PCI on Day 1

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: Due to early study termination and low sample size, statistical analyses were not performed.

End point values	Temanogrel 20 mg	Temanogrel 40 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	9	8	9	
Units: Millimeter of mercury*seconds				
arithmetic mean (standard deviation)	-8.1783 (± 15.35531)	0.0691 (± 13.27702)	-1.8907 (± 18.82659)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline to Post-PCI for Coronary Flow Reserve (CFR)

End point title	Change From Baseline to Post-PCI for Coronary Flow Reserve (CFR)

End point description:

The coronary flow reserve (CFR) was calculated from the ratio of baseline (i.e., resting transit time) to hyperemic mean transit time. FAS included all randomised subjects, irrespective of whether they received any study treatment. Here, 'Number of Subjects Analyzed' signifies subjects evaluable for this endpoint. Combined data for Stage A and Stage B was presented as pre-specified in protocol.

End point type	Secondary

End point timeframe:

From Baseline (prior to administration of study treatment) to 15 minutes post-PCI on Day 1

End point values	Temanogrel 20 mg	Temanogrel 40 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	9	8	9	
Units: Ratio				
arithmetic mean (standard deviation)	1.2744 (± 0.89307)	1.0238 (± 2.97729)	1.3787 (± 1.40440)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline to Post-PCI for Fractional Flow Reserve (FFR)

End point title	Change From Baseline to Post-PCI for Fractional Flow Reserve (FFR)

End point description:

The FFR was calculated from the ratio of distal to proximal mean pressures at maximal hyperemia (FFR=[distal coronary pressure/aortic pressure at maximum hyperemia]). FAS included all randomised subjects, irrespective of whether they received any study treatment. Here, 'Number of Subjects Analyzed' signifies subjects evaluable for this endpoint. Combined data for Stage A and Stage B was presented as pre-specified in protocol.

End point type	Secondary

End point timeframe:

From Baseline (prior to administration of study treatment) to 15 minutes post-PCI on Day 1

End point values	Temanogrel 20 mg	Temanogrel 40 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	9	8	9	
Units: Ratio				
arithmetic mean (standard deviation)	0.1346 (± 0.19620)	0.2494 (± 0.20758)	0.3123 (± 0.16562)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline to Post-PCI for Corrected Thrombolysis in Myocardial Infarction Frame Count (cTFC)

End point title	Change From Baseline to Post-PCI for Corrected Thrombolysis in Myocardial Infarction Frame Count (cTFC)

End point description:

The cTFC is a quantitative index of coronary flow and was calculated based upon the number of cine-frames that the intracoronary dye required to reach distal coronary landmarks. Safety set included all subjects in the FAS who received any study treatment. Here, 'Number of Subjects Analysed' signifies subjects evaluable for this endpoint. Combined data for Stage A and Stage B was presented as pre-specified in protocol.

End point type	Secondary

End point timeframe:

From Baseline (prior to administration of study treatment) to 15 minutes post-PCI on Day 1

End point values	Temanogrel 20 mg	Temanogrel 40 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	9	7	8	
Units: Frames per second				
arithmetic mean (standard deviation)	-6.54 (± 7.365)	-0.81 (± 6.320)	-8.93 (± 8.368)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects According to Change From Baseline to Post-PCI for Thrombolysis in Myocardial Infarction (TIMI) Flow Grade (TFG) Post-PCI

End point title	Number of Subjects According to Change From Baseline to Post-PCI for Thrombolysis in Myocardial Infarction (TIMI) Flow Grade (TFG) Post-PCI

End point description:

The TFG is a measure of epicardial perfusion and was graded on a standard scale from 0 to 3, where grade 0=no perfusion, grade 1=penetration without perfusion, grade 2=partial perfusion and grade 3= complete perfusion. Safety set included all subjects in the FAS who received any study treatment. Combined data for Stage A and Stage B was presented as pre-specified in protocol.

End point type	Secondary

End point timeframe:

Baseline (prior to administration of study treatment) and anytime between 0 to 15 minutes post-PCI on Day 1

End point values	Temanogrel 20 mg	Temanogrel 40 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10	8	9	
Units: Subjects				
Baseline, Grade 3	10	8	9	
0 to 15 min post-PCI, Grade 3	9	8	8	
0 to 15 min post-PCI, missing	1	0	1	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects According to Change From Baseline to Post-PCI in Thrombolysis in Myocardial Infarction Myocardial Perfusion Grade (TMPG) Post-PCI

End point title	Number of Subjects According to Change From Baseline to Post-PCI in Thrombolysis in Myocardial Infarction Myocardial Perfusion Grade (TMPG) Post-PCI

End point description:

The TMPG (also known as myocardial blush grade [MBG]), is a measure of myocardial perfusion in the capillary bed at the tissues level following contrast injection into the coronary artery. TMPG was graded on a scale from 0 to 3, where grade 0 = failure of dye to enter the microvasculature; grade 1 = dye slowly enters but fails to exit the microvasculature; grade 2 = delayed entry and exit of dye from the microvasculature; grade 3= normal entry and exit of dye from the microvasculature. Only those grades with non-zero subjects have been reported. Safety set included all subjects in the FAS who received any study treatment. Combined data for Stage A and Stage B was presented as pre-specified in protocol.

End point type	Secondary

End point timeframe:

Baseline (prior to administration of study treatment) and anytime between 0 to 15 minutes post-PCI on Day 1

End point values	Temanogrel 20 mg	Temanogrel 40 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10	8	9	
Units: Subjects				
Baseline, TMPG 2	1	0	1	
Baseline, TMPG 3	7	4	3	
Baseline Missing	2	4	5	
0 to 15 min post-PCI, TMPG value 3	9	6	6	
0 to 15 min post-PCI, Missing	1	2	3	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline to Post-PCI for Creatine Kinase (CK)

End point title	Change From Baseline to Post-PCI for Creatine Kinase (CK)

End point description:

Safety Set included all subjects in the FAS who received any study treatment. Here, 'n' signifies number of subjects evaluable at the specified timepoints. Combined data for Stage A and Stage B was presented as pre-specified in protocol. Here '99999' signifies that standard deviation could not be calculated for only one subject.

End point type	Secondary

End point timeframe:

Baseline (prior to administration of study treatment), anytime between 0 to 15 minutes, 6 hours post-PCI, and 24 hours post-PCI/discharge

End point values	Temanogrel 20 mg	Temanogrel 40 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10	8	9	
Units: Units per liter				
arithmetic mean (standard deviation)				
0 to 15 minutes post-PCI (n=10,8,9)	-11.7 (± 11.25)	-6.0 (± 5.68)	-5.9 (± 10.58)	
6 hours post-PCI (n=9,8,6)	0.9 (± 17.20)	1.5 (± 27.07)	-23.5 (± 41.03)	
24 hours post- PCI/discharge (n=6,1,3)	-33.7 (± 23.42)	233.0 (± 99999)	-6.0 (± 38.94)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline to Post-PCI for Creatine Kinase-Myocardial Band (CK-MB)

End point title	Change From Baseline to Post-PCI for Creatine Kinase-Myocardial Band (CK-MB)

End point description:

Safety Set included all subjects in the FAS who received any study treatment. Here, 'n' signifies number of subjects evaluable at the specified timepoints. Combined data for Stage A and Stage B was presented as pre-specified in protocol. Here '99999' signified that standard deviation could not be calculated for only one subject.

End point type	Secondary

End point timeframe:

Baseline (prior to administration of study treatment), anytime between 0 to 15 minutes, 6 hours post-PCI and 24 hours post-PCI/discharge

End point values	Temanogrel 20 mg	Temanogrel 40 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10	8	9	
Units: Micrograms per liter				
arithmetic mean (standard deviation)				
0 to 15 minutes Post-PCI (n=10,8,8)	-0.18 (± 0.290)	-0.18 (± 0.225)	-0.26 (± 0.490)	
6 Hours Post-PCI (n=9,8,6)	0.70 (± 1.260)	0.79 (± 2.208)	-0.63 (± 1.359)	
24 Hours Post- PCI/Discharge (n=6,1,3)	-0.05 (± 0.804)	31.80 (± 99999)	0.97 (± 0.643)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline to Post-PCI for Cardiac Troponin I

End point title	Change From Baseline to Post-PCI for Cardiac Troponin I

End point description:

Safety Set included all subjects in the FAS who received any study treatment. Here, 'Number Analyzed' signified number of subjects evaluable at the specified timepoints. Combined data for Stage A and Stage B was presented as pre-specified in protocol. Here '99999' signified that standard deviation could not be calculated for only one subject.

End point type	Secondary

End point timeframe:

Baseline (prior to administration of study treatment), anytime between 0 to15 minutes, 6 hours post-PCI and 24 hours post-PCI/discharge

End point values	Temanogrel 20 mg	Temanogrel 40 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10	8	9	
Units: Microgram per liter				
arithmetic mean (standard deviation)				
0-15 minutes Post-PCI (n=10,8,8)	-0.04 (± 0.126)	0.01 (± 0.035)	0.04 (± 0.052)	
6 Hours Post-PCI (n=9,8,6)	0.58 (± 1.310)	0.13 (± 0.354)	0.08 (± 0.204)	
24 Hours Post- PCI/Discharge (n=6,1,3)	-0.03 (± 0.197)	5.50 (± 99999)	0.30 (± 0.300)	

Statistical analyses

No statistical analyses for this end point

Secondary: Concentration of Temanogrel

End point title	Concentration of Temanogrel[2]

End point description:

Observed plasma concentration of temanogrel. Lower limit of quantification (LLOQ) of temanogrel was 0.500 nanograms/milliliter (ng/mL). Pharmacokinetic (PK) set included all subjects in the safety set with at least 1 post dose PK measurement. Here, 'n' signifies number of subjects evaluable at the specified timepoints. Combined data for Stage A and Stage B was presented as pre-specified in protocol. Here '99999' signifies that the data were not calculated as fewer than 50% of subjects had values above the lower limit of quantification or there were no measurable values.

End point type	Secondary

End point timeframe:

Pre-PCI, anytime between 0 to 15 minutes,1 hour, 3 hours, 6 hours post-PCI and 24 hours post PCI/discharge

Notes:

[2] - 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: The endpoint is specific to the arms reported.

End point values	Temanogrel 20 mg	Temanogrel 40 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	8		
Units: Nanograms per milliliter				
arithmetic mean (standard deviation)				
Pre-PCI (n=9,7)	1558.3889 (± 2156.89423)	1869.8571 (± 1815.65878)		
0 to 15 minutes post PCI (n=10,6)	126.9900 (± 31.08320)	265.0000 (± 109.83260)		
1 hour post PCI (n=6,6)	84.8667 (± 24.45278)	134.1667 (± 36.56455)		
3 hours post PCI (n=6,7)	41.8500 (± 17.23969)	87.1714 (± 90.12348)		
6 hours post PCI (n=9,8)	24.6522 (± 19.78224)	36.9000 (± 14.94380)		
24 hours post-procedure/discharge (n=4,0)	99999 (± 99999)	99999 (± 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Procedural Myocardial Injury

End point title	Number of Subjects With Procedural Myocardial Injury

End point description:

Procedural myocardial injury was defined as elevation of cardiac troponin (cTn) values greater than (>) 99th percentile upper reference limit (URL) in subjects with normal baseline values (<= 99th percentile URL) or elevation of cTn by > 20% of the baseline value in subjects with elevated cTn levels (>99th percentile URL). Safety Set included all subjects in the FAS who received any study treatment. Combined data for Stage A and Stage B was presented as pre-specified in protocol. All subjects reported under 'Number of Subjects Analyzed' contributed data to the table but may not have evaluable data for every row. Here 'Number Analyzed' indicates number of subjects evaluable at the specified timepoints.

End point type	Secondary

End point timeframe:

At 6 hours and 24 hours post-PCI/discharge on Day 1

End point values	Temanogrel 20 mg	Temanogrel 40 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10	8	9	
Units: Subjects				
6 Hours Post-PCI (n= 9,8,6)	3	1	1	
24 Hours Post-PCI/Discharge (n=6,1,3)	1	1	2	

Statistical analyses

No statistical analyses for this end point

Secondary: Concentration of AR295980

End point title	Concentration of AR295980[3]

End point description:

Observed plasma concentration of AR295980. PK set included all subjects in the safety set with at least 1 post dose PK measurement. Here, 'n' signifies number of subjects evaluable at the specified timepoints. Combined data for Stage A and Stage B was presented as pre-specified in protocol. Here '99999' signifies that the data were not calculated as fewer than 50% of subjects had values above the lower limit of quantification or there were no measurable values.

End point type	Secondary

End point timeframe:

Pre-PCI, anytime between 0 to 15 minutes,1 hour, 3 hours, 6 hours post-PCI, and 24 hours post PCI/discharge

Notes:

[3] - 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: The endpoint is specific to the arms reported.

End point values	Temanogrel 20 mg	Temanogrel 40 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	8		
Units: Nanograms per milliliter				
arithmetic mean (standard deviation)				
Pre-PCI (n=9,7)	1.0472 (± 0.87240)	3.2010 (± 3.97562)		
0 to 15 minutes post PCI (n=10,6)	6.3680 (± 2.61560)	6.8183 (± 2.24211)		
1 hour post PCI (n=6,6)	5.0750 (± 1.81783)	8.0783 (± 4.32397)		
3 hours post PCI (n=6,7)	3.6933 (± 1.18230)	5.5300 (± 2.48489)		
6 hours post PCI (n=9,8)	2.4678 (± 0.79325)	5.2650 (± 3.21979)		
24 hours post-PCI/discharge (n=4,0)	0.3518 (± 0.40765)	99999 (± 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Concentration of AR295981

End point title	Concentration of AR295981[4]

End point description:

Observed plasma concentration of AR295981. PK set included all subjects in the safety set with at least 1 post dose PK measurement. All subjects reported under 'Number of Subjects Analyzed' contributed data to the table but may not have evaluable data for every row. Here, 'n' signified number of subjects evaluable at the specified timepoints. Combined data for Stage A and Stage B was presented as pre-specified in protocol. Here '99999' signifies that the data were not calculated as fewer than 50% of subjects had values above the lower limit of quantification or there were no measurable values.

End point type	Secondary

End point timeframe:

Pre-PCI, anytime between 0 to 15 minutes,1 hour, 3 hours, 6 hours post-PCI, and 24 hours post PCI/discharge

Notes:

[4] - 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: The endpoint is specific to the arms reported.

End point values	Temanogrel 20 mg	Temanogrel 40 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	8		
Units: Nanograms per milliliter				
arithmetic mean (standard deviation)				
Pre-PCI (n=9,7)	1.8042 (± 1.11941)	5.9129 (± 8.69909)		
0 to 15 minutes post PCI (n=9,6)	0.9032 (± 0.46521)	1.9030 (± 1.05032)		
1 hour post PCI (n=6,6)	0.6743 (± 0.36798)	1.6575 (± 0.73395)		
3 hours post PCI (n=6,7)	0.4677 (± 0.37748)	1.0651 (± 0.32193)		
6 hours post PCI (n=9,8)	99999 (± 99999)	0.8685 (± 0.51239)		
24 hours post-PCI/discharge (n=4,0)	99999 (± 99999)	99999 (± 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Treatment-Emergent Adverse Events (TEAEs) by Severity

End point title	Number of Subjects with Treatment-Emergent Adverse Events (TEAEs) by Severity

End point description:

An adverse event (AE) was any untoward medical occurrence that did not necessarily have a causal relationship with study treatment.TEAE was an AE that occurred after initiation of study treatment that was not present at time of treatment start or an AE that increased in severity after initiation of medication,if event was present at time of treatment start. AEs were graded according to Common Terminology Criteria for Adverse Events(CTCAE)version 4.03 as grade1:mild;grade2:moderate;grade 3:severe,grade4:life threatening,grade5:death related to AE.Number of subjects with any TEAE and grade 3 or higher TEAE have been reported.Safety set included all subjects in the FAS who received any study treatment.

End point type	Secondary

End point timeframe:

From start of study treatment on day 1 to up to maximum of 10 days

End point values	Temanogrel 20 mg	Temanogrel 40 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10	8	9	
Units: Subjects				
Any TEAE	4	7	4	
Grade 3 or higher TEAE	0	2	1	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Treatment-Related TEAEs According to the Preferred Term

End point title	Number of Subjects With Treatment-Related TEAEs According to the Preferred Term

End point description:

An AE was any untoward medical occurrence that did not necessarily have a causal relationship with study treatment. TEAE was an AE that occurred after initiation of study treatment that was not present at the time of treatment start or an AE that increased in severity after the initiation of medication, if the event was present at the time of treatment start emerges. Relatedness was based on investigator's assessment. The safety set included all subjects in the FAS who received any study treatment.
Combined data for Stage A and Stage B is presented as pre-specified in protocol.

End point type	Secondary

End point timeframe:

From start of study treatment on day 1 to up to maximum of 10 days

End point values	Temanogrel 20 mg	Temanogrel 40 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10	8	9	
Units: Subjects				
Vascular access site haematoma	1	0	0	
Hypertension	0	1	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Serious Adverse Events (SAEs), Adverse Events Leading to Discontinuation of Study Treatment and Treatment-Related TEAEs

End point title	Number of Subjects with Serious Adverse Events (SAEs), Adverse Events Leading to Discontinuation of Study Treatment and Treatment-Related TEAEs

End point description:

An AE was any untoward medical occurrence that did not necessarily have a causal relationship with study treatment. TEAE was an AE that occurred after initiation of study treatment that was not present at the time of treatment start or an AE that increased in severity after the initiation of medication, if the event was present at the time of treatment start. SAE was an AE resulting in any of the following outcomes or considered medically significant: death; initial or prolonged inpatient hospitalization; life-threatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly or birth defect. Relatedness was based on investigator's assessment. Safety set included all subjects in the FAS who received any study treatment.

End point type	Secondary

End point timeframe:

From start of study treatment on day 1 to up to maximum of 10 days

End point values	Temanogrel 20 mg	Temanogrel 40 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10	8	9	
Units: Subjects				
SAEs	0	2	1	
Treatment discontinuation due to adverse events	0	0	0	
Treatment-Related TEAEs	1	1	0	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:	
From start of study treatment on Day 1 to up to maximum of 10 days	

Adverse event reporting additional description:

Same event may appear as both non-SAE and SAE but what is presented are distinct events. An event may be categorized as serious in 1 subject and non-serious in other, or a subject may have experienced both serious and non-serious event.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.0

Reporting groups

Reporting group title	Temanogrel 20mg

Reporting group description:

Subjects received a single intravenous (IV) dose of temanogrel 20 milligram (mg) on Day 1 following which the subjects underwent percutaneous coronary intervention (PCI). Subjects had a follow-up phone call 7 days after administration of study treatment.

Reporting group title	Placebo

Reporting group description:

Subjects received a single IV dose of placebo on Day 1 following which the subjects underwent PCI. Subjects had a follow-up phone call 7 days after administration of study treatment.

Reporting group title	Temanogrel 40mg

Reporting group description:

Subjects received a single IV dose of temanogrel 40mg on Day 1 following which the subjects underwent PCI. Subjects had a follow-up phone call 7 days after administration of study treatment.

Serious adverse events	Temanogrel 20mg	Placebo	Temanogrel 40mg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	2 / 8 (25.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Vascular access site haematoma			
alternative dictionary used: Medra v24.0 24.0			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	1 / 8 (12.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Aortic dissection			
alternative dictionary used: Medra v24.0 24.0			

subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	1 / 8 (12.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Cardiac disorders

Acute myocardial infarction

subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Temanogrel 20mg	Placebo	Temanogrel 40mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 10 (40.00%)	3 / 9 (33.33%)	7 / 8 (87.50%)
Investigations			
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Blood bilirubin increased			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Transaminases increased			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Injury, poisoning and procedural complications			
Procedural pain			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	1 / 8 (12.50%)
occurrences (all)	0	1	1
Vascular access site haematoma			
subjects affected / exposed	4 / 10 (40.00%)	1 / 9 (11.11%)	1 / 8 (12.50%)
occurrences (all)	4	1	1
Vascular disorders			
Aortic dissection			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Hypertension			

subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	2 / 8 (25.00%)
occurrences (all)	0	0	2
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Atrioventricular block second degree			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Cardiac arrest			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Cardiogenic shock			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Coronary artery dissection			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	1 / 8 (12.50%)
occurrences (all)	0	1	1
General disorders and administration site conditions			
Non-cardiac chest pain			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Oedema peripheral			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Hepatobiliary disorders			
Congestive hepatopathy			

subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			
Respiratory failure			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	0 / 8 (0.00%)
occurrences (all)	0	1	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
14 September 2020	Dosage and administration of study intervention was updated and procedures for collection of PK blood samples were updated.
17 May 2022	Changes to the frequency of blood collections and clarification regarding the allowed timing of Baseline coronary physiology indices.

Notes:

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.

This study was terminated early due to a business decision that was not due to any safety concerns. The number of subjects was smaller than originally planned and only summary statistics were therefore generated for primary and secondary endpoints.

Notes: