# 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<br>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<br>Units: Years | | | |
| arithmetic mean | 65.9 | 64.5 | 63.3 |
| standard deviation | ± 7.81 | ± 3.27 | ± 9.63 |
| Sex: Female, Male<br>Units: Subjects | | | |
| Female | 1 | 0 | 3 |
| Male | 9 | 8 | 6 |
| Race<br>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: