



Clinical trial results:

A Randomized, Placebo-controlled, Phase 2b Study to Evaluate the Safety and Efficacy of MEDI6012 in Acute ST Elevation Myocardial Infarction (REAL-TIMI 63B)

Summary

| | |
|--------------------------|----------------------|
| EudraCT number | 2017-004521-32 |
| Trial protocol | GB ES NL CZ SK HU PL |
| Global end of trial date | 18 January 2021 |

Results information

| | |
|--------------------------------|-----------------|
| Result version number | v1 (current) |
| This version publication date | 29 January 2022 |
| First version publication date | 29 January 2022 |

Trial information

Trial identification

| | |
|-----------------------|-------------|
| Sponsor protocol code | D5780C00007 |
|-----------------------|-------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT03578809 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | MedImmune LLC |
| Sponsor organisation address | OneMedImmune Way, Gaithersburg, United States, MD 20878 |
| Public contact | Global Clinical Lead, MedImmune LLC, +1 877-240-9479, information.center@astrazeneca.com |
| Scientific contact | Global Clinical Lead, MedImmune LLC, +1 877-240-9479, information.center@astrazeneca.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 | 08 September 2021 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 18 January 2021 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to evaluate the effect of MEDI6012 on reduction of infarct size compared with placebo.

Protection of trial subjects:

The conduct of this clinical study met all local legal and regulatory requirements. The study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and the International Conference on Harmonization guideline E6: Good Clinical Practice. Participating participant signed informed consent form and could withdraw from the study at any time without any disadvantage and without having to provide a reason for this decision. Only investigators qualified by training and experience were selected as appropriate experts to investigate the study drug.

Background therapy: -

Evidence for comparator: -

| | |
|---|--------------|
| Actual start date of recruitment | 05 June 2018 |
| 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 | Brazil: 7 |
| Country: Number of subjects enrolled | Czechia: 156 |
| Country: Number of subjects enrolled | Hungary: 101 |
| Country: Number of subjects enrolled | Israel: 53 |
| Country: Number of subjects enrolled | Netherlands: 116 |
| Country: Number of subjects enrolled | Poland: 11 |
| Country: Number of subjects enrolled | Russian Federation: 26 |
| Country: Number of subjects enrolled | Slovakia: 51 |
| Country: Number of subjects enrolled | Spain: 49 |
| Country: Number of subjects enrolled | United Kingdom: 23 |
| Worldwide total number of subjects | 593 |
| EEA total number of subjects | 484 |

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) | 370 |
| From 65 to 84 years | 223 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

This study was conducted in 10 countries (Brazil, Czech Republic, Hungary, Israel, Netherlands, Poland, Russian Federation, Slovakia, Spain, and the United Kingdom).

Pre-assignment

Screening details:

In total, 593 participants were randomized into the study and 575 participants were treated with the study drug.

Period 1

| | |
|------------------------------|---|
| Period 1 title | Overall Study (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind ^[1] |
| Roles blinded | Subject, Monitor, Data analyst, Carer, Assessor |

Arms

| | |
|------------------------------|-------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Cohort A: Placebo |

Arm description:

Participants received placebo matched to MEDI6012 on Day 1 prior to primary percutaneous coronary intervention (pPCI) followed by a second inpatient dose on Day 3 by intravenous (IV) push.

| | |
|--|---------------------------------|
| Arm type | Placebo |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection/infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Placebo matched to MEDI6012 was administered on Day 1 prior to pPCI followed by a second inpatient dose on Day 3 by IV push.

| | |
|------------------|--------------------|
| Arm title | Cohort A: MEDI6012 |
|------------------|--------------------|

Arm description:

Participants received loading dose of MEDI6012 300 mg on Day 1 prior to pPCI followed by a second inpatient dose of MEDI6012 150 mg on Day 3 by IV push.

| | |
|--|--|
| Arm type | Experimental |
| Investigational medicinal product name | MEDI6012 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Powder and solution for solution for injection |
| Routes of administration | Intravenous use |

Dosage and administration details:

Loading dose of MEDI6012 300 mg was administered on Day 1 prior to pPCI followed by a second inpatient dose of MEDI6012 150 mg on Day 3 by IV push.

| | |
|------------------|-------------------|
| Arm title | Cohort B: Placebo |
|------------------|-------------------|

Arm description:

Participants received placebo matched to MEDI6012 on Day 1 prior to pPCI followed by a second inpatient dose on Day 3, and outpatient maintenance doses on Days 10, 17, 24, and 31 by IV push.

| | |
|----------|---------|
| Arm type | Placebo |
|----------|---------|

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

Dosage and administration details:

Placebo matched to MEDI6012 was administered on Day 1 prior to pPCI followed by a second inpatient dose on Day 3, and outpatient maintenance doses on Days 10, 17, 24, and 31 by IV push.

| | |
|------------------|--------------------|
| Arm title | Cohort B: MEDI6012 |
|------------------|--------------------|

Arm description:

Participants received loading dose of MEDI6012 300 mg on Day 1 prior to pPCI followed by a second inpatient dose of MEDI6012 150 mg on Day 3, and outpatient maintenance doses of MEDI6012 100 mg on Days 10, 17, 24, and 31 by IV push.

| | |
|--|--|
| Arm type | Experimental |
| Investigational medicinal product name | MEDI6012 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Powder and solution for solution for injection |
| Routes of administration | Intravenous use |

Dosage and administration details:

Loading dose of MEDI6012 300 mg was administered on Day 1 prior to pPCI followed by a second inpatient dose of MEDI6012 150 mg on Day 3, and outpatient maintenance doses of MEDI6012 100 mg on Days 10, 17, 24, and 31 by IV push.

Notes:

[1] - The roles blinded appear to be inconsistent with a double blind trial.

Justification: For this 'Double blind' study, number of roles blinded were greater than one (Subject, Monitor, Carer, Data analyst, Assessor) and the Investigators were unblinded.

| Number of subjects in period 1 | Cohort A: Placebo | Cohort A: MEDI6012 | Cohort B: Placebo |
|---------------------------------------|-------------------|--------------------|-------------------|
| Started | 94 | 185 | 112 |
| Treated | 90 | 179 | 111 |
| Completed | 88 | 171 | 108 |
| Not completed | 6 | 14 | 4 |
| Adverse event, serious fatal | - | 2 | - |
| Consent withdrawn by subject | 3 | 5 | 2 |
| Unspecified | 3 | 6 | 2 |
| Lost to follow-up | - | 1 | - |

| Number of subjects in period 1 | Cohort B: MEDI6012 |
|---------------------------------------|--------------------|
| Started | 202 |
| Treated | 195 |
| Completed | 193 |
| Not completed | 9 |
| Adverse event, serious fatal | 1 |
| Consent withdrawn by subject | - |
| Unspecified | 8 |
| Lost to follow-up | - |

Baseline characteristics

Reporting groups

| | |
|--|--------------------|
| Reporting group title | Cohort A: Placebo |
| Reporting group description: Participants received placebo matched to MEDI6012 on Day 1 prior to primary percutaneous coronary intervention (pPCI) followed by a second inpatient dose on Day 3 by intravenous (IV) push. | |
| Reporting group title | Cohort A: MEDI6012 |
| Reporting group description: Participants received loading dose of MEDI6012 300 mg on Day 1 prior to pPCI followed by a second inpatient dose of MEDI6012 150 mg on Day 3 by IV push. | |
| Reporting group title | Cohort B: Placebo |
| Reporting group description: Participants received placebo matched to MEDI6012 on Day 1 prior to pPCI followed by a second inpatient dose on Day 3, and outpatient maintenance doses on Days 10, 17, 24, and 31 by IV push. | |
| Reporting group title | Cohort B: MEDI6012 |
| Reporting group description: Participants received loading dose of MEDI6012 300 mg on Day 1 prior to pPCI followed by a second inpatient dose of MEDI6012 150 mg on Day 3, and outpatient maintenance doses of MEDI6012 100 mg on Days 10, 17, 24, and 31 by IV push. | |

| Reporting group values | Cohort A: Placebo | Cohort A: MEDI6012 | Cohort B: Placebo |
|--|-------------------|--------------------|-------------------|
| Number of subjects | 94 | 185 | 112 |
| 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) | 62 | 122 | 58 |
| From 65-84 years | 32 | 63 | 54 |
| 85 years and over | 0 | 0 | 0 |
| Age Continuous Units: Years | | | |
| arithmetic mean | 59.7 | 59.9 | 62.6 |
| standard deviation | ± 10.3 | ± 10.2 | ± 10.8 |
| Sex: Female, Male Units: Participants | | | |
| Female | 20 | 35 | 27 |
| Male | 74 | 150 | 85 |
| Race (NIH/OMB) Units: Subjects | | | |
| American Indian or Alaska Native | 0 | 0 | 0 |
| Asian | 0 | 1 | 1 |
| Native Hawaiian or Other Pacific Islander | 0 | 0 | 0 |
| Black or African American | 0 | 0 | 1 |

| | | | |
|-------------------------|----|-----|-----|
| White | 94 | 182 | 110 |
| More than one race | 0 | 0 | 0 |
| Unknown or Not Reported | 0 | 2 | 0 |
| Ethnicity (NIH/OMB) | | | |
| Units: Subjects | | | |
| Hispanic or Latino | 2 | 8 | 2 |
| Not Hispanic or Latino | 92 | 177 | 110 |
| Unknown or Not Reported | 0 | 0 | 0 |

| Reporting group values | Cohort B: MEDI6012 | Total | |
|--|--------------------|-------|--|
| Number of subjects | 202 | 593 | |
| Age categorical | | | |
| Units: Subjects | | | |
| In utero | 0 | 0 | |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | |
| Newborns (0-27 days) | 0 | 0 | |
| Infants and toddlers (28 days-23 months) | 0 | 0 | |
| Children (2-11 years) | 0 | 0 | |
| Adolescents (12-17 years) | 0 | 0 | |
| Adults (18-64 years) | 128 | 370 | |
| From 65-84 years | 74 | 223 | |
| 85 years and over | 0 | 0 | |
| Age Continuous | | | |
| Units: Years | | | |
| arithmetic mean | 59.9 | | |
| standard deviation | ± 10.0 | - | |
| Sex: Female, Male | | | |
| Units: Participants | | | |
| Female | 49 | 131 | |
| Male | 153 | 462 | |
| Race (NIH/OMB) | | | |
| Units: Subjects | | | |
| American Indian or Alaska Native | 0 | 0 | |
| Asian | 3 | 5 | |
| Native Hawaiian or Other Pacific Islander | 0 | 0 | |
| Black or African American | 2 | 3 | |
| White | 194 | 580 | |
| More than one race | 0 | 0 | |
| Unknown or Not Reported | 3 | 5 | |
| Ethnicity (NIH/OMB) | | | |
| Units: Subjects | | | |
| Hispanic or Latino | 10 | 22 | |
| Not Hispanic or Latino | 192 | 571 | |
| Unknown or Not Reported | 0 | 0 | |

End points

End points reporting groups

| | |
|--|--------------------|
| Reporting group title | Cohort A: Placebo |
| Reporting group description: Participants received placebo matched to MEDI6012 on Day 1 prior to primary percutaneous coronary intervention (pPCI) followed by a second inpatient dose on Day 3 by intravenous (IV) push. | |
| Reporting group title | Cohort A: MEDI6012 |
| Reporting group description: Participants received loading dose of MEDI6012 300 mg on Day 1 prior to pPCI followed by a second inpatient dose of MEDI6012 150 mg on Day 3 by IV push. | |
| Reporting group title | Cohort B: Placebo |
| Reporting group description: Participants received placebo matched to MEDI6012 on Day 1 prior to pPCI followed by a second inpatient dose on Day 3, and outpatient maintenance doses on Days 10, 17, 24, and 31 by IV push. | |
| Reporting group title | Cohort B: MEDI6012 |
| Reporting group description: Participants received loading dose of MEDI6012 300 mg on Day 1 prior to pPCI followed by a second inpatient dose of MEDI6012 150 mg on Day 3, and outpatient maintenance doses of MEDI6012 100 mg on Days 10, 17, 24, and 31 by IV push. | |

Primary: Global Infarct Size

| | |
|--|------------------------------------|
| End point title | Global Infarct Size ^[1] |
| End point description: Global infarct size expressed as a percentage of left ventricle (LV) mass measured on delayed-enhanced cardiovascular magnetic resonance (CMR) imaging in 10-12 weeks post myocardial infarction (MI) is reported. Primary efficacy analysis population was analysed which included randomised participants with a Thrombolysis in Myocardial Infarction (TIMI) flow Grade 0-1 on initial angiography who received at least 2 doses of study drug and grouped according to assigned treatment. | |
| End point type | Primary |
| End point timeframe: 70 to 84 days post Day 1 dose | |
| 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: Statistical analysis was not applicable since the inferential statistics was not performed for the reported groups. | |

| End point values | Cohort A: Placebo | Cohort A: MEDI6012 | Cohort B: Placebo | Cohort B: MEDI6012 |
|--|------------------------|-------------------------|-------------------------|------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 43 | 97 | 61 | 108 |
| Units: Percentage of global infarct size | | | | |
| geometric mean (confidence interval 90%) | 5.453 (3.781 to 7.865) | 8.598 (7.228 to 10.229) | 9.004 (7.219 to 11.230) | 7.819 (6.658 to 9.183) |

Statistical analyses

No statistical analyses for this end point

Secondary: Left Ventricular Ejection Fraction (LVEF)

| | |
|-----------------|---|
| End point title | Left Ventricular Ejection Fraction (LVEF) |
|-----------------|---|

End point description:

The LVEF measured by cine magnetic resonance imaging (MRI) at 10-12 weeks post-MI is reported. Primary efficacy analysis population was analysed which included randomised participants with a TIMI flow Grade 0-1 on initial angiography who received at least 2 doses of study drug and grouped according to assigned treatment.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

70 to 84 days post Day 1 dose

| End point values | Cohort A: Placebo | Cohort A: MEDI6012 | Cohort B: Placebo | Cohort B: MEDI6012 |
|--|---------------------------|---------------------------|---------------------------|---------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 43 | 99 | 61 | 108 |
| Units: Percentage of LVEF | | | | |
| geometric mean (confidence interval 90%) | 47.626 (44.344 to 51.152) | 47.083 (45.167 to 49.079) | 47.329 (45.158 to 49.604) | 49.722 (48.117 to 51.381) |

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Non-calcified Plaque Volume (NCPV) in the Coronary Arteries in Cohort B

| | |
|-----------------|--|
| End point title | Change in Non-calcified Plaque Volume (NCPV) in the Coronary Arteries in Cohort B ^[2] |
|-----------------|--|

End point description:

Change in NCPV in the coronary arteries from index computed tomography angiography (CTA) to 10-12 weeks post-MI is reported. The index CTA was preferably to be performed between 48 to 72 hours post Dose 1 (could be done up to 5 days post Dose 1) but no earlier than 40 hours post Dose 1. Participants with creatinine clearance ≥ 60 mL/min (Cockcroft Gault equation) within 6 hours underwent an index coronary CTA no earlier than 40 hours following the first dose. The CTA analysis population was analysed which included randomised participants in the 6-dose regimen who received a full treatment course of study drug, were eligible, and had coronary CTA.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Day 1 dose (48 to 72 hours post Dose 1) through 70 to 84 days post Day 1 dose

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: Only those baseline period arms for which analysis was planned were reported in the end point.

| End point values | Cohort B: Placebo | Cohort B: MEDI6012 | | |
|--|------------------------|------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 60 | 121 | | |
| Units: mm ³ | | | | |
| geometric mean (confidence interval 90%) | 1.049 (0.915 to 1.203) | 0.998 (0.919 to 1.085) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Left Ventricular Mass by Late Gadolinium Enhancement (LGE)

| | |
|---|--|
| End point title | Left Ventricular Mass by Late Gadolinium Enhancement (LGE) |
| End point description: The left ventricular mass by LGE is reported. Primary efficacy analysis population was analysed which included randomised participants with a TIMI flow Grade 0-1 on initial angiography who received at least 2 doses of study drug and grouped according to assigned treatment. | |
| End point type | Secondary |
| End point timeframe: 70 to 84 days post Day 1 dose | |

| End point values | Cohort A: Placebo | Cohort A: MEDI6012 | Cohort B: Placebo | Cohort B: MEDI6012 |
|--------------------------------------|----------------------|-----------------------|----------------------|-----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 43 | 97 | 61 | 108 |
| Units: grams | | | | |
| arithmetic mean (standard deviation) | 119.740 (± 31.384) | 119.581 (± 23.949) | 115.221 (± 28.328) | 117.920 (± 24.821) |

Statistical analyses

No statistical analyses for this end point

Secondary: Left Ventricular Mass by Cine Magnetic Resonance Imaging (MRI)

| | |
|--|--|
| End point title | Left Ventricular Mass by Cine Magnetic Resonance Imaging (MRI) |
| End point description: The left ventricular mass by cine MRI is reported. Primary efficacy analysis population was analysed which included randomised participants with a TIMI flow Grade 0-1 on initial angiography who received at least 2 doses of study drug and grouped according to assigned treatment. | |
| End point type | Secondary |
| End point timeframe: 70 to 84 days post Day 1 dose | |

| End point values | Cohort A: Placebo | Cohort A: MEDI6012 | Cohort B: Placebo | Cohort B: MEDI6012 |
|--------------------------------------|-------------------------|-------------------------|-------------------------|-------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 43 | 99 | 61 | 108 |
| Units: grams | | | | |
| arithmetic mean (standard deviation) | 113.953 (\pm 31.261) | 113.870 (\pm 23.885) | 110.244 (\pm 28.009) | 111.533 (\pm 23.329) |

Statistical analyses

No statistical analyses for this end point

Secondary: Left Ventricular End-diastolic and End-systolic Volume

| | |
|---|--|
| End point title | Left Ventricular End-diastolic and End-systolic Volume |
| End point description: Left ventricular end-diastolic and end-systolic volume is reported. Primary efficacy analysis population was analysed which included randomised participants with a TIMI flow Grade 0-1 on initial angiography who received at least 2 doses of study drug and grouped according to assigned treatment. | |
| End point type | Secondary |
| End point timeframe: 70 to 84 days post Day 1 dose | |

| End point values | Cohort A: Placebo | Cohort A: MEDI6012 | Cohort B: Placebo | Cohort B: MEDI6012 |
|--|---------------------------------|---------------------------------|---------------------------------|---------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 43 | 99 | 61 | 108 |
| Units: mL | | | | |
| geometric mean (confidence interval 90%) | | | | |
| Left ventricular end-diastolic volume | 174.059 (161.956 to 187.066) | 176.523 (169.259 to 184.098) | 167.480 (157.010 to 178.649) | 172.733 (166.031 to 179.706) |
| Left ventricular end-systolic volume | 87.038 (78.229 to 96.838) | 89.594 (83.818 to 95.768) | 84.977 (77.205 to 93.532) | 83.676 (78.606 to 89.073) |

Statistical analyses

No statistical analyses for this end point

Secondary: Left Ventricular End-diastolic and End-systolic Volume Index

| | |
|-----------------|--|
| End point title | Left Ventricular End-diastolic and End-systolic Volume Index |
|-----------------|--|

End point description:

Left ventricular end-diastolic and end-systolic volume index is reported. Primary efficacy analysis population was analysed which included randomised participants with a TIMI flow Grade 0-1 on initial angiography who received at least 2 doses of study drug and grouped according to assigned treatment.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

70 to 84 days post Day 1 dose

| End point values | Cohort A: Placebo | Cohort A: MEDI6012 | Cohort B: Placebo | Cohort B: MEDI6012 |
|---|---------------------------|---------------------------|---------------------------|---------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 42 | 99 | 61 | 108 |
| Units: mL/m ² | | | | |
| geometric mean (confidence interval 90%) | | | | |
| Left ventricular end-diastolic volume index | 89.158 (84.324 to 94.269) | 90.280 (86.818 to 93.880) | 86.118 (81.401 to 91.107) | 87.258 (84.211 to 90.416) |
| Left ventricular end-systolic volume index | 44.491 (40.537 to 48.830) | 45.821 (42.970 to 48.863) | 43.695 (40.024 to 47.703) | 42.270 (39.845 to 44.842) |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Treatment Emergent Adverse Events (TEAEs) and Treatment Emergent Serious Adverse Events (TESAEs)

| | |
|-----------------|--|
| End point title | Number of Participants With Treatment Emergent Adverse Events (TEAEs) and Treatment Emergent Serious Adverse Events (TESAEs) |
|-----------------|--|

End point description:

An adverse event (AE) is any untoward medical occurrence in a participant who received study drug without regard to possibility of causal relationship. A serious adverse event (SAE) is an AE resulting in any of the following outcomes or deemed significant for any other reason: death; initial or prolonged inpatient hospitalization; life threatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly. The TEAEs are defined as events present at baseline that worsened in intensity after administration of study drug or events absent at baseline that emerged after administration of study drug. As-treated population was analysed which included all treated participants, grouped according to actual treatment received.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Day 1 through Day 195 post Day 1 dose

| End point values | Cohort A: Placebo | Cohort A: MEDI6012 | Cohort B: Placebo | Cohort B: MEDI6012 |
|-----------------------------|----------------------|-----------------------|----------------------|-----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 90 | 179 | 111 | 195 |
| Units: Participants | | | | |
| Any TEAEs | 49 | 114 | 70 | 136 |
| Any TSEAEs | 11 | 34 | 24 | 41 |

Statistical analyses

No statistical analyses for this end point

Secondary: Serum Concentration of MEDI6012 (Lecithin-cholesterol Acyltransferases [LCAT] Mass)

| | |
|-----------------|--|
| End point title | Serum Concentration of MEDI6012 (Lecithin-cholesterol Acyltransferases [LCAT] Mass) ^[3] |
|-----------------|--|

End point description:

Serum concentration of MEDI6012 is reported. Pharmacokinetic population was analysed which included all participants in the As-treated population who had at least one detectable serum concentration measurement for LCAT mass or activity. Here, 'n' denotes the number of participants who had adequate pharmacokinetic sample of MEDI6012 for the specified days, the arbitrary number '999999' denotes that no participants were evaluated for the specified time point, and the arbitrary numbers '99999' and '99999.9' denotes the data for mean and standard deviation (SD), respectively, which were not calculated because the concentration was below limit of quantification.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Pre- and post-dose on Days 1, 3, 17, and 31

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: Only those baseline period arms for which analysis was planned were reported in the end point.

| End point values | Cohort A: MEDI6012 | Cohort B: MEDI6012 | | |
|--------------------------------------|-----------------------|-----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 179 | 193 | | |
| Units: ng/mL | | | | |
| arithmetic mean (standard deviation) | | | | |
| Day 1 (pre-dose) (n = 3, 6) | 99999 (± 99999.9) | 99999 (± 99999.9) | | |
| Day 1 (post-dose) (n = 172, 183) | 76795.9 (± 31136.7) | 74661.2 (± 24561.6) | | |
| Day 3 (pre-dose) (n = 167, 180) | 28017.9 (± 11019.6) | 27738.8 (± 12892.4) | | |
| Day 3 (post-dose) (n = 160, 176) | 94653.8 (± 115895.1) | 87663.1 (± 93166.2) | | |
| Day 17 (pre-dose) (n = 0, 100) | 999999 (± 999999) | 4509.9 (± 2372.6) | | |
| Day 17 (post-dose) (n = 0, 153) | 999999 (± 999999) | 49111.0 (± 71552.1) | | |
| Day 31 (pre-dose) (n = 0, 80) | 999999 (± 999999) | 4954.8 (± 4193.9) | | |
| Day 31 (post-dose) (n = 0, 147) | 999999 (± 999999) | 67519.7 (± 224677.3) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Positive Anti-Drug Antibodies (ADA) to MEDI6012

| | |
|-----------------|---|
| End point title | Number of Participants With Positive Anti-Drug Antibodies (ADA) to MEDI6012 |
|-----------------|---|

End point description:

Number of participants with positive ADA titer to MEDI6012 are reported in 3 categories, ADA positive at any visit up to Day 70-84 follow-up visit, ADA positive with > 30% decrease in HDL-C from baseline (on the same date) at any visit up to D70-84 FU V, and ADA positive and > 30% decrease in HDL-C from baseline at Day 70-84 Follow-up Visit. Immunogenicity population was analysed which included all treated participants, grouped according to actual treatment received and had at least one serum sample for immunogenicity testing.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Predose on Day 1, Day 17, Day 31, 70 to 84 days, and on Day 195 post Day 1 dose

| End point values | Cohort A: Placebo | Cohort A: MEDI6012 | Cohort B: Placebo | Cohort B: MEDI6012 |
|---|----------------------|-----------------------|----------------------|-----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 90 | 179 | 111 | 194 |
| Units: Participants | | | | |
| At any visit up to Day 70-84 | 1 | 13 | 1 | 93 |
| with >30% decrease HDL-C, up to Day 70-84 | 1 | 3 | 0 | 1 |
| With >30% decrease HDL-C, at Day 70-84 | 1 | 0 | 0 | 1 |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Day 1 through Day 195 post Day 1 dose

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 23.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|-------------------|
| Reporting group title | MEDI6012 Cohort A |
|-----------------------|-------------------|

Reporting group description:

Participants received loading dose of MEDI6012 300 mg on Day 1 prior to pPCI followed by a second inpatient dose of MEDI6012 150 mg on Day 3 by IV push.

| | |
|-----------------------|------------------|
| Reporting group title | Placebo Cohort B |
|-----------------------|------------------|

Reporting group description:

Participants received placebo matched to MEDI6012 on Day 1 prior to pPCI followed by a second inpatient dose on Day 3, and outpatient maintenance doses on Days 10, 17, 24, and 31 by IV push.

| | |
|-----------------------|------------------|
| Reporting group title | Placebo Cohort A |
|-----------------------|------------------|

Reporting group description:

Participants received placebo matched to MEDI6012 on Day 1 prior to primary percutaneous coronary intervention (pPCI) followed by a second inpatient dose on Day 3 by intravenous (IV) push.

| | |
|-----------------------|-------------------|
| Reporting group title | MEDI6012 Cohort B |
|-----------------------|-------------------|

Reporting group description:

Participants received loading dose of MEDI6012 300 mg on Day 1 prior to pPCI followed by a second inpatient dose of MEDI6012 150 mg on Day 3, and outpatient maintenance doses of MEDI6012 100 mg on Days 10, 17, 24, and 31 by IV push.

| Serious adverse events | MEDI6012 Cohort A | Placebo Cohort B | Placebo Cohort A |
|---|-------------------|-------------------|------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 34 / 179 (18.99%) | 24 / 111 (21.62%) | 11 / 90 (12.22%) |
| number of deaths (all causes) | 2 | 0 | 0 |
| number of deaths resulting from adverse events | | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Lung neoplasm malignant | | | |
| subjects affected / exposed | 0 / 179 (0.00%) | 0 / 111 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lymphoma | | | |
| subjects affected / exposed | 0 / 179 (0.00%) | 1 / 111 (0.90%) | 0 / 90 (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 |

| | | | |
|---|-----------------|-----------------|----------------|
| Meningioma | | | |
| subjects affected / exposed | 1 / 179 (0.56%) | 0 / 111 (0.00%) | 0 / 90 (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 |
| Metastatic squamous cell carcinoma | | | |
| subjects affected / exposed | 0 / 179 (0.00%) | 0 / 111 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vascular disorders | | | |
| Aortic stenosis | | | |
| subjects affected / exposed | 0 / 179 (0.00%) | 1 / 111 (0.90%) | 0 / 90 (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 |
| Hypertensive crisis | | | |
| subjects affected / exposed | 1 / 179 (0.56%) | 0 / 111 (0.00%) | 0 / 90 (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 |
| Hypotension | | | |
| subjects affected / exposed | 1 / 179 (0.56%) | 2 / 111 (1.80%) | 1 / 90 (1.11%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Peripheral arterial occlusive disease | | | |
| subjects affected / exposed | 1 / 179 (0.56%) | 0 / 111 (0.00%) | 0 / 90 (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 |
| Peripheral ischaemia | | | |
| subjects affected / exposed | 0 / 179 (0.00%) | 0 / 111 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Phlebitis | | | |
| subjects affected / exposed | 0 / 179 (0.00%) | 1 / 111 (0.90%) | 0 / 90 (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 |
| Post thrombotic syndrome | | | |

| | | | |
|--|-----------------|-----------------|----------------|
| subjects affected / exposed | 0 / 179 (0.00%) | 0 / 111 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General disorders and administration site conditions | | | |
| Chest pain | | | |
| subjects affected / exposed | 1 / 179 (0.56%) | 0 / 111 (0.00%) | 0 / 90 (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 |
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 0 / 179 (0.00%) | 1 / 111 (0.90%) | 0 / 90 (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 |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 179 (0.00%) | 0 / 111 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Systemic inflammatory response syndrome | | | |
| subjects affected / exposed | 0 / 179 (0.00%) | 0 / 111 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vascular stent thrombosis | | | |
| subjects affected / exposed | 2 / 179 (1.12%) | 1 / 111 (0.90%) | 0 / 90 (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 |
| Reproductive system and breast disorders | | | |
| Prostatic haemorrhage | | | |
| subjects affected / exposed | 0 / 179 (0.00%) | 1 / 111 (0.90%) | 0 / 90 (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 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Dyspnoea | | | |

| | | | |
|---|-----------------|-----------------|----------------|
| subjects affected / exposed | 0 / 179 (0.00%) | 0 / 111 (0.00%) | 1 / 90 (1.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pleural effusion | | | |
| subjects affected / exposed | 0 / 179 (0.00%) | 0 / 111 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary congestion | | | |
| subjects affected / exposed | 0 / 179 (0.00%) | 0 / 111 (0.00%) | 1 / 90 (1.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary embolism | | | |
| subjects affected / exposed | 0 / 179 (0.00%) | 1 / 111 (0.90%) | 0 / 90 (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 |
| Psychiatric disorders | | | |
| Mental disorder | | | |
| subjects affected / exposed | 0 / 179 (0.00%) | 0 / 111 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Investigations | | | |
| Troponin increased | | | |
| subjects affected / exposed | 1 / 179 (0.56%) | 0 / 111 (0.00%) | 0 / 90 (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 |
| Electrocardiogram QT prolonged | | | |
| subjects affected / exposed | 0 / 179 (0.00%) | 0 / 111 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Troponin T increased | | | |
| subjects affected / exposed | 0 / 179 (0.00%) | 0 / 111 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Injury, poisoning and procedural | | | |

| | | | |
|---|-----------------|-----------------|----------------|
| complications | | | |
| Femur fracture | | | |
| subjects affected / exposed | 1 / 179 (0.56%) | 0 / 111 (0.00%) | 0 / 90 (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 |
| Intentional overdose | | | |
| subjects affected / exposed | 0 / 179 (0.00%) | 0 / 111 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Periprocedural myocardial infarction | | | |
| subjects affected / exposed | 0 / 179 (0.00%) | 0 / 111 (0.00%) | 1 / 90 (1.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Post procedural haematoma | | | |
| subjects affected / exposed | 0 / 179 (0.00%) | 1 / 111 (0.90%) | 0 / 90 (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 |
| Post procedural haematuria | | | |
| subjects affected / exposed | 0 / 179 (0.00%) | 0 / 111 (0.00%) | 1 / 90 (1.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Postpericardiotomy syndrome | | | |
| subjects affected / exposed | 0 / 179 (0.00%) | 0 / 111 (0.00%) | 1 / 90 (1.11%) |
| 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 | | | |
| Angina pectoris | | | |
| subjects affected / exposed | 3 / 179 (1.68%) | 0 / 111 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Acute myocardial infarction | | | |
| subjects affected / exposed | 3 / 179 (1.68%) | 0 / 111 (0.00%) | 2 / 90 (2.22%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|-----------------|-----------------|----------------|
| Angina unstable | | | |
| subjects affected / exposed | 2 / 179 (1.12%) | 2 / 111 (1.80%) | 1 / 90 (1.11%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 3 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Atrial fibrillation | | | |
| subjects affected / exposed | 0 / 179 (0.00%) | 2 / 111 (1.80%) | 0 / 90 (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 |
| Atrial flutter | | | |
| subjects affected / exposed | 1 / 179 (0.56%) | 1 / 111 (0.90%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Atrioventricular block complete | | | |
| subjects affected / exposed | 0 / 179 (0.00%) | 0 / 111 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Atrioventricular block second degree | | | |
| subjects affected / exposed | 0 / 179 (0.00%) | 1 / 111 (0.90%) | 0 / 90 (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 |
| Cardiac arrest | | | |
| subjects affected / exposed | 0 / 179 (0.00%) | 0 / 111 (0.00%) | 1 / 90 (1.11%) |
| 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 failure | | | |
| subjects affected / exposed | 5 / 179 (2.79%) | 2 / 111 (1.80%) | 1 / 90 (1.11%) |
| occurrences causally related to treatment / all | 0 / 6 | 0 / 3 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Cardiac failure acute | | | |
| subjects affected / exposed | 0 / 179 (0.00%) | 2 / 111 (1.80%) | 0 / 90 (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 |
| Cardiac failure congestive | | | |

| | | | |
|---|-----------------|-----------------|----------------|
| subjects affected / exposed | 0 / 179 (0.00%) | 1 / 111 (0.90%) | 0 / 90 (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 |
| Cardiac ventricular thrombosis | | | |
| subjects affected / exposed | 0 / 179 (0.00%) | 1 / 111 (0.90%) | 0 / 90 (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 |
| Coronary artery dissection | | | |
| subjects affected / exposed | 0 / 179 (0.00%) | 0 / 111 (0.00%) | 1 / 90 (1.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiogenic shock | | | |
| subjects affected / exposed | 1 / 179 (0.56%) | 0 / 111 (0.00%) | 0 / 90 (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 |
| Coronary artery stenosis | | | |
| subjects affected / exposed | 0 / 179 (0.00%) | 1 / 111 (0.90%) | 0 / 90 (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 |
| Dressler's syndrome | | | |
| subjects affected / exposed | 1 / 179 (0.56%) | 2 / 111 (1.80%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Intracardiac thrombus | | | |
| subjects affected / exposed | 0 / 179 (0.00%) | 1 / 111 (0.90%) | 0 / 90 (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 |
| Left ventricular dysfunction | | | |
| subjects affected / exposed | 0 / 179 (0.00%) | 1 / 111 (0.90%) | 0 / 90 (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 |
| Mitral valve incompetence | | | |

| | | | |
|---|-----------------|-----------------|----------------|
| subjects affected / exposed | 1 / 179 (0.56%) | 0 / 111 (0.00%) | 0 / 90 (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 |
| Myocardial infarction | | | |
| subjects affected / exposed | 1 / 179 (0.56%) | 0 / 111 (0.00%) | 0 / 90 (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 |
| Palpitations | | | |
| subjects affected / exposed | 1 / 179 (0.56%) | 0 / 111 (0.00%) | 0 / 90 (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 |
| Myocardial ischaemia | | | |
| subjects affected / exposed | 1 / 179 (0.56%) | 0 / 111 (0.00%) | 0 / 90 (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 |
| Pericardial haemorrhage | | | |
| subjects affected / exposed | 0 / 179 (0.00%) | 0 / 111 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Prinzmetal angina | | | |
| subjects affected / exposed | 1 / 179 (0.56%) | 0 / 111 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Right ventricular failure | | | |
| subjects affected / exposed | 1 / 179 (0.56%) | 0 / 111 (0.00%) | 0 / 90 (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 |
| Sinus tachycardia | | | |
| subjects affected / exposed | 0 / 179 (0.00%) | 1 / 111 (0.90%) | 0 / 90 (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 |
| Torsade de pointes | | | |

| | | | |
|---|-----------------|-----------------|----------------|
| subjects affected / exposed | 0 / 179 (0.00%) | 0 / 111 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ventricular arrhythmia | | | |
| subjects affected / exposed | 1 / 179 (0.56%) | 0 / 111 (0.00%) | 0 / 90 (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 |
| Ventricular extrasystoles | | | |
| subjects affected / exposed | 0 / 179 (0.00%) | 0 / 111 (0.00%) | 1 / 90 (1.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ventricular fibrillation | | | |
| subjects affected / exposed | 0 / 179 (0.00%) | 2 / 111 (1.80%) | 1 / 90 (1.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ventricular tachycardia | | | |
| subjects affected / exposed | 0 / 179 (0.00%) | 0 / 111 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| Cerebrovascular accident | | | |
| subjects affected / exposed | 0 / 179 (0.00%) | 1 / 111 (0.90%) | 1 / 90 (1.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ischaemic stroke | | | |
| subjects affected / exposed | 1 / 179 (0.56%) | 0 / 111 (0.00%) | 0 / 90 (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 |
| Syncope | | | |
| subjects affected / exposed | 0 / 179 (0.00%) | 0 / 111 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood and lymphatic system disorders | | | |

| | | | |
|---|-----------------|-----------------|----------------|
| Anaemia | | | |
| subjects affected / exposed | 2 / 179 (1.12%) | 0 / 111 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Thrombocytopenia | | | |
| subjects affected / exposed | 1 / 179 (0.56%) | 0 / 111 (0.00%) | 0 / 90 (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 |
| Ear and labyrinth disorders | | | |
| Vertigo | | | |
| subjects affected / exposed | 0 / 179 (0.00%) | 0 / 111 (0.00%) | 1 / 90 (1.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| Gastritis erosive | | | |
| subjects affected / exposed | 1 / 179 (0.56%) | 0 / 111 (0.00%) | 0 / 90 (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 |
| Diarrhoea | | | |
| subjects affected / exposed | 0 / 179 (0.00%) | 0 / 111 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 0 / 179 (0.00%) | 0 / 111 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Proctitis haemorrhagic | | | |
| subjects affected / exposed | 0 / 179 (0.00%) | 0 / 111 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatobiliary disorders | | | |
| Cholelithiasis | | | |

| | | | |
|---|-----------------|-----------------|----------------|
| subjects affected / exposed | 0 / 179 (0.00%) | 1 / 111 (0.90%) | 0 / 90 (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 |
| Drug-induced liver injury | | | |
| subjects affected / exposed | 0 / 179 (0.00%) | 0 / 111 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skin and subcutaneous tissue disorders | | | |
| Toxic skin eruption | | | |
| subjects affected / exposed | 0 / 179 (0.00%) | 0 / 111 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal and urinary disorders | | | |
| Acute kidney injury | | | |
| subjects affected / exposed | 1 / 179 (0.56%) | 0 / 111 (0.00%) | 0 / 90 (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 |
| Renal failure | | | |
| subjects affected / exposed | 0 / 179 (0.00%) | 0 / 111 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal impairment | | | |
| subjects affected / exposed | 1 / 179 (0.56%) | 1 / 111 (0.90%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ureterolithiasis | | | |
| subjects affected / exposed | 1 / 179 (0.56%) | 0 / 111 (0.00%) | 0 / 90 (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 |
| Musculoskeletal and connective tissue disorders | | | |
| Musculoskeletal chest pain | | | |
| subjects affected / exposed | 0 / 179 (0.00%) | 1 / 111 (0.90%) | 0 / 90 (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 |

| | | | |
|---|-----------------------------------|-----------------------------------|----------------------------------|
| Infections and infestations Bronchitis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 179 (0.56%) 0 / 1 0 / 0 | 1 / 111 (0.90%) 0 / 1 0 / 0 | 0 / 90 (0.00%) 0 / 0 0 / 0 |
| Infection subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 179 (0.56%) 0 / 1 0 / 0 | 0 / 111 (0.00%) 0 / 0 0 / 0 | 0 / 90 (0.00%) 0 / 0 0 / 0 |
| Orchitis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 179 (0.00%) 0 / 0 0 / 0 | 0 / 111 (0.00%) 0 / 0 0 / 0 | 1 / 90 (1.11%) 0 / 1 0 / 0 |
| Pneumonia subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 3 / 179 (1.68%) 0 / 3 0 / 1 | 0 / 111 (0.00%) 0 / 0 0 / 0 | 0 / 90 (0.00%) 0 / 0 0 / 0 |
| Respiratory tract infection viral subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 179 (0.00%) 0 / 0 0 / 0 | 0 / 111 (0.00%) 0 / 0 0 / 0 | 0 / 90 (0.00%) 0 / 0 0 / 0 |
| COVID-19 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 179 (0.56%) 0 / 1 0 / 0 | 0 / 111 (0.00%) 0 / 0 0 / 0 | 0 / 90 (0.00%) 0 / 0 0 / 0 |
| Hepatitis A subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 179 (0.00%) 0 / 0 0 / 0 | 0 / 111 (0.00%) 0 / 0 0 / 0 | 0 / 90 (0.00%) 0 / 0 0 / 0 |

| | | | |
|---|-------------------|--|--|
| Serious adverse events | MEDI6012 Cohort B | | |
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 41 / 195 (21.03%) | | |
| number of deaths (all causes) | 1 | | |
| number of deaths resulting from adverse events | | | |

| | | | |
|---|-----------------|--|--|
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Lung neoplasm malignant | | | |
| subjects affected / exposed | 1 / 195 (0.51%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Lymphoma | | | |
| subjects affected / exposed | 0 / 195 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Meningioma | | | |
| subjects affected / exposed | 0 / 195 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Metastatic squamous cell carcinoma | | | |
| subjects affected / exposed | 1 / 195 (0.51%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Vascular disorders | | | |
| Aortic stenosis | | | |
| subjects affected / exposed | 0 / 195 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hypertensive crisis | | | |
| subjects affected / exposed | 0 / 195 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hypotension | | | |
| subjects affected / exposed | 0 / 195 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Peripheral arterial occlusive disease | | | |
| subjects affected / exposed | 0 / 195 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | | |
|--|-----------------|--|--|--|
| Peripheral ischaemia | | | | |
| subjects affected / exposed | 1 / 195 (0.51%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Phlebitis | | | | |
| subjects affected / exposed | 0 / 195 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Post thrombotic syndrome | | | | |
| subjects affected / exposed | 1 / 195 (0.51%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| General disorders and administration site conditions | | | | |
| Chest pain | | | | |
| subjects affected / exposed | 0 / 195 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Non-cardiac chest pain | | | | |
| subjects affected / exposed | 2 / 195 (1.03%) | | | |
| occurrences causally related to treatment / all | 0 / 2 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pyrexia | | | | |
| subjects affected / exposed | 2 / 195 (1.03%) | | | |
| occurrences causally related to treatment / all | 0 / 2 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Systemic inflammatory response syndrome | | | | |
| subjects affected / exposed | 1 / 195 (0.51%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Vascular stent thrombosis | | | | |
| subjects affected / exposed | 1 / 195 (0.51%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |

| | | | |
|---|-----------------|--|--|
| Reproductive system and breast disorders | | | |
| Prostatic haemorrhage | | | |
| subjects affected / exposed | 0 / 195 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Dyspnoea | | | |
| subjects affected / exposed | 0 / 195 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pleural effusion | | | |
| subjects affected / exposed | 1 / 195 (0.51%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pulmonary congestion | | | |
| subjects affected / exposed | 0 / 195 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pulmonary embolism | | | |
| subjects affected / exposed | 0 / 195 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Psychiatric disorders | | | |
| Mental disorder | | | |
| subjects affected / exposed | 1 / 195 (0.51%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Investigations | | | |
| Troponin increased | | | |
| subjects affected / exposed | 0 / 195 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Electrocardiogram QT prolonged | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 1 / 195 (0.51%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Troponin T increased | | | |
| subjects affected / exposed | 1 / 195 (0.51%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Injury, poisoning and procedural complications | | | |
| Femur fracture | | | |
| subjects affected / exposed | 0 / 195 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Intentional overdose | | | |
| subjects affected / exposed | 1 / 195 (0.51%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Periprocedural myocardial infarction | | | |
| subjects affected / exposed | 0 / 195 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Post procedural haematoma | | | |
| subjects affected / exposed | 0 / 195 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Post procedural haematuria | | | |
| subjects affected / exposed | 0 / 195 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Postpericardiotomy syndrome | | | |
| subjects affected / exposed | 0 / 195 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cardiac disorders | | | |

| | | | | |
|---|-----------------|--|--|--|
| Angina pectoris | | | | |
| subjects affected / exposed | 3 / 195 (1.54%) | | | |
| occurrences causally related to treatment / all | 0 / 3 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Acute myocardial infarction | | | | |
| subjects affected / exposed | 0 / 195 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Angina unstable | | | | |
| subjects affected / exposed | 1 / 195 (0.51%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Atrial fibrillation | | | | |
| subjects affected / exposed | 2 / 195 (1.03%) | | | |
| occurrences causally related to treatment / all | 0 / 2 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Atrial flutter | | | | |
| subjects affected / exposed | 0 / 195 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Atrioventricular block complete | | | | |
| subjects affected / exposed | 1 / 195 (0.51%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Atrioventricular block second degree | | | | |
| subjects affected / exposed | 0 / 195 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Cardiac arrest | | | | |
| subjects affected / exposed | 1 / 195 (0.51%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Cardiac failure | | | | |

| | | | | |
|---|-----------------|--|--|--|
| subjects affected / exposed | 1 / 195 (0.51%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Cardiac failure acute | | | | |
| subjects affected / exposed | 3 / 195 (1.54%) | | | |
| occurrences causally related to treatment / all | 0 / 3 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Cardiac failure congestive | | | | |
| subjects affected / exposed | 0 / 195 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Cardiac ventricular thrombosis | | | | |
| subjects affected / exposed | 1 / 195 (0.51%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Coronary artery dissection | | | | |
| subjects affected / exposed | 0 / 195 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Cardiogenic shock | | | | |
| subjects affected / exposed | 0 / 195 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Coronary artery stenosis | | | | |
| subjects affected / exposed | 0 / 195 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Dressler's syndrome | | | | |
| subjects affected / exposed | 2 / 195 (1.03%) | | | |
| occurrences causally related to treatment / all | 0 / 2 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Intracardiac thrombus | | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 1 / 195 (0.51%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Left ventricular dysfunction | | | |
| subjects affected / exposed | 0 / 195 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Mitral valve incompetence | | | |
| subjects affected / exposed | 0 / 195 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Myocardial infarction | | | |
| subjects affected / exposed | 1 / 195 (0.51%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Palpitations | | | |
| subjects affected / exposed | 0 / 195 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Myocardial ischaemia | | | |
| subjects affected / exposed | 0 / 195 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pericardial haemorrhage | | | |
| subjects affected / exposed | 1 / 195 (0.51%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Prinzmetal angina | | | |
| subjects affected / exposed | 0 / 195 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Right ventricular failure | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 0 / 195 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Sinus tachycardia | | | |
| subjects affected / exposed | 0 / 195 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Torsade de pointes | | | |
| subjects affected / exposed | 1 / 195 (0.51%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Ventricular arrhythmia | | | |
| subjects affected / exposed | 0 / 195 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Ventricular extrasystoles | | | |
| subjects affected / exposed | 0 / 195 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Ventricular fibrillation | | | |
| subjects affected / exposed | 2 / 195 (1.03%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Ventricular tachycardia | | | |
| subjects affected / exposed | 1 / 195 (0.51%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Nervous system disorders | | | |
| Cerebrovascular accident | | | |
| subjects affected / exposed | 0 / 195 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Ischaemic stroke | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 1 / 195 (0.51%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Syncope | | | |
| subjects affected / exposed | 1 / 195 (0.51%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 1 / 195 (0.51%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Thrombocytopenia | | | |
| subjects affected / exposed | 0 / 195 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Ear and labyrinth disorders | | | |
| Vertigo | | | |
| subjects affected / exposed | 0 / 195 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal disorders | | | |
| Gastritis erosive | | | |
| subjects affected / exposed | 0 / 195 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Diarrhoea | | | |
| subjects affected / exposed | 1 / 195 (0.51%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 2 / 195 (1.03%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | |
|---|-----------------|--|--|
| Proctitis haemorrhagic | | | |
| subjects affected / exposed | 1 / 195 (0.51%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hepatobiliary disorders | | | |
| Cholelithiasis | | | |
| subjects affected / exposed | 0 / 195 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Drug-induced liver injury | | | |
| subjects affected / exposed | 1 / 195 (0.51%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Skin and subcutaneous tissue disorders | | | |
| Toxic skin eruption | | | |
| subjects affected / exposed | 1 / 195 (0.51%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Renal and urinary disorders | | | |
| Acute kidney injury | | | |
| subjects affected / exposed | 0 / 195 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Renal failure | | | |
| subjects affected / exposed | 1 / 195 (0.51%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Renal impairment | | | |
| subjects affected / exposed | 0 / 195 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Ureterolithiasis | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 0 / 195 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Musculoskeletal chest pain | | | |
| subjects affected / exposed | 0 / 195 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infections and infestations | | | |
| Bronchitis | | | |
| subjects affected / exposed | 1 / 195 (0.51%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infection | | | |
| subjects affected / exposed | 0 / 195 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Orchitis | | | |
| subjects affected / exposed | 0 / 195 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pneumonia | | | |
| subjects affected / exposed | 2 / 195 (1.03%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory tract infection viral | | | |
| subjects affected / exposed | 1 / 195 (0.51%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| COVID-19 | | | |
| subjects affected / exposed | 0 / 195 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | |
|---|-----------------|--|--|
| Hepatitis A | | | |
| subjects affected / exposed | 1 / 195 (0.51%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

Frequency threshold for reporting non-serious adverse events: 2 %

| Non-serious adverse events | MEDI6012 Cohort A | Placebo Cohort B | Placebo Cohort A |
|---|-------------------|-------------------|------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 74 / 179 (41.34%) | 47 / 111 (42.34%) | 28 / 90 (31.11%) |
| Vascular disorders | | | |
| Brachiocephalic arteriosclerosis | | | |
| subjects affected / exposed | 2 / 179 (1.12%) | 1 / 111 (0.90%) | 1 / 90 (1.11%) |
| occurrences (all) | 2 | 1 | 1 |
| Haematoma | | | |
| subjects affected / exposed | 4 / 179 (2.23%) | 2 / 111 (1.80%) | 0 / 90 (0.00%) |
| occurrences (all) | 4 | 2 | 0 |
| Hypertension | | | |
| subjects affected / exposed | 4 / 179 (2.23%) | 1 / 111 (0.90%) | 0 / 90 (0.00%) |
| occurrences (all) | 4 | 1 | 0 |
| Hypotension | | | |
| subjects affected / exposed | 3 / 179 (1.68%) | 7 / 111 (6.31%) | 0 / 90 (0.00%) |
| occurrences (all) | 3 | 7 | 0 |
| General disorders and administration site conditions | | | |
| Fatigue | | | |
| subjects affected / exposed | 4 / 179 (2.23%) | 4 / 111 (3.60%) | 3 / 90 (3.33%) |
| occurrences (all) | 4 | 4 | 3 |
| Pyrexia | | | |
| subjects affected / exposed | 4 / 179 (2.23%) | 4 / 111 (3.60%) | 1 / 90 (1.11%) |
| occurrences (all) | 4 | 4 | 1 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Chronic obstructive pulmonary disease | | | |
| subjects affected / exposed | 2 / 179 (1.12%) | 0 / 111 (0.00%) | 2 / 90 (2.22%) |
| occurrences (all) | 2 | 0 | 2 |
| Cough | | | |

| | | | |
|--|----------------------|----------------------|---------------------|
| subjects affected / exposed occurrences (all) | 8 / 179 (4.47%) 8 | 3 / 111 (2.70%) 3 | 2 / 90 (2.22%) 2 |
| Dyspnoea subjects affected / exposed occurrences (all) | 4 / 179 (2.23%) 4 | 3 / 111 (2.70%) 3 | 2 / 90 (2.22%) 2 |
| Epistaxis subjects affected / exposed occurrences (all) | 2 / 179 (1.12%) 2 | 2 / 111 (1.80%) 2 | 2 / 90 (2.22%) 2 |
| Psychiatric disorders | | | |
| Anxiety subjects affected / exposed occurrences (all) | 4 / 179 (2.23%) 4 | 1 / 111 (0.90%) 1 | 0 / 90 (0.00%) 0 |
| Insomnia subjects affected / exposed occurrences (all) | 2 / 179 (1.12%) 2 | 1 / 111 (0.90%) 1 | 0 / 90 (0.00%) 0 |
| Cardiac disorders | | | |
| Angina pectoris subjects affected / exposed occurrences (all) | 4 / 179 (2.23%) 5 | 4 / 111 (3.60%) 4 | 2 / 90 (2.22%) 2 |
| Atrial fibrillation subjects affected / exposed occurrences (all) | 6 / 179 (3.35%) 6 | 5 / 111 (4.50%) 5 | 2 / 90 (2.22%) 2 |
| Bradycardia subjects affected / exposed occurrences (all) | 0 / 179 (0.00%) 0 | 3 / 111 (2.70%) 3 | 1 / 90 (1.11%) 1 |
| Cardiac failure subjects affected / exposed occurrences (all) | 4 / 179 (2.23%) 4 | 3 / 111 (2.70%) 4 | 1 / 90 (1.11%) 1 |
| Cardiac ventricular thrombosis subjects affected / exposed occurrences (all) | 5 / 179 (2.79%) 5 | 0 / 111 (0.00%) 0 | 1 / 90 (1.11%) 1 |
| Palpitations subjects affected / exposed occurrences (all) | 5 / 179 (2.79%) 6 | 1 / 111 (0.90%) 1 | 1 / 90 (1.11%) 1 |
| Supraventricular extrasystoles | | | |

| | | | |
|---|------------------------|----------------------|---------------------|
| subjects affected / exposed occurrences (all) | 3 / 179 (1.68%) 3 | 1 / 111 (0.90%) 1 | 2 / 90 (2.22%) 2 |
| Ventricular extrasystoles subjects affected / exposed occurrences (all) | 5 / 179 (2.79%) 5 | 2 / 111 (1.80%) 2 | 0 / 90 (0.00%) 0 |
| Nervous system disorders | | | |
| Dizziness subjects affected / exposed occurrences (all) | 13 / 179 (7.26%) 13 | 5 / 111 (4.50%) 5 | 1 / 90 (1.11%) 1 |
| Headache subjects affected / exposed occurrences (all) | 7 / 179 (3.91%) 7 | 5 / 111 (4.50%) 5 | 4 / 90 (4.44%) 4 |
| Blood and lymphatic system disorders | | | |
| Anaemia subjects affected / exposed occurrences (all) | 3 / 179 (1.68%) 3 | 1 / 111 (0.90%) 1 | 0 / 90 (0.00%) 0 |
| Gastrointestinal disorders | | | |
| Abdominal pain upper subjects affected / exposed occurrences (all) | 0 / 179 (0.00%) 0 | 0 / 111 (0.00%) 0 | 3 / 90 (3.33%) 3 |
| Constipation subjects affected / exposed occurrences (all) | 1 / 179 (0.56%) 1 | 2 / 111 (1.80%) 2 | 1 / 90 (1.11%) 1 |
| Diarrhoea subjects affected / exposed occurrences (all) | 4 / 179 (2.23%) 4 | 2 / 111 (1.80%) 2 | 1 / 90 (1.11%) 1 |
| Nausea subjects affected / exposed occurrences (all) | 2 / 179 (1.12%) 2 | 3 / 111 (2.70%) 3 | 1 / 90 (1.11%) 1 |
| Toothache subjects affected / exposed occurrences (all) | 0 / 179 (0.00%) 0 | 0 / 111 (0.00%) 0 | 2 / 90 (2.22%) 2 |
| Vomiting subjects affected / exposed occurrences (all) | 2 / 179 (1.12%) 2 | 2 / 111 (1.80%) 2 | 3 / 90 (3.33%) 3 |
| Hepatobiliary disorders | | | |

| | | | |
|---|----------------------|----------------------|---------------------|
| Hepatic steatosis subjects affected / exposed occurrences (all) | 5 / 179 (2.79%) 5 | 1 / 111 (0.90%) 1 | 1 / 90 (1.11%) 1 |
| Renal and urinary disorders Renal failure subjects affected / exposed occurrences (all) | 3 / 179 (1.68%) 3 | 1 / 111 (0.90%) 1 | 2 / 90 (2.22%) 2 |
| Renal impairment subjects affected / exposed occurrences (all) | 1 / 179 (0.56%) 1 | 2 / 111 (1.80%) 2 | 2 / 90 (2.22%) 2 |
| Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) | 4 / 179 (2.23%) 4 | 0 / 111 (0.00%) 0 | 0 / 90 (0.00%) 0 |
| Back pain subjects affected / exposed occurrences (all) | 2 / 179 (1.12%) 2 | 3 / 111 (2.70%) 3 | 2 / 90 (2.22%) 2 |
| Pain in extremity subjects affected / exposed occurrences (all) | 1 / 179 (0.56%) 1 | 4 / 111 (3.60%) 4 | 0 / 90 (0.00%) 0 |
| Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all) | 2 / 179 (1.12%) 2 | 1 / 111 (0.90%) 1 | 0 / 90 (0.00%) 0 |
| Respiratory tract infection viral subjects affected / exposed occurrences (all) | 2 / 179 (1.12%) 2 | 1 / 111 (0.90%) 1 | 0 / 90 (0.00%) 0 |
| Urinary tract infection subjects affected / exposed occurrences (all) | 3 / 179 (1.68%) 3 | 2 / 111 (1.80%) 2 | 2 / 90 (2.22%) 2 |
| Metabolism and nutrition disorders Dyslipidaemia subjects affected / exposed occurrences (all) | 5 / 179 (2.79%) 5 | 2 / 111 (1.80%) 2 | 2 / 90 (2.22%) 2 |
| Hypokalaemia | | | |

| | | | |
|-----------------------------|-----------------|-----------------|----------------|
| subjects affected / exposed | 5 / 179 (2.79%) | 2 / 111 (1.80%) | 5 / 90 (5.56%) |
| occurrences (all) | 5 | 2 | 7 |
| Type 2 diabetes mellitus | | | |
| subjects affected / exposed | 3 / 179 (1.68%) | 3 / 111 (2.70%) | 1 / 90 (1.11%) |
| occurrences (all) | 3 | 3 | 1 |

| Non-serious adverse events | MEDI6012 Cohort B | | |
|---|-------------------|--|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 89 / 195 (45.64%) | | |
| Vascular disorders | | | |
| Brachiocephalic arteriosclerosis | | | |
| subjects affected / exposed | 4 / 195 (2.05%) | | |
| occurrences (all) | 4 | | |
| Haematoma | | | |
| subjects affected / exposed | 3 / 195 (1.54%) | | |
| occurrences (all) | 3 | | |
| Hypertension | | | |
| subjects affected / exposed | 6 / 195 (3.08%) | | |
| occurrences (all) | 6 | | |
| Hypotension | | | |
| subjects affected / exposed | 11 / 195 (5.64%) | | |
| occurrences (all) | 12 | | |
| General disorders and administration site conditions | | | |
| Fatigue | | | |
| subjects affected / exposed | 2 / 195 (1.03%) | | |
| occurrences (all) | 2 | | |
| Pyrexia | | | |
| subjects affected / exposed | 3 / 195 (1.54%) | | |
| occurrences (all) | 3 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Chronic obstructive pulmonary disease | | | |
| subjects affected / exposed | 0 / 195 (0.00%) | | |
| occurrences (all) | 0 | | |
| Cough | | | |

| | | | |
|--------------------------------|-----------------|--|--|
| subjects affected / exposed | 9 / 195 (4.62%) | | |
| occurrences (all) | 9 | | |
| Dyspnoea | | | |
| subjects affected / exposed | 6 / 195 (3.08%) | | |
| occurrences (all) | 6 | | |
| Epistaxis | | | |
| subjects affected / exposed | 2 / 195 (1.03%) | | |
| occurrences (all) | 2 | | |
| Psychiatric disorders | | | |
| Anxiety | | | |
| subjects affected / exposed | 6 / 195 (3.08%) | | |
| occurrences (all) | 6 | | |
| Insomnia | | | |
| subjects affected / exposed | 5 / 195 (2.56%) | | |
| occurrences (all) | 5 | | |
| Cardiac disorders | | | |
| Angina pectoris | | | |
| subjects affected / exposed | 6 / 195 (3.08%) | | |
| occurrences (all) | 6 | | |
| Atrial fibrillation | | | |
| subjects affected / exposed | 7 / 195 (3.59%) | | |
| occurrences (all) | 7 | | |
| Bradycardia | | | |
| subjects affected / exposed | 5 / 195 (2.56%) | | |
| occurrences (all) | 5 | | |
| Cardiac failure | | | |
| subjects affected / exposed | 9 / 195 (4.62%) | | |
| occurrences (all) | 9 | | |
| Cardiac ventricular thrombosis | | | |
| subjects affected / exposed | 0 / 195 (0.00%) | | |
| occurrences (all) | 0 | | |
| Palpitations | | | |
| subjects affected / exposed | 2 / 195 (1.03%) | | |
| occurrences (all) | 2 | | |
| Supraventricular extrasystoles | | | |

| | | | |
|--|------------------------|--|--|
| subjects affected / exposed occurrences (all) | 3 / 195 (1.54%) 3 | | |
| Ventricular extrasystoles subjects affected / exposed occurrences (all) | 5 / 195 (2.56%) 5 | | |
| Nervous system disorders Dizziness subjects affected / exposed occurrences (all) | 4 / 195 (2.05%) 4 | | |
| Headache subjects affected / exposed occurrences (all) | 12 / 195 (6.15%) 13 | | |
| Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all) | 6 / 195 (3.08%) 6 | | |
| Gastrointestinal disorders Abdominal pain upper subjects affected / exposed occurrences (all) | 2 / 195 (1.03%) 2 | | |
| Constipation subjects affected / exposed occurrences (all) | 5 / 195 (2.56%) 5 | | |
| Diarrhoea subjects affected / exposed occurrences (all) | 8 / 195 (4.10%) 9 | | |
| Nausea subjects affected / exposed occurrences (all) | 11 / 195 (5.64%) 14 | | |
| Toothache subjects affected / exposed occurrences (all) | 0 / 195 (0.00%) 0 | | |
| Vomiting subjects affected / exposed occurrences (all) | 3 / 195 (1.54%) 4 | | |
| Hepatobiliary disorders | | | |

| | | | |
|---|----------------------|--|--|
| Hepatic steatosis subjects affected / exposed occurrences (all) | 1 / 195 (0.51%) 1 | | |
| Renal and urinary disorders Renal failure subjects affected / exposed occurrences (all) | 0 / 195 (0.00%) 0 | | |
| Renal impairment subjects affected / exposed occurrences (all) | 2 / 195 (1.03%) 2 | | |
| Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) | 1 / 195 (0.51%) 1 | | |
| Back pain subjects affected / exposed occurrences (all) | 3 / 195 (1.54%) 3 | | |
| Pain in extremity subjects affected / exposed occurrences (all) | 2 / 195 (1.03%) 2 | | |
| Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all) | 5 / 195 (2.56%) 5 | | |
| Respiratory tract infection viral subjects affected / exposed occurrences (all) | 4 / 195 (2.05%) 4 | | |
| Urinary tract infection subjects affected / exposed occurrences (all) | 3 / 195 (1.54%) 3 | | |
| Metabolism and nutrition disorders Dyslipidaemia subjects affected / exposed occurrences (all) | 6 / 195 (3.08%) 6 | | |
| Hypokalaemia | | | |

| | | | |
|-----------------------------|-----------------|--|--|
| subjects affected / exposed | 1 / 195 (0.51%) | | |
| occurrences (all) | 1 | | |
| Type 2 diabetes mellitus | | | |
| subjects affected / exposed | 3 / 195 (1.54%) | | |
| occurrences (all) | 3 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-----------------|---|
| 09 January 2018 | Updated Table 'Treatment Period and Follow up Procedures: Cohort A (2 Dose Regimen)' to correct previous omissions and errors. |
| 28 March 2018 | The word 'prevent' was replaced with 'reduce' in the third secondary hypothesis. The use of estimated glomerular filtration rate (eGFR) criteria was removed and changed to creatinine clearance (CrCl) criteria throughout. Updated exclusion criteria. Subsection 'Cardiovascular MRI' was revised to remove 'no known history of contrast-induced nephropathy' and instead to give conditions for receiving contrast. Clarified that randomization will be stratified by infarct location. Updated Table 'Treatment Period and Follow-up Procedures' for Cohort A and Cohort B. The text that radiation dose would be calculated using a K factor of 0.014. Text was added to specify that the sponsor and principal investigator were to monitor the statistical assumptions in a blinded fashion and decide the exact time for interim analyses. |
| 14 June 2018 | For Inpatient Phase, Cohorts A and B, text was added that following Doses 1 and 2 for Cohort A, or Doses 1-3 for Cohort B, participants would be monitored for 2 hours in a location with personnel trained in Adult Advanced Life Support with resuscitation equipment available. For Outpatient Phase Cohort B, text was added that participants who did not undergo index CTA for any reason would not undergo the CTA at the end of the study. The title of the Cardiovascular MRI subsection was revised to read 'Administration of gadolinium Contrast for Cardiovascular MRI'. Under Coronary CTA, a sixth requirement was added that for follow up CTA, participants would need to have undergone an index CTA. The table footnote of Tables 9 and 10 were updated. Text was revised to read, "For CMR, participants will be required to meet Additional Study Requirements listed in the clinical study protocol Section 4.1.4, including no contraindication to MR imaging (eg, metallic implant, claustrophobia, implantable cardioverter-defibrillator, pacemaker) and, for the administration of gadolinium-based contrast, confirmation of CrCl \geq 30 mL/min (Cockcroft Gault equation) is required'. The text was revised to say that due to the acute nature of the study, members of the research team, and possibly the investigator, may be unblinded. |
| 18 April 2019 | Provided clarification for the exploratory safety objective and endpoints related to major cardiovascular events. Index CTA window altered from 'no earlier than 48 hours' to 'no earlier than 40 hours' post Dose 1. CMR window for repeat scans increased from 1 week to 4 weeks following the end-of-study visit (up to 112 days post Dose 1). The table footnote of Tables 9 and 10 were updated. The time frame of Day 70 to 84 was added to text in the extended follow up section. Text related to pharmacokinetics and ADA samples was revised. Text added to increase the window for repeat CMR scans from 1 week to 4 weeks following the end-of-study visit (up to 112 days post Dose 1) and removed tagged MRI and T1 mapping procedures. Text added regarding CTA in participants who had planned or underwent coronary artery bypass graft surgery. |
| 26 July 2019 | Sample size was changed from at least 414 to approximately 540; total numbers per cohort, sample size calculation and second interim analysis were updated to reflect this. The alpha threshold was amended to be a 1-sided alpha of 0.05. Number of study sites updated from 40 to 43. Under Coronary CTA, the fifth requirement was revised to read, "No contraindication to heart rate lowering using betablockers to allow for high quality, low-radiation dose CTA (per protocol). If heart rate is well controlled allowing for a high quality, low-radiation CTA without betablocker, then a contraindication to betablocker does not exclude the participant from coronary CTA". Descriptions of analysis populations updated. |

| | |
|-------------|--|
| 04 May 2020 | The guidance was added to the protocol in response to the coronavirus disease (COVID-19) pandemic to enable safety monitoring of participants through an extended blood sampling window, updated the footnotes of Table 9 and Table 10 accordingly. It was added that during the Extended Follow-up period, if the ADA test result became negative or the HDL-C was no longer > 30% decreased compared with baseline, the participant did not need to return for additional Extended Follow-up visit(s) and would be considered as having completed the Extended Follow-up period. It was clarified that 2 independent database locks may be conducted and details of these database locks were given. The end of the study (study completion) was defined as the date of the last protocol specified visit/assessment, which could be the date of the last Day 70 to 84 visit (including telephone contact), or the Extended Follow-up if required at Week 25, 39, or 52, or death for the last participant in the study, whichever occurred last. Throughout the protocol where '> 30% decrease in HDL-C' was cited, it was clarified that this refers to '> 30% decrease from baseline in HDL-C'. |
|-------------|--|

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported