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, Carer, Data analyst, 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 (± 31.261)	113.870 (± 23.885)	110.244 (± 28.009)	111.533 (± 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 TESAEs	11	34	24	41

Statistical analyses

No statistical analyses for this end point

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

End point title	Serum Concentration of MEDI6012 (Lecithin-cholesterol Acyltransferaes [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	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
Infection			
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
Orchitis			
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
Pneumonia			
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 / 1	0 / 0	0 / 0
Respiratory tract infection viral			
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
COVID-19			
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
Hepatitis A			
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

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

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

Hepatic steatosis			
subjects affected / exposed	5 / 179 (2.79%)	1 / 111 (0.90%)	1 / 90 (1.11%)
occurrences (all)	5	1	1
Renal and urinary disorders			
Renal failure			
subjects affected / exposed	3 / 179 (1.68%)	1 / 111 (0.90%)	2 / 90 (2.22%)
occurrences (all)	3	1	2
Renal impairment			
subjects affected / exposed	1 / 179 (0.56%)	2 / 111 (1.80%)	2 / 90 (2.22%)
occurrences (all)	1	2	2
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	4 / 179 (2.23%)	0 / 111 (0.00%)	0 / 90 (0.00%)
occurrences (all)	4	0	0
Back pain			
subjects affected / exposed	2 / 179 (1.12%)	3 / 111 (2.70%)	2 / 90 (2.22%)
occurrences (all)	2	3	2
Pain in extremity			
subjects affected / exposed	1 / 179 (0.56%)	4 / 111 (3.60%)	0 / 90 (0.00%)
occurrences (all)	1	4	0
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	2 / 179 (1.12%)	1 / 111 (0.90%)	0 / 90 (0.00%)
occurrences (all)	2	1	0
Respiratory tract infection viral			
subjects affected / exposed	2 / 179 (1.12%)	1 / 111 (0.90%)	0 / 90 (0.00%)
occurrences (all)	2	1	0
Urinary tract infection			
subjects affected / exposed	3 / 179 (1.68%)	2 / 111 (1.80%)	2 / 90 (2.22%)
occurrences (all)	3	2	2
Metabolism and nutrition disorders			
Dyslipidaemia			
subjects affected / exposed	5 / 179 (2.79%)	2 / 111 (1.80%)	2 / 90 (2.22%)
occurrences (all)	5	2	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) Ventricular extrasystoles subjects affected / exposed occurrences (all)	3 / 195 (1.54%) 3 5 / 195 (2.56%) 5		
Nervous system disorders Dizziness subjects affected / exposed occurrences (all) Headache subjects affected / exposed occurrences (all)	 4 / 195 (2.05%) 4 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) Constipation subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all) Toothache subjects affected / exposed occurrences (all) Vomiting subjects affected / exposed occurrences (all)	 2 / 195 (1.03%) 2 5 / 195 (2.56%) 5 8 / 195 (4.10%) 9 11 / 195 (5.64%) 14 0 / 195 (0.00%) 0 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) Renal impairment subjects affected / exposed occurrences (all)	0 / 195 (0.00%) 0 2 / 195 (1.03%) 2		
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) Back pain subjects affected / exposed occurrences (all) Pain in extremity subjects affected / exposed occurrences (all)	1 / 195 (0.51%) 1 3 / 195 (1.54%) 3 2 / 195 (1.03%) 2		
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all) Respiratory tract infection viral subjects affected / exposed occurrences (all) Urinary tract infection subjects affected / exposed occurrences (all)	5 / 195 (2.56%) 5 4 / 195 (2.05%) 4 3 / 195 (1.54%) 3		
Metabolism and nutrition disorders Dyslipidaemia subjects affected / exposed occurrences (all) Hypokalaemia	6 / 195 (3.08%) 6		

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 ≥ 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