Clinical trial results:
A Double-blind, Randomized, Placebo-controlled Phase 2 Study to Evaluate Efficacy, Safety, and Tolerability of Olpasiran (AMG 890) (a GalNAc-conjugated Small Interfering RNA [siRNA]) in Subjects With Elevated Lipoprotein(a)

Summary

EudraCT number	2019-003688-23
Trial protocol	DK NL IS
Global end of trial date	08 November 2022

Results information

Result version number	v1 (current)
This version publication date	10 August 2023
First version publication date	10 August 2023

Trial information

Trial identification

Sponsor protocol code	20180109

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04270760
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Amgen Inc.
Sponsor organisation address	One Amgen Center Drive, Thousand Oaks, CA, United States,
Public contact	Study Director, Amgen Inc., +1 8665726436, medinfo@amgen.com
Scientific contact	Study Director, Amgen Inc., +1 8665726436, medinfo@amgen.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	16 December 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	08 November 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of the trial was to evaluate the effect of olpasiran administered subcutaneously (SC) once every 12 weeks (Q12W) compared with placebo, on percent change from Baseline in lipoprotein(a) (Lp[a]) after 36 weeks of treatment.

Protection of trial subjects:

This study was conducted in accordance with International Council for Harmonisation Good Clinical Practice regulations/guidelines.

Background therapy:

Participants remained on standard of care per their local guidelines during the Treatment Period and Extended Safety Follow-up Period.

Evidence for comparator: -

Actual start date of recruitment	28 July 2020
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	14 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 43
Country: Number of subjects enrolled	Denmark: 10
Country: Number of subjects enrolled	Iceland: 11
Country: Number of subjects enrolled	Netherlands: 30
Country: Number of subjects enrolled	Canada: 26
Country: Number of subjects enrolled	United States: 142
Country: Number of subjects enrolled	Japan: 19
Worldwide total number of subjects	281
EEA total number of subjects	51

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)	163
From 65 to 84 years	118
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study was conducted at 34 centers in Australia, Denmark, Iceland, the Netherlands, Canada, the United States, and Japan between 28 July 2020 and 08 November 2022.

Pre-assignment

Screening details:

The Treatment Period was 48 weeks with investigational product (IP) administered SC Q12W or every 24 weeks (Q24W). After Week 48 there was an Extended Safety Follow-up Period without further dosing with IP for a minimum of 24 weeks.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Group 1: Olpasiran 10 mg Q12W

Arm description:

Participants were administered SC olpasiran 10 mg Q12W for 48 weeks with doses at Day 1, Week 12, Week 24, and Week 36. After Week 48 there was an Extended Safety Follow-up Period without further dosing with IP for a minimum of 24 weeks.

Arm type	Experimental
Investigational medicinal product name	Olpasiran
Investigational medicinal product code	AMG 890
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Administered via SC injection.

Arm title	Group 2: Olpasiran 75 mg Q12W

Arm description:

Participants were administered SC olpasiran 75 mg Q12W for 48 weeks with doses at Day 1, Week 12, Week 24, and Week 36. After Week 48 there was an Extended Safety Follow-up Period without further dosing with IP for a minimum of 24 weeks.

Arm type	Experimental
Investigational medicinal product name	Olpasiran
Investigational medicinal product code	AMG 890
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Administered via SC injection.

Arm title	Group 3: Olpasiran 225 mg Q12W

Arm description:

Participants were administered SC olpasiran 225 mg Q12W for 48 weeks with doses at Day 1, Week 12, Week 24, and Week 36. After Week 48 there was an Extended Safety Follow-up Period without further dosing with IP for a minimum of 24 weeks.

Arm type	Experimental

Investigational medicinal product name	Olpasiran
Investigational medicinal product code	AMG 890
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Administered via SC injection.

Arm title	Group 4: Olpasiran 225 mg Q24W

Arm description:

Participants were administered SC olpasiran 225 mg Q24W for 48 weeks with doses at Day 1 and Week 24. After Week 48 there was an Extended Safety Follow-up Period without further dosing with IP for a minimum of 24 weeks.

Arm type	Experimental
Investigational medicinal product name	Olpasiran
Investigational medicinal product code	AMG 890
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Administered via SC injection.

Arm title	Group 5: Placebo Q12W

Arm description:

Participants were administered SC placebo Q12W for 48 weeks with doses at Day 1, Week 12, Week 24, and Week 36. After Week 48 there was an Extended Safety Follow-up Period without further dosing with IP for a minimum of 24 weeks.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Administered via SC injection.

Number of subjects in period 1	Group 1: Olpasiran 10 mg Q12W	Group 2: Olpasiran 75 mg Q12W	Group 3: Olpasiran 225 mg Q12W
Started	58	58	56
Entered Extended Safety Follow-up Period	57	57	54
Completed	57	55	52
Not completed	1	3	4
Adverse event, serious fatal	-	-	-
Consent withdrawn by subject	-	1	3
Lost to follow-up	1	2	1

Number of subjects in period 1	Group 4: Olpasiran 225 mg Q24W	Group 5: Placebo Q12W
Started	55	54

Entered Extended Safety Follow-up Period	55	53
Completed	55	53
Not completed	0	1
Adverse event, serious fatal	-	1
Consent withdrawn by subject	-	-
Lost to follow-up	-	-

Baseline characteristics

Reporting groups	
Reporting group title	Group 1: Olpasiran 10 mg Q12W
Reporting group description:	
Participants were administered SC olpasiran 10 mg Q12W for 48 weeks with doses at Day 1, Week 12, Week 24, and Week 36. After Week 48 there was an Extended Safety Follow-up Period without further dosing with IP for a minimum of 24 weeks.	
Reporting group title	Group 2: Olpasiran 75 mg Q12W
Reporting group description:	
Participants were administered SC olpasiran 75 mg Q12W for 48 weeks with doses at Day 1, Week 12, Week 24, and Week 36. After Week 48 there was an Extended Safety Follow-up Period without further dosing with IP for a minimum of 24 weeks.	
Reporting group title	Group 3: Olpasiran 225 mg Q12W
Reporting group description:	
Participants were administered SC olpasiran 225 mg Q12W for 48 weeks with doses at Day 1, Week 12, Week 24, and Week 36. After Week 48 there was an Extended Safety Follow-up Period without further dosing with IP for a minimum of 24 weeks.	
Reporting group title	Group 4: Olpasiran 225 mg Q24W
Reporting group description:	
Participants were administered SC olpasiran 225 mg Q24W for 48 weeks with doses at Day 1 and Week 24. After Week 48 there was an Extended Safety Follow-up Period without further dosing with IP for a minimum of 24 weeks.	
Reporting group title	Group 5: Placebo Q12W
Reporting group description:	
Participants were administered SC placebo Q12W for 48 weeks with doses at Day 1, Week 12, Week 24, and Week 36. After Week 48 there was an Extended Safety Follow-up Period without further dosing with IP for a minimum of 24 weeks.	

Reporting group values	Group 1: Olpasiran 10 mg Q12W	Group 2: Olpasiran 75 mg Q12W	Group 3: Olpasiran 225 mg Q12W
Number of subjects	58	58	56
Age Categorical Units:			
18 - 64 years	31	35	37
65 - 74 years	19	17	18
75 - 84 years	8	6	1
Age Continuous Units: Years			
arithmetic mean	63.4	61.3	59.7
standard deviation	± 9.5	± 9.2	± 10.1
Sex: Female, Male Units:			
Female	12	23	15
Male	46	35	41
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	2	0	0
Not Hispanic or Latino	56	58	56
Unknown or Not Reported	0	0	0
Race/Ethnicity, Customized Units: Subjects			

Asian	6	5	5
Black or African American	0	1	2
White	52	52	47
Other	0	0	2

Reporting group values	Group 4: Olpasiran 225 mg Q24W	Group 5: Placebo Q12W	Total
Number of subjects	55	54	281
Age Categorical Units:			
18 - 64 years	31	29	163
65 - 74 years	19	17	90
75 - 84 years	5	8	28
Age Continuous Units: Years			
arithmetic mean	61.8	63.4	
standard deviation	± 9.4	± 8.9	-
Sex: Female, Male Units:			
Female	22	18	90
Male	33	36	191
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	2	2	6
Not Hispanic or Latino	53	52	275
Unknown or Not Reported	0	0	0
Race/Ethnicity, Customized Units: Subjects			
Asian	5	3	24
Black or African American	1	2	6
White	49	48	248
Other	0	1	3

End points

End points reporting groups

Reporting group title	Group 1: Olpasiran 10 mg Q12W
Reporting group description:	
Participants were administered SC olpasiran 10 mg Q12W for 48 weeks with doses at Day 1, Week 12, Week 24, and Week 36. After Week 48 there was an Extended Safety Follow-up Period without further dosing with IP for a minimum of 24 weeks.	
Reporting group title	Group 2: Olpasiran 75 mg Q12W
Reporting group description:	
Participants were administered SC olpasiran 75 mg Q12W for 48 weeks with doses at Day 1, Week 12, Week 24, and Week 36. After Week 48 there was an Extended Safety Follow-up Period without further dosing with IP for a minimum of 24 weeks.	
Reporting group title	Group 3: Olpasiran 225 mg Q12W
Reporting group description:	
Participants were administered SC olpasiran 225 mg Q12W for 48 weeks with doses at Day 1, Week 12, Week 24, and Week 36. After Week 48 there was an Extended Safety Follow-up Period without further dosing with IP for a minimum of 24 weeks.	
Reporting group title	Group 4: Olpasiran 225 mg Q24W
Reporting group description:	
Participants were administered SC olpasiran 225 mg Q24W for 48 weeks with doses at Day 1 and Week 24. After Week 48 there was an Extended Safety Follow-up Period without further dosing with IP for a minimum of 24 weeks.	
Reporting group title	Group 5: Placebo Q12W
Reporting group description:	
Participants were administered SC placebo Q12W for 48 weeks with doses at Day 1, Week 12, Week 24, and Week 36. After Week 48 there was an Extended Safety Follow-up Period without further dosing with IP for a minimum of 24 weeks.	

Primary: Percentage Change From Baseline in Lp(a) at Week 36

End point title	Percentage Change From Baseline in Lp(a) at Week 36
End point description:	
Least squares mean is from the repeated measures linear effects model which includes treatment group, stratification factors, scheduled visit and the interaction of treatment group with scheduled visit. Participants in the FAS with data available at each time point. FAS: includes all randomized participants who received at least one dose of IP.	
End point type	Primary
End point timeframe:	
Baseline and Week 36	

End point values	Group 1: Olpasiran 10 mg Q12W	Group 2: Olpasiran 75 mg Q12W	Group 3: Olpasiran 225 mg Q12W	Group 4: Olpasiran 225 mg Q24W
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	57	57	53	53
Units: Percentage Change in Lp(a)				
least squares mean (standard error)	-66.91 (± 1.78)	-93.78 (± 1.78)	-97.53 (± 1.82)	-96.89 (± 1.85)

End point values	Group 5: Placebo Q12W			
Subject group type	Reporting group			
Number of subjects analysed	51			
Units: Percentage Change in Lp(a)				
least squares mean (standard error)	3.60 (± 1.89)			

Statistical analyses

Statistical analysis title	Group 1 versus (vs) Group 5
Statistical analysis description:	
Treatment difference = percentage change in Group 1 - percentage change in Group 5 from Baseline at Week 36.	
Comparison groups	Group 1: Olpasiran 10 mg Q12W v Group 5: Placebo Q12W
Number of subjects included in analysis	108
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001 [1]
Method	Repeated measures linear effects model
Parameter estimate	Treatment difference
Point estimate	-70.51
Confidence interval	
level	95 %
sides	2-sided
lower limit	-75.12
upper limit	-65.9
Variability estimate	Standard error of the mean
Dispersion value	2.35

Notes:

[1] - Adjusted p-value is reported based on the Hochberg procedure to control the type I error for multiple comparisons. Each individual adjusted p-value is compared to 0.05 to determine statistical significance.

Statistical analysis title	Group 3 vs Group 5
Statistical analysis description:	
Treatment difference = percentage change in Group 3 - percentage change in Group 5 from Baseline at Week 36.	
Comparison groups	Group 3: Olpasiran 225 mg Q12W v Group 5: Placebo Q12W
Number of subjects included in analysis	104
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001 [2]
Method	Repeated measures linear effects model
Parameter estimate	Treatment difference
Point estimate	-101.13

Confidence interval	
level	95 %
sides	2-sided
lower limit	-105.79
upper limit	-96.47
Variability estimate	Standard error of the mean
Dispersion value	2.38

Notes:

[2] - Adjusted p-value is reported based on the Hochberg procedure to control the type I error for multiple comparisons. Each individual adjusted p-value is compared to 0.05 to determine statistical significance.

Statistical analysis title	Group 4 vs Group 5

Statistical analysis description:

Treatment difference = percentage change in Group 4 - percentage change in Group 5 from Baseline at Week 36.

Comparison groups	Group 4: Olpasiran 225 mg Q24W v Group 5: Placebo Q12W
Number of subjects included in analysis	104
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	Repeated measures linear effects model
Parameter estimate	Treatment difference
Point estimate	-100.49
Confidence interval	
level	95 %
sides	2-sided
lower limit	-105.16
upper limit	-95.82
Variability estimate	Standard error of the mean
Dispersion value	2.38

Statistical analysis title	Group 2 vs Group 5

Statistical analysis description:

Treatment difference = percentage change in Group 2 - percentage change in Group 5 from Baseline at Week 36.

Comparison groups	Group 2: Olpasiran 75 mg Q12W v Group 5: Placebo Q12W
Number of subjects included in analysis	108
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001 [3]
Method	Repeated measures linear effects model
Parameter estimate	Treatment difference
Point estimate	-97.38
Confidence interval	
level	95 %
sides	2-sided
lower limit	-101.98
upper limit	-92.77

Variability estimate	Standard error of the mean
Dispersion value	2.35

Notes:

[3] - Adjusted p-value is reported based on the Hochberg procedure to control the type I error for multiple comparisons. Each individual adjusted p-value is compared to 0.05 to determine statistical significance.

Secondary: Percentage Change From Baseline in Lp(a) at Week 48

End point title	Percentage Change From Baseline in Lp(a) at Week 48

End point description:

Least squares mean is from the repeated measures linear effects model which includes treatment group, stratification factors, scheduled visit and the interaction of treatment group with scheduled visit.

Participants in the FAS with data available at each time point. FAS: includes all randomized participants who received at least one dose of IP.

End point type	Secondary

End point timeframe:

Baseline and Week 48

End point values	Group 1: Olpasiran 10 mg Q12W	Group 2: Olpasiran 75 mg Q12W	Group 3: Olpasiran 225 mg Q12W	Group 4: Olpasiran 225 mg Q24W
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	57	57	54	53
Units: Percentage Change in Lp(a)				
least squares mean (standard error)	-64.89 (± 2.17)	-92.54 (± 2.17)	-97.29 (± 2.22)	-82.36 (± 2.25)

End point values	Group 5: Placebo Q12W			
Subject group type	Reporting group			
Number of subjects analysed	51			
Units: Percentage Change in Lp(a)				
least squares mean (standard error)	3.59 (± 2.30)			

Statistical analyses

Statistical analysis title	Group 1 vs Group 5

Statistical analysis description:

Treatment difference = percentage change in Group 1 - percentage change in Group 5 from Baseline at Week 48.

Comparison groups	Group 1: Olpasiran 10 mg Q12W v Group 5: Placebo Q12W

Number of subjects included in analysis	108
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	Repeated measures linear effects model
Parameter estimate	Treatment difference
Point estimate	-68.47
Confidence interval	
level	95 %
sides	2-sided
lower limit	-74.27
upper limit	-62.67
Variability estimate	Standard error of the mean
Dispersion value	2.96

Statistical analysis title	Group 2 vs Group 5
Statistical analysis description:	
Treatment difference = percentage change in Group 2 - percentage change in Group 5 from Baseline at Week 48.	
Comparison groups	Group 2: Olpasiran 75 mg Q12W v Group 5: Placebo Q12W
Number of subjects included in analysis	108
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	Repeated measures linear effects model
Parameter estimate	Treatment difference
Point estimate	-96.12
Confidence interval	
level	95 %
sides	2-sided
lower limit	-101.92
upper limit	-90.33
Variability estimate	Standard error of the mean
Dispersion value	2.96

Statistical analysis title	Group 3 vs Group 5
Statistical analysis description:	
Treatment difference = percentage change in Group 3 - percentage change in Group 5 from Baseline at Week 48.	
Comparison groups	Group 3: Olpasiran 225 mg Q12W v Group 5: Placebo Q12W
Number of subjects included in analysis	105
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	Repeated measures linear effects model
Parameter estimate	Treatment difference
Point estimate	-100.88

Confidence interval	
level	95 %
sides	2-sided
lower limit	-106.74
upper limit	-95.02
Variability estimate	Standard error of the mean
Dispersion value	2.99

Statistical analysis title	Group 4 vs Group 5
Statistical analysis description:	
Treatment difference = percentage change in Group 4 - percentage change in Group 5 from Baseline at Week 48.	
Comparison groups	Group 4: Olpasiran 225 mg Q24W v Group 5: Placebo Q12W
Number of subjects included in analysis	104
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	Repeated measures linear effects model
Parameter estimate	Treatment difference
Point estimate	-85.94
Confidence interval	
level	95 %
sides	2-sided
lower limit	-91.83
upper limit	-80.06
Variability estimate	Standard error of the mean
Dispersion value	3

Secondary: Percentage Change From Baseline in Low Density Lipoprotein Cholesterol (LDL-C) at Week 36 and Week 48

End point title	Percentage Change From Baseline in Low Density Lipoprotein Cholesterol (LDL-C) at Week 36 and Week 48
End point description:	
Least squares mean is from the repeated measures linear effects model which includes treatment group, stratification factors, scheduled visit and the interaction of treatment group with scheduled visit. Participants in the FAS with data available at each time point. FAS: includes all randomized participants who received at least one dose of IP.	
End point type	Secondary
End point timeframe:	
Baseline; Week 36 and Week 48	

End point values	Group 1: Olpasiran 10 mg Q12W	Group 2: Olpasiran 75 mg Q12W	Group 3: Olpasiran 225 mg Q12W	Group 4: Olpasiran 225 mg Q24W
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	57	57	54	53
Units: Percentage Change in LDL-C				
least squares mean (standard error)				
Week 36 (n = 57, 57, 53, 53, 51)	-17.425 (± 4.258)	-16.284 (± 4.259)	-16.733 (± 4.389)	-18.462 (± 4.428)
Week 48 (n = 57, 57, 54, 52, 51)	-14.743 (± 4.419)	-11.481 (± 4.418)	-17.308 (± 4.532)	-16.908 (± 4.608)

End point values	Group 5: Placebo Q12W			
Subject group type	Reporting group			
Number of subjects analysed	51			
Units: Percentage Change in LDL-C				
least squares mean (standard error)				
Week 36 (n = 57, 57, 53, 53, 51)	6.234 (± 4.520)			
Week 48 (n = 57, 57, 54, 52, 51)	10.113 (± 4.688)			

Statistical analyses

Statistical analysis title	Week 36: Group 1 vs Group 5

Statistical analysis description:

Treatment difference = percentage change in Group 1 - percentage change in Group 5 from Baseline at Week 36.

Comparison groups	Group 1: Olpasiran 10 mg Q12W v Group 5: Placebo Q12W
Number of subjects included in analysis	108
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	Repeated measures linear effects model
Parameter estimate	Treatment difference
Point estimate	-23.659
Confidence interval	
level	95 %
sides	2-sided
lower limit	-35.176
upper limit	-12.143
Variability estimate	Standard error of the mean
Dispersion value	5.874

Statistical analysis title	Week 36: Group 2 vs Group 5

Statistical analysis description:

Treatment difference = percentage change in Group 2 - percentage change in Group 5 from Baseline at Week 36.

Comparison groups	Group 2: Olpasiran 75 mg Q12W v Group 5: Placebo Q12W
Number of subjects included in analysis	108
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	Repeated measures linear effects model
Parameter estimate	Treatment difference
Point estimate	-22.518
Confidence interval	
level	95 %
sides	2-sided
lower limit	-34.036
upper limit	-11
Variability estimate	Standard error of the mean
Dispersion value	5.875

Statistical analysis title	Week 36: Group 3 vs Group 5

Statistical analysis description:

Treatment difference = percentage change in Group 3 - percentage change in Group 5 from Baseline at Week 36.

Comparison groups	Group 3: Olpasiran 225 mg Q12W v Group 5: Placebo Q12W
Number of subjects included in analysis	105
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	Repeated measures linear effects model
Parameter estimate	Treatment difference
Point estimate	-22.967
Confidence interval	
level	95 %
sides	2-sided
lower limit	-34.656
upper limit	-11.278
Variability estimate	Standard error of the mean
Dispersion value	5.962

Statistical analysis title	Week 36: Group 4 vs Group 5

Statistical analysis description:

Treatment difference = percentage change in Group 4 - percentage change in Group 5 from Baseline at Week 36.

Comparison groups	Group 4: Olpasiran 225 mg Q24W v Group 5: Placebo Q12W

Number of subjects included in analysis	104
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	Repeated measures linear effects model
Parameter estimate	Treatment difference
Point estimate	-24.696
Confidence interval	
level	95 %
sides	2-sided
lower limit	-36.399
upper limit	-12.993
Variability estimate	Standard error of the mean
Dispersion value	5.969

Statistical analysis title	Week 48: Group 2 vs Group 5
Statistical analysis description:	
Treatment difference = percentage change in Group 2 - percentage change in Group 5 from Baseline at Week 48.	
Comparison groups	Group 2: Olpasiran 75 mg Q12W v Group 5: Placebo Q12W
Number of subjects included in analysis	108
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	Repeated measures linear effects model
Parameter estimate	Treatment difference
Point estimate	-21.594
Confidence interval	
level	95 %
sides	2-sided
lower limit	-33.59
upper limit	-9.598
Variability estimate	Standard error of the mean
Dispersion value	6.118

Statistical analysis title	Week 48: Group 1 vs Group 5
Statistical analysis description:	
Treatment difference = percentage change in Group 1 - percentage change in Group 5 from Baseline at Week 48.	
Comparison groups	Group 1: Olpasiran 10 mg Q12W v Group 5: Placebo Q12W
Number of subjects included in analysis	108
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	Repeated measures linear effects model
Parameter estimate	Treatment difference
Point estimate	-24.856

Confidence interval	
level	95 %
sides	2-sided
lower limit	-36.853
upper limit	-12.859
Variability estimate	Standard error of the mean
Dispersion value	6.119

Statistical analysis title	Week 48: Group 3 vs Group 5
Statistical analysis description:	
Treatment difference = percentage change in Group 3 - percentage change in Group 5 from Baseline at Week 48.	
Comparison groups	Group 3: Olpasiran 225 mg Q12W v Group 5: Placebo Q12W
Number of subjects included in analysis	105
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	Repeated measures linear effects model
Parameter estimate	Treatment difference
Point estimate	-27.421
Confidence interval	
level	95 %
sides	2-sided
lower limit	-39.565
upper limit	-15.277
Variability estimate	Standard error of the mean
Dispersion value	6.194

Statistical analysis title	Week 48: Group 4 vs Group 5
Statistical analysis description:	
Treatment difference = percentage change in Group 4 - percentage change in Group 5 from Baseline at Week 48.	
Comparison groups	Group 4: Olpasiran 225 mg Q24W v Group 5: Placebo Q12W
Number of subjects included in analysis	104
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	Repeated measures linear effects model
Parameter estimate	Treatment difference
Point estimate	-27.021
Confidence interval	
level	95 %
sides	2-sided
lower limit	-39.24
upper limit	-14.801
Variability estimate	Standard error of the mean
Dispersion value	6.232

Secondary: Percentage Change From Baseline in Apolipoprotein (B) (ApoB) at Week 36 and Week 48

End point title	Percentage Change From Baseline in Apolipoprotein (B) (ApoB) at Week 36 and Week 48

End point description:

Least squares mean is from the repeated measures linear effects model which includes treatment group, stratification factors, scheduled visit and the interaction of treatment group with scheduled visit.

Participants in the FAS with data available at each time point. FAS: includes all randomized participants who received at least one dose of IP.

End point type	Secondary

End point timeframe:

Baseline; Week 36 and Week 48

End point values	Group 1: Olpasiran 10 mg Q12W	Group 2: Olpasiran 75 mg Q12W	Group 3: Olpasiran 225 mg Q12W	Group 4: Olpasiran 225 mg Q24W
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	57	57	54	53
Units: Percentage Change in ApoB				
least squares mean (standard error)				
Week 36 (n = 57, 57, 54, 53, 52)	-11.496 (± 2.886)	-9.302 (± 2.885)	-10.241 (± 2.960)	-11.378 (± 3.012)
Week 48 (n = 57, 57, 54, 53, 52)	-7.748 (± 3.307)	-4.768 (± 3.305)	-7.218 (± 3.393)	-9.548 (± 3.443)

End point values	Group 5: Placebo Q12W			
Subject group type	Reporting group			
Number of subjects analysed	52			
Units: Percentage Change in ApoB				
least squares mean (standard error)				
Week 36 (n = 57, 57, 54, 53, 52)	7.394 (± 3.066)			
Week 48 (n = 57, 57, 54, 53, 52)	12.292 (± 3.501)			

Statistical analyses

Statistical analysis title	Week 36: Group 1 vs Group 5

Statistical analysis description:

Treatment difference = percentage change in Group 1 - percentage change in Group 5 from Baseline at Week 36.

Comparison groups	Group 1: Olpasiran 10 mg Q12W v Group 5: Placebo Q12W

Number of subjects included in analysis	109
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	Repeated measures linear effects model
Parameter estimate	Treatment difference
Point estimate	-18.89
Confidence interval	
level	95 %
sides	2-sided
lower limit	-26.303
upper limit	-11.477
Variability estimate	Standard error of the mean
Dispersion value	3.779

Statistical analysis title	Week 36: Group 2 vs Group 5
Statistical analysis description:	
Treatment difference = percentage change in Group 2 - percentage change in Group 5 from Baseline at Week 36.	
Comparison groups	Group 2: Olpasiran 75 mg Q12W v Group 5: Placebo Q12W
Number of subjects included in analysis	109
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	Repeated measures linear effects model
Parameter estimate	Treatment difference
Point estimate	-16.696
Confidence interval	
level	95 %
sides	2-sided
lower limit	-24.107
upper limit	-9.284
Variability estimate	Standard error of the mean
Dispersion value	3.778

Statistical analysis title	Week 36: Group 3 vs Group 5
Statistical analysis description:	
Treatment difference = percentage change in Group 3 - percentage change in Group 5 from Baseline at Week 36.	
Comparison groups	Group 3: Olpasiran 225 mg Q12W v Group 5: Placebo Q12W
Number of subjects included in analysis	106
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	Repeated measures linear effects model
Parameter estimate	Treatment difference
Point estimate	-17.635

Confidence interval	
level	95 %
sides	2-sided
lower limit	-25.139
upper limit	-10.131
Variability estimate	Standard error of the mean
Dispersion value	3.825

Statistical analysis title	Week 36: Group 4 vs Group 5
Statistical analysis description:	
Treatment difference = percentage change in Group 4 - percentage change in Group 5 from Baseline at Week 36.	
Comparison groups	Group 4: Olpasiran 225 mg Q24W v Group 5: Placebo Q12W
Number of subjects included in analysis	105
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	Repeated measures linear effects model
Parameter estimate	Treatment difference
Point estimate	-18.772
Confidence interval	
level	95 %
sides	2-sided
lower limit	-26.303
upper limit	-11.241
Variability estimate	Standard error of the mean
Dispersion value	3.839

Statistical analysis title	Week 48: Group 1 vs Group 5
Statistical analysis description:	
Treatment difference = percentage change in Group 1 - percentage change in Group 5 from Baseline at Week 48.	
Comparison groups	Group 1: Olpasiran 10 mg Q12W v Group 5: Placebo Q12W
Number of subjects included in analysis	109
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	Repeated measures linear effects model
Parameter estimate	Treatment difference
Point estimate	-20.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	-28.757
upper limit	-11.323
Variability estimate	Standard error of the mean
Dispersion value	4.443

Statistical analysis title	Week 48: Group 2 vs Group 5
Statistical analysis description:	
Treatment difference = percentage change in Group 2 - percentage change in Group 5 from Baseline at Week 48.	
Comparison groups	Group 2: Olpasiran 75 mg Q12W v Group 5: Placebo Q12W
Number of subjects included in analysis	109
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	Repeated measures linear effects model
Parameter estimate	Treatment difference
Point estimate	-17.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	-25.774
upper limit	-8.345
Variability estimate	Standard error of the mean
Dispersion value	4.442

Statistical analysis title	Week 48: Group 3 vs Group 5
Statistical analysis description:	
Treatment difference = percentage change in Group 3 - percentage change in Group 5 from Baseline at Week 48.	
Comparison groups	Group 3: Olpasiran 225 mg Q12W v Group 5: Placebo Q12W
Number of subjects included in analysis	106
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	Repeated measures linear effects model
Parameter estimate	Treatment difference
Point estimate	-19.509
Confidence interval	
level	95 %
sides	2-sided
lower limit	-28.336
upper limit	-10.682
Variability estimate	Standard error of the mean
Dispersion value	4.5

Statistical analysis title	Week 48: Group 4 vs Group 5
Statistical analysis description:	
Treatment difference = percentage change in Group 4 - percentage change in Group 5 from Baseline at Week 48.	

Comparison groups	Group 4: Olpasiran 225 mg Q24W v Group 5: Placebo Q12W
Number of subjects included in analysis	105
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	Repeated measures linear effects model
Parameter estimate	Treatment difference
Point estimate	-21.839
Confidence interval	
level	95 %
sides	2-sided
lower limit	-30.7
upper limit	-12.979
Variability estimate	Standard error of the mean
Dispersion value	4.517

Secondary: Mean Serum Olpasiran Concentrations at Day 1, Week 24 and Week 48

End point title	Mean Serum Olpasiran Concentrations at Day 1, Week 24 and Week 48[4]

End point description:

Pharmacokinetic blood draws were collected at one timepoint during the 6-12 and 24-72 hour flexible time windows and at Week 48.

Lower limit of quantification (LLOQ) = 0.400 ng/mL. Values below the LLOQ were set to zero.

Participants in the FAS with data available at each time point. FAS: includes all randomized participants who received at least one dose of IP.

End point type	Secondary

End point timeframe:

Pre-dose and 1, 3, 6-12, and 24-72 hours post-dose on Day 1 and Week 24; Week 48

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Serum Olpasiran concentration data are reported for Olpasiran arms only as pre-specified.

End point values	Group 1: Olpasiran 10 mg Q12W	Group 2: Olpasiran 75 mg Q12W	Group 3: Olpasiran 225 mg Q12W	Group 4: Olpasiran 225 mg Q24W
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	55	56	49	52
Units: ng/mL				
arithmetic mean (standard deviation)				
Day 1: Pre-dose (n = 54, 52, 47, 51)	0.00 (± 0.00)	0.00 (± 0.00)	0.00 (± 0.00)	0.00 (± 0.00)
Day 1: 1 Hour Post-dose (n = 52, 44, 45, 46)	12.3 (± 6.9)	67.1 (± 47.4)	220 (± 218)	275 (± 450)
Day 1: 3 Hours Post-dose (n = 53, 44, 44, 48)	18 (± 9.85)	80.3 (± 43.2)	291 (± 273)	324 (± 383)
Day 1: 6-12 Hours Post-dose (n = 8, 9, 8, 16)	18.6 (± 10.1)	61.7 (± 36)	420 (± 432)	329 (± 191)
Day 1: 24-72 Hours Post-dose (n = 11, 12, 9, 17)	0.995 (± 0.946)	20.4 (± 13.2)	63.2 (± 59.7)	103 (± 47.3)
Week 24: Pre-dose (n = 55, 56, 49, 52)	0.00 (± 0.00)	0.0315 (± 0.134)	0.498 (± 1.88)	0.0645 (± 0.22)

Week 24: 1 Hour Post-dose (n = 52, 48, 48, 45)	12.4 (± 7.23)	73.6 (± 43.6)	204 (± 144)	253 (± 247)
Week 24: 3 Hours Post-dose (n = 53, 49, 46, 48)	16.3 (± 9.2)	96.3 (± 63.5)	278 (± 193)	332 (± 255)
Week 24: 6-12 Hours Post-dose (n = 8, 10, 7, 15)	17.2 (± 10.2)	76.3 (± 54.7)	271 (± 229)	315 (± 191)
Week 24: 24-72 Hours Post-dose (n = 7, 9, 8, 16)	1.27 (± 1.82)	17.3 (± 18.9)	99 (± 59.1)	96.3 (± 50.3)
Week 48 (n = 52, 50, 48, 51)	0.00 (± 0.00)	0.0599 (± 0.168)	0.533 (± 0.592)	0.127 (± 0.693)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Treatment Period: Median duration was 11.07 months. Extended Safety Follow-up Period: Median duration was 8.56 months.

Adverse event reporting additional description:

FAS: includes all randomized participants who received at least one dose of IP. For safety analysis FAS was used based on actual treatment received.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.1

Reporting groups

Reporting group title	Treatment Period: Olpasiran 225 mg Q12W

Reporting group description:

Group 3: Participants were administered SC olpasiran 225 mg Q12W for 48 weeks with doses at Day 1, Week 12, Week 24, and Week 36.

Reporting group title	Treatment Period: Olpasiran 75 mg Q12W

Reporting group description:

Group 2: Participants were administered SC olpasiran 75 mg Q12W for 48 weeks with doses at Day 1, Week 12, Week 24, and Week 36.

Reporting group title	Treatment Period: Olpasiran 10 mg Q12W

Reporting group description:

Group 1: Participants were administered SC olpasiran 10 mg Q12W for 48 weeks with doses at Day 1, Week 12, Week 24, and Week 36.

Reporting group title	Extended Safety Follow-up Period: Olpasiran 75 mg Q12W

Reporting group description:

Group 2: After Week 48 there was an Extended Safety Follow-up Period without further dosing with IP for a minimum of 24 weeks.

Reporting group title	Extended Safety Follow-up Period: Olpasiran 225 mg Q12W

Reporting group description:

Group 3: After Week 48 there was an Extended Safety Follow-up Period without further dosing with IP for a minimum of 24 weeks.

Reporting group title	Extended Safety Follow-up Period: Olpasiran 225 mg Q24W

Reporting group description:

Group 4: After Week 48 there was an Extended Safety Follow-up Period without further dosing with IP for a minimum of 24 weeks.

Reporting group title	Extended Safety Follow-up Period: Olpasiran 10 mg Q12W

Reporting group description:

Group 1: After Week 48 there was an Extended Safety Follow-up Period without further dosing with IP for a minimum of 24 weeks.

Reporting group title	Extended Safety Follow-up: Placebo Q12W

Reporting group description:

Group 5: After Week 48 there was an Extended Safety Follow-up Period without further dosing with IP for a minimum of 24 weeks.

Reporting group title	Treatment Period: Olpasiran 225 mg Q24W

Reporting group description:

Group 4: Participants were administered SC olpasiran 225 mg Q24W for 48 weeks with doses at Day 1 and Week 24.

Reporting group title	Treatment Period: Placebo Q12W

Reporting group description:

Group 5: Participants were administered SC placebo Q12W for 48 weeks with doses at Day 1, Week 12, Week 24, and Week 36.

Serious adverse events	Treatment Period: Olpasiran 225 mg Q12W	Treatment Period: Olpasiran 75 mg Q12W	Treatment Period: Olpasiran 10 mg Q12W
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 56 (10.71%)	3 / 58 (5.17%)	3 / 58 (5.17%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Gastrointestinal cancer metastatic			
subjects affected / exposed	0 / 56 (0.00%)	0 / 58 (0.00%)	0 / 58 (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
Breast cancer stage IV			
subjects affected / exposed	0 / 56 (0.00%)	0 / 58 (0.00%)	0 / 58 (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
Malignant melanoma stage I			
subjects affected / exposed	1 / 56 (1.79%)	0 / 58 (0.00%)	0 / 58 (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
Gastrointestinal carcinoma			
subjects affected / exposed	0 / 56 (0.00%)	0 / 58 (0.00%)	0 / 58 (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
Metastases to pancreas			
subjects affected / exposed	0 / 56 (0.00%)	0 / 58 (0.00%)	0 / 58 (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
Prostate cancer recurrent			
subjects affected / exposed	0 / 56 (0.00%)	0 / 58 (0.00%)	0 / 58 (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 / 56 (0.00%)	0 / 58 (0.00%)	0 / 58 (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
Hypertension			
subjects affected / exposed	0 / 56 (0.00%)	0 / 58 (0.00%)	0 / 58 (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
Iliac artery occlusion			
subjects affected / exposed	1 / 56 (1.79%)	0 / 58 (0.00%)	0 / 58 (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
General disorders and administration site conditions			
Injection site urticaria			
subjects affected / exposed	1 / 56 (1.79%)	0 / 58 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	1 / 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 / 56 (0.00%)	0 / 58 (0.00%)	0 / 58 (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
Injection site reaction			
subjects affected / exposed	1 / 56 (1.79%)	0 / 58 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Haemoptysis			
subjects affected / exposed	1 / 56 (1.79%)	0 / 58 (0.00%)	0 / 58 (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
Psychiatric disorders			
Depression			

subjects affected / exposed	0 / 56 (0.00%)	0 / 58 (0.00%)	0 / 58 (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
Product issues			
Device inappropriate shock delivery			
subjects affected / exposed	0 / 56 (0.00%)	0 / 58 (0.00%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 56 (0.00%)	0 / 58 (0.00%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rib fracture			
subjects affected / exposed	0 / 56 (0.00%)	1 / 58 (1.72%)	0 / 58 (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
Hip fracture			
subjects affected / exposed	0 / 56 (0.00%)	1 / 58 (1.72%)	0 / 58 (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
Femur fracture			
subjects affected / exposed	0 / 56 (0.00%)	0 / 58 (0.00%)	0 / 58 (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
Traumatic haematoma			
subjects affected / exposed	0 / 56 (0.00%)	0 / 58 (0.00%)	1 / 58 (1.72%)
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			
Atrial fibrillation			
subjects affected / exposed	0 / 56 (0.00%)	0 / 58 (0.00%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Angina pectoris			
subjects affected / exposed	0 / 56 (0.00%)	0 / 58 (0.00%)	0 / 58 (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
Angina unstable			
subjects affected / exposed	1 / 56 (1.79%)	0 / 58 (0.00%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bradycardia			
subjects affected / exposed	0 / 56 (0.00%)	0 / 58 (0.00%)	0 / 58 (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
Atrial flutter			
subjects affected / exposed	0 / 56 (0.00%)	0 / 58 (0.00%)	0 / 58 (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 / 56 (0.00%)	0 / 58 (0.00%)	0 / 58 (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
Ischaemic stroke			
subjects affected / exposed	0 / 56 (0.00%)	0 / 58 (0.00%)	0 / 58 (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
Syncope			
subjects affected / exposed	0 / 56 (0.00%)	0 / 58 (0.00%)	0 / 58 (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
Partial seizures			
subjects affected / exposed	0 / 56 (0.00%)	0 / 58 (0.00%)	0 / 58 (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
Seizure			

subjects affected / exposed	0 / 56 (0.00%)	0 / 58 (0.00%)	0 / 58 (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
Eye disorders			
Cataract			
subjects affected / exposed	0 / 56 (0.00%)	0 / 58 (0.00%)	0 / 58 (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 disorders			
Rectal haemorrhage			
subjects affected / exposed	0 / 56 (0.00%)	0 / 58 (0.00%)	0 / 58 (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
Diarrhoea			
subjects affected / exposed	1 / 56 (1.79%)	0 / 58 (0.00%)	0 / 58 (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
Colitis			
subjects affected / exposed	0 / 56 (0.00%)	0 / 58 (0.00%)	0 / 58 (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
Upper gastrointestinal haemorrhage			
subjects affected / exposed	0 / 56 (0.00%)	0 / 58 (0.00%)	0 / 58 (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			
Cholangitis			
subjects affected / exposed	0 / 56 (0.00%)	0 / 58 (0.00%)	0 / 58 (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			
Urticaria			

subjects affected / exposed	1 / 56 (1.79%)	0 / 58 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Urinoma			
subjects affected / exposed	0 / 56 (0.00%)	1 / 58 (1.72%)	0 / 58 (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
Ureterolithiasis			
subjects affected / exposed	0 / 56 (0.00%)	1 / 58 (1.72%)	0 / 58 (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
Musculoskeletal and connective tissue disorders			
Cervical spinal stenosis			
subjects affected / exposed	0 / 56 (0.00%)	0 / 58 (0.00%)	0 / 58 (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
Fistula			
subjects affected / exposed	0 / 56 (0.00%)	1 / 58 (1.72%)	0 / 58 (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
Osteoarthritis			
subjects affected / exposed	1 / 56 (1.79%)	0 / 58 (0.00%)	0 / 58 (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
Infections and infestations			
Cellulitis			
subjects affected / exposed	0 / 56 (0.00%)	0 / 58 (0.00%)	0 / 58 (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
Campylobacter infection			
subjects affected / exposed	0 / 56 (0.00%)	0 / 58 (0.00%)	0 / 58 (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 pneumonia			
subjects affected / exposed	0 / 56 (0.00%)	0 / 58 (0.00%)	0 / 58 (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
Abdominal abscess			
subjects affected / exposed	0 / 56 (0.00%)	1 / 58 (1.72%)	0 / 58 (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
Diverticulitis intestinal perforated			
subjects affected / exposed	0 / 56 (0.00%)	0 / 58 (0.00%)	0 / 58 (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
Influenza			
subjects affected / exposed	0 / 56 (0.00%)	0 / 58 (0.00%)	0 / 58 (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
Pneumonia			
subjects affected / exposed	0 / 56 (0.00%)	0 / 58 (0.00%)	0 / 58 (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
Diverticulitis			
subjects affected / exposed	0 / 56 (0.00%)	0 / 58 (0.00%)	0 / 58 (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
Urinary tract infection			
subjects affected / exposed	0 / 56 (0.00%)	0 / 58 (0.00%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vestibular neuronitis			
subjects affected / exposed	0 / 56 (0.00%)	0 / 58 (0.00%)	0 / 58 (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
Metabolism and nutrition disorders			

Obesity			
subjects affected / exposed	1 / 56 (1.79%)	0 / 58 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Extended Safety Follow-up Period: Olpasiran 75 mg Q12W	Extended Safety Follow-up Period: Olpasiran 225 mg Q12W	Extended Safety Follow-up Period: Olpasiran 225 mg Q24W
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 57 (3.51%)	6 / 54 (11.11%)	5 / 55 (9.09%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Gastrointestinal cancer metastatic			
subjects affected / exposed	0 / 57 (0.00%)	0 / 54 (0.00%)	0 / 55 (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
Breast cancer stage IV			
subjects affected / exposed	0 / 57 (0.00%)	0 / 54 (0.00%)	0 / 55 (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
Malignant melanoma stage I			
subjects affected / exposed	0 / 57 (0.00%)	0 / 54 (0.00%)	0 / 55 (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 carcinoma			
subjects affected / exposed	0 / 57 (0.00%)	0 / 54 (0.00%)	0 / 55 (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
Metastases to pancreas			
subjects affected / exposed	0 / 57 (0.00%)	0 / 54 (0.00%)	0 / 55 (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
Prostate cancer recurrent			

subjects affected / exposed	0 / 57 (0.00%)	0 / 54 (0.00%)	0 / 55 (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 / 57 (0.00%)	0 / 54 (0.00%)	0 / 55 (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
Hypertension			
subjects affected / exposed	0 / 57 (0.00%)	1 / 54 (1.85%)	0 / 55 (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
Iliac artery occlusion			
subjects affected / exposed	0 / 57 (0.00%)	0 / 54 (0.00%)	0 / 55 (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			
Injection site urticaria			
subjects affected / exposed	0 / 57 (0.00%)	0 / 54 (0.00%)	0 / 55 (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
Non-cardiac chest pain			
subjects affected / exposed	0 / 57 (0.00%)	0 / 54 (0.00%)	0 / 55 (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
Injection site reaction			
subjects affected / exposed	0 / 57 (0.00%)	0 / 54 (0.00%)	0 / 55 (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
Respiratory, thoracic and mediastinal disorders			
Haemoptysis			

subjects affected / exposed	0 / 57 (0.00%)	0 / 54 (0.00%)	0 / 55 (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
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 57 (0.00%)	1 / 54 (1.85%)	0 / 55 (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
Product issues			
Device inappropriate shock delivery			
subjects affected / exposed	0 / 57 (0.00%)	0 / 54 (0.00%)	0 / 55 (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			
Fall			
subjects affected / exposed	0 / 57 (0.00%)	0 / 54 (0.00%)	0 / 55 (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
Rib fracture			
subjects affected / exposed	0 / 57 (0.00%)	0 / 54 (0.00%)	0 / 55 (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
Hip fracture			
subjects affected / exposed	0 / 57 (0.00%)	0 / 54 (0.00%)	0 / 55 (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
Femur fracture			
subjects affected / exposed	1 / 57 (1.75%)	0 / 54 (0.00%)	0 / 55 (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
Traumatic haematoma			
subjects affected / exposed	0 / 57 (0.00%)	0 / 54 (0.00%)	0 / 55 (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

Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 57 (0.00%)	0 / 54 (0.00%)	1 / 55 (1.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina pectoris			
subjects affected / exposed	0 / 57 (0.00%)	0 / 54 (0.00%)	0 / 55 (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
Angina unstable			
subjects affected / exposed	0 / 57 (0.00%)	0 / 54 (0.00%)	0 / 55 (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
Bradycardia			
subjects affected / exposed	0 / 57 (0.00%)	0 / 54 (0.00%)	1 / 55 (1.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial flutter			
subjects affected / exposed	0 / 57 (0.00%)	0 / 54 (0.00%)	1 / 55 (1.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	0 / 57 (0.00%)	0 / 54 (0.00%)	0 / 55 (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
Ischaemic stroke			
subjects affected / exposed	0 / 57 (0.00%)	0 / 54 (0.00%)	0 / 55 (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
Syncope			
subjects affected / exposed	0 / 57 (0.00%)	0 / 54 (0.00%)	0 / 55 (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

Partial seizures			
subjects affected / exposed	0 / 57 (0.00%)	0 / 54 (0.00%)	0 / 55 (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
Seizure			
subjects affected / exposed	0 / 57 (0.00%)	0 / 54 (0.00%)	0 / 55 (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
Eye disorders			
Cataract			
subjects affected / exposed	0 / 57 (0.00%)	0 / 54 (0.00%)	0 / 55 (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 disorders			
Rectal haemorrhage			
subjects affected / exposed	0 / 57 (0.00%)	1 / 54 (1.85%)	0 / 55 (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
Diarrhoea			
subjects affected / exposed	0 / 57 (0.00%)	0 / 54 (0.00%)	0 / 55 (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
Colitis			
subjects affected / exposed	0 / 57 (0.00%)	0 / 54 (0.00%)	1 / 55 (1.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper gastrointestinal haemorrhage			
subjects affected / exposed	0 / 57 (0.00%)	0 / 54 (0.00%)	0 / 55 (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			
Cholangitis			

subjects affected / exposed	0 / 57 (0.00%)	0 / 54 (0.00%)	0 / 55 (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			
Urticaria			
subjects affected / exposed	0 / 57 (0.00%)	0 / 54 (0.00%)	0 / 55 (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			
Urinoma			
subjects affected / exposed	0 / 57 (0.00%)	0 / 54 (0.00%)	0 / 55 (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
Ureterolithiasis			
subjects affected / exposed	0 / 57 (0.00%)	0 / 54 (0.00%)	0 / 55 (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
Musculoskeletal and connective tissue disorders			
Cervical spinal stenosis			
subjects affected / exposed	0 / 57 (0.00%)	0 / 54 (0.00%)	0 / 55 (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
Fistula			
subjects affected / exposed	0 / 57 (0.00%)	0 / 54 (0.00%)	0 / 55 (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
Osteoarthritis			
subjects affected / exposed	0 / 57 (0.00%)	2 / 54 (3.70%)	0 / 55 (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
Infections and infestations			
Cellulitis			

subjects affected / exposed	1 / 57 (1.75%)	0 / 54 (0.00%)	0 / 55 (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
Campylobacter infection			
subjects affected / exposed	0 / 57 (0.00%)	0 / 54 (0.00%)	0 / 55 (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 pneumonia			
subjects affected / exposed	0 / 57 (0.00%)	0 / 54 (0.00%)	1 / 55 (1.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal abscess			
subjects affected / exposed	0 / 57 (0.00%)	0 / 54 (0.00%)	0 / 55 (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
Diverticulitis intestinal perforated			
subjects affected / exposed	0 / 57 (0.00%)	0 / 54 (0.00%)	1 / 55 (1.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			
subjects affected / exposed	0 / 57 (0.00%)	1 / 54 (1.85%)	0 / 55 (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
Pneumonia			
subjects affected / exposed	0 / 57 (0.00%)	0 / 54 (0.00%)	0 / 55 (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
Diverticulitis			
subjects affected / exposed	0 / 57 (0.00%)	0 / 54 (0.00%)	0 / 55 (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
Urinary tract infection			

subjects affected / exposed	0 / 57 (0.00%)	0 / 54 (0.00%)	0 / 55 (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
Vestibular neuronitis			
subjects affected / exposed	0 / 57 (0.00%)	0 / 54 (0.00%)	1 / 55 (1.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Obesity			
subjects affected / exposed	0 / 57 (0.00%)	0 / 54 (0.00%)	0 / 55 (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	Extended Safety Follow-up Period: Olpasiran 10 mg Q12W	Extended Safety Follow-up: Placebo Q12W	Treatment Period: Olpasiran 225 mg Q24W
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 57 (7.02%)	4 / 53 (7.55%)	4 / 55 (7.27%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Gastrointestinal cancer metastatic			
subjects affected / exposed	0 / 57 (0.00%)	1 / 53 (1.89%)	0 / 55 (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
Breast cancer stage IV			
subjects affected / exposed	0 / 57 (0.00%)	0 / 53 (0.00%)	0 / 55 (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
Malignant melanoma stage I			
subjects affected / exposed	0 / 57 (0.00%)	0 / 53 (0.00%)	0 / 55 (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 carcinoma			

subjects affected / exposed	0 / 57 (0.00%)	0 / 53 (0.00%)	0 / 55 (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
Metastases to pancreas			
subjects affected / exposed	0 / 57 (0.00%)	1 / 53 (1.89%)	0 / 55 (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
Prostate cancer recurrent			
subjects affected / exposed	0 / 57 (0.00%)	0 / 53 (0.00%)	0 / 55 (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 / 57 (0.00%)	0 / 53 (0.00%)	0 / 55 (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
Hypertension			
subjects affected / exposed	0 / 57 (0.00%)	0 / 53 (0.00%)	0 / 55 (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
Iliac artery occlusion			
subjects affected / exposed	0 / 57 (0.00%)	0 / 53 (0.00%)	0 / 55 (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			
Injection site urticaria			
subjects affected / exposed	0 / 57 (0.00%)	0 / 53 (0.00%)	0 / 55 (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
Non-cardiac chest pain			
subjects affected / exposed	0 / 57 (0.00%)	0 / 53 (0.00%)	0 / 55 (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

Injection site reaction			
subjects affected / exposed	0 / 57 (0.00%)	0 / 53 (0.00%)	1 / 55 (1.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Haemoptysis			
subjects affected / exposed	0 / 57 (0.00%)	0 / 53 (0.00%)	0 / 55 (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
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 57 (0.00%)	0 / 53 (0.00%)	0 / 55 (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
Product issues			
Device inappropriate shock delivery			
subjects affected / exposed	0 / 57 (0.00%)	0 / 53 (0.00%)	0 / 55 (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			
Fall			
subjects affected / exposed	0 / 57 (0.00%)	0 / 53 (0.00%)	0 / 55 (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
Rib fracture			
subjects affected / exposed	0 / 57 (0.00%)	0 / 53 (0.00%)	0 / 55 (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
Hip fracture			
subjects affected / exposed	0 / 57 (0.00%)	0 / 53 (0.00%)	0 / 55 (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
Femur fracture			

subjects affected / exposed	0 / 57 (0.00%)	0 / 53 (0.00%)	0 / 55 (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
Traumatic haematoma			
subjects affected / exposed	0 / 57 (0.00%)	0 / 53 (0.00%)	0 / 55 (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
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 57 (0.00%)	0 / 53 (0.00%)	1 / 55 (1.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina pectoris			
subjects affected / exposed	1 / 57 (1.75%)	0 / 53 (0.00%)	0 / 55 (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
Angina unstable			
subjects affected / exposed	0 / 57 (0.00%)	0 / 53 (0.00%)	0 / 55 (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
Bradycardia			
subjects affected / exposed	0 / 57 (0.00%)	0 / 53 (0.00%)	0 / 55 (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
Atrial flutter			
subjects affected / exposed	0 / 57 (0.00%)	0 / 53 (0.00%)	0 / 55 (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 / 57 (0.00%)	0 / 53 (0.00%)	0 / 55 (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
Ischaemic stroke			

subjects affected / exposed	0 / 57 (0.00%)	1 / 53 (1.89%)	0 / 55 (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
Syncope			
subjects affected / exposed	0 / 57 (0.00%)	0 / 53 (0.00%)	1 / 55 (1.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Partial seizures			
subjects affected / exposed	1 / 57 (1.75%)	0 / 53 (0.00%)	0 / 55 (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
Seizure			
subjects affected / exposed	0 / 57 (0.00%)	0 / 53 (0.00%)	1 / 55 (1.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Cataract			
subjects affected / exposed	1 / 57 (1.75%)	0 / 53 (0.00%)	0 / 55 (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
Gastrointestinal disorders			
Rectal haemorrhage			
subjects affected / exposed	0 / 57 (0.00%)	0 / 53 (0.00%)	0 / 55 (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
Diarrhoea			
subjects affected / exposed	0 / 57 (0.00%)	0 / 53 (0.00%)	0 / 55 (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
Colitis			
subjects affected / exposed	0 / 57 (0.00%)	0 / 53 (0.00%)	0 / 55 (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
Upper gastrointestinal haemorrhage			

subjects affected / exposed	1 / 57 (1.75%)	0 / 53 (0.00%)	0 / 55 (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
Hepatobiliary disorders			
Cholangitis			
subjects affected / exposed	0 / 57 (0.00%)	1 / 53 (1.89%)	0 / 55 (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
Skin and subcutaneous tissue disorders			
Urticaria			
subjects affected / exposed	0 / 57 (0.00%)	0 / 53 (0.00%)	1 / 55 (1.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Urinoma			
subjects affected / exposed	0 / 57 (0.00%)	0 / 53 (0.00%)	0 / 55 (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
Ureterolithiasis			
subjects affected / exposed	0 / 57 (0.00%)	0 / 53 (0.00%)	0 / 55 (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
Musculoskeletal and connective tissue disorders			
Cervical spinal stenosis			
subjects affected / exposed	0 / 57 (0.00%)	1 / 53 (1.89%)	0 / 55 (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
Fistula			
subjects affected / exposed	0 / 57 (0.00%)	0 / 53 (0.00%)	0 / 55 (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
Osteoarthritis			

subjects affected / exposed	0 / 57 (0.00%)	0 / 53 (0.00%)	0 / 55 (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
Infections and infestations			
Cellulitis			
subjects affected / exposed	0 / 57 (0.00%)	0 / 53 (0.00%)	0 / 55 (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
Campylobacter infection			
subjects affected / exposed	0 / 57 (0.00%)	0 / 53 (0.00%)	1 / 55 (1.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19 pneumonia			
subjects affected / exposed	0 / 57 (0.00%)	0 / 53 (0.00%)	0 / 55 (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
Abdominal abscess			
subjects affected / exposed	0 / 57 (0.00%)	0 / 53 (0.00%)	0 / 55 (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
Diverticulitis intestinal perforated			
subjects affected / exposed	0 / 57 (0.00%)	0 / 53 (0.00%)	0 / 55 (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
Influenza			
subjects affected / exposed	0 / 57 (0.00%)	0 / 53 (0.00%)	0 / 55 (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
Pneumonia			
subjects affected / exposed	0 / 57 (0.00%)	0 / 53 (0.00%)	0 / 55 (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
Diverticulitis			

subjects affected / exposed	0 / 57 (0.00%)	0 / 53 (0.00%)	1 / 55 (1.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 57 (0.00%)	0 / 53 (0.00%)	0 / 55 (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
Vestibular neuronitis			
subjects affected / exposed	0 / 57 (0.00%)	0 / 53 (0.00%)	0 / 55 (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
Metabolism and nutrition disorders			
Obesity			
subjects affected / exposed	0 / 57 (0.00%)	0 / 53 (0.00%)	0 / 55 (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	Treatment Period: Placebo Q12W		
Total subjects affected by serious adverse events			
subjects affected / exposed	8 / 54 (14.81%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Gastrointestinal cancer metastatic			
subjects affected / exposed	0 / 54 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Breast cancer stage IV			
subjects affected / exposed	1 / 54 (1.85%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Malignant melanoma stage I			

subjects affected / exposed	0 / 54 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal carcinoma			
subjects affected / exposed	1 / 54 (1.85%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metastases to pancreas			
subjects affected / exposed	0 / 54 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Prostate cancer recurrent			
subjects affected / exposed	1 / 54 (1.85%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Aortic stenosis			
subjects affected / exposed	1 / 54 (1.85%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypertension			
subjects affected / exposed	0 / 54 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Iliac artery occlusion			
subjects affected / exposed	0 / 54 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Injection site urticaria			
subjects affected / exposed	0 / 54 (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	1 / 54 (1.85%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injection site reaction			
subjects affected / exposed	0 / 54 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Haemoptysis			
subjects affected / exposed	0 / 54 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 54 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Product issues			
Device inappropriate shock delivery			
subjects affected / exposed	0 / 54 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 54 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Rib fracture			
subjects affected / exposed	0 / 54 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hip fracture			

subjects affected / exposed	0 / 54 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Femur fracture			
subjects affected / exposed	0 / 54 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Traumatic haematoma			
subjects affected / exposed	0 / 54 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 54 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Angina pectoris			
subjects affected / exposed	1 / 54 (1.85%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Angina unstable			
subjects affected / exposed	1 / 54 (1.85%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Bradycardia			
subjects affected / exposed	0 / 54 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Atrial flutter			
subjects affected / exposed	0 / 54 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			

Cerebrovascular accident				
subjects affected / exposed	1 / 54 (1.85%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Ischaemic stroke				
subjects affected / exposed	0 / 54 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Syncope				
subjects affected / exposed	0 / 54 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Partial seizures				
subjects affected / exposed	0 / 54 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Seizure				
subjects affected / exposed	0 / 54 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Eye disorders				
Cataract				
subjects affected / exposed	0 / 54 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
Rectal haemorrhage				
subjects affected / exposed	0 / 54 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Diarrhoea				
subjects affected / exposed	0 / 54 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Colitis			
subjects affected / exposed	0 / 54 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Upper gastrointestinal haemorrhage			
subjects affected / exposed	0 / 54 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Cholangitis			
subjects affected / exposed	0 / 54 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Urticaria			
subjects affected / exposed	0 / 54 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Urinoma			
subjects affected / exposed	0 / 54 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ureterolithiasis			
subjects affected / exposed	0 / 54 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Cervical spinal stenosis			
subjects affected / exposed	0 / 54 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Fistula			

subjects affected / exposed	0 / 54 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Osteoarthritis				
subjects affected / exposed	0 / 54 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Cellulitis				
subjects affected / exposed	0 / 54 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Campylobacter infection				
subjects affected / exposed	0 / 54 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
COVID-19 pneumonia				
subjects affected / exposed	0 / 54 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Abdominal abscess				
subjects affected / exposed	0 / 54 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Diverticulitis intestinal perforated				
subjects affected / exposed	0 / 54 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Influenza				
subjects affected / exposed	0 / 54 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia				

subjects affected / exposed	1 / 54 (1.85%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 1		
Diverticulitis			
subjects affected / exposed	0 / 54 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection			
subjects affected / exposed	0 / 54 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vestibular neuronitis			
subjects affected / exposed	0 / 54 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Obesity			
subjects affected / exposed	0 / 54 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Treatment Period: Olpasiran 225 mg Q12W	Treatment Period: Olpasiran 75 mg Q12W	Treatment Period: Olpasiran 10 mg Q12W
Total subjects affected by non-serious adverse events			
subjects affected / exposed	37 / 56 (66.07%)	40 / 58 (68.97%)	35 / 58 (60.34%)
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	1 / 56 (1.79%)	1 / 58 (1.72%)	0 / 58 (0.00%)
occurrences (all)	1	1	0
Fall			
subjects affected / exposed	1 / 56 (1.79%)	3 / 58 (5.17%)	2 / 58 (3.45%)
occurrences (all)	1	3	2
Vascular disorders			

Hypertension			
subjects affected / exposed	3 / 56 (5.36%)	2 / 58 (3.45%)	4 / 58 (6.90%)
occurrences (all)	3	3	4
Nervous system disorders			
Headache			
subjects affected / exposed	6 / 56 (10.71%)	7 / 58 (12.07%)	6 / 58 (10.34%)
occurrences (all)	7	9	9
Areflexia			
subjects affected / exposed	0 / 56 (0.00%)	3 / 58 (5.17%)	0 / 58 (0.00%)
occurrences (all)	0	5	0
Dizziness			
subjects affected / exposed	2 / 56 (3.57%)	3 / 58 (5.17%)	0 / 58 (0.00%)
occurrences (all)	2	3	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 56 (0.00%)	1 / 58 (1.72%)	3 / 58 (5.17%)
occurrences (all)	0	1	3
General disorders and administration site conditions			
Injection site erythema			
subjects affected / exposed	3 / 56 (5.36%)	3 / 58 (5.17%)	0 / 58 (0.00%)
occurrences (all)	5	3	0
Injection site bruising			
subjects affected / exposed	5 / 56 (8.93%)	4 / 58 (6.90%)	0 / 58 (0.00%)
occurrences (all)	6	5	0
Fatigue			
subjects affected / exposed	3 / 56 (5.36%)	8 / 58 (13.79%)	6 / 58 (10.34%)
occurrences (all)	3	11	8
Oedema peripheral			
subjects affected / exposed	1 / 56 (1.79%)	1 / 58 (1.72%)	2 / 58 (3.45%)
occurrences (all)	1	1	3
Non-cardiac chest pain			
subjects affected / exposed	1 / 56 (1.79%)	2 / 58 (3.45%)	2 / 58 (3.45%)
occurrences (all)	1	2	2
Injection site pruritus			
subjects affected / exposed	0 / 56 (0.00%)	0 / 58 (0.00%)	1 / 58 (1.72%)
occurrences (all)	0	0	1

Injection site pain			
subjects affected / exposed	1 / 56 (1.79%)	3 / 58 (5.17%)	2 / 58 (3.45%)
occurrences (all)	2	4	2
Immune system disorders			
Immunisation reaction			
subjects affected / exposed	2 / 56 (3.57%)	4 / 58 (6.90%)	8 / 58 (13.79%)
occurrences (all)	3	6	11
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	3 / 56 (5.36%)	0 / 58 (0.00%)	0 / 58 (0.00%)
occurrences (all)	3	0	0
Diarrhoea			
subjects affected / exposed	3 / 56 (5.36%)	3 / 58 (5.17%)	2 / 58 (3.45%)
occurrences (all)	3	3	2
Constipation			
subjects affected / exposed	1 / 56 (1.79%)	0 / 58 (0.00%)	3 / 58 (5.17%)
occurrences (all)	2	0	3
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 56 (1.79%)	1 / 58 (1.72%)	1 / 58 (1.72%)
occurrences (all)	1	1	1
Nausea			
subjects affected / exposed	2 / 56 (3.57%)	1 / 58 (1.72%)	2 / 58 (3.45%)
occurrences (all)	2	1	2
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 56 (0.00%)	1 / 58 (1.72%)	3 / 58 (5.17%)
occurrences (all)	0	1	3
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	3 / 56 (5.36%)	3 / 58 (5.17%)	2 / 58 (3.45%)
occurrences (all)	3	4	2
Back pain			
subjects affected / exposed	7 / 56 (12.50%)	5 / 58 (8.62%)	6 / 58 (10.34%)
occurrences (all)	7	5	6
Myalgia			

subjects affected / exposed	4 / 56 (7.14%)	1 / 58 (1.72%)	3 / 58 (5.17%)
occurrences (all)	4	1	4
Pain in extremity			
subjects affected / exposed	0 / 56 (0.00%)	1 / 58 (1.72%)	2 / 58 (3.45%)
occurrences (all)	0	1	2
Infections and infestations			
COVID-19			
subjects affected / exposed	7 / 56 (12.50%)	8 / 58 (13.79%)	1 / 58 (1.72%)
occurrences (all)	7	9	1
Gastroenteritis			
subjects affected / exposed	0 / 56 (0.00%)	4 / 58 (6.90%)	1 / 58 (1.72%)
occurrences (all)	0	4	2
Nasopharyngitis			
subjects affected / exposed	4 / 56 (7.14%)	2 / 58 (3.45%)	2 / 58 (3.45%)
occurrences (all)	4	2	2
Sinusitis			
subjects affected / exposed	0 / 56 (0.00%)	3 / 58 (5.17%)	0 / 58 (0.00%)
occurrences (all)	0	4	0
Upper respiratory tract infection			
subjects affected / exposed	2 / 56 (3.57%)	3 / 58 (5.17%)	4 / 58 (6.90%)
occurrences (all)	2	3	4
Urinary tract infection			
subjects affected / exposed	2 / 56 (3.57%)	4 / 58 (6.90%)	3 / 58 (5.17%)
occurrences (all)	2	4	3
Metabolism and nutrition disorders			
Type 2 diabetes mellitus			
subjects affected / exposed	1 / 56 (1.79%)	3 / 58 (5.17%)	3 / 58 (5.17%)
occurrences (all)	1	3	3

Non-serious adverse events	Extended Safety Follow-up Period: Olpasiran 75 mg Q12W	Extended Safety Follow-up Period: Olpasiran 225 mg Q12W	Extended Safety Follow-up Period: Olpasiran 225 mg Q24W
Total subjects affected by non-serious adverse events			
subjects affected / exposed	25 / 57 (43.86%)	21 / 54 (38.89%)	17 / 55 (30.91%)
Injury, poisoning and procedural complications			
Contusion			

subjects affected / exposed	2 / 57 (3.51%)	0 / 54 (0.00%)	0 / 55 (0.00%)
occurrences (all)	3	0	0
Fall			
subjects affected / exposed	1 / 57 (1.75%)	0 / 54 (0.00%)	2 / 55 (3.64%)
occurrences (all)	1	0	2
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 57 (1.75%)	0 / 54 (0.00%)	0 / 55 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 57 (1.75%)	2 / 54 (3.70%)	1 / 55 (1.82%)
occurrences (all)	1	2	1
Areflexia			
subjects affected / exposed	0 / 57 (0.00%)	1 / 54 (1.85%)	0 / 55 (0.00%)
occurrences (all)	0	1	0
Dizziness			
subjects affected / exposed	0 / 57 (0.00%)	0 / 54 (0.00%)	1 / 55 (1.82%)
occurrences (all)	0	0	1
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 57 (3.51%)	1 / 54 (1.85%)	0 / 55 (0.00%)
occurrences (all)	2	1	0
General disorders and administration site conditions			
Injection site erythema			
subjects affected / exposed	0 / 57 (0.00%)	0 / 54 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
Injection site bruising			
subjects affected / exposed	0 / 57 (0.00%)	0 / 54 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	1 / 57 (1.75%)	0 / 54 (0.00%)	0 / 55 (0.00%)
occurrences (all)	1	0	0
Oedema peripheral			
subjects affected / exposed	1 / 57 (1.75%)	2 / 54 (3.70%)	0 / 55 (0.00%)
occurrences (all)	1	2	0

Non-cardiac chest pain			
subjects affected / exposed	0 / 57 (0.00%)	0 / 54 (0.00%)	1 / 55 (1.82%)
occurrences (all)	0	0	1
Injection site pruritus			
subjects affected / exposed	0 / 57 (0.00%)	0 / 54 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
Injection site pain			
subjects affected / exposed	0 / 57 (0.00%)	0 / 54 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Immunisation reaction			
subjects affected / exposed	0 / 57 (0.00%)	2 / 54 (3.70%)	0 / 55 (0.00%)
occurrences (all)	0	3	0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 57 (1.75%)	0 / 54 (0.00%)	1 / 55 (1.82%)
occurrences (all)	1	0	1
Diarrhoea			
subjects affected / exposed	0 / 57 (0.00%)	0 / 54 (0.00%)	1 / 55 (1.82%)
occurrences (all)	0	0	1
Constipation			
subjects affected / exposed	0 / 57 (0.00%)	0 / 54 (0.00%)	1 / 55 (1.82%)
occurrences (all)	0	0	1
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 57 (0.00%)	1 / 54 (1.85%)	0 / 55 (0.00%)
occurrences (all)	0	1	0
Nausea			
subjects affected / exposed	0 / 57 (0.00%)	0 / 54 (0.00%)	2 / 55 (3.64%)
occurrences (all)	0	0	3
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 57 (1.75%)	0 / 54 (0.00%)	0 / 55 (0.00%)
occurrences (all)	2	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			

subjects affected / exposed	1 / 57 (1.75%)	1 / 54 (1.85%)	1 / 55 (1.82%)
occurrences (all)	1	1	1
Back pain			
subjects affected / exposed	1 / 57 (1.75%)	1 / 54 (1.85%)	1 / 55 (1.82%)
occurrences (all)	1	1	1
Myalgia			
subjects affected / exposed	0 / 57 (0.00%)	0 / 54 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	1 / 57 (1.75%)	0 / 54 (0.00%)	0 / 55 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
COVID-19			
subjects affected / exposed	11 / 57 (19.30%)	14 / 54 (25.93%)	10 / 55 (18.18%)
occurrences (all)	12	14	10
Gastroenteritis			
subjects affected / exposed	0 / 57 (0.00%)	1 / 54 (1.85%)	0 / 55 (0.00%)
occurrences (all)	0	1	0
Nasopharyngitis			
subjects affected / exposed	1 / 57 (1.75%)	0 / 54 (0.00%)	2 / 55 (3.64%)
occurrences (all)	1	0	2
Sinusitis			
subjects affected / exposed	1 / 57 (1.75%)	0 / 54 (0.00%)	0 / 55 (0.00%)
occurrences (all)	1	0	0
Upper respiratory tract infection			
subjects affected / exposed	2 / 57 (3.51%)	0 / 54 (0.00%)	1 / 55 (1.82%)
occurrences (all)	2	0	1
Urinary tract infection			
subjects affected / exposed	4 / 57 (7.02%)	1 / 54 (1.85%)	0 / 55 (0.00%)
occurrences (all)	5	1	0
Metabolism and nutrition disorders			
Type 2 diabetes mellitus			
subjects affected / exposed	1 / 57 (1.75%)	0 / 54 (0.00%)	0 / 55 (0.00%)
occurrences (all)	1	0	0

Non-serious adverse events	Extended Safety Follow-up Period: Olpasiran 10 mg	Extended Safety Follow-up: Placebo Q12W	Treatment Period: Olpasiran 225 mg Q24W

	Q12W		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	18 / 57 (31.58%)	17 / 53 (32.08%)	36 / 55 (65.45%)
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	1 / 57 (1.75%)	0 / 53 (0.00%)	0 / 55 (0.00%)
occurrences (all)	1	0	0
Fall			
subjects affected / exposed	0 / 57 (0.00%)	0 / 53 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 57 (0.00%)	1 / 53 (1.89%)	2 / 55 (3.64%)
occurrences (all)	0	1	2
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 57 (0.00%)	0 / 53 (0.00%)	6 / 55 (10.91%)
occurrences (all)	0	0	8
Areflexia			
subjects affected / exposed	0 / 57 (0.00%)	0 / 53 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
Dizziness			
subjects affected / exposed	0 / 57 (0.00%)	1 / 53 (1.89%)	1 / 55 (1.82%)
occurrences (all)	0	1	1
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 57 (1.75%)	1 / 53 (1.89%)	1 / 55 (1.82%)
occurrences (all)	1	1	1
General disorders and administration site conditions			
Injection site erythema			
subjects affected / exposed	0 / 57 (0.00%)	0 / 53 (0.00%)	4 / 55 (7.27%)
occurrences (all)	0	0	4
Injection site bruising			
subjects affected / exposed	0 / 57 (0.00%)	0 / 53 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
Fatigue			

subjects affected / exposed	2 / 57 (3.51%)	1 / 53 (1.89%)	2 / 55 (3.64%)
occurrences (all)	2	1	4
Oedema peripheral			
subjects affected / exposed	0 / 57 (0.00%)	0 / 53 (0.00%)	3 / 55 (5.45%)
occurrences (all)	0	0	3
Non-cardiac chest pain			
subjects affected / exposed	2 / 57 (3.51%)	0 / 53 (0.00%)	4 / 55 (7.27%)
occurrences (all)	2	0	4
Injection site pruritus			
subjects affected / exposed	0 / 57 (0.00%)	0 / 53 (0.00%)	3 / 55 (5.45%)
occurrences (all)	0	0	4
Injection site pain			
subjects affected / exposed	0 / 57 (0.00%)	0 / 53 (0.00%)	5 / 55 (9.09%)
occurrences (all)	0	0	6
Immune system disorders			
Immunisation reaction			
subjects affected / exposed	0 / 57 (0.00%)	0 / 53 (0.00%)	4 / 55 (7.27%)
occurrences (all)	0	0	8
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 57 (1.75%)	0 / 53 (0.00%)	2 / 55 (3.64%)
occurrences (all)	1	0	2
Diarrhoea			
subjects affected / exposed	0 / 57 (0.00%)	0 / 53 (0.00%)	1 / 55 (1.82%)
occurrences (all)	0	0	1
Constipation			
subjects affected / exposed	0 / 57 (0.00%)	0 / 53 (0.00%)	2 / 55 (3.64%)
occurrences (all)	0	0	2
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 57 (0.00%)	3 / 53 (5.66%)	0 / 55 (0.00%)
occurrences (all)	0	3	0
Nausea			
subjects affected / exposed	0 / 57 (0.00%)	1 / 53 (1.89%)	3 / 55 (5.45%)
occurrences (all)	0	1	3
Respiratory, thoracic and mediastinal disorders			

Cough			
subjects affected / exposed	0 / 57 (0.00%)	3 / 53 (5.66%)	0 / 55 (0.00%)
occurrences (all)	0	3	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 57 (0.00%)	1 / 53 (1.89%)	2 / 55 (3.64%)
occurrences (all)	0	1	3
Back pain			
subjects affected / exposed	3 / 57 (5.26%)	0 / 53 (0.00%)	1 / 55 (1.82%)
occurrences (all)	3	0	1
Myalgia			
subjects affected / exposed	2 / 57 (3.51%)	0 / 53 (0.00%)	4 / 55 (7.27%)
occurrences (all)	2	0	4
Pain in extremity			
subjects affected / exposed	1 / 57 (1.75%)	0 / 53 (0.00%)	3 / 55 (5.45%)
occurrences (all)	1	0	3
Infections and infestations			
COVID-19			
subjects affected / exposed	8 / 57 (14.04%)	10 / 53 (18.87%)	4 / 55 (7.27%)
occurrences (all)	8	10	4
Gastroenteritis			
subjects affected / exposed	0 / 57 (0.00%)	1 / 53 (1.89%)	2 / 55 (3.64%)
occurrences (all)	0	1	2
Nasopharyngitis			
subjects affected / exposed	3 / 57 (5.26%)	0 / 53 (0.00%)	1 / 55 (1.82%)
occurrences (all)	3	0	1
Sinusitis			
subjects affected / exposed	0 / 57 (0.00%)	0 / 53 (0.00%)	2 / 55 (3.64%)
occurrences (all)	0	0	2
Upper respiratory tract infection			
subjects affected / exposed	2 / 57 (3.51%)	1 / 53 (1.89%)	1 / 55 (1.82%)
occurrences (all)	4	1	1
Urinary tract infection			
subjects affected / exposed	0 / 57 (0.00%)	0 / 53 (0.00%)	1 / 55 (1.82%)
occurrences (all)	0	0	1
Metabolism and nutrition disorders			

Type 2 diabetes mellitus			
subjects affected / exposed	1 / 57 (1.75%)	0 / 53 (0.00%)	2 / 55 (3.64%)
occurrences (all)	1	0	2

Non-serious adverse events	Treatment Period: Placebo Q12W		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	29 / 54 (53.70%)		
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	3 / 54 (5.56%)		
occurrences (all)	4		
Fall			
subjects affected / exposed	1 / 54 (1.85%)		
occurrences (all)	1		
Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 54 (3.70%)		
occurrences (all)	2		
Nervous system disorders			
Headache			
subjects affected / exposed	4 / 54 (7.41%)		
occurrences (all)	6		
Areflexia			
subjects affected / exposed	0 / 54 (0.00%)		
occurrences (all)	0		
Dizziness			
subjects affected / exposed	2 / 54 (3.70%)		
occurrences (all)	3		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 54 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Injection site erythema			
subjects affected / exposed	0 / 54 (0.00%)		
occurrences (all)	0		
Injection site bruising			

subjects affected / exposed	4 / 54 (7.41%)		
occurrences (all)	6		
Fatigue			
subjects affected / exposed	3 / 54 (5.56%)		
occurrences (all)	4		
Oedema peripheral			
subjects affected / exposed	0 / 54 (0.00%)		
occurrences (all)	0		
Non-cardiac chest pain			
subjects affected / exposed	1 / 54 (1.85%)		
occurrences (all)	1		
Injection site pruritus			
subjects affected / exposed	0 / 54 (0.00%)		
occurrences (all)	0		
Injection site pain			
subjects affected / exposed	2 / 54 (3.70%)		
occurrences (all)	2		
Immune system disorders			
Immunisation reaction			
subjects affected / exposed	5 / 54 (9.26%)		
occurrences (all)	6		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	2 / 54 (3.70%)		
occurrences (all)	2		
Diarrhoea			
subjects affected / exposed	4 / 54 (7.41%)		
occurrences (all)	4		
Constipation			
subjects affected / exposed	2 / 54 (3.70%)		
occurrences (all)	2		
Gastrooesophageal reflux disease			
subjects affected / exposed	2 / 54 (3.70%)		
occurrences (all)	2		
Nausea			

subjects affected / exposed	1 / 54 (1.85%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 54 (1.85%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 54 (1.85%)		
occurrences (all)	1		
Back pain			
subjects affected / exposed	3 / 54 (5.56%)		
occurrences (all)	3		
Myalgia			
subjects affected / exposed	4 / 54 (7.41%)		
occurrences (all)	6		
Pain in extremity			
subjects affected / exposed	1 / 54 (1.85%)		
occurrences (all)	1		
Infections and infestations			
COVID-19			
subjects affected / exposed	6 / 54 (11.11%)		
occurrences (all)	6		
Gastroenteritis			
subjects affected / exposed	1 / 54 (1.85%)		
occurrences (all)	1		
Nasopharyngitis			
subjects affected / exposed	1 / 54 (1.85%)		
occurrences (all)	1		
Sinusitis			
subjects affected / exposed	0 / 54 (0.00%)		
occurrences (all)	0		
Upper respiratory tract infection			
subjects affected / exposed	2 / 54 (3.70%)		
occurrences (all)	2		
Urinary tract infection			

subjects affected / exposed occurrences (all)	1 / 54 (1.85%) 1		
Metabolism and nutrition disorders Type 2 diabetes mellitus subjects affected / exposed occurrences (all)	 2 / 54 (3.70%) 2		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
25 November 2020	Protocol amendment 1 was implemented to: - provide pandemic related guidance, - clarify the upper dosage limit for niacin and fish oil exclusion criteria, - modify exclusion criteria to include inherited or acquired known bleeding disorders.
01 April 2021	Protocol amendment 2 was implemented to: - update the number of participants from 240 to 290 and the participants per treatment from 48 to 58, - update the details of the planned interim analysis.
02 May 2022	Protocol amendment 3 was implemented to: - reduce the Extended Safety Follow-up Period from ≥ 40 weeks to a minimum of 24 weeks follow-up and removed the requirement for the participant's Lp(a) to return to 80% of Baseline levels, - update access to individual participant treatment assignments for Amgen (or designee) team members after the Treatment Period ended, the database was locked, and the snapshot was taken for the end of Treatment Period analysis.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported