



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 (\pm 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 (\pm 4.258) | -16.284 (\pm 4.259) | -16.733 (\pm 4.389) | -18.462 (\pm 4.428) |
| Week 48 (n = 57, 57, 54, 52, 51) | -14.743 (\pm 4.419) | -11.481 (\pm 4.418) | -17.308 (\pm 4.532) | -16.908 (\pm 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 (\pm 4.520) | | | |
| Week 48 (n = 57, 57, 54, 52, 51) | 10.113 (\pm 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, 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 occurrences (all) | 3 / 56 (5.36%) 3 | 2 / 58 (3.45%) 3 | 4 / 58 (6.90%) 4 |
| Nervous system disorders | | | |
| Headache subjects affected / exposed occurrences (all) | 6 / 56 (10.71%) 7 | 7 / 58 (12.07%) 9 | 6 / 58 (10.34%) 9 |
| Areflexia subjects affected / exposed occurrences (all) | 0 / 56 (0.00%) 0 | 3 / 58 (5.17%) 5 | 0 / 58 (0.00%) 0 |
| Dizziness subjects affected / exposed occurrences (all) | 2 / 56 (3.57%) 2 | 3 / 58 (5.17%) 3 | 0 / 58 (0.00%) 0 |
| Blood and lymphatic system disorders | | | |
| Anaemia subjects affected / exposed occurrences (all) | 0 / 56 (0.00%) 0 | 1 / 58 (1.72%) 1 | 3 / 58 (5.17%) 3 |
| General disorders and administration site conditions | | | |
| Injection site erythema subjects affected / exposed occurrences (all) | 3 / 56 (5.36%) 5 | 3 / 58 (5.17%) 3 | 0 / 58 (0.00%) 0 |
| Injection site bruising subjects affected / exposed occurrences (all) | 5 / 56 (8.93%) 6 | 4 / 58 (6.90%) 5 | 0 / 58 (0.00%) 0 |
| Fatigue subjects affected / exposed occurrences (all) | 3 / 56 (5.36%) 3 | 8 / 58 (13.79%) 11 | 6 / 58 (10.34%) 8 |
| Oedema peripheral subjects affected / exposed occurrences (all) | 1 / 56 (1.79%) 1 | 1 / 58 (1.72%) 1 | 2 / 58 (3.45%) 3 |
| Non-cardiac chest pain subjects affected / exposed occurrences (all) | 1 / 56 (1.79%) 1 | 2 / 58 (3.45%) 2 | 2 / 58 (3.45%) 2 |
| Injection site pruritus subjects affected / exposed occurrences (all) | 0 / 56 (0.00%) 0 | 0 / 58 (0.00%) 0 | 1 / 58 (1.72%) 1 |

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

| | | | |
|--|----------------------|----------------------|---------------------|
| subjects affected / exposed occurrences (all) | 4 / 56 (7.14%) 4 | 1 / 58 (1.72%) 1 | 3 / 58 (5.17%) 4 |
| Pain in extremity subjects affected / exposed occurrences (all) | 0 / 56 (0.00%) 0 | 1 / 58 (1.72%) 1 | 2 / 58 (3.45%) 2 |
| Infections and infestations COVID-19 subjects affected / exposed occurrences (all) | 7 / 56 (12.50%) 7 | 8 / 58 (13.79%) 9 | 1 / 58 (1.72%) 1 |
| Gastroenteritis subjects affected / exposed occurrences (all) | 0 / 56 (0.00%) 0 | 4 / 58 (6.90%) 4 | 1 / 58 (1.72%) 2 |
| Nasopharyngitis subjects affected / exposed occurrences (all) | 4 / 56 (7.14%) 4 | 2 / 58 (3.45%) 2 | 2 / 58 (3.45%) 2 |
| Sinusitis subjects affected / exposed occurrences (all) | 0 / 56 (0.00%) 0 | 3 / 58 (5.17%) 4 | 0 / 58 (0.00%) 0 |
| Upper respiratory tract infection subjects affected / exposed occurrences (all) | 2 / 56 (3.57%) 2 | 3 / 58 (5.17%) 3 | 4 / 58 (6.90%) 4 |
| Urinary tract infection subjects affected / exposed occurrences (all) | 2 / 56 (3.57%) 2 | 4 / 58 (6.90%) 4 | 3 / 58 (5.17%) 3 |
| Metabolism and nutrition disorders Type 2 diabetes mellitus subjects affected / exposed occurrences (all) | 1 / 56 (1.79%) 1 | 3 / 58 (5.17%) 3 | 3 / 58 (5.17%) 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 occurrences (all) | 2 / 57 (3.51%) 3 | 0 / 54 (0.00%) 0 | 0 / 55 (0.00%) 0 |
| Fall subjects affected / exposed occurrences (all) | 1 / 57 (1.75%) 1 | 0 / 54 (0.00%) 0 | 2 / 55 (3.64%) 2 |
| Vascular disorders Hypertension subjects affected / exposed occurrences (all) | 1 / 57 (1.75%) 1 | 0 / 54 (0.00%) 0 | 0 / 55 (0.00%) 0 |
| Nervous system disorders Headache subjects affected / exposed occurrences (all) | 1 / 57 (1.75%) 1 | 2 / 54 (3.70%) 2 | 1 / 55 (1.82%) 1 |
| Areflexia subjects affected / exposed occurrences (all) | 0 / 57 (0.00%) 0 | 1 / 54 (1.85%) 1 | 0 / 55 (0.00%) 0 |
| Dizziness subjects affected / exposed occurrences (all) | 0 / 57 (0.00%) 0 | 0 / 54 (0.00%) 0 | 1 / 55 (1.82%) 1 |
| Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all) | 2 / 57 (3.51%) 2 | 1 / 54 (1.85%) 1 | 0 / 55 (0.00%) 0 |
| General disorders and administration site conditions Injection site erythema subjects affected / exposed occurrences (all) | 0 / 57 (0.00%) 0 | 0 / 54 (0.00%) 0 | 0 / 55 (0.00%) 0 |
| Injection site bruising subjects affected / exposed occurrences (all) | 0 / 57 (0.00%) 0 | 0 / 54 (0.00%) 0 | 0 / 55 (0.00%) 0 |
| Fatigue subjects affected / exposed occurrences (all) | 1 / 57 (1.75%) 1 | 0 / 54 (0.00%) 0 | 0 / 55 (0.00%) 0 |
| Oedema peripheral subjects affected / exposed occurrences (all) | 1 / 57 (1.75%) 1 | 2 / 54 (3.70%) 2 | 0 / 55 (0.00%) 0 |

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

| | | | |
|--|------------------------|------------------------|------------------------|
| subjects affected / exposed occurrences (all) | 1 / 57 (1.75%) 1 | 1 / 54 (1.85%) 1 | 1 / 55 (1.82%) 1 |
| Back pain subjects affected / exposed occurrences (all) | 1 / 57 (1.75%) 1 | 1 / 54 (1.85%) 1 | 1 / 55 (1.82%) 1 |
| Myalgia subjects affected / exposed occurrences (all) | 0 / 57 (0.00%) 0 | 0 / 54 (0.00%) 0 | 0 / 55 (0.00%) 0 |
| Pain in extremity subjects affected / exposed occurrences (all) | 1 / 57 (1.75%) 1 | 0 / 54 (0.00%) 0 | 0 / 55 (0.00%) 0 |
| Infections and infestations COVID-19 subjects affected / exposed occurrences (all) | 11 / 57 (19.30%) 12 | 14 / 54 (25.93%) 14 | 10 / 55 (18.18%) 10 |
| Gastroenteritis subjects affected / exposed occurrences (all) | 0 / 57 (0.00%) 0 | 1 / 54 (1.85%) 1 | 0 / 55 (0.00%) 0 |
| Nasopharyngitis subjects affected / exposed occurrences (all) | 1 / 57 (1.75%) 1 | 0 / 54 (0.00%) 0 | 2 / 55 (3.64%) 2 |
| Sinusitis subjects affected / exposed occurrences (all) | 1 / 57 (1.75%) 1 | 0 / 54 (0.00%) 0 | 0 / 55 (0.00%) 0 |
| Upper respiratory tract infection subjects affected / exposed occurrences (all) | 2 / 57 (3.51%) 2 | 0 / 54 (0.00%) 0 | 1 / 55 (1.82%) 1 |
| Urinary tract infection subjects affected / exposed occurrences (all) | 4 / 57 (7.02%) 5 | 1 / 54 (1.85%) 1 | 0 / 55 (0.00%) 0 |
| Metabolism and nutrition disorders Type 2 diabetes mellitus subjects affected / exposed occurrences (all) | 1 / 57 (1.75%) 1 | 0 / 54 (0.00%) 0 | 0 / 55 (0.00%) 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 occurrences (all) | 0 / 57 (0.00%) 0 | 3 / 53 (5.66%) 3 | 0 / 55 (0.00%) 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia subjects affected / exposed occurrences (all) | 0 / 57 (0.00%) 0 | 1 / 53 (1.89%) 1 | 2 / 55 (3.64%) 3 |
| Back pain subjects affected / exposed occurrences (all) | 3 / 57 (5.26%) 3 | 0 / 53 (0.00%) 0 | 1 / 55 (1.82%) 1 |
| Myalgia subjects affected / exposed occurrences (all) | 2 / 57 (3.51%) 2 | 0 / 53 (0.00%) 0 | 4 / 55 (7.27%) 4 |
| Pain in extremity subjects affected / exposed occurrences (all) | 1 / 57 (1.75%) 1 | 0 / 53 (0.00%) 0 | 3 / 55 (5.45%) 3 |
| Infections and infestations | | | |
| COVID-19 subjects affected / exposed occurrences (all) | 8 / 57 (14.04%) 8 | 10 / 53 (18.87%) 10 | 4 / 55 (7.27%) 4 |
| Gastroenteritis subjects affected / exposed occurrences (all) | 0 / 57 (0.00%) 0 | 1 / 53 (1.89%) 1 | 2 / 55 (3.64%) 2 |
| Nasopharyngitis subjects affected / exposed occurrences (all) | 3 / 57 (5.26%) 3 | 0 / 53 (0.00%) 0 | 1 / 55 (1.82%) 1 |
| Sinusitis subjects affected / exposed occurrences (all) | 0 / 57 (0.00%) 0 | 0 / 53 (0.00%) 0 | 2 / 55 (3.64%) 2 |
| Upper respiratory tract infection subjects affected / exposed occurrences (all) | 2 / 57 (3.51%) 4 | 1 / 53 (1.89%) 1 | 1 / 55 (1.82%) 1 |
| Urinary tract infection subjects affected / exposed occurrences (all) | 0 / 57 (0.00%) 0 | 0 / 53 (0.00%) 0 | 1 / 55 (1.82%) 1 |
| Metabolism and nutrition disorders | | | |

| | | | |
|--|---------------------|---------------------|---------------------|
| Type 2 diabetes mellitus subjects affected / exposed occurrences (all) | 1 / 57 (1.75%) 1 | 0 / 53 (0.00%) 0 | 2 / 55 (3.64%) 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 occurrences (all) | 3 / 54 (5.56%) 4 | | |
| Fall subjects affected / exposed occurrences (all) | 1 / 54 (1.85%) 1 | | |
| Vascular disorders | | | |
| Hypertension subjects affected / exposed occurrences (all) | 2 / 54 (3.70%) 2 | | |
| Nervous system disorders | | | |
| Headache subjects affected / exposed occurrences (all) | 4 / 54 (7.41%) 6 | | |
| Areflexia subjects affected / exposed occurrences (all) | 0 / 54 (0.00%) 0 | | |
| Dizziness subjects affected / exposed occurrences (all) | 2 / 54 (3.70%) 3 | | |
| Blood and lymphatic system disorders | | | |
| Anaemia subjects affected / exposed occurrences (all) | 0 / 54 (0.00%) 0 | | |
| General disorders and administration site conditions | | | |
| Injection site erythema subjects affected / exposed occurrences (all) | 0 / 54 (0.00%) 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 occurrences (all) | 1 / 54 (1.85%) 1 | | |
| Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) | 1 / 54 (1.85%) 1 | | |
| Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) Back pain subjects affected / exposed occurrences (all) Myalgia subjects affected / exposed occurrences (all) Pain in extremity subjects affected / exposed occurrences (all) | 1 / 54 (1.85%) 1 3 / 54 (5.56%) 3 4 / 54 (7.41%) 6 1 / 54 (1.85%) 1 | | |
| Infections and infestations COVID-19 subjects affected / exposed occurrences (all) Gastroenteritis subjects affected / exposed occurrences (all) Nasopharyngitis subjects affected / exposed occurrences (all) Sinusitis subjects affected / exposed occurrences (all) Upper respiratory tract infection subjects affected / exposed occurrences (all) Urinary tract infection | 6 / 54 (11.11%) 6 1 / 54 (1.85%) 1 1 / 54 (1.85%) 1 0 / 54 (0.00%) 0 2 / 54 (3.70%) 2 | | |

| | | | |
|--|---------------------|--|--|
| 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: <ul style="list-style-type: none">- 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: <ul style="list-style-type: none">- 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: <ul style="list-style-type: none">- 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