



Clinical trial results:

A Phase 2, Double-Blind, Randomized, Placebo Controlled, Dose Ranging, Parallel Group Study to Evaluate the Effect of GS-6615 on Ventricular Arrhythmia in Subjects with Implantable Cardioverter-Defibrillator (ICD) or Cardiac Resynchronization Therapy-Defibrillator (CRT-D)

Summary

| | |
|--------------------------|-----------------|
| EudraCT number | 2013-004430-15 |
| Trial protocol | HU PL DK CZ NL |
| Global end of trial date | 14 October 2016 |

Results information

| | |
|--------------------------------|--|
| Result version number | v2 (current) |
| This version publication date | 18 May 2019 |
| First version publication date | 29 October 2017 |
| Version creation reason | <ul style="list-style-type: none">• Correction of full data setAdding text to "Limitations and Caveats" section |

Trial information

Trial identification

| | |
|-----------------------|----------------|
| Sponsor protocol code | GS-US-356-0101 |
|-----------------------|----------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02104583 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Gilead Sciences |
| Sponsor organisation address | 333 Lakeside Drive, Foster City, CA, United States, 94404 |
| Public contact | Clinical Trials Mailbox, Gilead Sciences , ClinicalTrialDisclosures@gilead.com |
| Scientific contact | Clinical Trials Mailbox, Gilead Sciences , ClinicalTrialDisclosures@gilead.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 | 14 October 2016 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 13 September 2016 |
| Global end of trial reached? | Yes |
| Global end of trial date | 14 October 2016 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to evaluate the effect of eleclazine (GS-6615) compared to placebo on the overall occurrence of appropriate Implantable Cardioverter-Defibrillator (ICD) interventions (antitachycardia pacing [ATP] or shock) in participants with ICD or Cardiac Resynchronization Therapy-Defibrillator (CRT-D) during the first 24 weeks of treatment.

Protection of trial subjects:

The protocol and consent/assent forms were submitted by each investigator to a duly constituted Independent Ethics Committee (IEC) or Institutional Review Board (IRB) for review and approval before study initiation. All revisions to the consent/assent forms (if applicable) after initial IEC/IRB approval were submitted by the investigator to the IEC/IRB for review and approval before implementation in accordance with regulatory requirements.

This study was conducted in accordance with recognized international scientific and ethical standards, including but not limited to the International Conference on Harmonization guideline for Good Clinical Practice (ICH GCP) and the original principles embodied in the Declaration of Helsinki.

Background therapy: -

Evidence for comparator: -

| | |
|---|-------------------|
| Actual start date of recruitment | 12 September 2014 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|--------------------|
| Country: Number of subjects enrolled | United States: 117 |
| Country: Number of subjects enrolled | Israel: 38 |
| Country: Number of subjects enrolled | Canada: 12 |
| Country: Number of subjects enrolled | Netherlands: 12 |
| Country: Number of subjects enrolled | Poland: 57 |
| Country: Number of subjects enrolled | Czech Republic: 8 |
| Country: Number of subjects enrolled | Denmark: 10 |
| Country: Number of subjects enrolled | Germany: 24 |
| Country: Number of subjects enrolled | Hungary: 35 |
| Worldwide total number of subjects | 313 |
| EEA total number of subjects | 146 |

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) | 139 |
| From 65 to 84 years | 174 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at study sites in North America, Europe and Asia. The first participant was screened on 12 September 2014. The last study visit occurred on 14 October 2016.

Pre-assignment

Screening details:

389 participants were screened.

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 | Cohort 1 Eleclazine 3 mg |

Arm description:

Single loading dose of eleclazine 30 mg on Day 1, followed by eleclazine 3 mg daily as maintenance for up to approximately 18 months

| | |
|--|--------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Eleclazine 3 mg |
| Investigational medicinal product code | |
| Other name | GS-6615 |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Eleclazine 3 mg orally daily for up to approximately 18 months

| | |
|------------------|------------------|
| Arm title | Cohort 1 Placebo |
|------------------|------------------|

Arm description:

Single loading dose of placebo to match eleclazine followed by placebo to match eleclazine once daily for up to approximately 18 months

| | |
|--|--------------------|
| Arm type | Placebo |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Placebo to match eleclazine for up to approximately 18 months

| | |
|------------------|--------------------------|
| Arm title | Cohort 2 Eleclazine 3 mg |
|------------------|--------------------------|

Arm description:

Cohort 2 randomization started following the initial safety evaluation in Cohort 1. Participants received single loading dose of eleclazine 30 mg on Day 1, followed by eleclazine 3 mg daily as maintenance for up to approximately 18 months.

| | |
|--|--------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Eleclazine 3 mg |
| Investigational medicinal product code | |
| Other name | GS-6615 |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Eleclazine 3 mg orally once daily for up to approximately 18 months

| | |
|------------------|--------------------------|
| Arm title | Cohort 2 Eleclazine 6 mg |
|------------------|--------------------------|

Arm description:

Cohort 2 randomization started following the initial safety evaluation in Cohort 1. Participants received single loading dose of eleclazine 30 mg on Day 1, followed by eleclazine 3 mg daily as maintenance for up to approximately 18 months

| | |
|--|--------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Eleclazine 6 mg |
| Investigational medicinal product code | |
| Other name | GS-6615 |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Eleclazine 6 mg (2 x 3 mg eleclazine tablets) orally daily for up to approximately 18 months

| | |
|------------------|------------------|
| Arm title | Cohort 2 Placebo |
|------------------|------------------|

Arm description:

Cohort 2 randomization started following the initial safety evaluation in Cohort 1. Single loading dose of placebo to match eleclazine followed by placebo to match eleclazine once daily for up to approximately 18 months.

| | |
|--|--------------------|
| Arm type | Placebo |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Placebo to match eleclazine for up to approximately 18 months

| Number of subjects in period 1^[1] | Cohort 1 Eleclazine 3 mg | Cohort 1 Placebo | Cohort 2 Eleclazine 3 mg |
|---|--------------------------|------------------|--------------------------|
| Started | 48 | 46 | 70 |
| Completed | 30 | 35 | 54 |
| Not completed | 18 | 11 | 16 |
| Subject required prohibited medication | - | 1 | 1 |
| Withdrew Consent | 3 | 2 | - |
| Adverse Event | 3 | 3 | 6 |
| Death | 2 | 1 | 3 |

| | | | |
|-----------------------------------|---|---|---|
| Investigator's Discretion | 1 | - | - |
| New ICD or CRT-D implanted | 2 | - | 1 |
| Subject required cardiac ablation | 6 | 4 | 4 |
| Protocol Violation | - | - | 1 |
| Lost to follow-up | 1 | - | - |

| Number of subjects in period 1 ^[1] | Cohort 2 Eleclazine 6 mg | Cohort 2 Placebo |
|--|-----------------------------|------------------|
| | | |
| Started | 73 | 75 |
| Completed | 57 | 63 |
| Not completed | 16 | 12 |
| Subject required prohibited medication | - | 1 |
| Withdrew Consent | 2 | 1 |
| Adverse Event | 6 | 1 |
| Death | 3 | 5 |
| Investigator's Discretion | - | - |
| New ICD or CRT-D implanted | - | - |
| Subject required cardiac ablation | 5 | 4 |
| Protocol Violation | - | - |
| Lost to follow-up | - | - |

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: One participant who was enrolled but never treated was not included in the subject disposition table.

Baseline characteristics

Reporting groups

| | |
|-----------------------|--------------------------|
| Reporting group title | Cohort 1 Eleclazine 3 mg |
|-----------------------|--------------------------|

Reporting group description:

Single loading dose of eleclazine 30 mg on Day 1, followed by eleclazine 3 mg daily as maintenance for up to approximately 18 months

| | |
|-----------------------|------------------|
| Reporting group title | Cohort 1 Placebo |
|-----------------------|------------------|

Reporting group description:

Single loading dose of placebo to match eleclazine followed by placebo to match eleclazine once daily for up to approximately 18 months

| | |
|-----------------------|--------------------------|
| Reporting group title | Cohort 2 Eleclazine 3 mg |
|-----------------------|--------------------------|

Reporting group description:

Cohort 2 randomization started following the initial safety evaluation in Cohort 1. Participants received single loading dose of eleclazine 30 mg on Day 1, followed by eleclazine 3 mg daily as maintenance for up to approximately 18 months.

| | |
|-----------------------|--------------------------|
| Reporting group title | Cohort 2 Eleclazine 6 mg |
|-----------------------|--------------------------|

Reporting group description:

Cohort 2 randomization started following the initial safety evaluation in Cohort 1. Participants received single loading dose of eleclazine 30 mg on Day 1, followed by eleclazine 3 mg daily as maintenance for up to approximately 18 months

| | |
|-----------------------|------------------|
| Reporting group title | Cohort 2 Placebo |
|-----------------------|------------------|

Reporting group description:

Cohort 2 randomization started following the initial safety evaluation in Cohort 1. Single loading dose of placebo to match eleclazine followed by placebo to match eleclazine once daily for up to approximately 18 months.

| Reporting group values | Cohort 1 Eleclazine 3 mg | Cohort 1 Placebo | Cohort 2 Eleclazine 3 mg |
|------------------------|--------------------------|------------------|--------------------------|
| Number of subjects | 48 | 46 | 70 |
| Age categorical | | | |
| Units: Subjects | | | |

| | | | |
|--|--------|-------|--------|
| Age continuous | | | |
| Safety Analysis Set: participants who received at least one dose of study drug | | | |
| Units: years | | | |
| arithmetic mean | 65 | 64 | 65 |
| standard deviation | ± 10.4 | ± 9.6 | ± 10.8 |
| Gender categorical | | | |
| Safety Analysis Set | | | |
| Units: Subjects | | | |
| Female | 4 | 5 | 8 |
| Male | 44 | 41 | 62 |
| Race | | | |
| Safety Analysis Set | | | |
| Units: Subjects | | | |
| American Indian or Alaska Native | 0 | 0 | 0 |
| Asian | 0 | 0 | 0 |
| Black | 1 | 1 | 0 |

| | | | |
|--|-----------|-----------|---------|
| Native Hawaiian or Pacific Islander | 0 | 0 | 0 |
| White | 47 | 45 | 70 |
| Not Permitted | 0 | 0 | 0 |
| Other | 0 | 0 | 0 |
| Ethnicity | | | |
| Safety Analysis Set | | | |
| Units: Subjects | | | |
| Hispanic or Latino | 1 | 0 | 0 |
| Not Hispanic or Latino | 47 | 45 | 70 |
| Not Permitted | 0 | 1 | 0 |
| Premature Ventricular Complex (PVC) | | | |
| Full Analysis Set: all randomized participants who received at least 1 dose of study drug. 46 participants in cohort 1 eleclazine 3 mg arm, 44 participants in cohort 1 placebo arm, 68 participants in cohort 2 eleclazine 3 mg arm, 73 participants in cohort 2 eleclazine 6 mg arm and 71 participants in cohort 2 placebo arm with available data were analyzed at baseline. | | | |
| Units: Count | | | |
| arithmetic mean | 11002 | 15560 | 10646 |
| standard deviation | ± 12494.1 | ± 25009.7 | ± 16107 |
| Non-Sustained Ventricular Tachycardia (nsVT) | | | |
| Full Analysis Set. 46 participants in cohort 1 eleclazine 3 mg arm, 44 participants in cohort 1 placebo arm, 68 participants in cohort 2 eleclazine 3 mg arm, 73 participants in cohort 2 eleclazine 6 mg arm and 71 participants in cohort 2 placebo arm with available data were analyzed at baseline. | | | |
| Units: Count | | | |
| arithmetic mean | 21 | 49 | 66 |
| standard deviation | ± 59.6 | ± 191.3 | ± 369.7 |
| Left Ventricular Ejection Fraction (LVEF) | | | |
| Full Analysis Set. 43 participants in cohort 1 eleclazine 3 mg arm, 45 participants in cohort 1 placebo arm, 57 participants in cohort 2 eleclazine 3 mg arm, 60 participants in cohort 2 eleclazine 3 mg arm and 66 participants in cohort 2 placebo arm with available data were analyzed at baseline. | | | |
| Units: Percentage | | | |
| arithmetic mean | 35 | 38 | 38 |
| standard deviation | ± 12.8 | ± 12.4 | ± 12.1 |

| Reporting group values | Cohort 2 Eleclazine 6 mg | Cohort 2 Placebo | Total |
|-------------------------------|--------------------------|------------------|-------|
| Number of subjects | 73 | 75 | 312 |
| Age categorical | | | |
| Units: Subjects | | | |

| | | | |
|--|-------|-------|-----|
| Age continuous | | | |
| Safety Analysis Set: participants who received at least one dose of study drug | | | |
| Units: years | | | |
| arithmetic mean | 65 | 64 | |
| standard deviation | ± 8.3 | ± 9.4 | - |
| Gender categorical | | | |
| Safety Analysis Set | | | |
| Units: Subjects | | | |
| Female | 7 | 8 | 32 |
| Male | 66 | 67 | 280 |
| Race | | | |
| Safety Analysis Set | | | |
| Units: Subjects | | | |
| American Indian or Alaska Native | 0 | 0 | 0 |

| | | | |
|--|-----------|--------|-----|
| Asian | 0 | 0 | 0 |
| Black | 2 | 1 | 5 |
| Native Hawaiian or Pacific Islander | 0 | 0 | 0 |
| White | 70 | 71 | 303 |
| Not Permitted | 1 | 2 | 3 |
| Other | 0 | 1 | 1 |
| Ethnicity | | | |
| Safety Analysis Set | | | |
| Units: Subjects | | | |
| Hispanic or Latino | 1 | 0 | 2 |
| Not Hispanic or Latino | 71 | 73 | 306 |
| Not Permitted | 1 | 2 | 4 |
| Premature Ventricular Complex (PVC) | | | |
| Full Analysis Set: all randomized participants who received at least 1 dose of study drug. 46 participants in cohort 1 eleclazine 3 mg arm, 44 participants in cohort 1 placebo arm, 68 participants in cohort 2 eleclazine 3 mg arm, 73 participants in cohort 2 eleclazine 6 mg arm and 71 participants in cohort 2 placebo arm with available data were analyzed at baseline. | | | |
| Units: Count | | | |
| arithmetic mean | 8194 | 6405 | |
| standard deviation | ± 10231.4 | ± 9073 | - |
| Non-Sustained Ventricular Tachycardia (nsVT) | | | |
| Full Analysis Set. 46 participants in cohort 1 eleclazine 3 mg arm, 44 participants in cohort 1 placebo arm, 68 participants in cohort 2 eleclazine 3 mg arm, 73 participants in cohort 2 eleclazine 6 mg arm and 71 participants in cohort 2 placebo arm with available data were analyzed at baseline. | | | |
| Units: Count | | | |
| arithmetic mean | 24 | 5 | |
| standard deviation | ± 69.1 | ± 12.3 | - |
| Left Ventricular Ejection Fraction (LVEF) | | | |
| Full Analysis Set. 43 participants in cohort 1 eleclazine 3 mg arm, 45 participants in cohort 1 placebo arm, 57 participants in cohort 2 eleclazine 3 mg arm, 60 participants in cohort 2 eleclazine 3 mg arm and 66 participants in cohort 2 placebo arm with available data were analyzed at baseline. | | | |
| Units: Percentage | | | |
| arithmetic mean | 38 | 40 | |
| standard deviation | ± 13.3 | ± 13.5 | - |

End points

End points reporting groups

| | |
|-----------------------|--------------------------|
| Reporting group title | Cohort 1 Eleclazine 3 mg |
|-----------------------|--------------------------|

Reporting group description:

Single loading dose of eleclazine 30 mg on Day 1, followed by eleclazine 3 mg daily as maintenance for up to approximately 18 months

| | |
|-----------------------|------------------|
| Reporting group title | Cohort 1 Placebo |
|-----------------------|------------------|

Reporting group description:

Single loading dose of placebo to match eleclazine followed by placebo to match eleclazine once daily for up to approximately 18 months

| | |
|-----------------------|--------------------------|
| Reporting group title | Cohort 2 Eleclazine 3 mg |
|-----------------------|--------------------------|

Reporting group description:

Cohort 2 randomization started following the initial safety evaluation in Cohort 1. Participants received single loading dose of eleclazine 30 mg on Day 1, followed by eleclazine 3 mg daily as maintenance for up to approximately 18 months.

| | |
|-----------------------|--------------------------|
| Reporting group title | Cohort 2 Eleclazine 6 mg |
|-----------------------|--------------------------|

Reporting group description:

Cohort 2 randomization started following the initial safety evaluation in Cohort 1. Participants received single loading dose of eleclazine 30 mg on Day 1, followed by eleclazine 3 mg daily as maintenance for up to approximately 18 months

| | |
|-----------------------|------------------|
| Reporting group title | Cohort 2 Placebo |
|-----------------------|------------------|

Reporting group description:

Cohort 2 randomization started following the initial safety evaluation in Cohort 1. Single loading dose of placebo to match eleclazine followed by placebo to match eleclazine once daily for up to approximately 18 months.

| | |
|----------------------------|----------------------------------|
| Subject analysis set title | Cohorts 1 and 2, Eleclazine 3 mg |
|----------------------------|----------------------------------|

| | |
|---------------------------|---------------|
| Subject analysis set type | Full analysis |
|---------------------------|---------------|

Subject analysis set description:

All randomized participants across cohorts 1 and 2 who received single loading dose of eleclazine 30 mg on Day 1, followed by eleclazine 3 mg daily as maintenance for up to approximately 20 months

| | |
|----------------------------|--------------------------|
| Subject analysis set title | Cohorts 1 and 2, Placebo |
|----------------------------|--------------------------|

| | |
|---------------------------|---------------|
| Subject analysis set type | Full analysis |
|---------------------------|---------------|

Subject analysis set description:

All randomized participants across cohorts 1 and 2 who received single loading dose of placebo to match eleclazine followed by placebo to match eleclazine once daily for up to approximately 20 months

Primary: Overall Occurrence (Total Number) of Appropriate Implantable Cardioverter-Defibrillator Device (ICD) Interventions (Anti-Tachycardia Pacing or Shock) Through Week 24

| | |
|-----------------|---|
| End point title | Overall Occurrence (Total Number) of Appropriate Implantable Cardioverter-Defibrillator Device (ICD) Interventions (Anti-Tachycardia Pacing or Shock) Through Week 24 |
|-----------------|---|

End point description:

The Full Analysis Set (FAS) for ICD/CRT-D (implantable cardioverter-defibrillator device/cardiac resynchronization therapy-defibrillator) event counts (FAS-ICD) was defined as FAS restricted to the subjects who had at least 1 postbaseline ICD/CRT-D interrogation.

Participants in the FAS-ICD analysis set with available data were analyzed.

| | |
|----------------------|---------|
| End point type | Primary |
| End point timeframe: | |
| Up to Week 24 | |

| End point values | Cohort 1 Eleclazine 3 mg | Cohort 1 Placebo | Cohort 2 Eleclazine 3 mg | Cohort 2 Eleclazine 6 mg |
|--------------------------------------|-----------------------------|---------------------|-----------------------------|-----------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 48 | 46 | 69 | 73 |
| Units: Number | | | | |
| arithmetic mean (standard deviation) | 3.3 (± 6.99) | 1.9 (± 3.79) | 2.6 (± 6.8) | 1.1 (± 2.09) |

| End point values | Cohort 2 Placebo | Cohorts 1 and 2, Eleclazine 3 mg | Cohorts 1 and 2, Placebo | |
|--------------------------------------|---------------------|--|-----------------------------|--|
| Subject group type | Reporting group | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 75 | 117 | 121 | |
| Units: Number | | | | |
| arithmetic mean (standard deviation) | 1.5 (± 3.92) | 2.8 (± 6.86) | 1.7 (± 3.86) | |

Statistical analyses

| | |
|-----------------------------------|---|
| Statistical analysis title | Number of Appropriate ICD Interventions |
|-----------------------------------|---|

Statistical analysis description:

The primary analysis of overall occurrence of appropriate ICD interventions through Week 24 was performed using a generalized linear model assuming a negative binomial distribution and log link. This model included terms for treatment, implanted device (ICD or CRT-D) and region (US or ROW). Least squares (LS) mean estimates and the corresponding 95% CIs (confidence intervals) were expressed in terms of appropriate ICD intervention average monthly incident rate through Week 24.

| | |
|---|---|
| Comparison groups | Cohorts 1 and 2, Eleclazine 3 mg v Cohorts 1 and 2, Placebo |
| Number of subjects included in analysis | 238 |
| Analysis specification | Pre-specified |
| Analysis type | other ^[1] |
| Parameter estimate | Eleclazine : Placebo Incident Rate Ratio |
| Point estimate | 1.52 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.86 |
| upper limit | 2.71 |

Notes:

[1] - Intergroup comparison

| Statistical analysis title | Number of Appropriate ICD Interventions |
|--|---|
| Statistical analysis description: | |
| The primary analysis of overall occurrence of appropriate ICD interventions through Week 24 was performed using a generalized linear model assuming a negative binomial distribution and log link. This model included terms for treatment, implanted device (ICD or CRT-D) and region (US or ROW). LS mean estimates and the corresponding 95% CIs were expressed in terms of appropriate ICD intervention average monthly incident rate through Week 24. | |
| Comparison groups | Cohort 2 Placebo v Cohort 2 Eleclazine 6 mg |
| Number of subjects included in analysis | 148 |
| Analysis specification | Pre-specified |
| Analysis type | other ^[2] |
| Parameter estimate | Eleclazine : Placebo Incident Rate Ratio |
| Point estimate | 0.82 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.34 |
| upper limit | 1.97 |

Notes:

[2] - Intergroup Comparison

Secondary: Overall Occurrence (Total Number) of Appropriate Implantable Cardioverter-Defibrillator Device (ICD) Interventions (Anti-Tachycardia Pacing or Shock) Through End of Study

| | |
|---|--|
| End point title | Overall Occurrence (Total Number) of Appropriate Implantable Cardioverter-Defibrillator Device (ICD) Interventions (Anti-Tachycardia Pacing or Shock) Through End of Study |
| End point description: | |
| Participants in the FAS-ICD analysis set with available data were analyzed. | |
| End point type | Secondary |
| End point timeframe: | |
| Up to 20 months | |

| End point values | Cohort 1 Eleclazine 3 mg | Cohort 1 Placebo | Cohort 2 Eleclazine 3 mg | Cohort 2 Eleclazine 6 mg |
|--------------------------------------|-----------------------------|---------------------|-----------------------------|-----------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 48 | 46 | 69 | 73 |
| Units: Number | | | | |
| arithmetic mean (standard deviation) | 5.0 (± 7.92) | 7.2 (± 20.89) | 3.8 (± 8.82) | 1.2 (± 2.11) |

| | | | | |
|------------------|---------------------|--|--|--|
| End point values | Cohort 2 Placebo | | | |
|------------------|---------------------|--|--|--|

| | | | | |
|--------------------------------------|-------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 75 | | | |
| Units: Number | | | | |
| arithmetic mean (standard deviation) | 2.0 (\pm 5.55) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Premature Ventricular Complex (PVC) Count as Assessed by Continuous Electrocardiogram [cECG] Monitoring)

| | |
|-----------------|--|
| End point title | Change From Baseline in Premature Ventricular Complex (PVC) Count as Assessed by Continuous Electrocardiogram [cECG] Monitoring) |
|-----------------|--|

End point description:

Change in PVC from baseline was measured in units of number of episodes/48 hours. Participants in the Full Analysis Set with available data were analyzed.

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

End point timeframe:

Baseline to Week 12

| End point values | Cohort 1 Eleclazine 3 mg | Cohort 1 Placebo | Cohort 2 Eleclazine 3 mg | Cohort 2 Eleclazine 6 mg |
|--------------------------------------|-----------------------------|-----------------------|-----------------------------|-----------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 48 | 40 | 58 | 56 |
| Units: Number | | | | |
| arithmetic mean (standard deviation) | 4282 (\pm 17651.5) | -2347 (\pm 8498.8) | -594 (\pm 13323.0) | -39 (\pm 13575.0) |

| End point values | Cohort 2 Placebo | | | |
|--------------------------------------|-----------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 63 | | | |
| Units: Number | | | | |
| arithmetic mean (standard deviation) | 1541 (\pm 11117.7) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Nonsustained Ventricular Tachycardia (nsVT)

Count as Assessed by Continuous Electrocardiogram [cECG] Monitoring)

| | |
|-----------------|--|
| End point title | Change From Baseline in Nonsustained Ventricular Tachycardia (nsVT) Count as Assessed by Continuous Electrocardiogram [cECG] Monitoring) |
|-----------------|--|

End point description:

Change in nsVT from baseline was measured in units of number of episodes/48 hours. Participants in the Full Analysis Set with available data were analyzed.

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

End point timeframe:

Baseline to Week 12

| End point values | Cohort 1 Eleclazine 3 mg | Cohort 1 Placebo | Cohort 2 Eleclazine 3 mg | Cohort 2 Eleclazine 6 mg |
|--------------------------------------|-----------------------------|---------------------|-----------------------------|-----------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 41 | 40 | 58 | 56 |
| Units: Number | | | | |
| arithmetic mean (standard deviation) | 44 (± 171.6) | -14 (± 52.2) | -67 (± 400.4) | 46 (± 388.4) |

| End point values | Cohort 2 Placebo | | | |
|--------------------------------------|---------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 63 | | | |
| Units: Number | | | | |
| arithmetic mean (standard deviation) | 2 (± 15.1) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Occurrence (Total Number) of VT (Ventricular Tachycardia)/VF (Ventricular Fibrillation) (Treated or Untreated) Through Week 24 and End of Study

| | |
|-----------------|---|
| End point title | Overall Occurrence (Total Number) of VT (Ventricular Tachycardia)/VF (Ventricular Fibrillation) (Treated or Untreated) Through Week 24 and End of Study |
|-----------------|---|

End point description:

Participants in the Full Analysis Set-ICD with available data were analyzed.

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

End point timeframe:

Up to Week 24; Up to 20 months

| End point values | Cohort 1 Eleclazine 3 mg | Cohort 1 Placebo | Cohort 2 Eleclazine 3 mg | Cohort 2 Eleclazine 6 mg |
|---|-----------------------------|---------------------|-----------------------------|-----------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 48 | 46 | 69 | 73 |
| Units: Number | | | | |
| arithmetic mean (standard deviation) | | | | |
| Total Number of Events Through Week 24 | 3.56 (± 7.554) | 2.07 (± 3.974) | 2.74 (± 6.825) | 1.44 (± 2.779) |
| Total Number of Events Through End of Study | 5.98 (± 8.907) | 7.83 (± 20.949) | 4.07 (± 9.088) | 1.56 (± 2.794) |

| End point values | Cohort 2 Placebo | | | |
|---|---------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 75 | | | |
| Units: Number | | | | |
| arithmetic mean (standard deviation) | | | | |
| Total Number of Events Through Week 24 | 1.61 (± 3.952) | | | |
| Total Number of Events Through End of Study | 2.17 (± 5.574) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Occurrence (Total Number) of Electrical Storms Through Week 24 and End of Study

| | |
|--------------------------------|---|
| End point title | Overall Occurrence (Total Number) of Electrical Storms Through Week 24 and End of Study |
| End point description: | |
| Full Analysis Set-ICD | |
| End point type | Secondary |
| End point timeframe: | |
| Up to Week 24; Up to 20 Months | |

| End point values | Cohort 1 Eleclazine 3 mg | Cohort 1 Placebo | Cohort 2 Eleclazine 3 mg | Cohort 2 Eleclazine 6 mg |
|---|-----------------------------|---------------------|-----------------------------|-----------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 48 | 46 | 69 | 73 |
| Units: Number | | | | |
| arithmetic mean (standard deviation) | | | | |
| Total Number of Events Through Week 24 | 0.15 (± 0.545) | 0.15 (± 0.631) | 0.23 (± 0.843) | 0.03 (± 0.164) |
| Total Number of Events Through End of Study | 0.21 (± 0.582) | 0.63 (± 2.037) | 0.35 (± 1.041) | 0.03 (± 0.164) |

| | | | | |
|---|---------------------|--|--|--|
| End point values | Cohort 2 Placebo | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 75 | | | |
| Units: Number | | | | |
| arithmetic mean (standard deviation) | | | | |
| Total Number of Events Through Week 24 | 0.09 (\pm 0.408) | | | |
| Total Number of Events Through End of Study | 0.12 (\pm 0.614) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Occurrence (Total Number) of Inappropriate ICD Interventions Through Week 24 and End of Study

| | |
|--------------------------------|---|
| End point title | Overall Occurrence (Total Number) of Inappropriate ICD Interventions Through Week 24 and End of Study |
| End point description: | |
| Full Analysis Set- ICD | |
| End point type | Secondary |
| End point timeframe: | |
| Up to Week 24; Up to 20 months | |

| | | | | |
|---|-----------------------------|---------------------|-----------------------------|-----------------------------|
| End point values | Cohort 1 Eleclazine 3 mg | Cohort 1 Placebo | Cohort 2 Eleclazine 3 mg | Cohort 2 Eleclazine 6 mg |
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 48 | 46 | 69 | 73 |
| Units: Number | | | | |
| arithmetic mean (standard deviation) | | | | |
| Total Number of Events Through Week 24 | 0.17 (\pm 0.753) | 0.15 (\pm 0.515) | 0.14 (\pm 0.772) | 0.12 (\pm 6.22) |
| Total Number of Events Through End of Study | 0.31 (\pm 1.613) | 0.41 (\pm 2.072) | 0.16 (\pm 0.779) | 0.14 (\pm 0.631) |

| | | | | |
|--------------------------------------|---------------------|--|--|--|
| End point values | Cohort 2 Placebo | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 75 | | | |
| Units: Number | | | | |
| arithmetic mean (standard deviation) | | | | |

| | | | | |
|---|---------------------|--|--|--|
| Total Number of Events Through Week 24 | 0.39 (\pm 2.283) | | | |
| Total Number of Events Through End of Study | 0.43 (\pm 2.395) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Left Ventricular Systolic and Diastolic Function as Assessed by Left Ventricular Ejection Fraction (LVEF)

| | |
|-----------------|---|
| End point title | Change in Left Ventricular Systolic and Diastolic Function as Assessed by Left Ventricular Ejection Fraction (LVEF) |
|-----------------|---|

End point description:

Participants in the Full Analysis Set with available data were analyzed.

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

End point timeframe:

Baseline to Week 12; Baseline to Week 24

| End point values | Cohort 1 Eleclazine 3 mg | Cohort 1 Placebo | Cohort 2 Eleclazine 3 mg | Cohort 2 Eleclazine 6 mg |
|--|-----------------------------|---------------------|-----------------------------|-----------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 48 | 46 | 70 | 73 |
| Units: Percentage | | | | |
| arithmetic mean (standard deviation) | | | | |
| At Week 12(N=41,39,50,46,58 in arms 1,2,3,4,5) | 3 (\pm 8.1) | 3 (\pm 6.2) | 3 (\pm 9.1) | 3 (\pm 8.2) |
| At Week 24(N=35,39,44,43,52 in arms 1,2,3,4,5) | 1 (\pm 12.3) | 2 (\pm 8.2) | 3 (\pm 10.0) | 1 (\pm 10.7) |

| End point values | Cohort 2 Placebo | | | |
|--|---------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 58 | | | |
| Units: Percentage | | | | |
| arithmetic mean (standard deviation) | | | | |
| At Week 12(N=41,39,50,46,58 in arms 1,2,3,4,5) | 1 (\pm 8.2) | | | |
| At Week 24(N=35,39,44,43,52 in arms 1,2,3,4,5) | 0 (\pm 8.3) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Time From Randomization to the First Occurrence of Appropriate ICD Interventions (ATP or Shock) or Cardiovascular (CV) Death

| | |
|--|--|
| End point title | Time From Randomization to the First Occurrence of Appropriate ICD Interventions (ATP or Shock) or Cardiovascular (CV) Death |
| End point description: The median time to the endpoint could only be estimated for the eleclazine 3 mg and placebo groups across cohorts 1 and 2; but first Quartile (Q1) value for cohort 2, eleclazine 6 mg group was 82.0, cohort 2, eleclazine 3 mg was 60.0 and cohort 2, placebo was 56.0. Full Analysis Set. | |
| End point type | Secondary |
| End point timeframe: Up to 20 months | |

| | | | | |
|----------------------------------|----------------------------------|--------------------------|--|--|
| End point values | Cohorts 1 and 2, Eleclazine 3 mg | Cohorts 1 and 2, Placebo | | |
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 118 | 121 | | |
| Units: Days | | | | |
| median (confidence interval 95%) | 243 (147.0 to 281.0) | 265 (130.0 to 496.0) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Time From Randomization to the First Occurrence of Cardiovascular (CV) Hospitalization, Emergency Room (ER) visit, or CV Death

| | |
|---|---|
| End point title | Time From Randomization to the First Occurrence of Cardiovascular (CV) Hospitalization, Emergency Room (ER) visit, or CV Death ^[3] |
| End point description: The median time to the endpoint could not be estimated for any of the treatment or placebo groups, therefore Q1 values were presented for this endpoint. Full Analysis Set. | |
| End point type | Secondary |
| End point timeframe: Up to 20 months | |

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Analyses for all participants from the missing baseline cohorts receiving eleclazine 3mg and placebo have been reported as participant analysis sets per treatment group across cohorts 1 and 2.

| | | | | |
|---|--------------------------|--------------------------|------------------|----------------------------------|
| End point values | Cohort 2 Eleclazine 3 mg | Cohort 2 Eleclazine 6 mg | Cohort 2 Placebo | Cohorts 1 and 2, Eleclazine 3 mg |
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 70 | 73 | 75 | 118 |
| Units: First Quartile (Q1) of the Median Days | | | | |

| | | | | |
|-------------------------|-------|-------|-------|-------|
| number (not applicable) | 125.0 | 193.0 | 189.0 | 144.0 |
|-------------------------|-------|-------|-------|-------|

| | | | | |
|---|--------------------------|--|--|--|
| End point values | Cohorts 1 and 2, Placebo | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 121 | | | |
| Units: First Quartile (Q1) of the Median Days | | | | |
| number (not applicable) | 190.0 | | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 20 months Plus 30 days

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 19.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|--------------------------|
| Reporting group title | Cohort 1 Eleclazine 3 mg |
|-----------------------|--------------------------|

Reporting group description:

Single loading dose of eleclazine 30 mg on Day 1, followed by eleclazine 3 mg daily as maintenance for up to approximately 18 months

| | |
|-----------------------|------------------|
| Reporting group title | Cohort 1 Placebo |
|-----------------------|------------------|

Reporting group description:

Single loading dose of placebo to match eleclazine followed by placebo to match eleclazine once daily for up to approximately 18 months

| | |
|-----------------------|--------------------------|
| Reporting group title | Cohort 2 Eleclazine 3 mg |
|-----------------------|--------------------------|

Reporting group description:

Cohort 2 randomization started following the initial safety evaluation in Cohort 1. Participants received single loading dose of eleclazine 30 mg on Day 1, followed by eleclazine 3 mg daily as maintenance for up to approximately 18 months.

| | |
|-----------------------|--------------------------|
| Reporting group title | Cohort 2 Eleclazine 6 mg |
|-----------------------|--------------------------|

Reporting group description:

Cohort 2 randomization started following the initial safety evaluation in Cohort 1. Participants received single loading dose of eleclazine 30 mg on Day 1, followed by eleclazine 3 mg daily as maintenance for up to approximately 18 months

| | |
|-----------------------|------------------|
| Reporting group title | Cohort 2 Placebo |
|-----------------------|------------------|

Reporting group description:

Cohort 2 randomization started following the initial safety evaluation in Cohort 1. Single loading dose of placebo to match eleclazine followed by placebo to match eleclazine once daily for up to approximately 18 months.

| Serious adverse events | Cohort 1 Eleclazine 3 mg | Cohort 1 Placebo | Cohort 2 Eleclazine 3 mg |
|---|--------------------------|------------------|--------------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 27 / 48 (56.25%) | 25 / 46 (54.35%) | 28 / 70 (40.00%) |
| number of deaths (all causes) | 2 | 2 | 3 |
| number of deaths resulting from adverse events | | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Acute leukaemia | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | 1 / 46 (2.17%) | 0 / 70 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| Endometrial cancer | | | |

| | | | |
|--|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 46 (0.00%) | 1 / 70 (1.43%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lung cancer metastatic | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 46 (0.00%) | 0 / 70 (0.00%) |
| 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 central nervous system | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 46 (0.00%) | 0 / 70 (0.00%) |
| 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 | | | |
| Hypotension | | | |
| subjects affected / exposed | 2 / 48 (4.17%) | 0 / 46 (0.00%) | 0 / 70 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Peripheral vascular disorder | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 46 (0.00%) | 1 / 70 (1.43%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Phlebitis | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | 1 / 46 (2.17%) | 0 / 70 (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 |
| General disorders and administration site conditions | | | |
| Chest discomfort | | | |
| subjects affected / exposed | 1 / 48 (2.08%) | 0 / 46 (0.00%) | 0 / 70 (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 |
| Chest pain | | | |
| subjects affected / exposed | 1 / 48 (2.08%) | 1 / 46 (2.17%) | 0 / 70 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|----------------|----------------|----------------|
| Phantom shocks | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 46 (0.00%) | 0 / 70 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Immune system disorders | | | |
| Cellulitis | | | |
| subjects affected / exposed | 1 / 48 (2.08%) | 1 / 46 (2.17%) | 0 / 70 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Acute respiratory failure | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 46 (0.00%) | 0 / 70 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Chronic obstructive pulmonary disease | | | |
| subjects affected / exposed | 3 / 48 (6.25%) | 0 / 46 (0.00%) | 0 / 70 (0.00%) |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dyspnoea | | | |
| subjects affected / exposed | 1 / 48 (2.08%) | 1 / 46 (2.17%) | 1 / 70 (1.43%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dyspnoea exertional | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | 1 / 46 (2.17%) | 0 / 70 (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 |
| Epistaxis | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 46 (0.00%) | 1 / 70 (1.43%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypoxia | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 46 (0.00%) | 0 / 70 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumothorax | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | 1 / 46 (2.17%) | 0 / 70 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory failure | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 46 (0.00%) | 0 / 70 (0.00%) |
| 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 | | | |
| Confusional state | | | |
| subjects affected / exposed | 1 / 48 (2.08%) | 0 / 46 (0.00%) | 0 / 70 (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 |
| Mental status changes | | | |
| subjects affected / exposed | 1 / 48 (2.08%) | 0 / 46 (0.00%) | 0 / 70 (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 |
| Product issues | | | |
| Device dislocation | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 46 (0.00%) | 0 / 70 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Device inappropriate shock delivery | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 46 (0.00%) | 1 / 70 (1.43%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Device malfunction | | | |
| subjects affected / exposed | 1 / 48 (2.08%) | 0 / 46 (0.00%) | 0 / 70 (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 |
| Investigations | | | |

| | | | |
|---|----------------|----------------|----------------|
| Anticoagulation drug level below therapeutic | | | |
| subjects affected / exposed | 1 / 48 (2.08%) | 0 / 46 (0.00%) | 0 / 70 (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 |
| Injury, poisoning and procedural complications | | | |
| Chemical burn of skin | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | 1 / 46 (2.17%) | 0 / 70 (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 |
| Fall | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 46 (0.00%) | 1 / 70 (1.43%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Humerus fracture | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 46 (0.00%) | 0 / 70 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Post procedural complication | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 46 (0.00%) | 1 / 70 (1.43%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Subdural haematoma | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 46 (0.00%) | 1 / 70 (1.43%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Tibia fracture | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | 1 / 46 (2.17%) | 0 / 70 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac disorders | | | |
| Acute coronary syndrome | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 46 (0.00%) | 0 / 70 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Acute myocardial infarction | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | 1 / 46 (2.17%) | 1 / 70 (1.43%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Acute right ventricular failure | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | 1 / 46 (2.17%) | 0 / 70 (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 |
| Angina unstable | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 46 (0.00%) | 1 / 70 (1.43%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Anginal equivalent | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 46 (0.00%) | 1 / 70 (1.43%) |
| 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 fibrillation | | | |
| subjects affected / exposed | 1 / 48 (2.08%) | 1 / 46 (2.17%) | 4 / 70 (5.71%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Atrial flutter | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 46 (0.00%) | 0 / 70 (0.00%) |
| 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 arrest | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 46 (0.00%) | 0 / 70 (0.00%) |
| 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 failure | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 46 (0.00%) | 2 / 70 (2.86%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Cardiac failure acute | | | |
| subjects affected / exposed | 1 / 48 (2.08%) | 1 / 46 (2.17%) | 0 / 70 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac failure chronic | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 46 (0.00%) | 1 / 70 (1.43%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Cardiac failure congestive | | | |
| subjects affected / exposed | 4 / 48 (8.33%) | 1 / 46 (2.17%) | 1 / 70 (1.43%) |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Cardiogenic shock | | | |
| subjects affected / exposed | 1 / 48 (2.08%) | 0 / 46 (0.00%) | 0 / 70 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Chronic left ventricular failure | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 46 (0.00%) | 1 / 70 (1.43%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Cor pulmonale | | | |
| subjects affected / exposed | 1 / 48 (2.08%) | 0 / 46 (0.00%) | 0 / 70 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Coronary artery disease | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | 1 / 46 (2.17%) | 2 / 70 (2.86%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Coronary artery stenosis | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 46 (0.00%) | 0 / 70 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Left ventricular dysfunction | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | 1 / 46 (2.17%) | 0 / 70 (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 |
| Myocardial infarction | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 46 (0.00%) | 0 / 70 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Palpitations | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 46 (0.00%) | 0 / 70 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Supraventricular tachycardia | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 46 (0.00%) | 0 / 70 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ventricular arrhythmia | | | |
| subjects affected / exposed | 3 / 48 (6.25%) | 2 / 46 (4.35%) | 5 / 70 (7.14%) |
| occurrences causally related to treatment / all | 1 / 5 | 0 / 3 | 0 / 5 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ventricular fibrillation | | | |
| subjects affected / exposed | 3 / 48 (6.25%) | 3 / 46 (6.52%) | 0 / 70 (0.00%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 4 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ventricular flutter | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 46 (0.00%) | 1 / 70 (1.43%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ventricular tachyarrhythmia | | | |

| | | | |
|---|------------------|------------------|-----------------|
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 46 (0.00%) | 1 / 70 (1.43%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ventricular tachycardia | | | |
| subjects affected / exposed | 11 / 48 (22.92%) | 10 / 46 (21.74%) | 7 / 70 (10.00%) |
| occurrences causally related to treatment / all | 0 / 14 | 0 / 15 | 0 / 8 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| Brain injury | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 46 (0.00%) | 0 / 70 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dizziness | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 46 (0.00%) | 1 / 70 (1.43%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatic encephalopathy | | | |
| subjects affected / exposed | 1 / 48 (2.08%) | 0 / 46 (0.00%) | 0 / 70 (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 |
| Ischaemic stroke | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 46 (0.00%) | 0 / 70 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Parosmia | | | |
| subjects affected / exposed | 1 / 48 (2.08%) | 0 / 46 (0.00%) | 0 / 70 (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 |
| Presyncope | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 46 (0.00%) | 0 / 70 (0.00%) |
| 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 | 2 / 48 (4.17%) | 0 / 46 (0.00%) | 1 / 70 (1.43%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | 1 / 46 (2.17%) | 0 / 70 (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 |
| Haemorrhagic anaemia | | | |
| subjects affected / exposed | 1 / 48 (2.08%) | 0 / 46 (0.00%) | 0 / 70 (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 |
| Eye disorders | | | |
| Retinal detachment | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 46 (0.00%) | 0 / 70 (0.00%) |
| 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 | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | 1 / 46 (2.17%) | 0 / 70 (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 |
| Coeliac artery compression syndrome | | | |
| subjects affected / exposed | 1 / 48 (2.08%) | 0 / 46 (0.00%) | 0 / 70 (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 |
| Constipation | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 46 (0.00%) | 0 / 70 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dry mouth | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 46 (0.00%) | 0 / 70 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|----------------|----------------|----------------|
| Gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 1 / 48 (2.08%) | 0 / 46 (0.00%) | 0 / 70 (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 |
| Inguinal hernia | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | 1 / 46 (2.17%) | 0 / 70 (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 |
| Large intestine polyp | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | 1 / 46 (2.17%) | 0 / 70 (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 |
| Nausea | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 46 (0.00%) | 0 / 70 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Oesophageal ulcer | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 46 (0.00%) | 1 / 70 (1.43%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Rectal haemorrhage | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 46 (0.00%) | 0 / 70 (0.00%) |
| 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 / 48 (0.00%) | 0 / 46 (0.00%) | 1 / 70 (1.43%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatobiliary disorders | | | |
| Acute hepatic failure | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 46 (0.00%) | 0 / 70 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hydrocholecystis | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 1 / 48 (2.08%) | 0 / 46 (0.00%) | 0 / 70 (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 |
| Skin and subcutaneous tissue disorders | | | |
| Petechiae | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 46 (0.00%) | 0 / 70 (0.00%) |
| 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 ulcer | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 46 (0.00%) | 0 / 70 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal and urinary disorders | | | |
| Acute kidney injury | | | |
| subjects affected / exposed | 1 / 48 (2.08%) | 1 / 46 (2.17%) | 0 / 70 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| Calculus urinary | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 46 (0.00%) | 0 / 70 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal impairment | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | 1 / 46 (2.17%) | 0 / 70 (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 |
| Urethral stenosis | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 46 (0.00%) | 0 / 70 (0.00%) |
| 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 retention | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 46 (0.00%) | 0 / 70 (0.00%) |
| 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 | | | |
| Arthralgia | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 46 (0.00%) | 0 / 70 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Arthritis | | | |
| subjects affected / exposed | 1 / 48 (2.08%) | 0 / 46 (0.00%) | 0 / 70 (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 |
| Gouty arthritis | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 46 (0.00%) | 0 / 70 (0.00%) |
| 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 | | | |
| Abscess limb | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 46 (0.00%) | 0 / 70 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bronchitis | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 46 (0.00%) | 0 / 70 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Clostridium difficile colitis | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 46 (0.00%) | 0 / 70 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Endocarditis pseudomonal | | | |
| subjects affected / exposed | 1 / 48 (2.08%) | 0 / 46 (0.00%) | 0 / 70 (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 |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | 1 / 46 (2.17%) | 1 / 70 (1.43%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|----------------|----------------|----------------|
| Septic shock | | | |
| subjects affected / exposed | 1 / 48 (2.08%) | 0 / 46 (0.00%) | 0 / 70 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Tooth infection | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 46 (0.00%) | 1 / 70 (1.43%) |
| 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 / 48 (0.00%) | 0 / 46 (0.00%) | 0 / 70 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Viral infection | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 46 (0.00%) | 0 / 70 (0.00%) |
| 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 | | | |
| Dehydration | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 46 (0.00%) | 0 / 70 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gout | | | |
| subjects affected / exposed | 1 / 48 (2.08%) | 0 / 46 (0.00%) | 0 / 70 (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 |
| Hyperkalaemia | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 46 (0.00%) | 0 / 70 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypoglycaemia | | | |
| subjects affected / exposed | 1 / 48 (2.08%) | 0 / 46 (0.00%) | 0 / 70 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| Serious adverse events | Cohort 2 Eleclazine 6 mg | Cohort 2 Placebo | |
|---|-----------------------------|------------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 26 / 73 (35.62%) | 26 / 75 (34.67%) | |
| number of deaths (all causes) | 4 | 5 | |
| number of deaths resulting from adverse events | | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Acute leukaemia | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 0 / 75 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Endometrial cancer | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 0 / 75 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lung cancer metastatic | | | |
| subjects affected / exposed | 1 / 73 (1.37%) | 0 / 75 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metastases to central nervous system | | | |
| subjects affected / exposed | 1 / 73 (1.37%) | 0 / 75 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vascular disorders | | | |
| Hypotension | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 0 / 75 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Peripheral vascular disorder | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 0 / 75 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Phlebitis | | | |

| | | | |
|--|----------------|----------------|--|
| subjects affected / exposed | 0 / 73 (0.00%) | 0 / 75 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General disorders and administration site conditions | | | |
| Chest discomfort | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 0 / 75 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Chest pain | | | |
| subjects affected / exposed | 2 / 73 (2.74%) | 1 / 75 (1.33%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Phantom shocks | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 1 / 75 (1.33%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Immune system disorders | | | |
| Cellulitis | | | |
| subjects affected / exposed | 1 / 73 (1.37%) | 0 / 75 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Acute respiratory failure | | | |
| subjects affected / exposed | 1 / 73 (1.37%) | 1 / 75 (1.33%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Chronic obstructive pulmonary disease | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 1 / 75 (1.33%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dyspnoea | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 0 / 73 (0.00%) | 0 / 75 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dyspnoea exertional | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 0 / 75 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Epistaxis | | | |
| subjects affected / exposed | 1 / 73 (1.37%) | 0 / 75 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypoxia | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 1 / 75 (1.33%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Pneumothorax | | | |
| subjects affected / exposed | 1 / 73 (1.37%) | 0 / 75 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory failure | | | |
| subjects affected / exposed | 1 / 73 (1.37%) | 0 / 75 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Psychiatric disorders | | | |
| Confusional state | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 0 / 75 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Mental status changes | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 0 / 75 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Product issues | | | |

| | | | |
|---|----------------|----------------|--|
| Device dislocation | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 1 / 75 (1.33%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Device inappropriate shock delivery | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 0 / 75 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Device malfunction | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 0 / 75 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Investigations | | | |
| Anticoagulation drug level below therapeutic | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 0 / 75 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Injury, poisoning and procedural complications | | | |
| Chemical burn of skin | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 0 / 75 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Fall | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 0 / 75 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Humerus fracture | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 1 / 75 (1.33%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Post procedural complication | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 0 / 73 (0.00%) | 0 / 75 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Subdural haematoma | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 0 / 75 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tibia fracture | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 0 / 75 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac disorders | | | |
| Acute coronary syndrome | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 1 / 75 (1.33%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Acute myocardial infarction | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 1 / 75 (1.33%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Acute right ventricular failure | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 0 / 75 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Angina unstable | | | |
| subjects affected / exposed | 1 / 73 (1.37%) | 0 / 75 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Anginal equivalent | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 0 / 75 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Atrial fibrillation | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 1 / 73 (1.37%) | 4 / 75 (5.33%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Atrial flutter | | | |
| subjects affected / exposed | 1 / 73 (1.37%) | 0 / 75 (0.00%) | |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac arrest | | | |
| subjects affected / exposed | 1 / 73 (1.37%) | 2 / 75 (2.67%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 2 | |
| Cardiac failure | | | |
| subjects affected / exposed | 3 / 73 (4.11%) | 2 / 75 (2.67%) | |
| occurrences causally related to treatment / all | 0 / 8 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 1 | |
| Cardiac failure acute | | | |
| subjects affected / exposed | 1 / 73 (1.37%) | 2 / 75 (2.67%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Cardiac failure chronic | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 0 / 75 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac failure congestive | | | |
| subjects affected / exposed | 2 / 73 (2.74%) | 1 / 75 (1.33%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Cardiogenic shock | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 0 / 75 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Chronic left ventricular failure | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 0 / 73 (0.00%) | 0 / 75 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cor pulmonale | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 0 / 75 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Coronary artery disease | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 1 / 75 (1.33%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Coronary artery stenosis | | | |
| subjects affected / exposed | 1 / 73 (1.37%) | 0 / 75 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Left ventricular dysfunction | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 0 / 75 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Myocardial infarction | | | |
| subjects affected / exposed | 1 / 73 (1.37%) | 0 / 75 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Palpitations | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 1 / 75 (1.33%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Supraventricular tachycardia | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 1 / 75 (1.33%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ventricular arrhythmia | | | |

| | | | |
|---|------------------|-----------------|--|
| subjects affected / exposed | 2 / 73 (2.74%) | 5 / 75 (6.67%) | |
| occurrences causally related to treatment / all | 1 / 2 | 1 / 5 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ventricular fibrillation | | | |
| subjects affected / exposed | 2 / 73 (2.74%) | 1 / 75 (1.33%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ventricular flutter | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 0 / 75 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ventricular tachyarrhythmia | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 1 / 75 (1.33%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ventricular tachycardia | | | |
| subjects affected / exposed | 10 / 73 (13.70%) | 8 / 75 (10.67%) | |
| occurrences causally related to treatment / all | 0 / 13 | 0 / 10 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorders | | | |
| Brain injury | | | |
| subjects affected / exposed | 1 / 73 (1.37%) | 0 / 75 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dizziness | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 1 / 75 (1.33%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatic encephalopathy | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 0 / 75 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ischaemic stroke | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 0 / 73 (0.00%) | 1 / 75 (1.33%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Parosmia | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 0 / 75 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Presyncope | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 1 / 75 (1.33%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Syncope | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 0 / 75 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 0 / 75 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haemorrhagic anaemia | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 0 / 75 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Eye disorders | | | |
| Retinal detachment | | | |
| subjects affected / exposed | 1 / 73 (1.37%) | 0 / 75 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 1 / 73 (1.37%) | 0 / 75 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |

| | | | |
|---|----------------|----------------|--|
| Coeliac artery compression syndrome | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 0 / 75 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Constipation | | | |
| subjects affected / exposed | 1 / 73 (1.37%) | 0 / 75 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dry mouth | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 1 / 75 (1.33%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 0 / 75 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Inguinal hernia | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 0 / 75 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Large intestine polyp | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 0 / 75 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nausea | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 1 / 75 (1.33%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Oesophageal ulcer | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 0 / 75 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Rectal haemorrhage | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 0 / 73 (0.00%) | 1 / 75 (1.33%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Upper gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 1 / 75 (1.33%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatobiliary disorders | | | |
| Acute hepatic failure | | | |
| subjects affected / exposed | 1 / 73 (1.37%) | 0 / 75 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hydrocholecystis | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 0 / 75 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Skin and subcutaneous tissue disorders | | | |
| Petechiae | | | |
| subjects affected / exposed | 1 / 73 (1.37%) | 0 / 75 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Skin ulcer | | | |
| subjects affected / exposed | 1 / 73 (1.37%) | 0 / 75 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal and urinary disorders | | | |
| Acute kidney injury | | | |
| subjects affected / exposed | 3 / 73 (4.11%) | 0 / 75 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Calculus urinary | | | |
| subjects affected / exposed | 1 / 73 (1.37%) | 0 / 75 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|----------------|----------------|--|
| Renal impairment | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 0 / 75 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urethral stenosis | | | |
| subjects affected / exposed | 1 / 73 (1.37%) | 0 / 75 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urinary retention | | | |
| subjects affected / exposed | 1 / 73 (1.37%) | 0 / 75 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 1 / 73 (1.37%) | 0 / 75 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Arthritis | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 0 / 75 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gouty arthritis | | | |
| subjects affected / exposed | 1 / 73 (1.37%) | 0 / 75 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Abscess limb | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 1 / 75 (1.33%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bronchitis | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 1 / 75 (1.33%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|----------------|----------------|--|
| Clostridium difficile colitis | | | |
| subjects affected / exposed | 1 / 73 (1.37%) | 0 / 75 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Endocarditis pseudomonal | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 0 / 75 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia | | | |
| subjects affected / exposed | 1 / 73 (1.37%) | 3 / 75 (4.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Septic shock | | | |
| subjects affected / exposed | 2 / 73 (2.74%) | 0 / 75 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 2 | 0 / 0 | |
| Tooth infection | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 0 / 75 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urinary tract infection | | | |
| subjects affected / exposed | 2 / 73 (2.74%) | 0 / 75 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Viral infection | | | |
| subjects affected / exposed | 1 / 73 (1.37%) | 0 / 75 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |
| subjects affected / exposed | 1 / 73 (1.37%) | 0 / 75 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gout | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 0 / 73 (0.00%) | 0 / 75 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hyperkalaemia | | | |
| subjects affected / exposed | 1 / 73 (1.37%) | 0 / 75 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypoglycaemia | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 0 / 75 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| Non-serious adverse events | Cohort 1 Eleclazine 3 mg | Cohort 1 Placebo | Cohort 2 Eleclazine 3 mg |
|---|-----------------------------|------------------|-----------------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 32 / 48 (66.67%) | 26 / 46 (56.52%) | 42 / 70 (60.00%) |
| Vascular disorders | | | |
| Hypotension | | | |
| subjects affected / exposed | 3 / 48 (6.25%) | 2 / 46 (4.35%) | 4 / 70 (5.71%) |
| occurrences (all) | 4 | 2 | 5 |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 3 / 48 (6.25%) | 1 / 46 (2.17%) | 1 / 70 (1.43%) |
| occurrences (all) | 4 | 1 | 1 |
| Chest discomfort | | | |
| subjects affected / exposed | 4 / 48 (8.33%) | 0 / 46 (0.00%) | 1 / 70 (1.43%) |
| occurrences (all) | 4 | 0 | 1 |
| Chest pain | | | |
| subjects affected / exposed | 1 / 48 (2.08%) | 3 / 46 (6.52%) | 3 / 70 (4.29%) |
| occurrences (all) | 1 | 3 | 3 |
| Fatigue | | | |
| subjects affected / exposed | 5 / 48 (10.42%) | 7 / 46 (15.22%) | 6 / 70 (8.57%) |
| occurrences (all) | 6 | 7 | 6 |
| Oedema peripheral | | | |

| | | | |
|---|--|---|--|
| subjects affected / exposed occurrences (all) | 3 / 48 (6.25%) 3 | 3 / 46 (6.52%) 3 | 2 / 70 (2.86%) 2 |
| Respiratory, thoracic and mediastinal disorders Dyspnoea subjects affected / exposed occurrences (all) | 5 / 48 (10.42%) 5 | 4 / 46 (8.70%) 4 | 7 / 70 (10.00%) 7 |
| Psychiatric disorders Anxiety subjects affected / exposed occurrences (all) Insomnia subjects affected / exposed occurrences (all) | 1 / 48 (2.08%) 1 0 / 48 (0.00%) 0 | 3 / 46 (6.52%) 3 5 / 46 (10.87%) 5 | 1 / 70 (1.43%) 1 1 / 70 (1.43%) 1 |
| Investigations Blood magnesium decreased subjects affected / exposed occurrences (all) Hepatic enzyme increased subjects affected / exposed occurrences (all) | 3 / 48 (6.25%) 3 1 / 48 (2.08%) 1 | 0 / 46 (0.00%) 0 3 / 46 (6.52%) 3 | 0 / 70 (0.00%) 0 0 / 70 (0.00%) 0 |
| Injury, poisoning and procedural complications Fall subjects affected / exposed occurrences (all) | 0 / 48 (0.00%) 0 | 0 / 46 (0.00%) 0 | 2 / 70 (2.86%) 2 |
| Cardiac disorders Atrial fibrillation subjects affected / exposed occurrences (all) Ventricular tachycardia subjects affected / exposed occurrences (all) | 4 / 48 (8.33%) 4 8 / 48 (16.67%) 23 | 2 / 46 (4.35%) 2 2 / 46 (4.35%) 2 | 4 / 70 (5.71%) 4 8 / 70 (11.43%) 10 |
| Nervous system disorders Dizziness subjects affected / exposed occurrences (all) Headache | 5 / 48 (10.42%) 5 | 4 / 46 (8.70%) 4 | 6 / 70 (8.57%) 7 |

| | | | |
|---|---------------------|---------------------|---------------------|
| subjects affected / exposed occurrences (all) | 4 / 48 (8.33%) 4 | 2 / 46 (4.35%) 2 | 3 / 70 (4.29%) 3 |
| Syncope subjects affected / exposed occurrences (all) | 2 / 48 (4.17%) 2 | 4 / 46 (8.70%) 4 | 2 / 70 (2.86%) 2 |
| Gastrointestinal disorders Constipation subjects affected / exposed occurrences (all) | 4 / 48 (8.33%) 4 | 1 / 46 (2.17%) 1 | 2 / 70 (2.86%) 2 |
| Diarrhoea subjects affected / exposed occurrences (all) | 3 / 48 (6.25%) 3 | 2 / 46 (4.35%) 2 | 5 / 70 (7.14%) 5 |
| Nausea subjects affected / exposed occurrences (all) | 2 / 48 (4.17%) 2 | 0 / 46 (0.00%) 0 | 4 / 70 (5.71%) 4 |
| Hepatobiliary disorders Cholelithiasis subjects affected / exposed occurrences (all) | 3 / 48 (6.25%) 3 | 0 / 46 (0.00%) 0 | 0 / 70 (0.00%) 0 |
| Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) | 3 / 48 (6.25%) 3 | 0 / 46 (0.00%) 0 | 1 / 70 (1.43%) 1 |
| Infections and infestations Pneumonia subjects affected / exposed occurrences (all) | 4 / 48 (8.33%) 5 | 1 / 46 (2.17%) 1 | 1 / 70 (1.43%) 1 |
| Urinary tract infection subjects affected / exposed occurrences (all) | 3 / 48 (6.25%) 3 | 4 / 46 (8.70%) 6 | 1 / 70 (1.43%) 2 |
| Metabolism and nutrition disorders Hypokalaemia subjects affected / exposed occurrences (all) | 3 / 48 (6.25%) 4 | 2 / 46 (4.35%) 2 | 2 / 70 (2.86%) 2 |
| Hyponatraemia | | | |

| | | | |
|-----------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 48 (0.00%) | 1 / 46 (2.17%) | 0 / 70 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |

| Non-serious adverse events | Cohort 2 Eleclazine 6 mg | Cohort 2 Placebo | |
|---|-----------------------------|------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 34 / 73 (46.58%) | 33 / 75 (44.00%) | |
| Vascular disorders | | | |
| Hypotension | | | |
| subjects affected / exposed | 2 / 73 (2.74%) | 2 / 75 (2.67%) | |
| occurrences (all) | 2 | 2 | |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 3 / 73 (4.11%) | 1 / 75 (1.33%) | |
| occurrences (all) | 3 | 1 | |
| Chest discomfort | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 0 / 75 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Chest pain | | | |
| subjects affected / exposed | 4 / 73 (5.48%) | 2 / 75 (2.67%) | |
| occurrences (all) | 4 | 2 | |
| Fatigue | | | |
| subjects affected / exposed | 3 / 73 (4.11%) | 5 / 75 (6.67%) | |
| occurrences (all) | 4 | 5 | |
| Oedema peripheral | | | |
| subjects affected / exposed | 2 / 73 (2.74%) | 3 / 75 (4.00%) | |
| occurrences (all) | 2 | 3 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Dyspnoea | | | |
| subjects affected / exposed | 2 / 73 (2.74%) | 5 / 75 (6.67%) | |
| occurrences (all) | 2 | 6 | |
| Psychiatric disorders | | | |
| Anxiety | | | |
| subjects affected / exposed | 1 / 73 (1.37%) | 0 / 75 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Insomnia | | | |

| | | | |
|---|----------------------|-----------------------|--|
| subjects affected / exposed occurrences (all) | 0 / 73 (0.00%) 0 | 0 / 75 (0.00%) 0 | |
| Investigations | | | |
| Blood magnesium decreased subjects affected / exposed occurrences (all) | 0 / 73 (0.00%) 0 | 0 / 75 (0.00%) 0 | |
| Hepatic enzyme increased subjects affected / exposed occurrences (all) | 1 / 73 (1.37%) 1 | 1 / 75 (1.33%) 1 | |
| Injury, poisoning and procedural complications | | | |
| Fall subjects affected / exposed occurrences (all) | 5 / 73 (6.85%) 5 | 1 / 75 (1.33%) 1 | |
| Cardiac disorders | | | |
| Atrial fibrillation subjects affected / exposed occurrences (all) | 2 / 73 (2.74%) 2 | 3 / 75 (4.00%) 3 | |
| Ventricular tachycardia subjects affected / exposed occurrences (all) | 7 / 73 (9.59%) 10 | 9 / 75 (12.00%) 14 | |
| Nervous system disorders | | | |
| Dizziness subjects affected / exposed occurrences (all) | 8 / 73 (10.96%) 8 | 2 / 75 (2.67%) 2 | |
| Headache subjects affected / exposed occurrences (all) | 3 / 73 (4.11%) 4 | 3 / 75 (4.00%) 3 | |
| Syncope subjects affected / exposed occurrences (all) | 1 / 73 (1.37%) 1 | 0 / 75 (0.00%) 0 | |
| Gastrointestinal disorders | | | |
| Constipation subjects affected / exposed occurrences (all) | 4 / 73 (5.48%) 4 | 2 / 75 (2.67%) 2 | |
| Diarrhoea | | | |

| | | | |
|---|---------------------|---------------------|--|
| subjects affected / exposed occurrences (all) | 4 / 73 (5.48%) 4 | 2 / 75 (2.67%) 2 | |
| Nausea subjects affected / exposed occurrences (all) | 3 / 73 (4.11%) 3 | 2 / 75 (2.67%) 2 | |
| Hepatobiliary disorders Cholelithiasis subjects affected / exposed occurrences (all) | 0 / 73 (0.00%) 0 | 0 / 75 (0.00%) 0 | |
| Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) | 3 / 73 (4.11%) 3 | 0 / 75 (0.00%) 0 | |
| Infections and infestations Pneumonia subjects affected / exposed occurrences (all) | 0 / 73 (0.00%) 0 | 0 / 75 (0.00%) 0 | |
| Urinary tract infection subjects affected / exposed occurrences (all) | 2 / 73 (2.74%) 2 | 2 / 75 (2.67%) 3 | |
| Metabolism and nutrition disorders Hypokalaemia subjects affected / exposed occurrences (all) | 1 / 73 (1.37%) 1 | 1 / 75 (1.33%) 1 | |
| Hyponatraemia subjects affected / exposed occurrences (all) | 4 / 73 (5.48%) 4 | 0 / 75 (0.00%) 0 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

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| An unplanned review of unblinded clinical trial data was performed in this study that was not prospectively specified in the protocol. There was no impact on the overall integrity or conclusions of the study. |
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Notes: