# Clinical trial results:
# A randomized, double-blind, double-dummy, multi-center study to assess safety and efficacy of BAY- 948862 in subjects with emergency presentation at the hospital because of worsening chronic heart failure with left ventricular systolic dysfunction and either type 2 diabetes mellitus with or without chronic kidney disease or moderate chronic kidney disease alone versus eplerenone

## Summary

| | |
|---|---|
| EudraCT number | 2012-002627-15 |
| Trial protocol | FI AT SE LT DE HU CZ NO NL PT DK IT ES BG GR PL |
| Global end of trial date | 22 January 2015 |

**Results information**

| | |
|---|---|
| Result version number | v2 |
| This version publication date | 08 September 2016 |
| First version publication date | 09 July 2016 |
| Version creation reason | • New data added to full data set<br>• Correction of full data set<br>Bayer sponsor contact information to be updated |

## Trial information

**Trial identification**

| | |
|---|---|
| Sponsor protocol code | BAY94-8862/14564 |

**Additional study identifiers**

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01807221 |
| WHO universal trial number (UTN) | - |

Notes:

**Sponsors**

| | |
|---|---|
| Sponsor organisation name | Bayer AG |
| Sponsor organisation address | Kaiser-Wilhelm-Allee, D-51368 Leverkusen, Germany, |
| Public contact | Therapeutic Area Head, Bayer AG, clinical-trials-contact@bayer.com |
| Scientific contact | Therapeutic Area Head, Bayer AG, clinical-trials-contact@bayer.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 | 22 January 2015 |
| Is this the analysis of the primary completion data? | No |

| | |
|---|---|
| Global end of trial reached? | Yes |
| Global end of trial date | 22 January 2015 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

Primary objective was to investigate efficacy (percentage of subjects with a relative decrease in N-terminal pro-hormone B-type natriuretic peptide [NT-proBNP] of more than 30 percent [%] from baseline to Day 90 [Day 90+/-2]) and safety of different oral doses of finerenone given once daily OD).

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 17 June 2013 |
| 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 | Netherlands: 28 |
| Country: Number of subjects enrolled | Norway: 5 |
| Country: Number of subjects enrolled | Poland: 117 |
| Country: Number of subjects enrolled | Portugal: 26 |
| Country: Number of subjects enrolled | Spain: 57 |
| Country: Number of subjects enrolled | Sweden: 29 |
| Country: Number of subjects enrolled | Austria: 22 |
| Country: Number of subjects enrolled | Bulgaria: 128 |
| Country: Number of subjects enrolled | Czech Republic: 21 |
| Country: Number of subjects enrolled | Denmark: 31 |
| Country: Number of subjects enrolled | Finland: 9 |
| Country: Number of subjects enrolled | France: 33 |
| Country: Number of subjects enrolled | Germany: 73 |
| Country: Number of subjects enrolled | Greece: 73 |

| | |
|---|---|
| Country: Number of subjects enrolled | Hungary: 144 |
| Country: Number of subjects enrolled | Italy: 67 |
| Country: Number of subjects enrolled | Lithuania: 80 |
| Country: Number of subjects enrolled | Turkey: 9 |
| Country: Number of subjects enrolled | United States: 39 |
| Country: Number of subjects enrolled | Taiwan: 32 |
| Country: Number of subjects enrolled | Australia: 9 |
| Country: Number of subjects enrolled | Canada: 58 |
| Country: Number of subjects enrolled | Israel: 153 |
| Country: Number of subjects enrolled | South Africa: 22 |
| Country: Number of subjects enrolled | Korea, Republic of: 21 |
| Worldwide total number of subjects | 1286 |
| EEA total number of subjects | 943 |

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) | 349 |
| From 65 to 84 years | 856 |
| 85 years and over | 81 |

## Subject disposition

### Recruitment

Recruitment details:

Study was conducted in 168 study centers in 25 countries worldwide, from 17 June 2013 (first subject first visit) to 09 December 2014 (last subject last visit).

### Pre-assignment

Screening details:

Out of 1286 enrolled subjects, 1066 subjects were randomized and 220 subjects were excluded due to screening failures.

### Period 1

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

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | Eplerenone (INSPRA®) |

Arm description:

Eplerenone 25 milligram (mg) capsule every other day (EOD), on Day 1, Day 3, Day 5, etc, along with placebo capsule (matched to Eplerenone capsule) on Day 2, Day 4, Day 6, etc., and placebo tablet (matched to Finerenone tablet) once daily (OD).The dose could be increased to 25 mg OD at Day 30 and to 50 mg OD at Day 60 (or 25 mg OD if no up-titration occurred on Day 30) if both up-titration steps were performed. Treatment duration was for 90 days.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Eplerenone |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

Subjects received 25mg of Eplerenone EOD up to Day 30. Potential up-titration to 25 mg OD after 30 days and 50 mg OD after 60 days.

| | |
|---|---|
| Investigational medicinal product name | Placebo tablet (matched to Finerenone tablet) |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Subjects received a single oral dose of placebo tablet (matched to Finerenone tablet) during any intervention period of the study.

| | |
|---|---|
| Investigational medicinal product name | Placebo capsule (matched to Eplerenone capsule) |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

Subjects received a single oral dose of placebo capsule (matched to Eplerenone capsule) during any intervention period of the study.

| | |
|---|---|
| **Arm title** | Finerenone (BAY94-8862) 2.5-5 mg OD |

Arm description:

Finerenone 2.5 mg immediate-release (IR) tablets OD and placebo capsule (matched to Eplerenone capsule) OD, with possible up-titration to 5 mg OD at Day 30 (Day 30±2) and sham up-titration at Day 60 (Day 60±2). Treatment duration was for 90 days.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Finerenone |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Subjects received 2.5 mg finerenone tablet OD in the morning, with possible up-titration to 5 mg OD.

| | |
|---|---|
| Investigational medicinal product name | Placebo capsule (matched to Eplerenone capsule) |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

Subjects received a single oral dose of placebo capsule (matched to Eplerenone capsule) during any intervention period of the study.

| | |
|---|---|
| **Arm title** | Finerenone (BAY94-8862) 5-10 mg OD |

Arm description:

Finerenone 5 mg IR tablets OD and placebo capsule (matched to Eplerenone capsule) OD, with possible up-titration to 10 mg OD at Day 30 (Day 30±2) and sham up-titration at Day 60 (Day 60±2). Treatment duration was for 90 days.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Finerenone |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Subjects received 5 mg finerenone tablet OD in the morning, with possible up-titration to 10 mg OD.

| | |
|---|---|
| Investigational medicinal product name | Placebo capsule (matched to Eplerenone capsule) |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

Subjects received a single oral dose of placebo capsule (matched to Eplerenone capsule) during any intervention period of the study.

| | |
|---|---|
| **Arm title** | Finerenone (BAY94-8862) 7.5-15 mg OD |

Arm description:

Finerenone 7.5 mg IR tablet OD and placebo capsule (matched to Eplerenone capsule) OD, with possible up-titration to 15 mg OD at Day 30 (Day 30±2) and sham up-titration at Day 60 (Day 60±2). Treatment duration was for 90 days.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Finerenone |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Subjects received 7.5 mg finerenone tablet OD in the morning, with possible up-titration to 15 mg OD.

| | |
|---|---|
| Investigational medicinal product name | Placebo capsule (matched to Eplerenone capsule) |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

Subjects received a single oral dose of placebo capsule (matched to Eplerenone capsule) during any intervention period of the study.

| | |
|---|---|
| **Arm title** | Finerenone (BAY94-8862) 10-20 mg OD |

Arm description:

Finerenone 10 mg IR tablet OD and placebo capsule (matched to Eplerenone capsule) OD, with possible up-titration to 20 mg OD at Day 30 (Day 30±2) and sham up-titration at Day 60 (Day 60±2). Treatment duration was for 90 days.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Finerenone |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Subjects received 10 mg finerenone tablet OD in the morning, with possible up-titration to 20 mg OD.

| | |
|---|---|
| Investigational medicinal product name | Placebo capsule (matched to Eplerenone capsule) |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

Subjects received a single oral dose of placebo capsule (matched to Eplerenone capsule) during any intervention period of the study.

| | |
|---|---|
| **Arm title** | Finerenone (BAY94-8862) 15-20 mg OD |

Arm description:

Finerenone 15 mg IR tablet OD and placebo capsule (matched to Eplerenone capsule) OD, with possible up-titration to 20 mg OD at Day 30 (Day 30±2) and sham up-titration at Day 60 (Day 60±2). Treatment duration was for 90 days.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Finerenone |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Subjects received 15 mg finerenone tablet OD in the morning, with possible up-titration to 20 mg OD.

| | |
|---|---|
| Investigational medicinal product name | Placebo capsule (matched to Eplerenone capsule) |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

Subjects received a single oral dose of placebo capsule (matched to Eplerenone capsule) during any intervention period of the study.

| Number of subjects in period 1[1] | Eplerenone (INSPRA®) | Finerenone (BAY94-8862) 2.5-5 mg OD | Finerenone (BAY94-8862) 5-10 mg OD |
|---|---|---|---|
| Started | 224 | 173 | 165 |
| Completed | 144 | 121 | 122 |
| Not completed | 80 | 52 | 43 |
| Consent withdrawn by subject | 33 | 15 | 8 |
| Physician decision | 2 | 1 | - |
| Logistical difficulties | - | 1 | - |
| Protocol violation | - | 2 | 1 |
| Death | 7 | 9 | 4 |
| Adverse event | 33 | 22 | 26 |
| Non-compliance | 1 | 2 | - |
| Sponsor decision | 2 | - | 1 |
| Lost to follow-up | 1 | - | 2 |
| Progressive disease | 1 | - | 1 |

| Number of subjects in period 1[1] | Finerenone (BAY94-8862) 7.5-15 mg OD | Finerenone (BAY94-8862) 10-20 mg OD | Finerenone (BAY94-8862) 15-20 mg OD |
|---|---|---|---|
| Started | 169 | 170 | 165 |
| Completed | 123 | 134 | 124 |
| Not completed | 46 | 36 | 41 |
| Consent withdrawn by subject | 14 | 16 | 13 |
| Physician decision | - | - | - |
| Logistical difficulties | - | 1 | - |
| Protocol violation | 2 | - | 1 |
| Death | 2 | 1 | 6 |
| Adverse event | 25 | 18 | 21 |
| Non-compliance | 1 | - | - |
| Sponsor decision | 1 | - | - |
| Lost to follow-up | 1 | - | - |
| Progressive disease | - | - | - |

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: Not all the enrolled subjects were treated with study drugs. As baseline only included treated subjects, the worldwide number enrolled in the trial differs with the number of subjects reported in the baseline period.

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | Eplerenone (INSPRA®) |
| Reporting group description: | |
| Eplerenone 25 milligram (mg) capsule every other day (EOD), on Day 1, Day 3, Day 5, etc, along with placebo capsule (matched to Eplerenone capsule) on Day 2, Day 4, Day 6, etc., and placebo tablet (matched to Finerenone tablet) once daily (OD).The dose could be increased to 25 mg OD at Day 30 and to 50 mg OD at Day 60 (or 25 mg OD if no up-titration occurred on Day 30) if both up-titration steps were performed. Treatment duration was for 90 days. | |
| Reporting group title | Finerenone (BAY94-8862) 2.5-5 mg OD |
| Reporting group description: | |
| Finerenone 2.5 mg immediate-release (IR) tablets OD and placebo capsule (matched to Eplerenone capsule) OD, with possible up-titration to 5 mg OD at Day 30 (Day 30±2) and sham up-titration at Day 60 (Day 60±2). Treatment duration was for 90 days. | |
| Reporting group title | Finerenone (BAY94-8862) 5-10 mg OD |
| Reporting group description: | |
| Finerenone 5 mg IR tablets OD and placebo capsule (matched to Eplerenone capsule) OD, with possible up-titration to 10 mg OD at Day 30 (Day 30±2) and sham up-titration at Day 60 (Day 60±2). Treatment duration was for 90 days. | |
| Reporting group title | Finerenone (BAY94-8862) 7.5-15 mg OD |
| Reporting group description: | |
| Finerenone 7.5 mg IR tablet OD and placebo capsule (matched to Eplerenone capsule) OD, with possible up-titration to 15 mg OD at Day 30 (Day 30±2) and sham up-titration at Day 60 (Day 60±2). Treatment duration was for 90 days. | |
| Reporting group title | Finerenone (BAY94-8862) 10-20 mg OD |
| Reporting group description: | |
| Finerenone 10 mg IR tablet OD and placebo capsule (matched to Eplerenone capsule) OD, with possible up-titration to 20 mg OD at Day 30 (Day 30±2) and sham up-titration at Day 60 (Day 60±2). Treatment duration was for 90 days. | |
| Reporting group title | Finerenone (BAY94-8862) 15-20 mg OD |
| Reporting group description: | |
| Finerenone 15 mg IR tablet OD and placebo capsule (matched to Eplerenone capsule) OD, with possible up-titration to 20 mg OD at Day 30 (Day 30±2) and sham up-titration at Day 60 (Day 60±2). Treatment duration was for 90 days. | |

| Reporting group values | Eplerenone (INSPRA®) | Finerenone (BAY94-8862) 2.5-5 mg OD | Finerenone (BAY94-8862) 5-10 mg OD |
|---|---|---|---|
| Number of subjects | 224 | 173 | 165 |
| Age Categorical<br>Units: Subjects | | | |
| Age Continuous<br>Units: years | | | |
| arithmetic mean | 72.38 | 72.53 | 71.81 |
| standard deviation | ± 9.92 | ± 9.74 | ± 10.55 |
| Gender Categorical<br>Units: Subjects | | | |
| Female | 51 | 37 | 38 |
| Male | 173 | 136 | 127 |

| Reporting group values | Finerenone (BAY94-8862) 7.5-15 mg OD | Finerenone (BAY94-8862) 10-20 mg OD | Finerenone (BAY94-8862) 15-20 mg OD |
|---|---|---|---|

| | | | |
|---|---|---|---|
| Number of subjects | 169 | 170 | 165 |
| Age Categorical<br>Units: Subjects | | | |

| | | | |
|---|---|---|---|
| Age Continuous<br>Units: years | | | |
| arithmetic mean | 69.27 | 71.27 | 69.2 |
| standard deviation | ± 9.83 | ± 10.27 | ± 10.15 |
| Gender Categorical<br>Units: Subjects | | | |
| Female | 44 | 41 | 31 |
| Male | 125 | 129 | 134 |

| **Reporting group values** | Total | | |
|---|---|---|---|
| Number of subjects | 1066 | | |
| Age Categorical<br>Units: Subjects | | | |

| | | | |
|---|---|---|---|
| Age Continuous<br>Units: years | | | |
| arithmetic mean | | | |
| standard deviation | - | | |
| Gender Categorical<br>Units: Subjects | | | |
| Female | 242 | | |
| Male | 824 | | |

## End points

### End points reporting groups

| | |
|---|---|
| Reporting group title | Eplerenone (INSPRA®) |
| Reporting group description: | |
| Eplerenone 25 milligram (mg) capsule every other day (EOD), on Day 1, Day 3, Day 5, etc, along with placebo capsule (matched to Eplerenone capsule) on Day 2, Day 4, Day 6, etc., and placebo tablet (matched to Finerenone tablet) once daily (OD).The dose could be increased to 25 mg OD at Day 30 and to 50 mg OD at Day 60 (or 25 mg OD if no up-titration occurred on Day 30) if both up-titration steps were performed. Treatment duration was for 90 days. | |
| Reporting group title | Finerenone (BAY94-8862) 2.5-5 mg OD |
| Reporting group description: | |
| Finerenone 2.5 mg immediate-release (IR) tablets OD and placebo capsule (matched to Eplerenone capsule) OD, with possible up-titration to 5 mg OD at Day 30 (Day 30±2) and sham up-titration at Day 60 (Day 60±2). Treatment duration was for 90 days. | |
| Reporting group title | Finerenone (BAY94-8862) 5-10 mg OD |
| Reporting group description: | |
| Finerenone 5 mg IR tablets OD and placebo capsule (matched to Eplerenone capsule) OD, with possible up-titration to 10 mg OD at Day 30 (Day 30±2) and sham up-titration at Day 60 (Day 60±2). Treatment duration was for 90 days. | |
| Reporting group title | Finerenone (BAY94-8862) 7.5-15 mg OD |
| Reporting group description: | |
| Finerenone 7.5 mg IR tablet OD and placebo capsule (matched to Eplerenone capsule) OD, with possible up-titration to 15 mg OD at Day 30 (Day 30±2) and sham up-titration at Day 60 (Day 60±2). Treatment duration was for 90 days. | |
| Reporting group title | Finerenone (BAY94-8862) 10-20 mg OD |
| Reporting group description: | |
| Finerenone 10 mg IR tablet OD and placebo capsule (matched to Eplerenone capsule) OD, with possible up-titration to 20 mg OD at Day 30 (Day 30±2) and sham up-titration at Day 60 (Day 60±2). Treatment duration was for 90 days. | |
| Reporting group title | Finerenone (BAY94-8862) 15-20 mg OD |
| Reporting group description: | |
| Finerenone 15 mg IR tablet OD and placebo capsule (matched to Eplerenone capsule) OD, with possible up-titration to 20 mg OD at Day 30 (Day 30±2) and sham up-titration at Day 60 (Day 60±2). Treatment duration was for 90 days. | |
| Subject analysis set title | Safety analysis set (SAF) |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: | |
| (N=1055) All randomized subjects who took at least one dose of study drug and with data after beginning of treatment. | |
| Subject analysis set title | Full Analysis set (FAS) |
| Subject analysis set type | Full analysis |
| Subject analysis set description: | |
| (N=1002) All subjects of the SAF who had baseline and at least one post-baseline NT-proBNP value or who died or experienced permanent (≥5 consecutive days) withdrawal of study drug after cardiovascular (CV) hospitalization or after emergency presentation for WCHF. | |
| Subject analysis set title | Per-protocol analysis set (N=PPS) |
| Subject analysis set type | Per protocol |
| Subject analysis set description: | |
| (654) All subjects of the FAS who had valid NT-proBNP data at Day 60 (Day 60±2) or later and had no major protocol deviations. | |
| Subject analysis set title | Pharmacokinetic analysis set (N=PKS) |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: | |
| (786) All finerenone-treated subjects with at least one valid finerenone plasma concentration and without any protocol deviation that would interfere with the evaluation of the PK data. | |

## Primary: Percentage of Subjects With a Relative Decrease in NTproBNP of More Than 30 % From Baseline to Day 90 (Day 90±2)

| End point title | Percentage of Subjects With a Relative Decrease in NTproBNP of More Than 30 % From Baseline to Day 90 (Day 90±2) |
|---|---|

End point description:

N-terminal pro-B type natriuretic peptide (NT-proBNP) levels in the blood are used for screening, diagnosis of acute and chronic heart failure (CHF) and may be useful to establish prognosis in heart failure.

| End point type | Primary |
|---|---|

End point timeframe:

At Day 90 (Day 90±2)

| End point values | Eplerenone (INSPRA®) | Finerenone (BAY94-8862) 2.5-5 mg OD | Finerenone (BAY94-8862) 5-10 mg OD | Finerenone (BAY94-8862) 7.5-15 mg OD |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 207[1] | 162[2] | 157[3] | 158[4] |
| Units: Percentage of Subjects | | | | |
| number (confidence interval 90%) | 37.2 (31.6 to 43.1) | 30.9 (24.9 to 37.4) | 32.5 (26.3 to 39.2) | 37.3 (30.9 to 44.1) |

Notes:

[1] - FAS

[2] - FAS

[3] - FAS

[4] - FAS

| End point values | Finerenone (BAY94-8862) 10-20 mg OD | Finerenone (BAY94-8862) 15-20 mg OD | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 160[5] | 158[6] | | |
| Units: Percentage of Subjects | | | | |
| number (confidence interval 90%) | 38.8 (32.3 to 45.5) | 34.2 (27.9 to 40.9) | | |

Notes:

[5] - FAS

[6] - FAS

### Statistical analyses

| Statistical analysis title | Statistical Analysis 1 |
|---|---|

Statistical analysis description:

Estimates and two-sided 90% confidence intervals are provided for each treatment group and for the treatment differences пBi - пC. Clopper-Pearson confidence intervals were calculated for each treatment group, while for treatment differences the exact unconditional confidence limits were calculated.

| Comparison groups | Eplerenone (INSPRA®) v Finerenone (BAY94-8862) 2.5-5 mg OD |
|---|---|

| | |
|---|---|
| Number of subjects included in analysis | 369 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.8771 |
| Method | Chi-squared |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -6.3 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | -14.9 |
| upper limit | 2.3 |

| **Statistical analysis title** | Statistical Analysis 2 |
|---|---|

Statistical analysis description:

Estimates and two-sided 90% confidence intervals are provided for each treatment group and for the treatment differences πBi - πC. Clopper-Pearson confidence intervals were calculated for each treatment group, while for treatment differences the exact unconditional confidence limits were calculated.

| | |
|---|---|
| Comparison groups | Eplerenone (INSPRA®) v Finerenone (BAY94-8862) 5-10 mg OD |
| Number of subjects included in analysis | 364 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.7945 |
| Method | Chi-squared |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -4.7 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | -13.4 |
| upper limit | 4 |

| **Statistical analysis title** | Statistical Analysis 3 |
|---|---|

Statistical analysis description:

Estimates and two-sided 90% confidence intervals are provided for each treatment group and for the treatment differences πBi - πC. Clopper-Pearsonconfidence intervals were calculated for each treatment group, while for treatment differences the exact unconditional confidence limits were calculated.

| | |
|---|---|
| Comparison groups | Eplerenone (INSPRA®) v Finerenone (BAY94-8862) 7.5-15 mg OD |
| Number of subjects included in analysis | 365 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.5 |
| Method | Chi-squared |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 0.1 |

| | |
|---|---|
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | -8.5 |
| upper limit | 8.8 |

| **Statistical analysis title** | Statistical Analysis 4 |
|---|---|

Statistical analysis description:

Estimates and two-sided 90% confidence intervals are provided for each treatment group and for the treatment differences πBi - πC. Clopper-Pearsonconfidence intervals were calculated for each treatment group, while for treatment differences the exact unconditional confidence limits were calculated.

| | |
|---|---|
| Comparison groups | Eplerenone (INSPRA®) v Finerenone (BAY94-8862) 10-20 mg OD |
| Number of subjects included in analysis | 367 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.4225 |
| Method | Chi-squared |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 1.6 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | -7.1 |
| upper limit | 10.2 |

| **Statistical analysis title** | Statistical Analysis 5 |
|---|---|

Statistical analysis description:

Estimates and two-sided 90% confidence intervals are provided for each treatment group and for the treatment differences πBi - πC. Clopper-Pearson confidence intervals were calculated for each treatment group, while for treatment differences the exact unconditional confidence limits were calculated.

| | |
|---|---|
| Comparison groups | Eplerenone (INSPRA®) v Finerenone (BAY94-8862) 15-20 mg OD |
| Number of subjects included in analysis | 365 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.6865 |
| Method | Chi-squared |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -3 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | -11.7 |
| upper limit | 5.7 |

## Secondary: Number of Subjects With Death due to any Cause

| End point title | Number of Subjects With Death due to any Cause |
|---|---|

End point description:

Death due to any cause include cardiovascular (CV) death and Non-CV death. Non-CV death was classified by 2 subcategories: non-malignant causes and malignant causes. End of treatment is defined as the last study drug intake + 3 days.

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

End point timeframe:

Day 30, 60, 90, End of Treatment, End of Follow-up (30 days post-last dose)

| End point values | Eplerenone (INSPRA®) | Finerenone (BAY94-8862) 2.5-5 mg OD | Finerenone (BAY94-8862) 5-10 mg OD | Finerenone (BAY94-8862) 7.5-15 mg OD |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 207[7] | 162[8] | 157[9] | 158[10] |
| Units: Subjects | | | | |
| Day 30 | 6 | 5 | 1 | 1 |
| Day 60 | 7 | 7 | 3 | 2 |
| Day 90 | 9 | 10 | 4 | 4 |
| End of Treatment | 9 | 10 | 4 | 5 |
| End of Follow-up | 15 | 16 | 7 | 11 |

Notes:

[7] - FAS

[8] - FAS

[9] - FAS

[10] - FAS

| End point values | Finerenone (BAY94-8862) 10-20 mg OD | Finerenone (BAY94-8862) 15-20 mg OD | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 160[11] | 158[12] | | |
| Units: Subjects | | | | |
| Day 30 | 0 | 2 | | |
| Day 60 | 0 | 4 | | |
| Day 90 | 1 | 5 | | |
| End of Treatment | 1 | 5 | | |
| End of Follow-up | 2 | 8 | | |

Notes:

[11] - FAS

[12] - FAS

### Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Subjects With Cardiovascular Hospitalization

| End point title | Number of Subjects With Cardiovascular Hospitalization |
|---|---|

End point description:

Hospitalizations were defined as any unplanned admission to hospital, i.e. completion of hospital admission procedures and one overnight [i.e. date change] stay or until the death of subject occurred.

Hospitalizations and deaths were classified by 2 primary categories: CV and non-CV. The pre-specified subcategories for CV hospitalizations were as follows: 1. Worsening heart failure, 2.Acute myocardial infarction, 3. Arrhythmia, 4.Transient ischemic attack and stroke, 5. Other CV hospitalizations. End of treatment is defined as the last study drug intake + 3 days.

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

End point timeframe:

Day 30, 60, 90, End of Treatment, End of Follow-up (30 days post-last dose)

| **End point values** | Eplerenone (INSPRA®) | Finerenone (BAY94-8862) 2.5-5 mg OD | Finerenone (BAY94-8862) 5-10 mg OD | Finerenone (BAY94-8862) 7.5-15 mg OD |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 207[13] | 162[14] | 157[15] | 158[16] |
| Units: Subjects | | | | |
| Day 30 | 28 | 23 | 14 | 8 |
| Day 60 | 43 | 33 | 23 | 21 |
| Day 90 | 45 | 35 | 26 | 29 |
| End of Treatment | 46 | 35 | 26 | 29 |
| End of Follow-up | 56 | 43 | 38 | 36 |

Notes:

[13] - FAS

[14] - FAS

[15] - FAS

[16] - FAS

| **End point values** | Finerenone (BAY94-8862) 10-20 mg OD | Finerenone (BAY94-8862) 15-20 mg OD | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 160[17] | 158[18] | | |
| Units: Subjects | | | | |
| Day 30 | 7 | 15 | | |
| Day 60 | 15 | 23 | | |
| Day 90 | 22 | 28 | | |
| End of Treatment | 22 | 29 | | |
| End of Follow-up | 27 | 34 | | |

Notes:

[17] - FAS

[18] - FAS

### Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Subjects With Emergency Presentations for Worsening Chronic Heart Failure (WCHF)

| End point title | Number of Subjects With Emergency Presentations for Worsening Chronic Heart Failure (WCHF) |
|---|---|

End point description:

Emergency presentations for WCHF were defined as newly developing signs and symptoms of WCHF after start of treatment with study drug, requiring an additional emergency presentation to hospital and IV treatment with diuretics and/or positive inotropic agents. End of treatment is defined as the last study drug intake + 3 days.

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

End point timeframe:

Day 30, 60, 90, End of Treatment, End of Follow-up (30 days post-last dose)

| **End point values** | Eplerenone (INSPRA®) | Finerenone (BAY94-8862) 2.5-5 mg OD | Finerenone (BAY94-8862) 5-10 mg OD | Finerenone (BAY94-8862) 7.5-15 mg OD |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 207[19] | 162[20] | 157[21] | 158[22] |
| Units: Subjects | | | | |
| Day 30 | 21 | 19 | 12 | 9 |
| Day 60 | 35 | 30 | 20 | 17 |
| Day 90 | 37 | 32 | 22 | 24 |
| End of Treatment | 37 | 32 | 22 | 24 |
| End of Follow-up | 47 | 40 | 30 | 30 |

Notes:

[19] - FAS

[20] - FAS

[21] - FAS

[22] - FAS

| **End point values** | Finerenone (BAY94-8862) 10-20 mg OD | Finerenone (BAY94-8862) 15-20 mg OD | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 160[23] | 158[24] | | |
| Units: Subjects | | | | |
| Day 30 | 7 | 15 | | |
| Day 60 | 14 | 22 | | |
| Day 90 | 18 | 28 | | |
| End of Treatment | 18 | 30 | | |
| End of Follow-up | 26 | 34 | | |

Notes:

[23] - FAS

[24] - FAS

### Statistical analyses

No statistical analyses for this end point

## Secondary: Effect of Dose on B-type natriuretic peptide (BNP)

| End point title | Effect of Dose on B-type natriuretic peptide (BNP) |
|---|---|

End point description:

B-type natriuretic peptide (BNP) levels in the blood are used for screening, diagnosis of acute chronic heart failure (CHF) and may be useful to establish prognosis in heart failure.

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

End point timeframe:

Day 30, 60, 90, End of Treatment, End of Follow-up (30 days post-last dose)

| End point values | Eplerenone (INSPRA®) | Finerenone (BAY94-8862) 2.5-5 mg OD | Finerenone (BAY94-8862) 5-10 mg OD | Finerenone (BAY94-8862) 7.5-15 mg OD |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 203[25] | 156[26] | 151[27] | 156[28] |
| Units: picogram per milliliter (pg/mL) | | | | |
| geometric mean (standard deviation) | | | | |
| Baseline (n=203, 156, 151, 156, 158, 155) | 594.29 (± 2.601) | 677.906 (± 2.637) | 574.245 (± 2.543) | 570.776 (± 2.741) |
| Day 30 (n=176, 136, 136, 141, 139, 133) | 0.925 (± 2.02) | 0.944 (± 1.952) | 0.878 (± 1.713) | 0.832 (± 1.959) |
| Day 60 (n=148, 130, 128, 125, 133, 128) | 0.783 (± 2.194) | 0.864 (± 2.139) | 0.854 (± 1.854) | 0.79 (± 2.179) |
| Day 90 (n=141, 119, 122, 119, 127, 120) | 0.723 (± 2.202) | 0.813 (± 2.412) | 0.839 (± 1.93) | 0.719 (± 2.204) |
| Last on-Treatment (n=180,145,139,145,143,140) | 0.757 (± 2.231) | 0.84 (± 2.349) | 0.853 (± 1.931) | 0.732 (± 2.185) |
| Premature discontinuation (n=33,23,22,19,21,22) | 0.896 (± 0.896) | 1.104 (± 2.15) | 1.006 (± 2.422) | 0.884 (± 1.973) |
| Follow-up (n=165,128,136,126,143,136) | 0.795 (± 2.232) | 0.815 (± 2.388) | 0.886 (± 2.199) | 0.726 (± 2.397) |

Notes:

[25] - FAS

[26] - FAS

[27] - FAS

[28] - FAS

| End point values | Finerenone (BAY94-8862) 10-20 mg OD | Finerenone (BAY94-8862) 15-20 mg OD | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 158[29] | 155[30] | | |
| Units: picogram per milliliter (pg/mL) | | | | |
| geometric mean (standard deviation) | | | | |
| Baseline (n=203, 156, 151, 156, 158, 155) | 606.08 (± 2.598) | 552.032 (± 2.698) | | |
| Day 30 (n=176, 136, 136, 141, 139, 133) | 0.852 (± 1.901) | 0.879 (± 1.968) | | |
| Day 60 (n=148, 130, 128, 125, 133, 128) | 0.711 (± 2.116) | 0.824 (± 2.142) | | |
| Day 90 (n=141, 119, 122, 119, 127, 120) | 0.706 (± 2.34) | 0.771 (± 2.197) | | |
| Last on-Treatment (n=180,145,139,145,143,140) | 0.702 (± 2.28) | 0.777 (± 2.173) | | |
| Premature discontinuation (n=33,23,22,19,21,22) | 0.848 (± 2.218) | 1.044 (± 2.174) | | |
| Follow-up (n=165,128,136,126,143,136) | 0.729 (± 2.487) | 0.852 (± 2.169) | | |

Notes:

[29] - FAS

[30] - FAS

## Statistical analyses

No statistical analyses for this end point

## Secondary: Effect of Dose on N-terminal prohormone of B-type natriuretic peptide (NT-proBNP)

| End point title | Effect of Dose on N-terminal prohormone of B-type natriuretic peptide (NT-proBNP) |
|---|---|

End point description:

N-terminal pro-B type natriuretic peptide (NT-proBNP) levels in the blood are used for screening, diagnosis of acute chronic heart failure (CHF) and may be useful to establish prognosis in heart failure.

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

End point timeframe:

Day 30, 60, 90, End of Treatment, End of Follow-up (30 days post-last dose)

| **End point values** | Eplerenone (INSPRA®) | Finerenone (BAY94-8862) 2.5-5 mg OD | Finerenone (BAY94-8862) 5-10 mg OD | Finerenone (BAY94-8862) 7.5-15 mg OD |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 207[31] | 162[32] | 157[33] | 158[34] |
| Units: pg/mL | | | | |
| geometric mean (standard deviation) | | | | |
| Baseline (n=207, 162, 157, 158, 160, 158) | 4730.17 (± 2.938) | 4793.43 (± 3.084) | 4184.631 (± 3.093) | 3776.859 (± 3.395) |
| Day 30 (n=177, 137, 139, 145, 141, 136) | 0.883 (± 2.458) | 0.98 (± 2.158) | 0.874 (± 2.14) | 0.888 (± 2.123) |
| Day 60 (n=153, 131, 127, 125, 137, 130) | 0.749 (± 2.73) | 0.822 (± 2.423) | 0.814 (± 2.178) | 0.81 (± 2.268) |
| Day 90 (n=142, 119, 120, 118, 129, 121) | 0.688 (± 2.59) | 0.789 (± 2.661) | 0.765 (± 2.214) | 0.783 (± 2.454) |
| Last on-Treatment (n=180,145,139,146,143,141) | 0.755 (± 2.522) | 0.841 (± 2.552) | 0.797 (± 2.215) | 0.81 (± 2.35) |
| Premature discontinuation (n= 36,23,24,21,22,25) | 0.948 (± 2.684) | 1.369 (± 2.087) | 1.267 (± 2.261) | 0.927 (± 1.864) |
| Follow-up (n=165,130,139,131,144,137) | 0.747 (± 2.616) | 0.747 (± 2.741) | 0.887 (± 2.604) | 0.809 (± 2.647) |

Notes:

[31] - FAS

[32] - FAS

[33] - FAS

[34] - FAS

| **End point values** | Finerenone (BAY94-8862) 10-20 mg OD | Finerenone (BAY94-8862) 15-20 mg OD | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 160[35] | 158[36] | | |
| Units: pg/mL | | | | |
| geometric mean (standard deviation) | | | | |
| Baseline (n=207, 162, 157, 158, 160, 158) | 4163.898 (± 2.734) | 3791.677 (± 3.013) | | |
| Day 30 (n=177, 137, 139, 145, 141, 136) | 0.822 (± 2.217) | 0.921 (± 2.136) | | |
| Day 60 (n=153, 131, 127, 125, 137, 130) | 0.748 (± 2.496) | 0.829 (± 2.288) | | |

| | | | | |
|---|---|---|---|---|
| Day 90 (n=142, 119, 120, 118, 129, 121) | 0.728 (± 2.795) | 0.771 (± 2.471) | | |
| Last on-Treatment (n=180,145,139,146,143,141) | 0.735 (± 2.717) | 0.771 (± 2.479) | | |
| Premature discontinuation (n= 36,23,24,21,22,25) | 1.133 (± 2.981) | 0.965 (± 2.352) | | |
| Follow-up (n=165,130,139,131,144,137) | 0.746 (± 2.472) | 0.849 (± 2.348) | | |

Notes:

[35] - FAS

[36] - FAS

### Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline in Health-Related Quality of Life to Day 30 (Day 30±2) and Day 90 (Day 90±2) Assessed by the Kansas City Cardiomyopathy Questionnaire (KCCQ)

| | |
|---|---|
| End point title | Change From Baseline in Health-Related Quality of Life to Day 30 (Day 30±2) and Day 90 (Day 90±2) Assessed by the Kansas City Cardiomyopathy Questionnaire (KCCQ) |

End point description:

The KCCQ was the leading health related quality of life measure for subjects with CHF. KCCQ was a 23 item questionnaire that independently measures the impact of subjects HF, or its treatment, on 7 distinct domains: self-administered instrument that quantifies physical function, symptoms (frequency, severity and recent change), social function, self-efficacy and knowledge, and quality of life. KCCQ clinical summary score is a composite assessment of physical limitations and total symptom scores. Results from the total symptom summary score are presented. Scores are transformed to a range of 0-100, in which higher scores reflect better health status. In the below table, categorical data represents change from baseline data at respective time points.

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

End point timeframe:

Baseline, Day 30, Day 90

| **End point values** | Eplerenone (INSPRA®) | Finerenone (BAY94-8862) 2.5-5 mg OD | Finerenone (BAY94-8862) 5-10 mg OD | Finerenone (BAY94-8862) 7.5-15 mg OD |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 203 | 161 | 156 | 158 |
| Units: Units on a Scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (n= 203, 161, 156, 158, 160, 157) | 43.7 (± 23) | 42.8 (± 22.6) | 45.4 (± 24) | 42.1 (± 23.2) |
| Day 30 (n=177, 141, 137, 145, 141, 141) | 20.5 (± 26.2) | 18.2 (± 22.7) | 19.3 (± 26.5) | 23 (± 24.4) |
| Day 90 (n=141, 118, 121, 118, 129, 119) | 24.3 (± 27.6) | 21.3 (± 27.2) | 24.5 (± 27) | 29.3 (± 28.6) |

| **End point values** | Finerenone (BAY94-8862) 10-20 mg OD | Finerenone (BAY94-8862) 15-20 mg OD | | |
|---|---|---|---|---|

| Subject group type | Reporting group | Reporting group | | |
|---|---|---|---|---|
| Number of subjects analysed | 160 | 157 | | |
| Units: Units on a Scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (n= 203, 161, 156, 158, 160, 157) | 42.3 (± 23.7) | 43.2 (± 22.5) | | |
| Day 30 (n=177, 141, 137, 145, 141, 141) | 24.9 (± 22.9) | 20.6 (± 27) | | |
| Day 90 (n=141, 118, 121, 118, 129, 119) | 28.3 (± 23.8) | 22.2 (± 30.6) | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change from Baseline With Transitions From Baseline With Respect to EuroQol Group 5-Dimension, 3-Level Questionnaire (EQ-5D-3L)

| End point title | Change from Baseline With Transitions From Baseline With Respect to EuroQol Group 5-Dimension, 3-Level Questionnaire (EQ-5D-3L) |
|---|---|

End point description:

EQ-5D-3L: participant rated questionnaire to assess health-related quality of life. It consists of EQ-5D descriptive system and EQ-5D Visual Analog Scale (VAS). EQ-5D-3L descriptive system comprises the following 5 dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Each dimension has 3 levels: no problems (1), some problems (2), and extreme problems (3). The 5 dimensional 3-level systems are converted into a single index utility score. Values for theoretically possible health states are calculated using a regression model and weighted according to the social preferences of the European general population. For this population, the possible EQ-5D-3L index scores ranges from -0.11 (that is, 3 for all 5 dimensions) to 1.0 (that is, 1 for all 5 dimensions), where higher scores indicate a better health state.

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

End point timeframe:

Day 30, 90 any End of Follow-up (30 days post-last dose)

| End point values | Eplerenone (INSPRA®) | Finerenone (BAY94-8862) 2.5-5 mg OD | Finerenone (BAY94-8862) 5-10 mg OD | Finerenone (BAY94-8862) 7.5-15 mg OD |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 207[37] | 162[38] | 157[39] | 158[40] |
| Units: Scores on scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (n=201, 160, 156, 157, 158,158) | 0.58 (± 0.25) | 0.59 (± 0.25) | 0.62 (± 0.23) | 0.58 (± 0.23) |
| Day 30 (n=173, 141,137,143,139,135) | 0.06 (± 0.23) | 0.02 (± 0.24) | 0.02 (± 0.23) | 0.07 (± 0.22) |
| Day 90 (n=139, 117,122,117,126,120) | 0.08 (± 0.24) | 0.03 (± 0.27) | 0.04 (± 0.25) | 0.08 (± 0.2) |
| Last on-treatment (n=174, 143,138,145,138,140) | 0.06 (± 0.23) | 0.04 (± 0.28) | 0.04 (± 0.25) | 0.08 (± 0.22) |
| Premature discontinuation (n=33,20,19,21,17,23) | -0.12 (± 0.25) | -0.06 (± 0.29) | -0.09 (± 0.24) | -0.1 (± 0.24) |
| Follow-up (n=161,129,136,133,144,139) | 0.06 (± 0.26) | 0.01 (± 0.25) | 0.01 (± 0.27) | 0.08 (± 0.23) |

Notes:

[37] - FAS

[38] - FAS

[39] - FAS

[40] - FAS

| **End point values** | Finerenone (BAY94-8862) 10-20 mg OD | Finerenone (BAY94-8862) 15-20 mg OD | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 160[41] | 158[42] | | |
| Units: Scores on scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (n=201, 160, 156, 157, 158,158) | 0.56 (± 0.25) | 0.59 (± 0.24) | | |
| Day 30 (n=173, 141,137,143,139,135) | 0.06 (± 0.23) | 0.02 (± 0.25) | | |
| Day 90 (n=139, 117,122,117,126,120) | 0.1 (± 0.24) | 0.06 (± 0.28) | | |
| Last on-treatment (n=174, 143,138,145,138,140) | 0.09 (± 0.24) | 0.06 (± 0.28) | | |
| Premature discontinuation (n=33,20,19,21,17,23) | -0.05 (± 0.25) | 0 (± 0.29) | | |
| Follow-up (n=161,129,136,133,144,139) | 0.07 (± 0.23) | 0.04 (± 0.28) | | |

Notes:

[41] - FAS

[42] - FAS

### Statistical analyses

No statistical analyses for this end point

### Other pre-specified: Change From Baseline in Serum Potassium at Specified Time Points

| End point title | Change From Baseline in Serum Potassium at Specified Time Points |
|---|---|

End point description:

Serum Potassium is a standard clinical chemistry parameter. In the below table, categorical data represents change from baseline data at respective time points.

| End point type | Other pre-specified |
|---|---|

End point timeframe:

From Baseline until the end of follow-up (30 days post dose)

| **End point values** | Eplerenone (INSPRA®) | Finerenone (BAY94-8862) 2.5-5 mg OD | Finerenone (BAY94-8862) 5-10 mg OD | Finerenone (BAY94-8862) 7.5-15 mg OD |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 221 | 172 | 162 | 167 |
| Units: millimoles per liter (mmol/L) | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (n=221,172,162,167,168,163) | 4.159 (± 0.495) | 4.081 (± 0.501) | 4.211 (± 0.541) | 4.174 (± 0.443) |
| Day 30 (Day 30±2) (n=178,136,137,142,143,137) | 0.057 (± 0.608) | 0.135 (± 0.573) | 0.075 (± 0.523) | 0.085 (± 0.475) |

| | | | | |
|---|---|---|---|---|
| Day 60 (Day 60±2) (n=151,130,125,129,134,129) | 0.179 (± 0.589) | 0.091 (± 0.568) | 0.131 (± 0.566) | 0.171 (± 0.54) |
| Day 90 (Day 90±2) (n=143,117,118,121,128,119) | 0.307 (± 0.609) | 0.184 (± 0.574) | 0.153 (± 0.516) | 0.164 (± 0.579) |
| Last on-Treatment (n=208,164,155,162,163,156) | 0.257 (± 0.647) | 0.159 (± 0.585) | 0.151 (± 0.562) | 0.219 (± 0.628) |
| Follow-up (n=164,131,139,134,145,137) | 0.117 (± 0.621) | 0.226 (± 0.694) | 0.054 (± 0.623) | 0.05 (± 0.572) |

| **End point values** | Finerenone (BAY94-8862) 10-20 mg OD | Finerenone (BAY94-8862) 15-20 mg OD | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 168 | 163 | | |
| Units: millimoles per liter (mmol/L) | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (n=221,172,162,167,168,163) | 4.131 (± 0.506) | 4.117 (± 0.506) | | |
| Day 30 (Day 30±2) (n=178,136,137,142,143,137) | 0.21 (± 0.592) | 0.193 (± 0.556) | | |
| Day 60 (Day 60±2) (n=151,130,125,129,134,129) | 0.274 (± 0.522) | 0.216 (± 0.547) | | |
| Day 90 (Day 90±2) (n=143,117,118,121,128,119) | 0.275 (± 0.58) | 0.245 (± 0.574) | | |
| Last on-Treatment (n=208,164,155,162,163,156) | 0.306 (± 0.66) | 0.295 (± 0.611) | | |
| Follow-up (n=164,131,139,134,145,137) | 0.175 (± 0.559) | 0.036 (± 0.556) | | |

## Statistical analyses

No statistical analyses for this end point

## Other pre-specified: Change From Baseline in Blood Pressure Systolic Blood Pressure (SBP) at Specified Time Points

| End point title | Change From Baseline in Blood Pressure Systolic Blood Pressure (SBP) at Specified Time Points |
|---|---|

End point description:

Systolic blood pressure (SBP) is a directly non-invasively measured hemodynamic parameter. In the below table, categorical data represents change from baseline data at respective time points.

| End point type | Other pre-specified |
|---|---|

End point timeframe:

Day 30, 60, 90, End of Treatment, End of Follow-up (30 days post-last dose)

| End point values | Eplerenone (INSPRA®) | Finerenone (BAY94-8862) 2.5-5 mg OD | Finerenone (BAY94-8862) 5-10 mg OD | Finerenone (BAY94-8862) 7.5-15 mg OD |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 218[43] | 171[44] | 160[45] | 165[46] |
| Units: millimeter of mercury (mmHg) | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (n=218,171,160,165,169,163) | 120.554 (± 18.706) | 119.492 (± 16.348) | 118.498 (± 14.355) | 119.087 (± 16.677) |
| Day 7 (n=204,158,154,158,163,157) | -0.541 (± 13.894) | -3.178 (± 13.72) | -2.565 (± 12.278) | 0.568 (± 12.733) |
| Day 14 (n=49,27,40,36,37,32) | -3.442 (± 14.258) | -4.488 (± 10.31) | 4.142 (± 15.001) | 1.241 (± 13.561) |
| Day 30 (n=177,143,138,147,145,139) | 0.067 (± 15.312) | -0.824 (± 15.747) | -0.367 (± 14.984) | 0.374 (± 14.433) |
| Day 60 (n=155,128,130,129,139,131) | 0.684 (± 16.315) | 0.337 (± 14.176) | -1.249 (± 13.659) | -1.811 (± 14.462) |
| Day 90 (n=141,119,121,121,131,122) | -0.967 (± 16.408) | 0.922 (± 15.847) | 0.047 (± 15.643) | -0.664 (± 15.018) |
| Last on-Treatment (n=201,160,153,160,163,157) | -1.723 (± 16.065) | -0.33 (± 16.259) | -1.42 (± 15.469) | -0.192 (± 15.082) |
| Premature discontinuation (n=37,24,24,23,25,24) | -2.991 (± 16.456) | -0.41 (± 13.936) | -2.167 (± 19.963) | 9.391 (± 22.378) |
| Follow-up (n=165,131,141,135,153,143) | 0.188 (± 16.751) | 2.869 (± 15.502) | 1.95 (± 16.148) | -0.928 (± 17.953) |

Notes:

[43] - SAF

[44] - SAF

[45] - SAF

[46] - SAF

| End point values | Finerenone (BAY94-8862) 10-20 mg OD | Finerenone (BAY94-8862) 15-20 mg OD | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 169[47] | 163[48] | | |
| Units: millimeter of mercury (mmHg) | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (n=218,171,160,165,169,163) | 116.024 (± 16.895) | 116.941 (± 16.548) | | |
| Day 7 (n=204,158,154,158,163,157) | 0.162 (± 15.416) | -0.546 (± 13.498) | | |
| Day 14 (n=49,27,40,36,37,32) | -3.099 (± 12.591) | -2.906 (± 15.406) | | |
| Day 30 (n=177,143,138,147,145,139) | 1.786 (± 15.039) | 0.899 (± 14.608) | | |
| Day 60 (n=155,128,130,129,139,131) | 0.981 (± 15.525) | 0.667 (± 14.83) | | |
| Day 90 (n=141,119,121,121,131,122) | 1.216 (± 17.831) | 0.956 (± 15.743) | | |
| Last on-Treatment (n=201,160,153,160,163,157) | 1.072 (± 17.123) | 0.516 (± 16.429) | | |
| Premature discontinuation (n=37,24,24,23,25,24) | -2.32 (± 11.963) | -0.028 (± 15.42) | | |
| Follow-up (n=165,131,141,135,153,143) | 2.041 (± 16.189) | 3.037 (± 16.782) | | |

Notes:

[47] - SAF

[48] - SAF

## Statistical analyses

No statistical analyses for this end point

## Other pre-specified: Change From Baseline in Blood Pressure Diastolic Blood Pressure (DBP) at Specified Time Points

| End point title | Change From Baseline in Blood Pressure Diastolic Blood Pressure (DBP) at Specified Time Points |
|---|---|

End point description:

Diastolic blood pressure (DBP) is a directly non-invasively measured hemodynamic parameter. In the below table, categorical data represents change from baseline data at respective time points.

| End point type | Other pre-specified |
|---|---|

End point timeframe:

Day 30, 60, 90, End of Treatment, End of Follow-up (30 days post-last dose)

| **End point values** | Eplerenone (INSPRA®) | Finerenone (BAY94-8862) 2.5-5 mg OD | Finerenone (BAY94-8862) 5-10 mg OD | Finerenone (BAY94-8862) 7.5-15 mg OD |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 218[49] | 171[50] | 160[51] | 165[52] |
| Units: millimeter for mercury (mmHg) | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (n=218,171,160,165,169,163) | 71.633 (± 11.647) | 71.044 (± 10.762) | 71.442 (± 8.508) | 70.61 (± 9.692) |
| Day 7 (n=204,158,154,158,163,157) | -1.351 (± 10.237) | -1.693 (± 9.911) | -2.143 (± 9.848) | 0.013 (± 9.733) |
| Day 14 (n=49,27,40,36,37,32) | -3.442 (± 10.089) | -0.537 (± 9.59) | 1.608 (± 9.423) | -0.083 (± 7.421) |
| Day 30 (n=177,143,138,147,145,139) | -0.503 (± 10.826) | 0.146 (± 10.667) | -0.845 (± 8.91) | -0.068 (± 9.633) |
| Day 60 (n=155,128,130,129,139,131) | -0.613 (± 11.096) | -0.199 (± 11.297) | -2.144 (± 9.552) | -0.85 (± 10.472) |
| Day 90 (n=141,119,121,121,131,122) | -0.716 (± 11.035) | -0.106 (± 11.148) | -1.738 (± 9.015) | -1.121 (± 9.96) |
| Last on-Treatment (n=201,160,153,160,163,157) | -1.003 (± 10.841) | -0.466 (± 11.532) | -2.383 (± 10.064) | -0.777 (± 9.842) |
| Premature discontinuation (n= 36,24,24,23,25,24) | -3.185 (± 11.853) | 0.868 (± 9.239) | -2.194 (± 15.522) | 4.101 (± 12.151) |
| Follow-up (n=165,131,141,135,153,143) | -1.218 (± 11.477) | 0.696 (± 13.172) | -0.444 (± 10.197) | -1.16 (± 11.114) |

Notes:

[49] - SAF

[50] - SAF

[51] - SAF

[52] - SAF

| End point values | Finerenone (BAY94-8862) 10-20 mg OD | Finerenone (BAY94-8862) 15-20 mg OD | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 169[53] | 163[54] | | |
| Units: millimeter for mercury (mmHg) | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (n=218,171,160,165,169,163) | 70.343 (± 10.394) | 71.145 (± 9.809) | | |
| Day 7 (n=204,158,154,158,163,157) | -0.738 (± 10.534) | -1.166 (± 8.964) | | |
| Day 14 (n=49,27,40,36,37,32) | -2.387 (± 10.51) | -0.625 (± 9.41) | | |
| Day 30 (n=177,143,138,147,145,139) | -0.094 (± 10.086) | -1.163 (± 9.622) | | |
| Day 60 (n=155,128,130,129,139,131) | 0.17 (± 10.312) | -0.575 (± 10.427) | | |
| Day 90 (n=141,119,121,121,131,122) | -0.545 (± 11.212) | -0.877 (± 11.327) | | |
| Last on-Treatment (n=201,160,153,160,163,157) | -0.44 (± 10.716) | -1.121 (± 11.52) | | |
| Premature discontinuation (n= 36,24,24,23,25,24) | -2.96 (± 9.199) | -0.083 (± 10.113) | | |
| Follow-up (n=165,131,141,135,153,143) | -0.298 (± 11.521) | -0.172 (± 10.211) | | |

Notes:

[53] - SAF

[54] - SAF

### Statistical analyses

No statistical analyses for this end point

## Other pre-specified: Change From Baseline in in Heart rate at Specified Time Points

| End point title | Change From Baseline in in Heart rate at Specified Time Points |
|---|---|

End point description:

Heart rate (HR) is a directly non-invasively measured hemodynamic parameter. In the below table, categorical data represents change from baseline data at respective time points.

| End point type | Other pre-specified |
|---|---|

End point timeframe:

Day 30, 60, 90, End of Treatment, End of Follow-up (30 days post-last dose)

| End point values | Eplerenone (INSPRA®) | Finerenone (BAY94-8862) 2.5-5 mg OD | Finerenone (BAY94-8862) 5-10 mg OD | Finerenone (BAY94-8862) 7.5-15 mg OD |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 217[55] | 171[56] | 160[57] | 165[58] |
| Units: Beats per minute (Beats/min) | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (n=217,171,160,165,169,162) | 74.957 (± 13.813) | 73.369 (± 13.396) | 72.681 (± 12.623) | 74.184 (± 12.369) |
| Day 7 (n=203,158,153,158,163,157) | -0.8 (± 10.751) | 1.073 (± 13.5) | -0.63 (± 11.696) | -0.719 (± 10.77) |

| | | | | |
|---|---|---|---|---|
| Day 14 (n=49,27,40,36,37,32) | -3.109 (± 15.101) | 0.599 (± 16.387) | 1.842 (± 14.988) | -1.324 (± 13.666) |
| Day 30(n=176,143,138,147,145,139) | 0.294 (± 13.61) | 1.064 (± 14.128) | 0.435 (± 13.63) | -0.349 (± 12.636) |
| Day 60 (n=155,128,130,129,139,131) | 0.297 (± 13.033) | -0.975 (± 14.953) | -1.741 (± 10.86) | -2.318 (± 14.225) |
| Day 90 (n=141,119,121,121,131,122) | -0.189 (± 12.289) | -1.647 (± 13.001) | -2.89 (± 12.034) | -2.212 (± 12.041) |
| Last on-Treatment (n=201,160,153,160,163,157) | -0.216 (± 13.172) | -0.476 (± 14.516) | -2.453 (± 11.945) | -1.94 (± 11.563) |
| Premature discontinuation (n= 36,24,24,23,25,23) | -2.278 (± 15.909) | -1.424 (± 15.587) | -0.222 (± 7.591) | 1.101 (± 10.22) |
| Follow-up (n=165,131,141,135,153,143) | -1.281 (± 13.789) | -2.057 (± 13.982) | -0.626 (± 14.196) | -1.326 (± 15.488) |

Notes:

[55] - SAF

[56] - SAF

[57] - SAF

[58] - SAF

| **End point values** | Finerenone (BAY94-8862) 10-20 mg OD | Finerenone (BAY94-8862) 15-20 mg OD | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 169[59] | 162[60] | | |
| Units: Beats per minute (Beats/min) | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (n=217,171,160,165,169,162) | 73.852 (± 11.999) | 74.329 (± 13.187) | | |
| Day 7 (n=203,158,153,158,163,157) | -0.548 (± 11.144) | -1.176 (± 13.398) | | |
| Day 14 (n=49,27,40,36,37,32) | 0.423 (± 11.247) | -3.969 (± 13.715) | | |
| Day 30(n=176,143,138,147,145,139) | -0.802 (± 11.311) | -1.633 (± 12.719) | | |
| Day 60 (n=155,128,130,129,139,131) | 0.192 (± 13.377) | -1.608 (± 13.828) | | |
| Day 90 (n=141,119,121,121,131,122) | -0.71 (± 13.777) | -1.145 (± 14.284) | | |
| Last on-Treatment (n=201,160,153,160,163,157) | -0.162 (± 13.265) | -2.066 (± 15.649) | | |
| Premature discontinuation (n= 36,24,24,23,25,23) | 4.733 (± 13.646) | -2.072 (± 19.731) | | |
| Follow-up (n=165,131,141,135,153,143) | 0.834 (± 14.159) | -1.317 (± 14.636) | | |

Notes:

[59] - SAF

[60] - SAF

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

From the start of study treatment until 3 days after last dose of study drug

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

### Dictionary used

| | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 17.1 |

### Reporting groups

| | |
|---|---|
| Reporting group title | Eplerenone (INSPRA®) |

Reporting group description:

Eplerenone 25mg capsule every other day (EOD), on Day 1, Day 3, Day 5, etc, along with placebo capsule (matched to Eplerenone capsule) on Day 2, Day 4, Day 6, etc., and placebo tablet (matched to Finerenone tablet) once daily (OD). The dose could be increased to 25 mg OD at Day 30 and to 50 mg OD at Day 60 (or 25 mg OD if no up-titration occurred on Day 30) if both up-titration steps were performed. Treatment duration was for 90 days.

| | |
|---|---|
| Reporting group title | Finerenone(BAY94-8862) 2.5-5 mg OD |

Reporting group description:

Finerenone 2.5 mg immediate-release (IR) tablets OD and placebo-matched to Eplerenone capsule OD, with possible up-titration to 5 mg OD at Day 30 (Day 30±2) and sham up-titration at Day 60 (Day 60±2). Treatment duration was for 90 days.

| | |
|---|---|
| Reporting group title | Finerenone (BAY94-8862) 15-20 mg OD |

Reporting group description:

Finerenone 15 mg IR tablet OD and placebo-matched to Eplerenone capsule OD, with possible up-titration to 20 mg OD at Day 30 (Day 30±2) and sham up-titration at Day 60 (Day 60±2). Treatment duration was for 90 days.

| | |
|---|---|
| Reporting group title | Finerenone (BAY94-8862) 7.5-15 mg OD |

Reporting group description:

Finerenone 7.5 mg IR tablet OD and placebo-matched to Eplerenone capsule OD, with possible up-titration to 15 mg OD at Day 30 (Day 30±2) and sham up-titration at Day 60 (Day 60±2). Treatment duration was for 90 days.

| | |
|---|---|
| Reporting group title | Finerenone (BAY94-8862) 10-20 mg OD |

Reporting group description:

Finerenone 10 mg IR tablet OD and placebo-matched to Eplerenone capsule OD, with possible up-titration to 20 mg OD at Day 30 (Day 30±2) and sham up-titration at Day 60 (Day 60±2). Treatment duration was for 90 days.

| | |
|---|---|
| Reporting group title | Finerenone (BAY94-8862) 5-10 mg OD |

Reporting group description:

Finerenone 5 mg IR tablets OD and placebo-matched to Eplerenone capsule OD, with possible up-titration to 10 mg OD at Day 30 (Day 30±2) and sham up-titration at Day 60 (Day 60±2). Treatment duration was for 90 days.

| Serious adverse events | Eplerenone (INSPRA®) | Finerenone(BAY94-8862) 2.5-5 mg OD | Finerenone (BAY94-8862) 15-20 mg OD |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 77 / 221 (34.84%) | 72 / 172 (41.86%) | 57 / 163 (34.97%) |
| number of deaths (all causes) | 19 | 17 | 9 |
| number of deaths resulting from adverse events | | | |

| | | | |
|---|---|---|---|
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Metastases to liver | | | |
| subjects affected / exposed | 0 / 221 (0.00%) | 1 / 172 (0.58%) | 0 / 163 (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 |
| Rectal adenocarcinoma | | | |
| subjects affected / exposed | 0 / 221 (0.00%) | 0 / 172 (0.00%) | 1 / 163 (0.61%) |
| 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 neoplasm | | | |
| subjects affected / exposed | 0 / 221 (0.00%) | 0 / 172 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vascular disorders | | | |
| Aortic stenosis | | | |
| subjects affected / exposed | 0 / 221 (0.00%) | 0 / 172 (0.00%) | 1 / 163 (0.61%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Circulatory collapse | | | |
| subjects affected / exposed | 1 / 221 (0.45%) | 0 / 172 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypotension | | | |
| subjects affected / exposed | 1 / 221 (0.45%) | 1 / 172 (0.58%) | 1 / 163 (0.61%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Orthostatic hypotension | | | |
| subjects affected / exposed | 1 / 221 (0.45%) | 0 / 172 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Peripheral ischaemia | | | |
| subjects affected / exposed | 0 / 221 (0.00%) | 0 / 172 (0.00%) | 1 / 163 (0.61%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|---|---|---|
| Deep vein thrombosis | | | |
| subjects affected / exposed | 0 / 221 (0.00%) | 0 / 172 (0.00%) | 1 / 163 (0.61%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Femoral artery occlusion | | | |
| subjects affected / exposed | 1 / 221 (0.45%) | 0 / 172 (0.00%) | 0 / 163 (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 |
| Haemodynamic instability | | | |
| subjects affected / exposed | 0 / 221 (0.00%) | 0 / 172 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Surgical and medical procedures | | | |
| Cardiac pacemaker insertion | | | |
| subjects affected / exposed | 0 / 221 (0.00%) | 0 / 172 (0.00%) | 0 / 163 (0.00%) |
| 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 pacemaker removal | | | |
| subjects affected / exposed | 0 / 221 (0.00%) | 0 / 172 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardioversion | | | |
| subjects affected / exposed | 2 / 221 (0.90%) | 0 / 172 (0.00%) | 0 / 163 (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 |
| Foot amputation | | | |
| subjects affected / exposed | 0 / 221 (0.00%) | 1 / 172 (0.58%) | 0 / 163 (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 |
| Toe amputation | | | |
| subjects affected / exposed | 0 / 221 (0.00%) | 1 / 172 (0.58%) | 0 / 163 (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 |
| Implantable defibrillator insertion | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 221 (0.45%) | 2 / 172 (1.16%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ventricular assist device insertion | | | |
| subjects affected / exposed | 0 / 221 (0.00%) | 0 / 172 (0.00%) | 0 / 163 (0.00%) |
| 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 rehabilitation therapy | | | |
| subjects affected / exposed | 0 / 221 (0.00%) | 0 / 172 (0.00%) | 1 / 163 (0.61%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac resynchronisation therapy | | | |
| subjects affected / exposed | 0 / 221 (0.00%) | 2 / 172 (1.16%) | 1 / 163 (0.61%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac ablation | | | |
| subjects affected / exposed | 0 / 221 (0.00%) | 0 / 172 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Tooth extraction | | | |
| subjects affected / exposed | 0 / 221 (0.00%) | 0 / 172 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Percutaneous coronary intervention | | | |
| subjects affected / exposed | 1 / 221 (0.45%) | 0 / 172 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General disorders and administration site conditions | | | |
| Chest pain | | | |
| subjects affected / exposed | 0 / 221 (0.00%) | 1 / 172 (0.58%) | 0 / 163 (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 |
| Malaise | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 221 (0.00%) | 1 / 172 (0.58%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 221 (0.00%) | 0 / 172 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Sudden death | | | |
| subjects affected / exposed | 1 / 221 (0.45%) | 2 / 172 (1.16%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 1 / 2 | 0 / 0 |
| Sudden cardiac death | | | |
| subjects affected / exposed | 0 / 221 (0.00%) | 1 / 172 (0.58%) | 0 / 163 (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 |
| Oedema due to cardiac disease | | | |
| subjects affected / exposed | 0 / 221 (0.00%) | 0 / 172 (0.00%) | 1 / 163 (0.61%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Implant site haematoma | | | |
| subjects affected / exposed | 0 / 221 (0.00%) | 1 / 172 (0.58%) | 0 / 163 (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 |
| Implant site ulcer | | | |
| subjects affected / exposed | 0 / 221 (0.00%) | 1 / 172 (0.58%) | 0 / 163 (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 |
| Stent-graft endoleak | | | |
| subjects affected / exposed | 1 / 221 (0.45%) | 0 / 172 (0.00%) | 0 / 163 (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 |
| Reproductive system and breast disorders | | | |
| Benign prostatic hyperplasia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 221 (0.00%) | 1 / 172 (0.58%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Acute pulmonary oedema | | | |
| subjects affected / exposed | 0 / 221 (0.00%) | 0 / 172 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Choking | | | |
| subjects affected / exposed | 0 / 221 (0.00%) | 0 / 172 (0.00%) | 0 / 163 (0.00%) |
| 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 | 2 / 221 (0.90%) | 0 / 172 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 1 / 3 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cough | | | |
| subjects affected / exposed | 0 / 221 (0.00%) | 0 / 172 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dyspnoea | | | |
| subjects affected / exposed | 1 / 221 (0.45%) | 0 / 172 (0.00%) | 1 / 163 (0.61%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dyspnoea exertional | | | |
| subjects affected / exposed | 0 / 221 (0.00%) | 0 / 172 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Epistaxis | | | |
| subjects affected / exposed | 0 / 221 (0.00%) | 1 / 172 (0.58%) | 0 / 163 (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 |
| Lung disorder | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 221 (0.45%) | 0 / 172 (0.00%) | 0 / 163 (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 |
| Pleural effusion | | | |
| subjects affected / exposed | 1 / 221 (0.45%) | 0 / 172 (0.00%) | 1 / 163 (0.61%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonitis | | | |
| subjects affected / exposed | 0 / 221 (0.00%) | 0 / 172 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary embolism | | | |
| subjects affected / exposed | 1 / 221 (0.45%) | 0 / 172 (0.00%) | 0 / 163 (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 |
| Pulmonary oedema | | | |
| subjects affected / exposed | 0 / 221 (0.00%) | 0 / 172 (0.00%) | 2 / 163 (1.23%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory failure | | | |
| subjects affected / exposed | 0 / 221 (0.00%) | 0 / 172 (0.00%) | 1 / 163 (0.61%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Obstructive airways disorder | | | |
| subjects affected / exposed | 0 / 221 (0.00%) | 1 / 172 (0.58%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Psychiatric disorders | | | |
| Completed suicide | | | |
| subjects affected / exposed | 0 / 221 (0.00%) | 0 / 172 (0.00%) | 1 / 163 (0.61%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Delirium | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 221 (0.45%) | 0 / 172 (0.00%) | 0 / 163 (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 |
| Sleep disorder | | | |
| subjects affected / exposed | 0 / 221 (0.00%) | 0 / 172 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Mental status changes | | | |
| subjects affected / exposed | 0 / 221 (0.00%) | 0 / 172 (0.00%) | 1 / 163 (0.61%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Psychotic disorder | | | |
| subjects affected / exposed | 0 / 221 (0.00%) | 0 / 172 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Investigations | | | |
| Blood creatinine increased | | | |
| subjects affected / exposed | 1 / 221 (0.45%) | 0 / 172 (0.00%) | 0 / 163 (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 |
| Blood potassium increased | | | |
| subjects affected / exposed | 0 / 221 (0.00%) | 1 / 172 (0.58%) | 2 / 163 (1.23%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 2 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| International normalised ratio increased | | | |
| subjects affected / exposed | 0 / 221 (0.00%) | 1 / 172 (0.58%) | 1 / 163 (0.61%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Computerised tomogram abdomen abnormal | | | |
| subjects affected / exposed | 1 / 221 (0.45%) | 0 / 172 (0.00%) | 0 / 163 (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 |
| Troponin T increased | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 221 (0.00%) | 0 / 172 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatic enzyme increased | | | |
| subjects affected / exposed | 0 / 221 (0.00%) | 0 / 172 (0.00%) | 1 / 163 (0.61%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Injury, poisoning and procedural complications | | | |
| Accident | | | |
| subjects affected / exposed | 1 / 221 (0.45%) | 0 / 172 (0.00%) | 0 / 163 (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 |
| Femur fracture | | | |
| subjects affected / exposed | 0 / 221 (0.00%) | 0 / 172 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hip fracture | | | |
| subjects affected / exposed | 0 / 221 (0.00%) | 1 / 172 (0.58%) | 0 / 163 (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 |
| Incisional hernia | | | |
| subjects affected / exposed | 0 / 221 (0.00%) | 1 / 172 (0.58%) | 0 / 163 (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 |
| Overdose | | | |
| subjects affected / exposed | 0 / 221 (0.00%) | 0 / 172 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Subdural haematoma | | | |
| subjects affected / exposed | 1 / 221 (0.45%) | 0 / 172 (0.00%) | 0 / 163 (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 |
| Contusion | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 221 (0.00%) | 0 / 172 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Brain contusion | | | |
| subjects affected / exposed | 1 / 221 (0.45%) | 0 / 172 (0.00%) | 0 / 163 (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 |
| Allergic transfusion reaction | | | |
| subjects affected / exposed | 0 / 221 (0.00%) | 1 / 172 (0.58%) | 0 / 163 (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 |
| Toxicity to various agents | | | |
| subjects affected / exposed | 0 / 221 (0.00%) | 0 / 172 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac disorders | | | |
| Acute myocardial infarction | | | |
| subjects affected / exposed | 1 / 221 (0.45%) | 1 / 172 (0.58%) | 0 / 163 (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 |
| Angina pectoris | | | |
| subjects affected / exposed | 1 / 221 (0.45%) | 1 / 172 (0.58%) | 0 / 163 (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 |
| Atrial fibrillation | | | |
| subjects affected / exposed | 0 / 221 (0.00%) | 1 / 172 (0.58%) | 1 / 163 (0.61%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Atrial flutter | | | |
| subjects affected / exposed | 0 / 221 (0.00%) | 0 / 172 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Atrial tachycardia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 221 (0.45%) | 0 / 172 (0.00%) | 0 / 163 (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 |
| Atrioventricular block complete | | | |
| subjects affected / exposed | 0 / 221 (0.00%) | 0 / 172 (0.00%) | 0 / 163 (0.00%) |
| 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 | 3 / 221 (1.36%) | 1 / 172 (0.58%) | 2 / 163 (1.23%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 2 |
| Cardiac failure | | | |
| subjects affected / exposed | 21 / 221 (9.50%) | 16 / 172 (9.30%) | 13 / 163 (7.98%) |
| occurrences causally related to treatment / all | 0 / 27 | 0 / 26 | 0 / 14 |
| deaths causally related to treatment / all | 0 / 3 | 0 / 2 | 0 / 0 |
| Cardiac failure acute | | | |
| subjects affected / exposed | 6 / 221 (2.71%) | 6 / 172 (3.49%) | 5 / 163 (3.07%) |
| occurrences causally related to treatment / all | 0 / 6 | 1 / 6 | 0 / 5 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Cardiac failure chronic | | | |
| subjects affected / exposed | 13 / 221 (5.88%) | 9 / 172 (5.23%) | 12 / 163 (7.36%) |
| occurrences causally related to treatment / all | 1 / 16 | 0 / 11 | 0 / 16 |
| deaths causally related to treatment / all | 0 / 2 | 0 / 3 | 0 / 2 |
| Cardiac failure congestive | | | |
| subjects affected / exposed | 4 / 221 (1.81%) | 5 / 172 (2.91%) | 3 / 163 (1.84%) |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 5 | 0 / 7 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiogenic shock | | | |
| subjects affected / exposed | 1 / 221 (0.45%) | 1 / 172 (0.58%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Coronary artery disease | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 2 / 221 (0.90%) | 0 / 172 (0.00%) | 0 / 163 (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 |
| Coronary artery occlusion | | | |
| subjects affected / exposed | 1 / 221 (0.45%) | 0 / 172 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Coronary artery stenosis | | | |
| subjects affected / exposed | 1 / 221 (0.45%) | 0 / 172 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Left ventricular failure | | | |
| subjects affected / exposed | 0 / 221 (0.00%) | 1 / 172 (0.58%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| Mitral valve incompetence | | | |
| subjects affected / exposed | 0 / 221 (0.00%) | 1 / 172 (0.58%) | 0 / 163 (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 | 1 / 221 (0.45%) | 0 / 172 (0.00%) | 0 / 163 (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 |
| Myocardial ischaemia | | | |
| subjects affected / exposed | 1 / 221 (0.45%) | 0 / 172 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pericardial haemorrhage | | | |
| subjects affected / exposed | 0 / 221 (0.00%) | 0 / 172 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Right ventricular failure | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 221 (0.00%) | 0 / 172 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Sick sinus syndrome | | | |
| subjects affected / exposed | 0 / 221 (0.00%) | 1 / 172 (0.58%) | 0 / 163 (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 |
| Supraventricular tachycardia | | | |
| subjects affected / exposed | 0 / 221 (0.00%) | 0 / 172 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ventricular arrhythmia | | | |
| subjects affected / exposed | 1 / 221 (0.45%) | 0 / 172 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ventricular fibrillation | | | |
| subjects affected / exposed | 3 / 221 (1.36%) | 3 / 172 (1.74%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 4 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| Ventricular tachycardia | | | |
| subjects affected / exposed | 2 / 221 (0.90%) | 4 / 172 (2.33%) | 1 / 163 (0.61%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 8 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Left ventricular dysfunction | | | |
| subjects affected / exposed | 0 / 221 (0.00%) | 1 / 172 (0.58%) | 0 / 163 (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 |
| Cardiopulmonary failure | | | |
| subjects affected / exposed | 1 / 221 (0.45%) | 0 / 172 (0.00%) | 0 / 163 (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 |
| Acute coronary syndrome | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 221 (0.00%) | 1 / 172 (0.58%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac ventricular thrombosis | | | |
| subjects affected / exposed | 0 / 221 (0.00%) | 1 / 172 (0.58%) | 0 / 163 (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 |
| Ventricular tachyarrhythmia | | | |
| subjects affected / exposed | 1 / 221 (0.45%) | 0 / 172 (0.00%) | 0 / 163 (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 |
| Cardiovascular insufficiency | | | |
| subjects affected / exposed | 0 / 221 (0.00%) | 0 / 172 (0.00%) | 1 / 163 (0.61%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Nervous system disorders | | | |
| Cerebellar syndrome | | | |
| subjects affected / exposed | 0 / 221 (0.00%) | 1 / 172 (0.58%) | 0 / 163 (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 |
| Cerebrovascular accident | | | |
| subjects affected / exposed | 0 / 221 (0.00%) | 0 / 172 (0.00%) | 1 / 163 (0.61%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dizziness | | | |
| subjects affected / exposed | 1 / 221 (0.45%) | 0 / 172 (0.00%) | 0 / 163 (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 |
| Embolic stroke | | | |
| subjects affected / exposed | 0 / 221 (0.00%) | 1 / 172 (0.58%) | 0 / 163 (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 |
| Haemorrhage intracranial | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 221 (0.45%) | 0 / 172 (0.00%) | 0 / 163 (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 |
| Loss of consciousness | | | |
| subjects affected / exposed | 1 / 221 (0.45%) | 0 / 172 (0.00%) | 0 / 163 (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 |
| Nervous system disorder | | | |
| subjects affected / exposed | 1 / 221 (0.45%) | 0 / 172 (0.00%) | 0 / 163 (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 |
| Status epilepticus | | | |
| subjects affected / exposed | 0 / 221 (0.00%) | 0 / 172 (0.00%) | 0 / 163 (0.00%) |
| 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 / 221 (0.90%) | 0 / 172 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vocal cord paralysis | | | |
| subjects affected / exposed | 0 / 221 (0.00%) | 1 / 172 (0.58%) | 0 / 163 (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 |
| Cerebrovascular insufficiency | | | |
| subjects affected / exposed | 0 / 221 (0.00%) | 0 / 172 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ischaemic stroke | | | |
| subjects affected / exposed | 2 / 221 (0.90%) | 0 / 172 (0.00%) | 1 / 163 (0.61%) |
| 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 | 1 / 221 (0.45%) | 1 / 172 (0.58%) | 0 / 163 (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 |
| Eye disorders | | | |
| Cataract | | | |
| subjects affected / exposed | 0 / 221 (0.00%) | 1 / 172 (0.58%) | 0 / 163 (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 |
| Cataract nuclear | | | |
| subjects affected / exposed | 0 / 221 (0.00%) | 0 / 172 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vitreous haemorrhage | | | |
| subjects affected / exposed | 0 / 221 (0.00%) | 1 / 172 (0.58%) | 0 / 163 (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 |
| Gastrointestinal disorders | | | |
| Constipation | | | |
| subjects affected / exposed | 1 / 221 (0.45%) | 1 / 172 (0.58%) | 0 / 163 (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 |
| Diarrhoea | | | |
| subjects affected / exposed | 0 / 221 (0.00%) | 1 / 172 (0.58%) | 0 / 163 (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 |
| Gastritis erosive | | | |
| subjects affected / exposed | 0 / 221 (0.00%) | 0 / 172 (0.00%) | 1 / 163 (0.61%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 0 / 221 (0.00%) | 0 / 172 (0.00%) | 1 / 163 (0.61%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Inguinal hernia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 221 (0.00%) | 0 / 172 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pancreatitis | | | |
| subjects affected / exposed | 0 / 221 (0.00%) | 1 / 172 (0.58%) | 0 / 163 (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 |
| Small intestinal perforation | | | |
| subjects affected / exposed | 0 / 221 (0.00%) | 0 / 172 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Intestinal haemorrhage | | | |
| subjects affected / exposed | 0 / 221 (0.00%) | 0 / 172 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatobiliary disorders | | | |
| Acute hepatic failure | | | |
| subjects affected / exposed | 0 / 221 (0.00%) | 0 / 172 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatitis | | | |
| subjects affected / exposed | 0 / 221 (0.00%) | 0 / 172 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skin and subcutaneous tissue disorders | | | |
| Skin ulcer | | | |
| subjects affected / exposed | 0 / 221 (0.00%) | 0 / 172 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Stasis dermatitis | | | |
| subjects affected / exposed | 0 / 221 (0.00%) | 0 / 172 (0.00%) | 1 / 163 (0.61%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diabetic foot | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 221 (0.45%) | 1 / 172 (0.58%) | 0 / 163 (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 |
| Renal and urinary disorders | | | |
| Azotaemia | | | |
| subjects affected / exposed | 1 / 221 (0.45%) | 0 / 172 (0.00%) | 0 / 163 (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 |
| Haematuria | | | |
| subjects affected / exposed | 0 / 221 (0.00%) | 1 / 172 (0.58%) | 1 / 163 (0.61%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nephrolithiasis | | | |
| subjects affected / exposed | 0 / 221 (0.00%) | 0 / 172 (0.00%) | 1 / 163 (0.61%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nephropathy toxic | | | |
| subjects affected / exposed | 0 / 221 (0.00%) | 0 / 172 (0.00%) | 1 / 163 (0.61%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal failure | | | |
| subjects affected / exposed | 1 / 221 (0.45%) | 2 / 172 (1.16%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 2 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal failure acute | | | |
| subjects affected / exposed | 0 / 221 (0.00%) | 5 / 172 (2.91%) | 1 / 163 (0.61%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 5 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| Renal failure chronic | | | |
| subjects affected / exposed | 0 / 221 (0.00%) | 0 / 172 (0.00%) | 3 / 163 (1.84%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 2 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal impairment | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 221 (0.00%) | 0 / 172 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Endocrine disorders | | | |
| Hyperthyroidism | | | |
| subjects affected / exposed | 1 / 221 (0.45%) | 0 / 172 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Muscle haemorrhage | | | |
| subjects affected / exposed | 0 / 221 (0.00%) | 0 / 172 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Rhabdomyolysis | | | |
| subjects affected / exposed | 0 / 221 (0.00%) | 0 / 172 (0.00%) | 0 / 163 (0.00%) |
| 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 | | | |
| Bronchitis | | | |
| subjects affected / exposed | 0 / 221 (0.00%) | 1 / 172 (0.58%) | 0 / 163 (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 |
| Bronchopneumonia | | | |
| subjects affected / exposed | 1 / 221 (0.45%) | 1 / 172 (0.58%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cellulitis | | | |
| subjects affected / exposed | 0 / 221 (0.00%) | 0 / 172 (0.00%) | 0 / 163 (0.00%) |
| 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 | | | |
| subjects affected / exposed | 0 / 221 (0.00%) | 0 / 172 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|---|---|---|
| Erysipelas | | | |
| subjects affected / exposed | 2 / 221 (0.90%) | 1 / 172 (0.58%) | 0 / 163 (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 |
| Gastrointestinal infection | | | |
| subjects affected / exposed | 0 / 221 (0.00%) | 0 / 172 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infection | | | |
| subjects affected / exposed | 0 / 221 (0.00%) | 0 / 172 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lymphangitis | | | |
| subjects affected / exposed | 0 / 221 (0.00%) | 0 / 172 (0.00%) | 1 / 163 (0.61%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Necrotising fasciitis | | | |
| subjects affected / exposed | 0 / 221 (0.00%) | 1 / 172 (0.58%) | 0 / 163 (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 |
| Osteomyelitis | | | |
| subjects affected / exposed | 0 / 221 (0.00%) | 1 / 172 (0.58%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia | | | |
| subjects affected / exposed | 1 / 221 (0.45%) | 3 / 172 (1.74%) | 3 / 163 (1.84%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 3 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia legionella | | | |
| subjects affected / exposed | 0 / 221 (0.00%) | 0 / 172 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Sepsis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 221 (0.45%) | 0 / 172 (0.00%) | 0 / 163 (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 |
| Septic shock | | | |
| subjects affected / exposed | 2 / 221 (0.90%) | 0 / 172 (0.00%) | 0 / 163 (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 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 221 (0.00%) | 1 / 172 (0.58%) | 0 / 163 (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 |
| Urinary tract infection | | | |
| subjects affected / exposed | 0 / 221 (0.00%) | 1 / 172 (0.58%) | 1 / 163 (0.61%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Rectal abscess | | | |
| subjects affected / exposed | 0 / 221 (0.00%) | 0 / 172 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Staphylococcal bacteraemia | | | |
| subjects affected / exposed | 1 / 221 (0.45%) | 0 / 172 (0.00%) | 0 / 163 (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 |
| Pneumococcal sepsis | | | |
| subjects affected / exposed | 0 / 221 (0.00%) | 0 / 172 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Asymptomatic bacteriuria | | | |
| subjects affected / exposed | 0 / 221 (0.00%) | 0 / 172 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Escherichia infection | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 221 (0.00%) | 0 / 172 (0.00%) | 1 / 163 (0.61%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory tract infection viral | | | |
| subjects affected / exposed | 0 / 221 (0.00%) | 0 / 172 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory tract infection | | | |
| subjects affected / exposed | 0 / 221 (0.00%) | 0 / 172 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Enterocolitis bacterial | | | |
| subjects affected / exposed | 0 / 221 (0.00%) | 0 / 172 (0.00%) | 0 / 163 (0.00%) |
| 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 | 1 / 221 (0.45%) | 0 / 172 (0.00%) | 0 / 163 (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 |
| Diabetes mellitus | | | |
| subjects affected / exposed | 1 / 221 (0.45%) | 0 / 172 (0.00%) | 1 / 163 (0.61%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hyperkalaemia | | | |
| subjects affected / exposed | 5 / 221 (2.26%) | 6 / 172 (3.49%) | 6 / 163 (3.68%) |
| occurrences causally related to treatment / all | 5 / 5 | 4 / 6 | 5 / 6 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypoglycaemia | | | |
| subjects affected / exposed | 1 / 221 (0.45%) | 0 / 172 (0.00%) | 0 / 163 (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 |
| Hypokalaemia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 221 (0.00%) | 0 / 172 (0.00%) | 2 / 163 (1.23%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hyponatraemia | | | |
| subjects affected / exposed | 0 / 221 (0.00%) | 1 / 172 (0.58%) | 1 / 163 (0.61%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypovolaemia | | | |
| subjects affected / exposed | 1 / 221 (0.45%) | 1 / 172 (0.58%) | 0 / 163 (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 |
| Type 2 diabetes mellitus | | | |
| subjects affected / exposed | 0 / 221 (0.00%) | 0 / 172 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| **Serious adverse events** | Finerenone (BAY94-8862) 7.5-15 mg OD | Finerenone (BAY94-8862) 10-20 mg OD | Finerenone (BAY94-8862) 5-10 mg OD |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 52 / 167 (31.14%) | 46 / 169 (27.22%) | 47 / 163 (28.83%) |
| number of deaths (all causes) | 12 | 2 | 9 |
| number of deaths resulting from adverse events | | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Metastases to liver | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Rectal adenocarcinoma | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lung neoplasm | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 167 (0.00%) | 1 / 169 (0.59%) | 0 / 163 (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 |
| Vascular disorders | | | |
| Aortic stenosis | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Circulatory collapse | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypotension | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | 0 / 169 (0.00%) | 0 / 163 (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 |
| Orthostatic hypotension | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | 0 / 169 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Peripheral ischaemia | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | 0 / 169 (0.00%) | 0 / 163 (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 |
| Deep vein thrombosis | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | 1 / 163 (0.61%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Femoral artery occlusion | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haemodynamic instability | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 167 (0.00%) | 1 / 169 (0.59%) | 0 / 163 (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 |
| Surgical and medical procedures | | | |
| Cardiac pacemaker insertion | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 2 / 169 (1.18%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac pacemaker removal | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 1 / 169 (0.59%) | 0 / 163 (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 |
| Cardioversion | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Foot amputation | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | 0 / 169 (0.00%) | 0 / 163 (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 |
| Toe amputation | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Implantable defibrillator insertion | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | 0 / 163 (0.00%) |
| 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 assist device insertion | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | 1 / 163 (0.61%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac rehabilitation therapy | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | 0 / 163 (0.00%) |
| 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 resynchronisation therapy | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | 0 / 169 (0.00%) | 0 / 163 (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 |
| Cardiac ablation | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 1 / 169 (0.59%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Tooth extraction | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | 0 / 169 (0.00%) | 0 / 163 (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 |
| Percutaneous coronary intervention | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General disorders and administration site conditions | | | |
| Chest pain | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | 1 / 169 (0.59%) | 0 / 163 (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 |
| Malaise | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pyrexia | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | 0 / 169 (0.00%) | 0 / 163 (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 |
| Sudden death | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 167 (0.60%) | 0 / 169 (0.00%) | 1 / 163 (0.61%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| Sudden cardiac death | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | 2 / 163 (1.23%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| Oedema due to cardiac disease | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Implant site haematoma | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Implant site ulcer | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Stent-graft endoleak | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| **Reproductive system and breast disorders** | | | |
| Benign prostatic hyperplasia | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | 1 / 163 (0.61%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| **Respiratory, thoracic and mediastinal disorders** | | | |
| Acute pulmonary oedema | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 1 / 169 (0.59%) | 0 / 163 (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 |

| | | | |
|---|---|---|---|
| Choking | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | 1 / 163 (0.61%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Chronic obstructive pulmonary disease | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 1 / 169 (0.59%) | 0 / 163 (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 |
| Cough | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | 0 / 169 (0.00%) | 0 / 163 (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 |
| Dyspnoea | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dyspnoea exertional | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | 0 / 169 (0.00%) | 0 / 163 (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 |
| Epistaxis | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lung disorder | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pleural effusion | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonitis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 167 (0.60%) | 0 / 169 (0.00%) | 0 / 163 (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 |
| Pulmonary embolism | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | 1 / 163 (0.61%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary oedema | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory failure | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Obstructive airways disorder | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | 0 / 163 (0.00%) |
| 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 | | | |
| Completed suicide | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Delirium | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Sleep disorder | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | 0 / 169 (0.00%) | 0 / 163 (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 | 0 / 167 (0.00%) | 0 / 169 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Psychotic disorder | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 1 / 169 (0.59%) | 0 / 163 (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 |
| Investigations | | | |
| Blood creatinine increased | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood potassium increased | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | 1 / 169 (0.59%) | 2 / 163 (1.23%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 1 | 2 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| International normalised ratio increased | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Computerised tomogram abdomen abnormal | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Troponin T increased | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | 1 / 163 (0.61%) |
| 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 enzyme increased | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Injury, poisoning and procedural | | | |

| | | | |
|---|---|---|---|
| complications | | | |
| Accident | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Femur fracture | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | 0 / 169 (0.00%) | 0 / 163 (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 |
| Hip fracture | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Incisional hernia | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Overdose | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | 1 / 163 (0.61%) |
| 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 / 167 (0.00%) | 0 / 169 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Contusion | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 1 / 169 (0.59%) | 0 / 163 (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 |
| Brain contusion | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Allergic transfusion reaction | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Toxicity to various agents | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | 1 / 163 (0.61%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac disorders | | | |
| Acute myocardial infarction | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 1 / 169 (0.59%) | 0 / 163 (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 pectoris | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Atrial fibrillation | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | 2 / 169 (1.18%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Atrial flutter | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | 1 / 163 (0.61%) |
| 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 tachycardia | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | 0 / 169 (0.00%) | 0 / 163 (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 |
| Atrioventricular block complete | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 1 / 169 (0.59%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac arrest | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 167 (0.60%) | 0 / 169 (0.00%) | 1 / 163 (0.61%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Cardiac failure | | | |
| subjects affected / exposed | 21 / 167 (12.57%) | 11 / 169 (6.51%) | 15 / 163 (9.20%) |
| occurrences causally related to treatment / all | 1 / 33 | 0 / 12 | 0 / 17 |
| deaths causally related to treatment / all | 0 / 4 | 0 / 0 | 0 / 2 |
| Cardiac failure acute | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | 3 / 169 (1.78%) | 3 / 163 (1.84%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 4 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac failure chronic | | | |
| subjects affected / exposed | 8 / 167 (4.79%) | 6 / 169 (3.55%) | 7 / 163 (4.29%) |
| occurrences causally related to treatment / all | 0 / 9 | 0 / 6 | 0 / 7 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac failure congestive | | | |
| subjects affected / exposed | 2 / 167 (1.20%) | 0 / 169 (0.00%) | 2 / 163 (1.23%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiogenic shock | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Coronary artery disease | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Coronary artery occlusion | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Coronary artery stenosis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | 0 / 163 (0.00%) |
| 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 failure | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Mitral valve incompetence | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Myocardial infarction | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Myocardial ischaemia | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pericardial haemorrhage | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | 0 / 169 (0.00%) | 0 / 163 (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 |
| Right ventricular failure | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 1 / 169 (0.59%) | 0 / 163 (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 |
| Sick sinus syndrome | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | 0 / 163 (0.00%) |
| 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 / 167 (0.00%) | 0 / 169 (0.00%) | 1 / 163 (0.61%) |
| 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 arrhythmia | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 1 / 169 (0.59%) | 0 / 163 (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 |
| Ventricular fibrillation | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | 0 / 163 (0.00%) |
| 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 tachycardia | | | |
| subjects affected / exposed | 3 / 167 (1.80%) | 1 / 169 (0.59%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Left ventricular dysfunction | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiopulmonary failure | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | 0 / 163 (0.00%) |
| 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 coronary syndrome | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | 0 / 163 (0.00%) |
| 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 ventricular thrombosis | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | 0 / 163 (0.00%) |
| 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 tachyarrhythmia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiovascular insufficiency | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| Cerebellar syndrome | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cerebrovascular accident | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | 0 / 169 (0.00%) | 0 / 163 (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 |
| Dizziness | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Embolic stroke | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haemorrhage intracranial | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Loss of consciousness | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorder | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Status epilepticus | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 1 / 169 (0.59%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Syncope | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | 0 / 169 (0.00%) | 1 / 163 (0.61%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vocal cord paralysis | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cerebrovascular insufficiency | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | 1 / 163 (0.61%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ischaemic stroke | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | 0 / 169 (0.00%) | 0 / 163 (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 |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Eye disorders | | | |
| Cataract | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cataract nuclear | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 167 (0.60%) | 0 / 169 (0.00%) | 0 / 163 (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 |
| Vitreous haemorrhage | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | 0 / 163 (0.00%) |
| 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 | | | |
| Constipation | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 1 / 169 (0.59%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diarrhoea | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastritis erosive | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 1 / 169 (0.59%) | 0 / 163 (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 |
| Gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 1 / 169 (0.59%) | 0 / 163 (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 |
| Inguinal hernia | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 1 / 169 (0.59%) | 0 / 163 (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 |
| Pancreatitis | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Small intestinal perforation | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 167 (0.00%) | 1 / 169 (0.59%) | 0 / 163 (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 |
| Intestinal haemorrhage | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 1 / 169 (0.59%) | 0 / 163 (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 |
| Hepatobiliary disorders | | | |
| Acute hepatic failure | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | 1 / 163 (0.61%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatitis | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | 1 / 163 (0.61%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skin and subcutaneous tissue disorders | | | |
| Skin ulcer | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 1 / 169 (0.59%) | 0 / 163 (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 |
| Stasis dermatitis | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diabetic foot | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 1 / 169 (0.59%) | 0 / 163 (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 |
| Renal and urinary disorders | | | |
| Azotaemia | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|---|---|---|
| Haematuria | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | 1 / 163 (0.61%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nephrolithiasis | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nephropathy toxic | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | 0 / 163 (0.00%) |
| 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 failure | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | 0 / 169 (0.00%) | 1 / 163 (0.61%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal failure acute | | | |
| subjects affected / exposed | 4 / 167 (2.40%) | 2 / 169 (1.18%) | 1 / 163 (0.61%) |
| occurrences causally related to treatment / all | 1 / 4 | 0 / 2 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal failure chronic | | | |
| subjects affected / exposed | 2 / 167 (1.20%) | 0 / 169 (0.00%) | 1 / 163 (0.61%) |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal impairment | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | 1 / 169 (0.59%) | 0 / 163 (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 |
| Endocrine disorders | | | |
| Hyperthyroidism | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | 0 / 163 (0.00%) |
| 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 | | | |
| Muscle haemorrhage | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | 1 / 163 (0.61%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Rhabdomyolysis | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | 0 / 169 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Bronchitis | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 1 / 169 (0.59%) | 1 / 163 (0.61%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bronchopneumonia | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | 0 / 169 (0.00%) | 0 / 163 (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 |
| Cellulitis | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | 2 / 163 (1.23%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Endocarditis | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | 0 / 169 (0.00%) | 0 / 163 (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 |
| Erysipelas | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | 0 / 163 (0.00%) |
| 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 infection | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | 0 / 169 (0.00%) | 0 / 163 (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 |

| | | | |
|---|---|---|---|
| Infection | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 1 / 169 (0.59%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lymphangitis | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Necrotising fasciitis | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Osteomyelitis | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | 2 / 169 (1.18%) | 3 / 163 (1.84%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia legionella | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | 1 / 163 (0.61%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Sepsis | | | |
| subjects affected / exposed | 2 / 167 (1.20%) | 2 / 169 (1.18%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| Septic shock | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | 1 / 163 (0.61%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Upper respiratory tract infection | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urinary tract infection | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 1 / 169 (0.59%) | 0 / 163 (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 |
| Rectal abscess | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 1 / 169 (0.59%) | 0 / 163 (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 |
| Staphylococcal bacteraemia | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumococcal sepsis | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | 0 / 169 (0.00%) | 0 / 163 (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 |
| Asymptomatic bacteriuria | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | 0 / 169 (0.00%) | 0 / 163 (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 |
| Escherichia infection | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory tract infection viral | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | 1 / 163 (0.61%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory tract infection | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 167 (0.60%) | 1 / 169 (0.59%) | 0 / 163 (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 |
| Enterocolitis bacterial | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | 1 / 163 (0.61%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diabetes mellitus | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hyperkalaemia | | | |
| subjects affected / exposed | 7 / 167 (4.19%) | 5 / 169 (2.96%) | 4 / 163 (2.45%) |
| occurrences causally related to treatment / all | 6 / 7 | 5 / 5 | 3 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypoglycaemia | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypokalaemia | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | 1 / 169 (0.59%) | 0 / 163 (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 |
| Hyponatraemia | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 2 / 169 (1.18%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypovolaemia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | 0 / 163 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Type 2 diabetes mellitus | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | 0 / 169 (0.00%) | 0 / 163 (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 |

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

| **Non-serious adverse events** | Eplerenone (INSPRA®) | Finerenone(BAY94-8862) 2.5-5 mg OD | Finerenone (BAY94-8862) 15-20 mg OD |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 85 / 221 (38.46%) | 63 / 172 (36.63%) | 65 / 163 (39.88%) |
| Investigations | | | |
| Blood creatinine increased | | | |
| subjects affected / exposed | 12 / 221 (5.43%) | 5 / 172 (2.91%) | 8 / 163 (4.91%) |
| occurrences (all) | 14 | 5 | 9 |
| Vascular disorders | | | |
| Hypotension | | | |
| subjects affected / exposed | 11 / 221 (4.98%) | 7 / 172 (4.07%) | 8 / 163 (4.91%) |
| occurrences (all) | 13 | 7 | 8 |
| Cardiac disorders | | | |
| Cardiac failure | | | |
| subjects affected / exposed | 13 / 221 (5.88%) | 14 / 172 (8.14%) | 10 / 163 (6.13%) |
| occurrences (all) | 14 | 20 | 10 |
| Nervous system disorders | | | |
| Dizziness | | | |
| subjects affected / exposed | 12 / 221 (5.43%) | 8 / 172 (4.65%) | 6 / 163 (3.68%) |
| occurrences (all) | 13 | 8 | 7 |
| Gastrointestinal disorders | | | |
| Diarrhoea | | | |
| subjects affected / exposed | 8 / 221 (3.62%) | 6 / 172 (3.49%) | 7 / 163 (4.29%) |
| occurrences (all) | 8 | 6 | 9 |
| Nausea | | | |
| subjects affected / exposed | 7 / 221 (3.17%) | 9 / 172 (5.23%) | 6 / 163 (3.68%) |
| occurrences (all) | 7 | 12 | 6 |

| | | | |
|---|---|---|---|
| Respiratory, thoracic and mediastinal disorders | | | |
| Dyspnoea | | | |
| subjects affected / exposed | 11 / 221 (4.98%) | 12 / 172 (6.98%) | 10 / 163 (6.13%) |
| occurrences (all) | 12 | 13 | 11 |
| Renal and urinary disorders | | | |
| Renal impairment | | | |
| subjects affected / exposed | 8 / 221 (3.62%) | 6 / 172 (3.49%) | 9 / 163 (5.52%) |
| occurrences (all) | 10 | 8 | 9 |
| Metabolism and nutrition disorders | | | |
| Hyperkalaemia | | | |
| subjects affected / exposed | 8 / 221 (3.62%) | 5 / 172 (2.91%) | 9 / 163 (5.52%) |
| occurrences (all) | 9 | 5 | 9 |
| Hypokalaemia | | | |
| subjects affected / exposed | 34 / 221 (15.38%) | 20 / 172 (11.63%) | 17 / 163 (10.43%) |
| occurrences (all) | 44 | 26 | 20 |

| **Non-serious adverse events** | Finerenone (BAY94-8862) 7.5-15 mg OD | Finerenone (BAY94-8862) 10-20 mg OD | Finerenone (BAY94-8862) 5-10 mg OD |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 50 / 167 (29.94%) | 50 / 169 (29.59%) | 59 / 163 (36.20%) |
| Investigations | | | |
| Blood creatinine increased | | | |
| subjects affected / exposed | 3 / 167 (1.80%) | 4 / 169 (2.37%) | 7 / 163 (4.29%) |
| occurrences (all) | 3 | 4 | 7 |
| Vascular disorders | | | |
| Hypotension | | | |
| subjects affected / exposed | 11 / 167 (6.59%) | 7 / 169 (4.14%) | 11 / 163 (6.75%) |
| occurrences (all) | 14 | 7 | 12 |
| Cardiac disorders | | | |
| Cardiac failure | | | |
| subjects affected / exposed | 5 / 167 (2.99%) | 7 / 169 (4.14%) | 10 / 163 (6.13%) |
| occurrences (all) | 6 | 7 | 11 |
| Nervous system disorders | | | |
| Dizziness | | | |
| subjects affected / exposed | 6 / 167 (3.59%) | 7 / 169 (4.14%) | 6 / 163 (3.68%) |
| occurrences (all) | 6 | 7 | 7 |
| Gastrointestinal disorders | | | |

| | | | |
|---|---|---|---|
| Diarrhoea | | | |
| subjects affected / exposed | 10 / 167 (5.99%) | 6 / 169 (3.55%) | 6 / 163 (3.68%) |
| occurrences (all) | 11 | 6 | 6 |
| Nausea | | | |
| subjects affected / exposed | 5 / 167 (2.99%) | 2 / 169 (1.18%) | 2 / 163 (1.23%) |
| occurrences (all) | 7 | 2 | 2 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Dyspnoea | | | |
| subjects affected / exposed | 6 / 167 (3.59%) | 3 / 169 (1.78%) | 7 / 163 (4.29%) |
| occurrences (all) | 7 | 4 | 7 |
| Renal and urinary disorders | | | |
| Renal impairment | | | |
| subjects affected / exposed | 6 / 167 (3.59%) | 8 / 169 (4.73%) | 7 / 163 (4.29%) |
| occurrences (all) | 10 | 11 | 9 |
| Metabolism and nutrition disorders | | | |
| Hyperkalaemia | | | |
| subjects affected / exposed | 7 / 167 (4.19%) | 6 / 169 (3.55%) | 7 / 163 (4.29%) |
| occurrences (all) | 7 | 6 | 10 |
| Hypokalaemia | | | |
| subjects affected / exposed | 15 / 167 (8.98%) | 14 / 169 (8.28%) | 21 / 163 (12.88%) |
| occurrences (all) | 30 | 18 | 28 |

## More information

## Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 21 January 2014 | 1. The specification that potassium was to be monitored in serum was removed; potassium during the treatment period could be monitored in serum or plasma. A paragraph detailing the prohibited use of potassium lowering agents was added. 2. The inclusion criteria were modified with respect to the inclusion of women of childbearing potential. 3. A cap of 45% for subjects with atrial fibrillation was introduced. 4. Definitions of "mineralocorticoid receptor antagonist (MRA) naïve" and "previous MRA use" for stratification were added. 5. It was clarified that concomitant treatment with an angiotensin-converting enzyme inhibitor (ACEI) and an angiotensin receptor blocker (ARB) was prohibited. Diltiazem was removed from the list of moderate cytochrome P450 isoenzyme 3A4 (CYP3A4) inhibitory. 6. A pregnancy test was added at the screening visit for women of childbearing potential. 7. It was clarified that the latest assessed left ventricular ejection fraction (LVEF) value recorded for medical history had to be prior to the screening visit. 8. The symptom burden domain and the total symptom scale were added to the KCCQ. 9. The requirement to report adverse event (AEs) of special interest as serious adverse event (SAEs) was added. 10. An un-blinding waiver and exemption from expedited reporting requirements were introduced for specific disease related AEs. 11. The assessment schedule if the screening visit and Visit 1 (Day 1) took place on the same day was clarified. 12. The definition of the SAF was modified to all randomized subjects who took at least one dose of study drug and with data after beginning of treatment. 13. Further details were added on general statistical considerations, the analysis of the primary efficacy variable, health related quality of life, AEs, safety laboratory parameters, and safety biomarkers, and subgroup analyses. |

Notes:

## 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.

Occurrence of "±" in relation with geometric CV is autogenerated and cannot be deleted. Decimal places were automatically truncated if last decimal equals zero.

Notes:

## Online references

http://www.ncbi.nlm.nih.gov/pubmed/25678098

http://www.ncbi.nlm.nih.gov/pubmed/27130705