



Clinical trial results:

Factor XI LICA to Reduce Thrombotic Events in End-Stage Renal Disease Patients on Hemodialysis: A Phase 2, Randomized, Double-Blind, Placebo-Controlled Study of the Safety, Pharmacokinetics, and Pharmacodynamics of Multiple Doses of BAY 2976217

Summary

| | |
|--------------------------|-------------------|
| EudraCT number | 2019-003927-39 |
| Trial protocol | CZ DE LV GR BG HU |
| Global end of trial date | 12 May 2022 |

Results information

| | |
|--------------------------------|--------------|
| Result version number | v1 (current) |
| This version publication date | 22 May 2023 |
| First version publication date | 22 May 2023 |

Trial information

Trial identification

| | |
|-----------------------|------------------|
| Sponsor protocol code | BAY2976217/21170 |
|-----------------------|------------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT04534114 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | Bayer AG |
| Sponsor organisation address | Kaiser Wilhelm Allee, Leverkusen, Germany, D-51368 |
| 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 | 12 May 2022 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 12 May 2022 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The main objective was to evaluate the safety of fesomersen as compared to placebo.

Protection of trial subjects:

The conduct of this clinical study met all local legal and regulatory requirements. The study was conducted in accordance with ethical principles that have their origin in the Declaration of Helsinki and the International Council for Harmonization guideline E6: Good Clinical Practice. Before entering the study, the informed consent was read by and explained to all the 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 | 04 September 2020 |
| 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 | Belgium: 11 |
| Country: Number of subjects enrolled | Bulgaria: 21 |
| Country: Number of subjects enrolled | Czechia: 14 |
| Country: Number of subjects enrolled | Germany: 9 |
| Country: Number of subjects enrolled | Greece: 23 |
| Country: Number of subjects enrolled | Hungary: 10 |
| Country: Number of subjects enrolled | Canada: 8 |
| Country: Number of subjects enrolled | Japan: 32 |
| Country: Number of subjects enrolled | Korea, Republic of: 1 |
| Country: Number of subjects enrolled | Latvia: 7 |
| Country: Number of subjects enrolled | Spain: 21 |
| Country: Number of subjects enrolled | Russian Federation: 88 |
| Country: Number of subjects enrolled | Taiwan: 9 |
| Country: Number of subjects enrolled | Ukraine: 36 |
| Country: Number of subjects enrolled | United States: 17 |
| Worldwide total number of subjects | 307 |
| EEA total number of subjects | 116 |

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) | 200 |
| From 65 to 84 years | 102 |
| 85 years and over | 5 |

Subject disposition

Recruitment

Recruitment details:

Study was conducted at 69 study centers in 15 countries between 04-SEP-2020 (first subject first visit) and 12-MAY-2022 (last subject last visit).

Pre-assignment

Screening details:

From 359 subjects screened, 51 subjects were screening failure and a total of 308 subjects were randomized and 307 were treated either with fesomersen or placebo.

Period 1

| | |
|------------------------------|--------------------------------|
| Period 1 title | Main treatment period |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator, Monitor |

Arms

| | |
|------------------------------|------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Fesomersen 40 mg |

Arm description:

Subjects received monthly subcutaneous treatment with 40 mg fesomersen (Factor XI LICA).
LICA=Ligand conjugated antisense oligonucleotide.

| | |
|--|------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Fesomersen sodium |
| Investigational medicinal product code | BAY2976217 |
| Other name | Factor XI LICA |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Subcutaneous treatment with 40 mg fesomersen.

| | |
|------------------|------------------|
| Arm title | Fesomersen 80 mg |
|------------------|------------------|

Arm description:

Subjects received monthly subcutaneous treatment with 80 mg fesomersen (Factor XI LICA).
LICA=Ligand conjugated antisense oligonucleotide.

| | |
|--|------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Fesomersen sodium |
| Investigational medicinal product code | BAY2976217 |
| Other name | Factor XI LICA |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Subcutaneous treatment with 80 mg fesomersen.

| | |
|------------------|-------------------|
| Arm title | Fesomersen 120 mg |
|------------------|-------------------|

Arm description:

Subjects received monthly subcutaneous treatment with 120 mg fesomersen (Factor XI LICA).
LICA=Ligand conjugated antisense oligonucleotide.

| | |
|----------|--------------|
| Arm type | Experimental |
|----------|--------------|

| | |
|--|------------------------|
| Investigational medicinal product name | Fesomersen sodium |
| Investigational medicinal product code | BAY2976217 |
| Other name | Factor XI LICA |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Subcutaneous treatment with 120 mg fesomersen.

| | |
|------------------|---------|
| Arm title | Placebo |
|------------------|---------|

Arm description:

Subjects received monthly subcutaneous treatment with matching placebo to fesomersen (Factor XI LICA). LICA=Ligand conjugated antisense oligonucleotide.

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

Dosage and administration details:

Matching placebo.

| Number of subjects in period 1 | Fesomersen 40 mg | Fesomersen 80 mg | Fesomersen 120 mg |
|--|------------------|------------------|-------------------|
| Started | 77 | 79 | 76 |
| Completed | 67 | 66 | 64 |
| Not completed | 10 | 13 | 12 |
| Adverse event, serious fatal | 1 | - | - |
| COVID-19 pandemic: Adverse event | - | 1 | 1 |
| Physician decision | - | - | - |
| COVID-19 pandemic: withdrawal following protocol | 1 | 3 | 3 |
| Participant decision | 1 | 3 | 3 |
| COVID-19 pandemic: Death | - | 1 | - |
| Adverse event, non-fatal | 4 | 2 | 1 |
| Protocol-specified withdrawal criterion met | 2 | 1 | 4 |
| Other reason | 1 | 1 | - |
| COVID-19 pandemic: Participant decision | - | 1 | - |

| Number of subjects in period 1 | Placebo |
|---------------------------------------|---------|
| Started | 75 |
| Completed | 61 |
| Not completed | 14 |
| Adverse event, serious fatal | 1 |
| COVID-19 pandemic: Adverse event | - |
| Physician decision | 1 |

| | |
|--|---|
| COVID-19 pandemic: withdrawal following protocol | 1 |
| Participant decision | 1 |
| COVID-19 pandemic: Death | 2 |
| Adverse event, non-fatal | 2 |
| Protocol-specified withdrawal criterion met | 6 |
| Other reason | - |
| COVID-19 pandemic: Participant decision | - |

Period 2

| | |
|------------------------------|--------------------------------|
| Period 2 title | Extension treatment period |
| Is this the baseline period? | No |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator, Monitor |

Arms

| | |
|------------------------------|------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Fesomersen 40 mg |

Arm description:

Subjects received monthly subcutaneous treatment with 40 mg fesomersen (Factor XI LICA).
LICA=Ligand conjugated antisense oligonucleotide.

| | |
|--|------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Fesomersen sodium |
| Investigational medicinal product code | BAY2976217 |
| Other name | Factor XI LICA |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Subcutaneous treatment with 40 mg fesomersen.

| | |
|------------------|------------------|
| Arm title | Fesomersen 80 mg |
|------------------|------------------|

Arm description:

Subjects received monthly subcutaneous treatment with 80 mg fesomersen (Factor XI LICA).
LICA=Ligand conjugated antisense oligonucleotide.

| | |
|--|------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Fesomersen sodium |
| Investigational medicinal product code | BAY2976217 |
| Other name | Factor XI LICA |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Subcutaneous treatment with 80 mg fesomersen.

| | |
|------------------|-------------------|
| Arm title | Fesomersen 120 mg |
|------------------|-------------------|

Arm description:

Subjects received monthly subcutaneous treatment with 120 mg fesomersen (Factor XI LICA).
LICA=Ligand conjugated antisense oligonucleotide.

| | |
|--|------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Fesomersen sodium |
| Investigational medicinal product code | BAY2976217 |
| Other name | Factor XI LICA |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Subcutaneous treatment with 120 mg fesomersen.

| | |
|------------------|---------|
| Arm title | Placebo |
|------------------|---------|

Arm description:

Subjects received monthly subcutaneous treatment with matching placebo to fesomersen (Factor XI LICA). LICA=Ligand conjugated antisense oligonucleotide.

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

Dosage and administration details:

Matching placebo.

| Number of subjects in period 2^[1] | Fesomersen 40 mg | Fesomersen 80 mg | Fesomersen 120 mg |
|---|------------------|------------------|-------------------|
| Started | 62 | 61 | 63 |
| Completed | 59 | 57 | 62 |
| Not completed | 3 | 4 | 1 |
| Adverse event, serious fatal | - | - | 1 |
| COVID-19 pandemic: withdrawal following protocol | 1 | - | - |
| COVID-19 pandemic: Death | - | - | - |
| Protocol-specified withdrawal criterion met | 2 | 2 | - |
| Adverse event, non-fatal | - | 1 | - |
| Other reason | - | 1 | - |

| Number of subjects in period 2^[1] | Placebo |
|---|---------|
| Started | 58 |
| Completed | 53 |
| Not completed | 5 |
| Adverse event, serious fatal | 2 |
| COVID-19 pandemic: withdrawal following protocol | - |
| COVID-19 pandemic: Death | 1 |
| Protocol-specified withdrawal criterion met | 1 |
| Adverse event, non-fatal | 1 |

| | |
|--------------|---|
| Other reason | - |
|--------------|---|

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: Not all subjects completed main treatment period entered extension treatment period.

Baseline characteristics

Reporting groups

| | |
|--|-------------------|
| Reporting group title | Fesomersen 40 mg |
| Reporting group description: Subjects received monthly subcutaneous treatment with 40 mg fesomersen (Factor XI LICA). LICA=Ligand conjugated antisense oligonucleotide. | |
| Reporting group title | Fesomersen 80 mg |
| Reporting group description: Subjects received monthly subcutaneous treatment with 80 mg fesomersen (Factor XI LICA). LICA=Ligand conjugated antisense oligonucleotide. | |
| Reporting group title | Fesomersen 120 mg |
| Reporting group description: Subjects received monthly subcutaneous treatment with 120 mg fesomersen (Factor XI LICA). LICA=Ligand conjugated antisense oligonucleotide. | |
| Reporting group title | Placebo |
| Reporting group description: Subjects received monthly subcutaneous treatment with matching placebo to fesomersen (Factor XI LICA). LICA=Ligand conjugated antisense oligonucleotide. | |

| Reporting group values | Fesomersen 40 mg | Fesomersen 80 mg | Fesomersen 120 mg |
|---|------------------|------------------|-------------------|
| Number of subjects | 77 | 79 | 76 |
| Age categorical Units: Subjects | | | |
| In utero | | | |
| Preterm newborn infants (gestational age < 37 wks) | | | |
| Newborns (0-27 days) | | | |
| Infants and toddlers (28 days-23 months) | | | |
| Children (2-11 years) | | | |
| Adolescents (12-17 years) | | | |
| Adults (18-64 years) | | | |
| From 65-84 years | | | |
| 85 years and over | | | |
| Age continuous Units: years | | | |
| arithmetic mean | 60.4 | 58.0 | 57.7 |
| standard deviation | ± 13.2 | ± 14.4 | ± 13.3 |
| Gender categorical Units: Subjects | | | |
| Female | 35 | 20 | 30 |
| Male | 42 | 59 | 46 |
| Race Units: Subjects | | | |
| Asian | 12 | 8 | 11 |
| Black or African american | 2 | 1 | 4 |
| Not reported | 1 | 0 | 0 |
| White | 62 | 70 | 61 |
| Ethnicity Units: Subjects | | | |

| | | | |
|------------------------|----|----|----|
| Hispanic or latino | 3 | 6 | 1 |
| Not hispanic or latino | 74 | 73 | 75 |
| Not reported | 0 | 0 | 0 |

| Reporting group values | Placebo | Total | |
|---|---------|-------|--|
| Number of subjects | 75 | 307 | |
| Age categorical Units: Subjects | | | |
| In utero | | 0 | |
| Preterm newborn infants (gestational age < 37 wks) | | 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) | | 0 | |
| From 65-84 years | | 0 | |
| 85 years and over | | 0 | |
| Age continuous Units: years | | | |
| arithmetic mean | 58.6 | | |
| standard deviation | ± 11.9 | - | |
| Gender categorical Units: Subjects | | | |
| Female | 22 | 107 | |
| Male | 53 | 200 | |
| Race Units: Subjects | | | |
| Asian | 13 | 44 | |
| Black or African american | 1 | 8 | |
| Not reported | 0 | 1 | |
| White | 61 | 254 | |
| Ethnicity Units: Subjects | | | |
| Hispanic or latino | 2 | 12 | |
| Not hispanic or latino | 72 | 294 | |
| Not reported | 1 | 1 | |

End points

End points reporting groups

| | |
|--|------------------------------------|
| Reporting group title | Fesomersen 40 mg |
| Reporting group description: Subjects received monthly subcutaneous treatment with 40 mg fesomersen (Factor XI LICA). LICA=Ligand conjugated antisense oligonucleotide. | |
| Reporting group title | Fesomersen 80 mg |
| Reporting group description: Subjects received monthly subcutaneous treatment with 80 mg fesomersen (Factor XI LICA). LICA=Ligand conjugated antisense oligonucleotide. | |
| Reporting group title | Fesomersen 120 mg |
| Reporting group description: Subjects received monthly subcutaneous treatment with 120 mg fesomersen (Factor XI LICA). LICA=Ligand conjugated antisense oligonucleotide. | |
| Reporting group title | Placebo |
| Reporting group description: Subjects received monthly subcutaneous treatment with matching placebo to fesomersen (Factor XI LICA). LICA=Ligand conjugated antisense oligonucleotide. | |
| Reporting group title | Fesomersen 40 mg |
| Reporting group description: Subjects received monthly subcutaneous treatment with 40 mg fesomersen (Factor XI LICA). LICA=Ligand conjugated antisense oligonucleotide. | |
| Reporting group title | Fesomersen 80 mg |
| Reporting group description: Subjects received monthly subcutaneous treatment with 80 mg fesomersen (Factor XI LICA). LICA=Ligand conjugated antisense oligonucleotide. | |
| Reporting group title | Fesomersen 120 mg |
| Reporting group description: Subjects received monthly subcutaneous treatment with 120 mg fesomersen (Factor XI LICA). LICA=Ligand conjugated antisense oligonucleotide. | |
| Reporting group title | Placebo |
| Reporting group description: Subjects received monthly subcutaneous treatment with matching placebo to fesomersen (Factor XI LICA). LICA=Ligand conjugated antisense oligonucleotide. | |
| Subject analysis set title | Safety analysis set (SAF) |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: Safety analysis set (SAF) includes all randomized subjects who received at least one dose of the study intervention according to actual treatment arm received. | |
| Subject analysis set title | Pharmacokinetic analysis set (PKS) |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: Pharmacokinetic analysis set (PKS) includes all fesomersen-treated subjects with at least 1 PK sample in accordance with the PK sampling schedule and without deviation from the protocol that would interfere with the evaluation of the PK data were included in the PK analysis. | |
| Subject analysis set title | Pharmacodynamic set (PDS) |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: Pharmacodynamic set (PDS) includes all subjects with at least 1 PD sample in accordance with the PD sampling schedule and without deviation from the protocol that would interfere with the evaluation of the PD data were included in the PD analysis. | |

Primary: Incidence of composite of major bleeding (MB) and clinically-relevant non-major bleeding (CRNMB) during the main treatment period and within the on-treatment time window, as assessed by blinded central independent adjudication committee (CIAC)

| | |
|-----------------|---|
| End point title | Incidence of composite of major bleeding (MB) and clinically-relevant non-major bleeding (CRNMB) during the main treatment period and within the on-treatment time window, as assessed by blinded central independent adjudication committee (CIAC) |
|-----------------|---|

End point description:

MB is defined as symptomatic bleeding and: 1) Fatal bleeding, and/or; 2) Bleeding in a critical area or organ, such as intracranial, intraspinal, intraocular, retroperitoneal, intraarticular or pericardial, or intramuscular with compartment syndrome, and/or; 3) Bleeding causing a fall in hemoglobin level of 20 g/L (2.0 g/dL) (1.24 mmol/L) or more, or leading to transfusion of two or more units of whole blood or red cells. CRNMB is defined as any sign or symptom of hemorrhage that does not fit the criteria for the ISTH definition of major bleeding but does meet at least one of the following criteria: 1) Requiring medical intervention by a healthcare professional; 2) Leading to hospitalization or increased level of care; 3) Prompting a face-to-face evaluation. n/100 person-years: number of subjects with incident events divided by the cumulative at-risk time in the reference population, where a subject is no longer at risk once an incident event occurred.

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

| End point values | Fesomersen 40 mg | Fesomersen 80 mg | Fesomersen 120 mg | Placebo |
|----------------------------------|-------------------|-------------------|-------------------|-------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 77 ^[1] | 79 ^[2] | 76 ^[3] | 75 ^[4] |
| Units: n/100 person-years | | | | |
| number (confidence interval 95%) | 9.0 (2.5 to 18.9) | 9.1 (2.5 to 19.1) | 6.1 (1.1 to 14.5) | 9.7 (2.7 to 20.4) |

Notes:

[1] - SAF

[2] - SAF

[3] - SAF

[4] - SAF

Statistical analyses

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

Statistical analysis description:

Fesomersen groups were compared to the placebo group using two-sided log-rank tests. Due to the exploratory nature of these analyses, no multiplicity adjustment was done. Cause-specific hazard ratio and corresponding 2-sided 95% confidence intervals, comparing the hazards for the event-of-interest in each of the Fesomersen groups with the placebo group were estimated based on three separate cause-specific Cox proportional hazards models as exploratory analysis.

| | |
|---|-----------------------------|
| Comparison groups | Fesomersen 40 mg v Placebo |
| Number of subjects included in analysis | 152 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.944 |
| Method | Logrank |
| Parameter estimate | Cause specific Hazard ratio |
| Point estimate | 0.94 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.19 |
| upper limit | 4.68 |

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

Statistical analysis description:

Fesomersen groups were compared to the placebo group using two-sided log-rank tests. Due to the exploratory nature of these analyses, no multiplicity adjustment was done. Cause-specific hazard ratio and corresponding 2-sided 95% confidence intervals, comparing the hazards for the event-of-interest in each of the Fesomersen groups with the placebo group were estimated based on three separate cause-specific Cox proportional hazards models as exploratory analysis.

| | |
|---|-----------------------------|
| Comparison groups | Fesomersen 80 mg v Placebo |
| Number of subjects included in analysis | 154 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.953 |
| Method | Logrank |
| Parameter estimate | Cause specific Hazard ratio |
| Point estimate | 0.95 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.19 |
| upper limit | 4.72 |

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

Statistical analysis description:

Fesomersen groups were compared to the placebo group using two-sided log-rank tests. Due to the exploratory nature of these analyses, no multiplicity adjustment was done. Cause-specific hazard ratio and corresponding 2-sided 95% confidence intervals, comparing the hazards for the event-of-interest in each of the Fesomersen groups with the placebo group were estimated based on three separate cause-specific Cox proportional hazards models as exploratory analysis.

| | |
|---|-----------------------------|
| Comparison groups | Fesomersen 120 mg v Placebo |
| Number of subjects included in analysis | 151 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.605 |
| Method | Logrank |
| Parameter estimate | Cause specific Hazard ratio |
| Point estimate | 0.63 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.1 |
| upper limit | 3.75 |

Secondary: Incidence of composite of MB and CRNMB during the main and extended treatment periods and within the on-treatment time window, as assessed by blinded CIAC

| | |
|-----------------|--|
| End point title | Incidence of composite of MB and CRNMB during the main and extended treatment periods and within the on-treatment time window, as assessed by blinded CIAC |
|-----------------|--|

End point description:

MB is defined as symptomatic bleeding and: 1) Fatal bleeding, and/or; 2) Bleeding in a critical area or organ, such as intracranial, intraspinal, intraocular, retroperitoneal, intraarticular or pericardial, or intramuscular with compartment syndrome, and/or; 3) Bleeding causing a fall in hemoglobin level of 20 g/L (2.0 g/dL) (1.24 mmol/L) or more, or leading to transfusion of two or more units of whole blood or red cells. CRNMB is defined as any sign or symptom of hemorrhage that does not fit the criteria for the ISTH definition of major bleeding but does meet at least one of the following criteria: 1) Requiring medical intervention by a healthcare professional; 2) Leading to hospitalization or increased level of care; 3) Prompting a face-to-face evaluation. n/100 person-years: number of subjects with incident events divided by the cumulative at-risk time in the reference population, where a subject is no longer at risk once an incident event occurred.

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

End point timeframe:

Up to 48 weeks

| End point values | Fesomersen 40 mg | Fesomersen 80 mg | Fesomersen 120 mg | Placebo |
|----------------------------------|--------------------|-------------------|-------------------|-------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 77 ^[5] | 79 ^[6] | 76 ^[7] | 75 ^[8] |
| Units: n/100 person-years | | | | |
| number (confidence interval 95%) | 10.7 (4.2 to 19.7) | 8.6 (2.9 to 16.7) | 6.4 (1.7 to 13.3) | 7.0 (1.9 to 14.8) |

Notes:

[5] - SAF

[6] - SAF

[7] - SAF

[8] - SAF

Statistical analyses

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

Statistical analysis description:

Fesomersen groups were compared to the placebo group using two-sided log-rank tests. Due to the exploratory nature of these analyses, no multiplicity adjustment was done. Cause-specific hazard ratio and corresponding 2-sided 95% confidence intervals, comparing the hazards for the event-of-interest in each of the Fesomersen groups with the placebo group were estimated based on three separate cause-specific Cox proportional hazards models as exploratory analysis.

| | |
|---|-----------------------------|
| Comparison groups | Fesomersen 40 mg v Placebo |
| Number of subjects included in analysis | 152 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.612 |
| Method | Logrank |
| Parameter estimate | Cause specific Hazard ratio |
| Point estimate | 1.45 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.34 |
| upper limit | 6.08 |

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

Statistical analysis description:

Fesomersen groups were compared to the placebo group using two-sided log-rank tests. Due to the exploratory nature of these analyses, no multiplicity adjustment was done. Cause-specific hazard ratio and corresponding 2-sided 95% confidence intervals, comparing the hazards for the event-of-interest in each of the Fesomersen groups with the placebo group were estimated based on three separate cause-specific Cox proportional hazards models as exploratory analysis.

| | |
|---|-----------------------------|
| Comparison groups | Fesomersen 80 mg v Placebo |
| Number of subjects included in analysis | 154 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.757 |
| Method | Logrank |
| Parameter estimate | Cause specific Hazard ratio |
| Point estimate | 1.27 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.28 |
| upper limit | 5.66 |

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

Statistical analysis description:

Fesomersen groups were compared to the placebo group using two-sided log-rank tests. Due to the exploratory nature of these analyses, no multiplicity adjustment was done. Cause-specific hazard ratio and corresponding 2-sided 95% confidence intervals, comparing the hazards for the event-of-interest in each of the Fesomersen groups with the placebo group were estimated based on three separate cause-specific Cox proportional hazards models as exploratory analysis.

| | |
|---|-----------------------------|
| Comparison groups | Fesomersen 120 mg v Placebo |
| Number of subjects included in analysis | 151 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.909 |
| Method | Logrank |
| Parameter estimate | Cause specific Hazard ratio |
| Point estimate | 0.91 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.18 |
| upper limit | 4.52 |

Secondary: Number of subjects with treatment-emergent adverse events (TEAEs) during the main treatment period and within the on-treatment time window and their severity

| | |
|-----------------|---|
| End point title | Number of subjects with treatment-emergent adverse events (TEAEs) during the main treatment period and within the on-treatment time window and their severity |
|-----------------|---|

End point description:

TEAEs were analyzed during the on-treatment time window within the main treatment period in the safety analysis set (SAF). Data observed from the randomization date until the end of the main treatment period. TEAEs were defined as events occurring after first study intervention administration and up to 20 weeks after last study intervention administration.

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

End point timeframe:

Up to 24 weeks

| End point values | Fesomersen 40 mg | Fesomersen 80 mg | Fesomersen 120 mg | Placebo |
|--|-------------------|--------------------|--------------------|--------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 77 ^[9] | 79 ^[10] | 76 ^[11] | 75 ^[12] |
| Units: Subjects | | | | |
| Any TEAE | 54 | 56 | 55 | 55 |
| Maximum intensity for any TEAE: Mild | 28 | 28 | 22 | 27 |
| Maximum intensity for any TEAE: Moderate | 17 | 24 | 28 | 19 |
| Maximum intensity for any TEAE: Severe | 9 | 4 | 5 | 9 |

Notes:

[9] - SAF

[10] - SAF

[11] - SAF

[12] - SAF

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with TEAEs during the main and extended treatment periods and within the on-treatment time window and their severity

| | |
|-----------------|---|
| End point title | Number of subjects with TEAEs during the main and extended treatment periods and within the on-treatment time window and their severity |
|-----------------|---|

End point description:

TEAEs were analyzed during during main and extended treatment periods in the safety analysis set (SAF). Data observed from the randomization date until the end of the extension treatment period. TEAEs were defined as events occurring after first study intervention administration and up to 20 weeks after last study intervention administration.

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

End point timeframe:

Up to 48 weeks

| End point values | Fesomersen 40 mg | Fesomersen 80 mg | Fesomersen 120 mg | Placebo |
|--|--------------------|--------------------|--------------------|--------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 77 ^[13] | 79 ^[14] | 76 ^[15] | 75 ^[16] |
| Units: Subjects | | | | |
| Any TEAE | 61 | 62 | 58 | 56 |
| Maximum intensity for any TEAE: Mild | 26 | 25 | 20 | 26 |
| Maximum intensity for any TEAE: Moderate | 24 | 31 | 30 | 18 |
| Maximum intensity for any TEAE: Severe | 11 | 6 | 8 | 12 |

Notes:

[13] - SAF

[14] - SAF

[15] - SAF

[16] - SAF

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with TEAEs during the main and extended treatment periods and until 20 weeks after the last study intervention dose and their severity

| | |
|-----------------|---|
| End point title | Number of subjects with TEAEs during the main and extended treatment periods and until 20 weeks after the last study intervention dose and their severity |
|-----------------|---|

End point description:

TEAEs occurring from first study intervention intake until 20 weeks after last study intervention intake.

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

End point timeframe:

Up to 48 weeks

| End point values | Fesomersen 40 mg | Fesomersen 80 mg | Fesomersen 120 mg | Placebo |
|--|--------------------|--------------------|--------------------|--------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 77 ^[17] | 79 ^[18] | 76 ^[19] | 75 ^[20] |
| Units: Subjects | | | | |
| Any TEAE | 64 | 63 | 62 | 59 |
| Maximum intensity for any TEAE: Mild | 21 | 21 | 18 | 21 |
| Maximum intensity for any TEAE: Moderate | 28 | 33 | 33 | 22 |
| Maximum intensity for any TEAE: Severe | 15 | 9 | 11 | 16 |

Notes:

[17] - SAF

[18] - SAF

[19] - SAF

Statistical analyses

No statistical analyses for this end point

Secondary: Trough concentrations (Ctrough) of three dose levels of fesomersen

| | |
|-----------------|--|
| End point title | Trough concentrations (Ctrough) of three dose levels of fesomersen ^[21] |
|-----------------|--|

End point description:

Trough (pre-dose) fesomersen-equivalent plasma concentrations (Ctrough) for 3 dose levels of fesomersen were summarized descriptively by dose level and visit: Visit 12, Visit 14, Visit 16, Visit 18 (main treatment period).

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

End point timeframe:

At visits V12 (Day 57), V14 (Day 85), V16 (Day 113), V18 (Day 141)

Notes:

[21] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Ctrough was not measured for the placebo group.

| End point values | Fesomersen 40 mg | Fesomersen 80 mg | Fesomersen 120 mg | |
|---|-------------------------|------------------------|------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 77 ^[22] | 79 ^[23] | 76 ^[24] | |
| Units: µg/mL | | | | |
| geometric mean (geometric coefficient of variation) | | | | |
| Visit 12 (n=62, 57, 55) | 0.000454 (± 118.753791) | 0.000704 (± 80.938271) | 0.001186 (± 76.691406) | |
| Visit 14 (n=62, 60, 62) | 0.000490 (± 92.511801) | 0.000792 (± 82.170296) | 0.001246 (± 97.530820) | |
| Visit 16 (n=58, 56, 60) | 0.000572 (± 85.974878) | 0.000789 (± 68.188121) | 0.001346 (± 81.805680) | |
| Visit 18 (n=64, 53, 59) | 0.000521 (± 106.848825) | 0.000828 (± 91.024162) | 0.001424 (± 92.709743) | |

Notes:

[22] - PKS

[23] - PKS

[24] - PKS

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum change in FXI (coagulation factor XI) antigen levels during the main treatment period

| | |
|-----------------|---|
| End point title | Maximum change in FXI (coagulation factor XI) antigen levels during the main treatment period |
|-----------------|---|

End point description:

The secondary endpoint of change in FXI antigen levels during the main treatment period was an optional secondary endpoint only as mentioned in the integrated clinical protocol amendment version 3.0 and was not analyzed in this study as the FXI activity assay is sufficient to describe the effect on FXI level in plasma.

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

End point timeframe:

Up to 24 weeks

| End point values | Fesomersen 40 mg | Fesomersen 80 mg | Fesomersen 120 mg | Placebo |
|--------------------------------------|-------------------|-------------------|-------------------|-------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 0 ^[25] | 0 ^[26] | 0 ^[27] | 0 ^[28] |
| Units: U/mL | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline | () | () | () | () |
| Visit 5 (Day 1) | () | () | () | () |

Notes:

[25] - Not analyzed as the FXI activity assay is sufficient to describe the effect on FXI level in plasma.

[26] - Not analyzed as the FXI activity assay is sufficient to describe the effect on FXI level in plasma.

[27] - Not analyzed as the FXI activity assay is sufficient to describe the effect on FXI level in plasma.

[28] - Not analyzed as the FXI activity assay is sufficient to describe the effect on FXI level in plasma.

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum change in FXI activity levels during the main treatment period

| | |
|-----------------|--|
| End point title | Maximum change in FXI activity levels during the main treatment period |
|-----------------|--|

End point description:

The FXIa activity was measured by a fluorogenic activated FXIa activity (AXIA) assay. Absolute change from baseline at each visit until Visit 22 (Day 169) are reported.

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

End point timeframe:

Up to 24 weeks

| End point values | Fesomersen 40 mg | Fesomersen 80 mg | Fesomersen 120 mg | Placebo |
|--------------------------------------|--------------------|--------------------|--------------------|--------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 77 ^[29] | 79 ^[30] | 76 ^[31] | 75 ^[32] |
| Units: U/mL | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline | 0.00 (± 0.00) | 0.00 (± 0.00) | 0.00 (± 0.00) | 0.00 (± 0.00) |
| Visit 5 (Day 1): Pre-dose | 0.06 (± 0.06) | 0.05 (± 0.06) | 0.05 (± 0.05) | 0.04 (± 0.05) |
| Visit 5 (Day 1): 5 Hours | 0.09 (± 0.09) | 0.11 (± 0.12) | 0.13 (± 0.13) | 0.10 (± 0.08) |
| Visit 6 (Day 2): 22 Hours | 0.13 (± 0.11) | 0.12 (± 0.12) | 0.15 (± 0.13) | 0.14 (± 0.13) |
| Visit 7 (Day 8) | 0.21 (± 0.15) | 0.32 (± 0.15) | 0.43 (± 0.18) | 0.08 (± 0.07) |

| | | | | |
|------------------------------|---------------|---------------|---------------|---------------|
| Visit 8 (Day 15) | 0.34 (± 0.23) | 0.48 (± 0.21) | 0.61 (± 0.24) | 0.12 (± 0.09) |
| Visit 9 (Day 22) | 0.37 (± 0.26) | 0.50 (± 0.23) | 0.63 (± 0.25) | 0.11 (± 0.09) |
| Visit 10 (Day 29): Pre-dose | 0.34 (± 0.26) | 0.44 (± 0.21) | 0.60 (± 0.25) | 0.09 (± 0.07) |
| Visit 10 (Day 29): 5 Hours | 0.32 (± 0.25) | 0.43 (± 0.22) | 0.58 (± 0.25) | 0.12 (± 0.14) |
| Visit 11 (Day 43) | 0.47 (± 0.29) | 0.59 (± 0.25) | 0.76 (± 0.27) | 0.09 (± 0.08) |
| Visit 12 (Day 57): Pre-dose | 0.42 (± 0.26) | 0.55 (± 0.24) | 0.69 (± 0.28) | 0.11 (± 0.10) |
| Visit 13 (Day 71) | 0.52 (± 0.26) | 0.66 (± 0.24) | 0.76 (± 0.25) | 0.15 (± 0.13) |
| Visit 14 (Day 85): Pre-dose | 0.46 (± 0.27) | 0.59 (± 0.26) | 0.72 (± 0.24) | 0.14 (± 0.12) |
| Visit 16 (Day 113): Pre-dose | 0.46 (± 0.26) | 0.57 (± 0.28) | 0.75 (± 0.25) | 0.16 (± 0.16) |
| Visit 18 (Day 141): Pre-dose | 0.47 (± 0.27) | 0.56 (± 0.28) | 0.72 (± 0.25) | 0.12 (± 0.09) |
| Visit 19 (Day 148) | 0.52 (± 0.27) | 0.63 (± 0.29) | 0.76 (± 0.26) | 0.15 (± 0.16) |
| Visit 20 (Day 155) | 0.52 (± 0.28) | 0.65 (± 0.29) | 0.77 (± 0.25) | 0.15 (± 0.17) |
| Visit 21 (Day 162) | 0.50 (± 0.30) | 0.64 (± 0.28) | 0.75 (± 0.26) | 0.16 (± 0.20) |
| Visit 22 (Day 169): Pre-dose | 0.46 (± 0.29) | 0.59 (± 0.28) | 0.73 (± 0.25) | 0.17 (± 0.21) |

Notes:

[29] - PDS

[30] - PDS

[31] - PDS

[32] - PDS

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first study intervention up to 64 Weeks.

Adverse event reporting additional description:

Adverse event reporting for the all-cause mortality considers all deaths that occurred at any time during the study before the last contact, up to 64 Weeks.

| | |
|-----------------|----------------|
| Assessment type | Non-systematic |
|-----------------|----------------|

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 25.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|------------------|
| Reporting group title | Fesomersen 40 mg |
|-----------------------|------------------|

Reporting group description:

Subjects received subcutaneous treatment with 40 mg fesomersen.

| | |
|-----------------------|---------|
| Reporting group title | Placebo |
|-----------------------|---------|

Reporting group description:

Subjects received subcutaneous treatment with matching placebo to fesomersen.

| | |
|-----------------------|-------------------|
| Reporting group title | Fesomersen 120 mg |
|-----------------------|-------------------|

Reporting group description:

Subjects received subcutaneous treatment with 120 mg fesomersen.

| | |
|-----------------------|------------------|
| Reporting group title | Fesomersen 80 mg |
|-----------------------|------------------|

Reporting group description:

Subjects received subcutaneous treatment with 80 mg fesomersen.

| Serious adverse events | Fesomersen 40 mg | Placebo | Fesomersen 120 mg |
|---|------------------|------------------|-------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 19 / 77 (24.68%) | 20 / 75 (26.67%) | 17 / 76 (22.37%) |
| number of deaths (all causes) | 2 | 7 | 2 |
| number of deaths resulting from adverse events | 1 | 6 | 1 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Endometrial cancer | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 0 / 75 (0.00%) | 1 / 76 (1.32%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pancreatic neoplasm | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 0 / 75 (0.00%) | 0 / 76 (0.00%) |
| 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 | | | |

| | | | |
|--|----------------|----------------|----------------|
| Hypertension | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 75 (1.33%) | 0 / 76 (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 |
| Peripheral arterial occlusive disease | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 75 (1.33%) | 1 / 76 (1.32%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Subclavian vein thrombosis | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 75 (1.33%) | 0 / 76 (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 |
| Peripheral artery thrombosis | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 0 / 75 (0.00%) | 0 / 76 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Superficial vein thrombosis | | | |
| subjects affected / exposed | 1 / 77 (1.30%) | 0 / 75 (0.00%) | 0 / 76 (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 |
| Surgical and medical procedures | | | |
| Renal transplant | | | |
| subjects affected / exposed | 3 / 77 (3.90%) | 1 / 75 (1.33%) | 0 / 76 (0.00%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 1 | 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 / 77 (1.30%) | 0 / 75 (0.00%) | 0 / 76 (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 |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 75 (1.33%) | 0 / 76 (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 |

| | | | |
|---|----------------|----------------|----------------|
| Swelling | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 75 (1.33%) | 0 / 76 (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 |
| Device related thrombosis | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 75 (1.33%) | 0 / 76 (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 | | | |
| Pulmonary embolism | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 0 / 75 (0.00%) | 1 / 76 (1.32%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Investigations | | | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 0 / 75 (0.00%) | 1 / 76 (1.32%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Klebsiella test positive | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 0 / 75 (0.00%) | 0 / 76 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Transplant evaluation | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 75 (1.33%) | 0 / 76 (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 |
| Injury, poisoning and procedural complications | | | |
| Arteriovenous fistula thrombosis | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 3 / 75 (4.00%) | 2 / 76 (2.63%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 7 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Concussion | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 77 (0.00%) | 0 / 75 (0.00%) | 1 / 76 (1.32%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hip fracture | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 0 / 75 (0.00%) | 1 / 76 (1.32%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Shunt occlusion | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 75 (1.33%) | 0 / 76 (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 |
| Arteriovenous graft thrombosis | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 75 (1.33%) | 0 / 76 (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 |
| Arteriovenous fistula site complication | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 75 (1.33%) | 0 / 76 (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 |
| Arteriovenous graft site haemorrhage | | | |
| subjects affected / exposed | 1 / 77 (1.30%) | 0 / 75 (0.00%) | 0 / 76 (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 |
| Shunt stenosis | | | |
| subjects affected / exposed | 1 / 77 (1.30%) | 0 / 75 (0.00%) | 0 / 76 (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 |
| Vascular graft thrombosis | | | |
| subjects affected / exposed | 1 / 77 (1.30%) | 0 / 75 (0.00%) | 0 / 76 (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 |
| Delayed graft function | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 77 (0.00%) | 0 / 75 (0.00%) | 0 / 76 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Arteriovenous graft site pseudoaneurysm | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 0 / 75 (0.00%) | 0 / 76 (0.00%) |
| 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 | | | |
| Arrhythmia | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 0 / 75 (0.00%) | 1 / 76 (1.32%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Atrial fibrillation | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 0 / 75 (0.00%) | 1 / 76 (1.32%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Atrial flutter | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 0 / 75 (0.00%) | 0 / 76 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac arrest | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 75 (1.33%) | 0 / 76 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Coronary artery disease | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 75 (1.33%) | 0 / 76 (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 failure congestive | | | |
| subjects affected / exposed | 1 / 77 (1.30%) | 0 / 75 (0.00%) | 0 / 76 (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 |
| Supraventricular tachycardia | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 77 (0.00%) | 0 / 75 (0.00%) | 1 / 76 (1.32%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ventricular fibrillation | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 75 (1.33%) | 0 / 76 (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 |
| Bradyarrhythmia | | | |
| subjects affected / exposed | 1 / 77 (1.30%) | 0 / 75 (0.00%) | 0 / 76 (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 / 77 (0.00%) | 1 / 75 (1.33%) | 0 / 76 (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 |
| Nervous system disorders | | | |
| Carotid artery stenosis | | | |
| subjects affected / exposed | 1 / 77 (1.30%) | 0 / 75 (0.00%) | 0 / 76 (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 |
| Encephalopathy | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 75 (1.33%) | 0 / 76 (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 |
| Cerebral ischaemia | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 0 / 75 (0.00%) | 0 / 76 (0.00%) |
| 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 | 1 / 77 (1.30%) | 0 / 75 (0.00%) | 0 / 76 (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 |
| Transient ischaemic attack | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 75 (1.33%) | 0 / 76 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Post cardiac arrest syndrome | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 75 (1.33%) | 0 / 76 (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 |
| Blood and lymphatic system disorders | | | |
| Thrombocytopenia | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 75 (1.33%) | 0 / 76 (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 |
| Spleen ischaemia | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 75 (1.33%) | 0 / 76 (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 | | | |
| Abdominal adhesions | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 0 / 75 (0.00%) | 0 / 76 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diarrhoea | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 75 (1.33%) | 0 / 76 (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 |
| Duodenal ulcer haemorrhage | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 0 / 75 (0.00%) | 0 / 76 (0.00%) |
| 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 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 0 / 75 (0.00%) | 0 / 76 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal haemorrhage | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 1 / 77 (1.30%) | 0 / 75 (0.00%) | 0 / 76 (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 |
| Intestinal ischaemia | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 75 (1.33%) | 0 / 76 (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 |
| Intestinal obstruction | | | |
| subjects affected / exposed | 1 / 77 (1.30%) | 0 / 75 (0.00%) | 0 / 76 (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 |
| Small intestinal haemorrhage | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 0 / 75 (0.00%) | 1 / 76 (1.32%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Large intestine perforation | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 75 (1.33%) | 0 / 76 (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 |
| Obstructive pancreatitis | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 0 / 75 (0.00%) | 0 / 76 (0.00%) |
| 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 | | | |
| Bile duct stone | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 0 / 75 (0.00%) | 0 / 76 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cholecystitis | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 0 / 75 (0.00%) | 0 / 76 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cholangitis | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 77 (0.00%) | 0 / 75 (0.00%) | 0 / 76 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cholecystitis acute | | | |
| subjects affected / exposed | 1 / 77 (1.30%) | 0 / 75 (0.00%) | 0 / 76 (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 |
| Hepatic ischaemia | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 75 (1.33%) | 0 / 76 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Pain in extremity | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 0 / 75 (0.00%) | 1 / 76 (1.32%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Osteoarthritis | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 0 / 75 (0.00%) | 1 / 76 (1.32%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Rotator cuff syndrome | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 0 / 75 (0.00%) | 1 / 76 (1.32%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Cellulitis | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 2 / 75 (2.67%) | 1 / 76 (1.32%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diverticulitis | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 75 (1.33%) | 0 / 76 (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 |

| | | | |
|---|----------------|----------------|----------------|
| Gangrene | | | |
| subjects affected / exposed | 1 / 77 (1.30%) | 1 / 75 (1.33%) | 0 / 76 (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 |
| Orchitis | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 75 (1.33%) | 0 / 76 (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 / 77 (0.00%) | 0 / 75 (0.00%) | 1 / 76 (1.32%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Peritonitis | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 75 (1.33%) | 0 / 76 (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 / 77 (1.30%) | 0 / 75 (0.00%) | 0 / 76 (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 |
| Sepsis | | | |
| subjects affected / exposed | 1 / 77 (1.30%) | 1 / 75 (1.33%) | 1 / 76 (1.32%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| Staphylococcal bacteraemia | | | |
| subjects affected / exposed | 1 / 77 (1.30%) | 0 / 75 (0.00%) | 0 / 76 (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 |
| Coronavirus infection | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 0 / 75 (0.00%) | 1 / 76 (1.32%) |
| 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 syndrome | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 77 (0.00%) | 0 / 75 (0.00%) | 0 / 76 (0.00%) |
| 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 access site infection | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 75 (1.33%) | 0 / 76 (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 sepsis | | | |
| subjects affected / exposed | 1 / 77 (1.30%) | 0 / 75 (0.00%) | 0 / 76 (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 |
| COVID-19 | | | |
| subjects affected / exposed | 1 / 77 (1.30%) | 2 / 75 (2.67%) | 4 / 76 (5.26%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | 0 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| COVID-19 pneumonia | | | |
| subjects affected / exposed | 2 / 77 (2.60%) | 1 / 75 (1.33%) | 1 / 76 (1.32%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolism and nutrition disorders | | | |
| Hyperkalaemia | | | |
| subjects affected / exposed | 1 / 77 (1.30%) | 0 / 75 (0.00%) | 0 / 76 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|------------------|--|--|
| Serious adverse events | Fesomersen 80 mg | | |
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 18 / 79 (22.78%) | | |
| number of deaths (all causes) | 1 | | |
| number of deaths resulting from adverse events | 1 | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Endometrial cancer | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pancreatic neoplasm | | | |
| subjects affected / exposed | 1 / 79 (1.27%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Peripheral arterial occlusive disease | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Subclavian vein thrombosis | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Peripheral artery thrombosis | | | |
| subjects affected / exposed | 1 / 79 (1.27%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Superficial vein thrombosis | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Surgical and medical procedures | | | |
| Renal transplant | | | |
| subjects affected / exposed | 4 / 79 (5.06%) | | |
| occurrences causally related to treatment / all | 0 / 4 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| General disorders and administration | | | |

| | | | |
|---|----------------|--|--|
| site conditions | | | |
| Chest pain | | | |
| subjects affected / exposed | 1 / 79 (1.27%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Swelling | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Device related thrombosis | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Pulmonary embolism | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Investigations | | | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Klebsiella test positive | | | |
| subjects affected / exposed | 1 / 79 (1.27%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Transplant evaluation | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Injury, poisoning and procedural complications | | | |
| Arteriovenous fistula thrombosis | | | |
| subjects affected / exposed | 1 / 79 (1.27%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Concussion | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hip fracture | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Shunt occlusion | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Arteriovenous graft thrombosis | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Arteriovenous fistula site complication | | | |
| subjects affected / exposed | 1 / 79 (1.27%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Arteriovenous graft site haemorrhage | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | | |
|---|----------------|--|--|--|
| Shunt stenosis | | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Vascular graft thrombosis | | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Delayed graft function | | | | |
| subjects affected / exposed | 1 / 79 (1.27%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Arteriovenous graft site pseudoaneurysm | | | | |
| subjects affected / exposed | 1 / 79 (1.27%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Cardiac disorders | | | | |
| Arrhythmia | | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Atrial fibrillation | | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Atrial flutter | | | | |
| subjects affected / exposed | 1 / 79 (1.27%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Cardiac arrest | | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |

| | | | |
|---|----------------|--|--|
| Coronary artery disease | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cardiac failure congestive | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Supraventricular tachycardia | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Ventricular fibrillation | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Bradyarrhythmia | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Acute coronary syndrome | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Nervous system disorders | | | |
| Carotid artery stenosis | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Encephalopathy | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cerebral ischaemia | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 1 / 79 (1.27%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Loss of consciousness | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Transient ischaemic attack | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Post cardiac arrest syndrome | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Blood and lymphatic system disorders | | | |
| Thrombocytopenia | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Spleen ischaemia | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal disorders | | | |
| Abdominal adhesions | | | |
| subjects affected / exposed | 1 / 79 (1.27%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Diarrhoea | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Duodenal ulcer haemorrhage | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 1 / 79 (1.27%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastritis | | | |
| subjects affected / exposed | 1 / 79 (1.27%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Intestinal ischaemia | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Intestinal obstruction | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Small intestinal haemorrhage | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Large intestine perforation | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Obstructive pancreatitis | | | |
| subjects affected / exposed | 1 / 79 (1.27%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hepatobiliary disorders | | | |
| Bile duct stone | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 1 / 79 (1.27%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cholecystitis | | | |
| subjects affected / exposed | 1 / 79 (1.27%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cholangitis | | | |
| subjects affected / exposed | 1 / 79 (1.27%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cholecystitis acute | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hepatic ischaemia | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Pain in extremity | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Osteoarthritis | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Rotator cuff syndrome | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infections and infestations | | | |

| | | | | |
|---|----------------|--|--|--|
| Cellulitis | | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Diverticulitis | | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Gangrene | | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Orchitis | | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Osteomyelitis | | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Peritonitis | | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pneumonia | | | | |
| subjects affected / exposed | 1 / 79 (1.27%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Sepsis | | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Staphylococcal bacteraemia | | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Coronavirus infection | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Sepsis syndrome | | | |
| subjects affected / exposed | 1 / 79 (1.27%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Vascular access site infection | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Staphylococcal sepsis | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| COVID-19 | | | |
| subjects affected / exposed | 1 / 79 (1.27%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| COVID-19 pneumonia | | | |
| subjects affected / exposed | 4 / 79 (5.06%) | | |
| occurrences causally related to treatment / all | 0 / 4 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Metabolism and nutrition disorders | | | |
| Hyperkalaemia | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

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

| Non-serious adverse events | Fesomersen 40 mg | Placebo | Fesomersen 120 mg |
|---|------------------|------------------|-------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 31 / 77 (40.26%) | 21 / 75 (28.00%) | 30 / 76 (39.47%) |
| Investigations | | | |
| N-terminal prohormone brain natriuretic peptide increased | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 0 / 75 (0.00%) | 0 / 76 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 3 / 77 (3.90%) | 7 / 75 (9.33%) | 6 / 76 (7.89%) |
| occurrences (all) | 5 | 8 | 8 |
| Hypotension | | | |
| subjects affected / exposed | 6 / 77 (7.79%) | 1 / 75 (1.33%) | 8 / 76 (10.53%) |
| occurrences (all) | 27 | 1 | 12 |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 4 / 77 (5.19%) | 1 / 75 (1.33%) | 3 / 76 (3.95%) |
| occurrences (all) | 4 | 1 | 5 |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 4 / 77 (5.19%) | 4 / 75 (5.33%) | 3 / 76 (3.95%) |
| occurrences (all) | 6 | 5 | 5 |
| Thrombocytopenia | | | |
| subjects affected / exposed | 3 / 77 (3.90%) | 2 / 75 (2.67%) | 7 / 76 (9.21%) |
| occurrences (all) | 5 | 4 | 11 |
| General disorders and administration site conditions | | | |
| Pyrexia | | | |
| subjects affected / exposed | 7 / 77 (9.09%) | 4 / 75 (5.33%) | 2 / 76 (2.63%) |
| occurrences (all) | 8 | 4 | 3 |
| Gastrointestinal disorders | | | |
| Diarrhoea | | | |
| subjects affected / exposed | 5 / 77 (6.49%) | 2 / 75 (2.67%) | 3 / 76 (3.95%) |
| occurrences (all) | 9 | 2 | 3 |
| Nausea | | | |

| | | | |
|---|---|---|--|
| subjects affected / exposed occurrences (all) | 3 / 77 (3.90%) 3 | 3 / 75 (4.00%) 3 | 1 / 76 (1.32%) 1 |
| Psychiatric disorders Insomnia subjects affected / exposed occurrences (all) | 2 / 77 (2.60%) 3 | 2 / 75 (2.67%) 3 | 3 / 76 (3.95%) 3 |
| Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all) Muscle spasms subjects affected / exposed occurrences (all) | 4 / 77 (5.19%) 4 4 / 77 (5.19%) 10 | 2 / 75 (2.67%) 5 3 / 75 (4.00%) 13 | 4 / 76 (5.26%) 4 5 / 76 (6.58%) 7 |

| | | | |
|---|---|--|--|
| Non-serious adverse events | Fesomersen 80 mg | | |
| Total subjects affected by non-serious adverse events subjects affected / exposed | 27 / 79 (34.18%) | | |
| Investigations N-terminal prohormone brain natriuretic peptide increased subjects affected / exposed occurrences (all) | 4 / 79 (5.06%) 4 | | |
| Vascular disorders Hypertension subjects affected / exposed occurrences (all) Hypotension subjects affected / exposed occurrences (all) | 5 / 79 (6.33%) 9 4 / 79 (5.06%) 12 | | |
| Nervous system disorders Headache subjects affected / exposed occurrences (all) | 3 / 79 (3.80%) 4 | | |
| Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all) Thrombocytopenia | 4 / 79 (5.06%) 9 | | |

| | | | |
|--|--|--|--|
| subjects affected / exposed occurrences (all) | 7 / 79 (8.86%) 13 | | |
| General disorders and administration site conditions Pyrexia subjects affected / exposed occurrences (all) | 3 / 79 (3.80%) 4 | | |
| Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all) | 2 / 79 (2.53%) 2 4 / 79 (5.06%) 4 | | |
| Psychiatric disorders Insomnia subjects affected / exposed occurrences (all) | 4 / 79 (5.06%) 4 | | |
| Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all) Muscle spasms subjects affected / exposed occurrences (all) | 3 / 79 (3.80%) 3 3 / 79 (3.80%) 5 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-------------------|---|
| 29 September 2020 | This amendment was prepared to address the change in the new contraception guidance as requested by Health Authorities. Additionally, the number of procedures and visits was decreased to reduce the burden on the participants. This reduction does not impact the participants' safety nor affect the benefit-risk assessment. |
| 07 July 2021 | The rationale of this amendment was to implement the possibility of local laboratory safety assessments in case centrally provided laboratory kits are not available due to COVID-19-related logistical reasons. Further it was to update the requirements for discontinuation of study intervention and the rules for prohibited medications intake. Minor corrections and clarifications were also added. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported