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

[20] - 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	3 / 77 (3.90%)	3 / 75 (4.00%)	1 / 76 (1.32%)
occurrences (all)	3	3	1
Psychiatric disorders			
Insomnia			
subjects affected / exposed	2 / 77 (2.60%)	2 / 75 (2.67%)	3 / 76 (3.95%)
occurrences (all)	3	3	3
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	4 / 77 (5.19%)	2 / 75 (2.67%)	4 / 76 (5.26%)
occurrences (all)	4	5	4
Muscle spasms			
subjects affected / exposed	4 / 77 (5.19%)	3 / 75 (4.00%)	5 / 76 (6.58%)
occurrences (all)	10	13	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	4 / 79 (5.06%)		
occurrences (all)	4		
Vascular disorders			
Hypertension			
subjects affected / exposed	5 / 79 (6.33%)		
occurrences (all)	9		
Hypotension			
subjects affected / exposed	4 / 79 (5.06%)		
occurrences (all)	12		
Nervous system disorders			
Headache			
subjects affected / exposed	3 / 79 (3.80%)		
occurrences (all)	4		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	4 / 79 (5.06%)		
occurrences (all)	9		
Thrombocytopenia			

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