



Clinical trial results:

A Phase 3 Multicenter, Open-Label Study to Evaluate the Safety of Daily Oral Dosing of Tafamidis Meglumine (PF-06291826-83) 20 mg or 80 mg [or Tafamidis (PF-06291826-00) 61 mg] in Subjects Diagnosed With Transthyretin Cardiomyopathy (ATTR-CM)

Summary

EudraCT number	2016-000868-42
Trial protocol	ES BE CZ DE SE NL GB IT
Global end of trial date	02 November 2023

Results information

Result version number	v1 (current)
This version publication date	07 November 2024
First version publication date	07 November 2024

Trial information

Trial identification

Sponsor protocol code	B3461045
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02791230
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Pfizer Inc.
Sponsor organisation address	235 E 42nd Street,, New York, United States, NY 10017
Public contact	Pfizer ClinicalTrials.gov Call Center, Pfizer Inc., 001 8007181021, ClinicalTrials.gov_Inquiries@pfizer.com
Scientific contact	Pfizer ClinicalTrials.gov Call Center, Pfizer Inc., 001 8007181021, ClinicalTrials.gov_Inquiries@pfizer.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	02 May 2024
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	02 November 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of this trial is to obtain additional, long-term, safety data for tafamidis in subjects with transthyretin amyloid cardiomyopathy (ATTR-CM) and to provide investigational product, tafamidis, to enrolled subjects until local availability by prescription for the ATTR-CM indication.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Council for Harmonization (ICH) Good Clinical Practice (GCP) Guidelines. All the local regulatory requirements pertinent to safety of trials participants were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	13 June 2016
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	Argentina: 20
Country: Number of subjects enrolled	Australia: 77
Country: Number of subjects enrolled	Canada: 191
Country: Number of subjects enrolled	Czechia: 56
Country: Number of subjects enrolled	Germany: 35
Country: Number of subjects enrolled	Brazil: 1
Country: Number of subjects enrolled	French Southern Territories: 206
Country: Number of subjects enrolled	Hong Kong: 5
Country: Number of subjects enrolled	Italy: 20
Country: Number of subjects enrolled	Japan: 35
Country: Number of subjects enrolled	Belgium: 35
Country: Number of subjects enrolled	Spain: 187
Country: Number of subjects enrolled	Sweden: 4
Country: Number of subjects enrolled	Netherlands: 13
Country: Number of subjects enrolled	Taiwan: 23
Country: Number of subjects enrolled	Ireland: 1
Country: Number of subjects enrolled	United States: 819
Worldwide total number of subjects	1728
EEA total number of subjects	351

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)	121
From 65 to 84 years	1374
85 years and over	233

Subject disposition

Recruitment

Recruitment details:

The study consisted of two cohorts: Cohort A & B. Cohort A: Participants diagnosed with ATTR-CM who completed 30 months of participation in parent study [B3461028 (NCT01994889)] were enrolled in this extension study B3461045. Cohort B: Participants diagnosed with ATTR-CM who did not participate in parent study were enrolled in this extension study.

Pre-assignment

Screening details:

A total of 1733 participants were enrolled in this current extension study.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Cohort A: Tafamidis (Parent and Extension Study)

Arm description:

Participants who received tafamidis 20 milligram (mg) or 80 mg orally once daily in the parent study for 30 months (complete participation), after enrollment in the current extension study, continued to receive the same dose and later switched to tafamidis 61 mg (or 80 mg in regions where 61 mg tafamidis was unavailable), orally once daily along with standard of care for up to 60 months.

Arm type	Experimental
Investigational medicinal product name	Tafamidis meglumine
Investigational medicinal product code	PF-06291826
Other name	
Pharmaceutical forms	Capsule, soft
Routes of administration	Oral use

Dosage and administration details:

Participants received tafamidis 20mg or 80 mg (4 capsules of 20 mg each), and later switched to 61 mg capsule (where available) orally once daily for 60 months.

Arm title	Cohort A: Placebo (Parent Study)/Tafamidis (Extension Study)
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Arm description:

Participants who received placebo orally once daily in the parent study for 30 months (complete participation), after enrollment in the current extension study, received tafamidis 20 mg or 80 mg and later switched to tafamidis 61 mg (or 80 mg in regions where 61 mg tafamidis was unavailable), orally once daily along with standard of care for up to 60 months.

Arm type	Experimental
Investigational medicinal product name	Tafamidis meglumine
Investigational medicinal product code	PF-06291826
Other name	
Pharmaceutical forms	Capsule, soft
Routes of administration	Oral use

Dosage and administration details:

Participants received tafamidis 20 mg or 80 mg (4 capsules of 20 mg each), and later switched to 61 mg capsule (where available) orally once daily for 60 months.

Arm title	Cohort B: Tafamidis (Only in extension study)
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Arm description:

Participants who did not participate in the parent study and received tafamidis at a dose of 61 mg (or 80 mg in regions where 61 mg tafamidis was unavailable), once daily along with standard of care for up to

60 months.

Arm type	Experimental
Investigational medicinal product name	Tafamidis meglumine
Investigational medicinal product code	PF-06291826
Other name	
Pharmaceutical forms	Capsule, soft
Routes of administration	Oral use

Dosage and administration details:

Participants received tafamidis 61 mg capsule where available (or 80 mg (4 capsules of 20 mg each)), orally once daily for 60 months.

Number of subjects in period 1	Cohort A: Tafamidis (Parent and Extension Study)	Cohort A: Placebo (Parent Study)/Tafamidis (Extension Study)	Cohort B: Tafamidis (Only in extension study)
Started	170	82	1476
Completed	84	31	988
Not completed	86	51	488
Consent withdrawn by subject	24	13	172
Adverse Event	10	9	66
Failure to Meet Randomization Criteria	3	2	15
Death	38	25	184
Study sites terminated by sponsor	1	-	5
Unspecified	9	1	28
Medication Error Without Associated Adverse Event	-	1	1
Lost to follow-up	-	-	10
Lack of efficacy	1	-	3
Protocol deviation	-	-	4

Baseline characteristics

Reporting groups

Reporting group title	Cohort A: Tafamidis (Parent and Extension Study)
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Reporting group description:

Participants who received tafamidis 20 milligram (mg) or 80 mg orally once daily in the parent study for 30 months (complete participation), after enrollment in the current extension study, continued to receive the same dose and later switched to tafamidis 61 mg (or 80 mg in regions where 61 mg tafamidis was unavailable), orally once daily along with standard of care for up to 60 months.

Reporting group title	Cohort A: Placebo (Parent Study)/Tafamidis (Extension Study)
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Reporting group description:

Participants who received placebo orally once daily in the parent study for 30 months (complete participation), after enrollment in the current extension study, received tafamidis 20 mg or 80 mg and later switched to tafamidis 61 mg (or 80 mg in regions where 61 mg tafamidis was unavailable), orally once daily along with standard of care for up to 60 months.

Reporting group title	Cohort B: Tafamidis (Only in extension study)
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Reporting group description:

Participants who did not participate in the parent study and received tafamidis at a dose of 61 mg (or 80 mg in regions where 61 mg tafamidis was unavailable), once daily along with standard of care for up to 60 months.

Reporting group values	Cohort A: Tafamidis (Parent and Extension Study)	Cohort A: Placebo (Parent Study)/Tafamidis (Extension Study)	Cohort B: Tafamidis (Only in extension study)
Number of subjects	170	82	1476
Age categorical Units: Participants			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	9	6	106
From 65-84 years	142	72	1160
85 years and over	19	4	210
Age Continuous Units: Years			
arithmetic mean	76.73	76.41	76.51
standard deviation	± 6.75	± 6.47	± 7.75
Sex: Female, Male Units: Participants			
Female	13	8	165
Male	157	74	1311
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	9	5	66
Native Hawaiian or Other Pacific Islander	0	0	0

Black or African American	15	5	139
White	144	72	1252
More than one race	0	0	0
Unknown or Not Reported	2	0	19
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	5	1	37
Not Hispanic or Latino	164	81	1433
Unknown or Not Reported	1	0	6

Reporting group values	Total		
Number of subjects	1728		
Age categorical			
Units: Participants			
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)	121		
From 65-84 years	1374		
85 years and over	233		
Age Continuous			
Units: Years			
arithmetic mean			
standard deviation	-		
Sex: Female, Male			
Units: Participants			
Female	186		
Male	1542		
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	0		
Asian	80		
Native Hawaiian or Other Pacific Islander	0		
Black or African American	159		
White	1468		
More than one race	0		
Unknown or Not Reported	21		
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	43		
Not Hispanic or Latino	1678		
Unknown or Not Reported	7		

End points

End points reporting groups

Reporting group title	Cohort A: Tafamidis (Parent and Extension Study)
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Reporting group description:

Participants who received tafamidis 20 milligram (mg) or 80 mg orally once daily in the parent study for 30 months (complete participation), after enrollment in the current extension study, continued to receive the same dose and later switched to tafamidis 61 mg (or 80 mg in regions where 61 mg tafamidis was unavailable), orally once daily along with standard of care for up to 60 months.

Reporting group title	Cohort A: Placebo (Parent Study)/Tafamidis (Extension Study)
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Reporting group description:

Participants who received placebo orally once daily in the parent study for 30 months (complete participation), after enrollment in the current extension study, received tafamidis 20 mg or 80 mg and later switched to tafamidis 61 mg (or 80 mg in regions where 61 mg tafamidis was unavailable), orally once daily along with standard of care for up to 60 months.

Reporting group title	Cohort B: Tafamidis (Only in extension study)
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Reporting group description:

Participants who did not participate in the parent study and received tafamidis at a dose of 61 mg (or 80 mg in regions where 61 mg tafamidis was unavailable), once daily along with standard of care for up to 60 months.

Subject analysis set title	Cohort A: Tafamidis(Parent study) & Tafamidis(Extension Study)
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Subject analysis set type	Per protocol
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Subject analysis set description:

Participants who received tafamidis 20 mg or 80 mg orally once daily in the parent study for 30 months (complete participation) and after enrollment in the current extension study, continued to receive the same dose and later switched to tafamidis 61 mg (or 80 mg in regions where 61 mg tafamidis was unavailable), orally once daily along with standard of care for up to 60 months.

Subject analysis set title	Cohort A: Placebo (Parent Study) & Tafamidis (Extension Study)
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Subject analysis set type	Per protocol
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Subject analysis set description:

Participants who received placebo orally once daily in the parent study for 30 months (complete participation) and after enrollment in the current extension study, received tafamidis 20 mg or 80 mg and later switched to tafamidis 61 mg (or 80 mg in regions where 61 mg tafamidis was unavailable), orally once daily along with standard of care for up to 60 months.

Primary: Time to All-Cause Mortality: Cohort A

End point title	Time to All-Cause Mortality: Cohort A
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End point description:

Time to all-cause mortality was calculated from first dose of randomized treatment in parent study (PS) B3461028 to all-cause mortality events which included death, heart transplants & cardiac mechanical assist device implantation treated as death. Treated participants from PS who discontinued before this study were included as planned. Data from participants who dropped out for liver-only transplantation were handled like all censored participants. Censored participants were participants completed or discontinued from study, were alive at analysis. Combined mortality analysis (CMA) set included all participants in Intent-To-Treat (ITT) analysis set from study B3461028. Mortality analyses in B3461045 for Cohort A included combined data from participants in B3461028, including participants who died, discontinued in B3461028, or were not enrolled into B3461045 (i.e. ITT Analysis Set from B3461028) with mortality data through participation in B3461045. Analysis was based on pooled dose

End point type	Primary
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End point timeframe:

From first dose of randomized treatment in parent study (B3461028) up to 28 days post last dose of study treatment in current extension study (B3461045), [approximately up to 91 months]

End point values	Cohort A: Tafamidis(Parent study) & Tafamidis(Extension Study)	Cohort A: Placebo (Parent Study) & Tafamidis (Extension Study)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	264	177		
Units: Months				
median (confidence interval 95%)	58.7 (50.3 to 68.4)	35.8 (29.7 to 41.1)		

Statistical analyses

Statistical analysis title	Tafamidis PS & ES vs Placebo PS & Tafamidis ES
Comparison groups	Cohort A: Tafamidis(Parent study) & Tafamidis(Extension Study) v Cohort A: Placebo (Parent Study) & Tafamidis (Extension Study)
Number of subjects included in analysis	441
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0001
Method	Cox proportional hazards model
Parameter estimate	Hazard ratio (HR)
Point estimate	0.6202
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.4865
upper limit	0.7906

Primary: Number of Participants With All-Cause Mortality Events: Cohort B

End point title	Number of Participants With All-Cause Mortality Events: Cohort B ^{[1][2]}
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End point description:

All cause mortality included all participants who had discontinue for transplantation (i.e, heart transplantation and combined heart and liver transplantation) or for implantation of a cardiac mechanical assist device, were handled in the same manner as death. Data from participants who dropped out for a liver-only transplantation were handled in the same manner as the data from all other censored participants. Censored participants were participants who completed study or discontinued from the study (including discontinued by sponsor or participants withdrew, or discontinued due to AE), or alive at the time of analysis. Safety analysis population consisted of all participants (Cohort B) who were enrolled in this study and who had taken at least 1 dose of study medication.

End point type	Primary
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End point timeframe:

B3461045: From first dose of treatment up to 28 days post last dose of study treatment (approximately up to 61 months)

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: No statistical analyses was planned for this primary end point

[2] - 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: The end point is reporting statistics for the arms specified

End point values	Cohort B: Tafamidis (Only in extension study)			
Subject group type	Reporting group			
Number of subjects analysed	1476			
Units: Participants	345			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Treatment-Emergent Adverse Events (AEs)

End point title	Number of Participants With Treatment-Emergent Adverse Events (AEs) ^[3]
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End point description:

An AEs was any untoward medical occurrence who received investigational product or medical device; the event need not necessarily have causal relationship with treatment or usage. Treatment emergent AE was defined as an event that emerged during treatment period that was absent before treatment or worsened during the treatment period relative to pretreatment state. AEs included both SAEs and all Non-SAEs. A serious adverse event (SAE) was any untoward medical occurrence at any dose that: resulted in death; was life-threatening (immediate risk of death); required inpatient hospitalization or prolongation of existing hospitalization; resulted in persistent or significant disability/incapacity; resulted in congenital anomaly/birth defect; considered an important medical event. Safety analysis population consisted of all participants (Cohorts A&B) who were enrolled in this study & taken at least 1 dose of study medication. This analysis (cohort A) was based on pooled dose groups, as per the SAP.

End point type	Primary
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End point timeframe:

B3461045: From first dose of treatment up to 28 days post last dose of study treatment (approximately up to 61 months)

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: No statistical analyses was planned for this primary end point

End point values	Cohort A: Tafamidis (Parent and Extension Study)	Cohort A: Placebo (Parent Study)/Tafamid is (Extension Study)	Cohort B: Tafamidis (Only in extension study)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	170	82	1476	
Units: Participants	168	79	1294	

Statistical analyses

Other pre-specified: Time to Cardiovascular-Related Mortality Events: Cohort A

End point title	Time to Cardiovascular-Related Mortality Events: Cohort A
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End point description:

Time to cardiovascular-related mortality was calculated from first dose of randomized treatment in B3461028. Participants who discontinued for transplantation (that is heart transplantation and combined heart and liver transplantation) or for implantation of cardiac mechanical assist device were treated as a death. Treated participants from the parent study who discontinued prior to the start of this study were also included in this analysis as planned. Kaplan-Meier method was used. CMA set included all participants in the ITT analysis set from study B3461028 (NCT01994889). Mortality analyses in study B3461045 for Cohort A participants were combined data from participants in study B3461028 (NCT01994889), including participants who died, discontinued in B3461028, or were not enrolled into B3461045 (i.e. ITT Analysis Set from B3461028 [NCT01994889]) with mortality data through participation in the B3461045 study. This analysis was based on the pooled dose groups, as per the SAP.

End point type	Other pre-specified
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End point timeframe:

From first dose of randomized treatment in parent study (B3461028) up to 28 days post last dose of study treatment in current extension study (B3461045), [approximately up to 91 months]

End point values	Cohort A: Tafamidis(Parent study) & Tafamidis(Extension Study)	Cohort A: Placebo (Parent Study) & Tafamidis (Extension Study)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	264	177		
Units: Months				
median (confidence interval 95%)	70.2 (63.4 to 88.8)	40.8 (34.1 to 50.7)		

Statistical analyses

Statistical analysis title	Tafamidis PS & ES vs Placebo PS & Tafamidis ES
Comparison groups	Cohort A: Tafamidis(Parent study) & Tafamidis(Extension Study) v Cohort A: Placebo (Parent Study) & Tafamidis (Extension Study)
Number of subjects included in analysis	441
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0005
Method	Cox Proportional Hazards model
Parameter estimate	Hazard ratio
Point estimate	0.6133
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.4666
upper limit	0.8062

Other pre-specified: Number of Participants With Cardiovascular Related Mortality Events: Cohort B

End point title	Number of Participants With Cardiovascular Related Mortality Events: Cohort B ^[4]
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End point description:

Deaths adjudicated as cardiovascular-related and indeterminate were reported. Cardiovascular-related mortality events included deaths, heart transplants and cardiac mechanical assist devices implantation treated as death. Cardiovascular relatedness was based on clinical judgement. Safety analysis population included all participants who were enrolled in this study and taken at least 1 dose of study medication.

End point type	Other pre-specified
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End point timeframe:

B3461045: From first dose of treatment up to 28 days post last dose of study treatment (approximately up to 61 months)

Notes:

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

Justification: The end point is reporting statistics for the arms specified

End point values	Cohort B: Tafamidis (Only in extension study)			
Subject group type	Reporting group			
Number of subjects analysed	1476			
Units: Participants	204			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Mean Annualized Rate of All Cause Hospitalizations

End point title	Mean Annualized Rate of All Cause Hospitalizations
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End point description:

Annual rate of all cause hospitalization was calculated for each participant as the participant's number of all cause hospitalizations divided by this participant's duration on study in years. Hospitalization was defined as any initial admission (even less than 24 hours) in a hospital or equivalent healthcare facility or any prolongation of an existing admission. Only all cause hospitalizations where the participant was admitted to a hospital during the current extension study were included in this analysis. Any hospitalizations prior to randomization date were not included. Safety analysis population included all participants who were enrolled in this study and taken at least 1 dose of study medication. This analysis (Cohort A) was based on the pooled dose groups, as per the SAP.

End point type	Other pre-specified
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End point timeframe:

B3461045: From first dose of treatment up to 28 days post last dose of study treatment (approximately up to 61 months)

End point values	Cohort A: Tafamidis (Parent and Extension Study)	Cohort A: Placebo (Parent Study)/Tafamid is (Extension Study)	Cohort B: Tafamidis (Only in extension study)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	170	82	1476	
Units: Hospitalization/year				
arithmetic mean (standard deviation)	1.67 (± 5.830)	1.84 (± 2.275)	0.96 (± 5.117)	

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Mean Annualized Rate of Cardiovascular (CV)-Related Hospitalizations

End point title	Mean Annualized Rate of Cardiovascular (CV)-Related Hospitalizations
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End point description:

Annual rate of CV related hospitalization was calculated for each participant as the participant's number of CV related hospitalizations divided by this participant's duration on study in years. CV-related hospitalizations included hospitalizations due to heart failure, arrhythmia, myocardial infarction, stroke, and other cardiovascular-related events. Hospitalization was defined as any initial admission (even less than 24 hours) in a hospital or equivalent healthcare facility or any prolongation of an existing admission. Admission also included transfer within the hospital to an acute/intensive care unit (e.g., from the psychiatric wing to a medical floor, medical floor to a coronary care unit, or neurological floor to a tuberculosis unit). Safety analysis population consisted of all participants (Cohorts A and B) who were enrolled in this study and taken at least 1 dose of study medication. This analysis (Cohort A) was based on the pooled dose groups, as per the SAP.

End point type	Other pre-specified
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End point timeframe:

B3461045: From first dose of treatment up to 28 days post last dose of study treatment (approximately up to 61 months)

End point values	Cohort A: Tafamidis (Parent and Extension Study)	Cohort A: Placebo (Parent Study)/Tafamid is (Extension Study)	Cohort B: Tafamidis (Only in extension study)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	170	82	1476	
Units: CV related hospitalization/year				
arithmetic mean (standard deviation)	1.09 (± 5.409)	1.14 (± 1.899)	0.50 (± 1.567)	

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change From Baseline in Kansas City Cardiomyopathy Questionnaire (KCCQ) Clinical Summary Scores at Months 12, 30, 42, 60 and 90: Cohort A

End point title	Change From Baseline in Kansas City Cardiomyopathy Questionnaire (KCCQ) Clinical Summary Scores at Months 12, 30, 42, 60 and 90: Cohort A
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End point description:

KCCQ: 23-item, self-administered questionnaire assesses health status & health-related Quality of life (QoL) in participants with heart failure. KCCQ has 8 domains: physical limitations, symptom stability, symptom frequency, symptom burden, total symptom (mean of symptom frequency & symptom burden), self-efficacy, quality of life & social limitations. Scores were generated for each domain & scaled from 0 (worst)-100 (best possible status). KCCQ-clinical summary score=mean of domains- physical limitation & total symptoms & transformed to single score which ranged from 0 -100, higher scores =better health status. Data for change from baseline is reported as least square (LS) mean. CMA set was analyzed. All participants reported under "Number of Participants Analyzed" contributed data to table; however, may not have evaluable data for every row. "Number Analyzed (n)" =number of participants evaluable at specified time points. Therefore, this analysis was based on the pooled dose

End point type	Other pre-specified
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End point timeframe:

B3461028: Baseline (Day 1, pre-dose), Months 12, 30; B3461045: Months 42, 60 and 90 (time points were relative to Day 1 from B3461028; 42, 60 and 90 Months were 12, 30 and 60 Months of B3461045)

End point values	Cohort A: Tafamidis(Parent study) & Tafamidis(Extension Study)	Cohort A: Placebo (Parent Study) & Tafamidis (Extension Study)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	264	177		
Units: Units on a scale				
least squares mean (standard error)				
Change at Month 12 (n= 221, 145)	-3.17 (± 1.016)	-10.2 (± 1.316)		
Change at Month 30 (n= 170, 84)	-7.41 (± 1.185)	-19.9 (± 1.999)		
Change at Month 42 (n= 143, 54)	-11.2 (± 1.483)	-25.4 (± 2.143)		
Change at Month 60 (n= 64, 22)	-11.8 (± 1.756)	-25.1 (± 3.287)		
Change at Month 90 (n= 9, 2)	-17.4 (± 2.758)	-56.9 (± 1.868)		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change From Baseline in KCCQ Overall Score at Months 12, 30, 42, 60, 90: Cohort A

End point title	Change From Baseline in KCCQ Overall Score at Months 12, 30, 42, 60, 90: Cohort A
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End point description:

KCCQ: 23-item, self-administered questionnaire assesses health status & health-related QoL in participants with heart failure. KCCQ has 8 domains: physical limitations, symptom stability, symptom

frequency, symptom burden, total symptom (mean of symptom frequency and symptom burden), self-efficacy, quality of life & social limitations). Scores were generated for each domain and scaled from 0 (worst)-100 (best possible status). KCCQ-overall score=mean of domains-physical limitation, total symptoms, quality of life, social limitation & transformed to single score which ranged from 0 (worst)-100 (best possible status), higher scores=better health status. Data for change from baseline reported as LS mean. CMA set was analyzed. All participants reported under "Number of Participants Analyzed" contributed data to table; may not have evaluable data for every row. "n"=number of participants evaluable at specified time points. Therefore, this analysis was based on the pooled dose groups, as per the SAP.

End point type	Other pre-specified
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End point timeframe:

B3461028: Baseline (Day 1, pre-dose), Months 12, 30; B3461045: Months 42, 60 and 90 (time points were relative to Day 1 from B3461028; 42, 60 and 90 Months were 12, 30 and 60 Months of B3461045)

End point values	Cohort A: Tafamidis(Parent study) & Tafamidis(Extension Study)	Cohort A: Placebo (Parent Study) & Tafamidis (Extension Study)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	264	177		
Units: Units on a scale				
least squares mean (standard error)				
Change at Month 12 (n= 221, 145)	-1.97 (± 1.131)	-9.69 (± 1.428)		
Change at Month 30 (n= 170, 84)	-6.07 (± 1.399)	-19.5 (± 1.908)		
Change at Month 42 (n= 143, 54)	-8.81 (± 1.470)	-24.0 (± 2.114)		
Change at Month 60 (n= 64, 22)	-8.56 (± 1.646)	-24.5 (± 3.020)		
Change at Month 90 (n= 9, 2)	-18.1 (± 2.617)	-52.6 (± 1.791)		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change from Baseline in KCCQ Total Symptom Score at Months 12, 30, 42, 60 and 90: Cohort A

End point title	Change from Baseline in KCCQ Total Symptom Score at Months 12, 30, 42, 60 and 90: Cohort A
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End point description:

KCCQ: 23-item, self-administered questionnaire assesses health status & health-related QoL in participants with heart failure. KCCQ has 8 domains: physical limitations, symptom stability, symptom frequency, symptom burden, total symptom (mean of symptom frequency and symptom burden), self-efficacy, quality of life & social limitations). Scores were generated for each domain and scaled from 0 (worst)-100 (best possible status). KCCQ Total Symptoms score=mean of the domains- symptom frequency & symptom burden and transformed to single score which ranged from 0 (worst)-100 (best possible status), higher scores=better health status. Data for change from baseline reported as LS mean. CMA set was analyzed. All participants reported under "Number of Participants Analyzed" contributed data to table; may not have evaluable data for every row. "n"=number of participants evaluable at specified time points. Therefore, this analysis was based on the pooled dose groups, as per the SAP.

End point type	Other pre-specified
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End point timeframe:

B3461028: Baseline (Day 1, pre-dose), Months 12, 30; B3461045: Months 42, 60 and 90 (time points were relative to Day 1 from B3461028; 42, 60 and 90 Months were 12, 30 and 60 Months of B3461045)

End point values	Cohort A: Tafamidis(Parent study) & Tafamidis(Extension Study)	Cohort A: Placebo (Parent Study) & Tafamidis (Extension Study)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	264	177		
Units: Units on a scale				
least squares mean (standard error)				
Change at Month 12 (n= 221, 145)	-2.90 (± 1.182)	-10.3 (± 1.494)		
Change at Month 30 (n= 170, 84)	-5.92 (± 1.279)	-18.7 (± 2.276)		
Change at Month 42 (n= 143, 54)	-9.29 (± 1.699)	-22.5 (± 2.237)		
Change at Month 60 (n= 64, 22)	-8.94 (± 1.858)	-19.0 (± 3.693)		
Change at Month 90 (n= 9, 2)	-16.4 (± 2.654)	-56.0 (± 1.958)		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change From Baseline in KCCQ Clinical Summary Scores at Months 12, 30 and 54: Cohort B

End point title	Change From Baseline in KCCQ Clinical Summary Scores at Months 12, 30 and 54: Cohort B ^[5]
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End point description:

KCCQ: 23-item, self-administered questionnaire assesses health status & health-related QoL in participants with heart failure. KCCQ has 8 domains: physical limitations, symptom stability, symptom frequency, symptom burden, total symptom (mean of symptom frequency and symptom burden), self-efficacy, quality of life and social limitations). Scores were generated for each domain and scaled from 0 (worst)-100 (best possible status). KCCQ-clinical summary score=mean of domains- physical limitation and total symptoms and transformed to single score which ranged from 0 (worst) -100 (best possible status), higher scores = better health status. Data for change from baseline reported as mean. Safety analysis set. All participants reported under "Number of Participants Analyzed" contributed data to table; may not have evaluable data for every row. "n"=number of participants evaluable at specified time points.

End point type	Other pre-specified
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End point timeframe:

B3461045: Baseline (Day 1, pre-dose), Months 12, 30 and 54

Notes:

[5] - 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: The end point is reporting statistics for the arms specified

End point values	Cohort B: Tafamidis (Only in extension study)			
Subject group type	Reporting group			
Number of subjects analysed	830			
Units: Units on a scale				
arithmetic mean (standard deviation)				
Change at Month 12 (n= 830)	-0.242 (± 17.7032)			
Change at Month 30 (n=237)	-3.086 (± 20.4276)			
Change at Month 54 (n=42)	-3.988 (± 18.7931)			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change From Baseline in KCCQ Overall Score at Months 12, 30 and 54: Cohort B

End point title	Change From Baseline in KCCQ Overall Score at Months 12, 30 and 54: Cohort B ^[6]
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End point description:

KCCQ: 23-item, self-administered questionnaire assesses health status & health-related QoL in participants with heart failure. KCCQ has 8 domains: physical limitations, symptom stability, symptom frequency, symptom burden, total symptom (mean of symptom frequency and symptom burden), self-efficacy, quality of life & social limitations). Scores were generated for each domain and scaled from 0 (worst)-100 (best possible status). KCCQ-overall score=mean of domains-physical limitation, total symptoms, quality of life, social limitation & transformed to single score which ranged from 0 (worst)-100 (best possible status), higher scores=better health status. Data for change from baseline reported as mean. Safety analysis set. All participants reported under "Number of Participants Analyzed" contributed data to table; may not have evaluable data for every row. "n" =number of participants evaluable at specified time points.

End point type	Other pre-specified
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End point timeframe:

B3461045: Baseline (Day 1, pre-dose), Months 12, 30 and 54

Notes:

[6] - 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: The end point is reporting statistics for the arms specified

End point values	Cohort B: Tafamidis (Only in extension study)			
Subject group type	Reporting group			
Number of subjects analysed	830			
Units: Units on a scale				
arithmetic mean (standard deviation)				
Change at Month 12 (n= 830)	0.443 (± 18.2575)			
Change at Month 30 (n= 237)	-1.378 (± 20.9437)			

Change at Month 54 (n=42)	-2.093 (\pm 19.5085)			
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Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change From Baseline in KCCQ Total Symptom Score at Months 12, 30 and 54: Cohort B

End point title	Change From Baseline in KCCQ Total Symptom Score at Months 12, 30 and 54: Cohort B ^[7]
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End point description:

KCCQ: 23-item, self-administered questionnaire assesses health status & health-related QoL in participants with heart failure. KCCQ has 8 domains: physical limitations, symptom stability, symptom frequency, symptom burden, total symptom(mean of symptom frequency and symptom burden),self-efficacy, quality of life & social limitations). Scores were generated for each domain and scaled from 0 (worst)-100 (best possible status). KCCQ Total Symptoms score=mean of the domains- symptom frequency & symptom burden and transformed to single score which ranged from 0 (worst)-100 (best possible status),higher scores=better health status. Data for change from baseline reported as mean. Safety analysis set. All participants reported under "Number of Participants Analyzed" contributed data to table; may not have evaluable data for every row."n"=number of participants evaluable at specified time points.

End point type	Other pre-specified
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End point timeframe:

B3461045: Baseline (Day 1, pre-dose), Months 12, 30 and 54

Notes:

[7] - 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: The end point is reporting statistics for the arms specified

End point values	Cohort B: Tafamidis (Only in extension study)			
Subject group type	Reporting group			
Number of subjects analysed	829			
Units: Units on a scale				
arithmetic mean (standard deviation)				
Change at Month 12 (n= 829)	0.738 (\pm 19.1549)			
Change at Month 30 (n= 237)	-1.112 (\pm 20.7952)			
Change at Month 54 (n=42)	-1.885 (\pm 19.4433)			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Number of Participants With Shift From Baseline in New York

Heart Association (NYHA) Classification at Months 6, 12, 18, 24, 30, 36, 42, 48, 54 and 60

End point title	Number of Participants With Shift From Baseline in New York Heart Association (NYHA) Classification at Months 6, 12, 18, 24, 30, 36, 42, 48, 54 and 60
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End point description:

NYHA classification: Class (CI) I: Participants with Cardiovascular disease (CVD) but without resulting limitation of physical activity (PA). Ordinary PA does not cause fatigue, palpitation, dyspnea or anginal pain; CI II: Participants with CVD resulting in slight limitation of PA & comfortable at rest. Ordinary PA results in fatigue, palpitation, dyspnea or angina pain; CI III: participants with CVD resulting in marked limitation of PA & comfortable at rest. Less than ordinary PA causes fatigue, palpitation, dyspnea or anginal pain; CI IV: participants with CVD resulting in inability to carry on any PA without discomfort. Symptoms of cardiac insufficiency/anginal syndrome may present even at rest. If any PA is undertaken, discomfort is increased. Safety analysis set. All participants reported "No. of Participants Analyzed" contributed data to table, may not be evaluable data for every row. n = participants evaluable at specified timepoints. Analysis (Cohort A) based on pooled dose groups, as per SAP.

End point type	Other pre-specified
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End point timeframe:

B3461045: Baseline (Day 1, pre-dose), Months 6, 12, 18, 24, 30, 36, 42, 48, 54 and 60

End point values	Cohort A: Tafamidis (Parent and Extension Study)	Cohort A: Placebo (Parent Study)/Tafamidis (Extension Study)	Cohort B: Tafamidis (Only in extension study)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	170	82	1476	
Units: Participants				
Month 6 CI I (Baseline) to CI I (n=155, 66, 1249)	13	4	132	
Month 12 CI I (Baseline) to CI I (n=142, 54, 850)	10	4	94	
Month 18 CI I (Baseline) to CI I (n=123, 47, 611)	5	4	64	
Month 24 CI I (Baseline) to CI I (n=105, 40, 434)	4	4	42	
Month 30 CI I (Baseline) to CI I (n=64, 23, 291)	1	1	27	
Month 36 CI I (Baseline) to CI I (n=43, 17, 223)	1	2	21	
Month 42 CI I (Baseline) to CI I (n=31, 8, 163)	0	0	16	
Month 48 CI I (Baseline) to CI I (n=27, 7, 99)	0	0	6	
Month 54 CI I (Baseline) to CI I (n=18, 4, 44)	0	0	1	
Month 60 CI I (Baseline) to CI I (n=9, 2, 0)	0	0	0	
Month 6 CI I (Baseline) to CI II (n=155, 66, 1249)	4	2	70	
Month 12 CI I (Baseline) to CI II (n=142, 54, 850)	5	0	60	
Month 18 CI I (Baseline) to CI II (n=123, 47, 611)	3	0	45	
Month 24 CI I (Baseline) to CI II (n=105, 40, 434)	4	1	40	

Month 30 CI I (Baseline) to CI II (n=64,23,291)	1	0	32	
Month 36 CI I (Baseline) to CI II (n=43,17,223)	4	0	18	
Month 42 CI I (Baseline) to CI II (n=31,8,163)	3	1	11	
Month 48 CI I (Baseline) to CI II (n=27,7,99)	2	0	8	
Month 54 CI I (Baseline) to CI II (n=18,4,44)	0	0	3	
Month 60 CI I (Baseline) to CI II (n= 9,2,0)	0	0	0	
Month 6 CI I (Baseline) to CI III (n=155,66,1249)	0	0	8	
Month 12 CI I (Baseline) to CI III (n=142,54,850)	1	0	3	
Month 18 CI I (Baseline) to CI III (n=123,47,611)	0	0	3	
Month 24 CI I (Baseline) to CI III (n=105,40,434)	2	1	0	
Month 30 CI I (Baseline) to CI III (n=64,23,291)	0	0	1	
Month 36 CI I (Baseline) to CI III (n=43,17,223)	0	0	0	
Month 42 CI I (Baseline) to CI III (n=31,8,163)	0	0	1	
Month 48 CI I (Baseline) to CI III (n=27,7,99)	0	0	0	
Month 54 CI I (Baseline) to CI III (n=18,4,44)	0	0	0	
Month 60 CI I (Baseline) to CI III (n= 9,2,0)	0	0	0	
Month 6 CI I (Baseline) to CI IV (n=155,66,1249)	0	0	0	
Month 12 CI I (Baseline) to CI IV (n=142,54,850)	0	0	0	
Month 18 CI I (Baseline) to CI IV (n=123,47,611)	0	0	0	
Month 24 CI I (Baseline) to CI IV (n=105,40,434)	0	0	0	
Month 30 CI I (Baseline) to CI IV (n=64,23,291)	0	0	0	
Month 36 CI I (Baseline) to CI IV (n=43,17,223)	0	0	0	
Month 42 CI I (Baseline) to CI IV (n=31,8,163)	0	0	0	
Month 48 CI I (Baseline) to CI IV (n=27,7,99)	0	0	0	
Month 54 CI I (Baseline) to CI IV (n=18,4,44)	0	0	0	
Month 60 CI I (Baseline) to CI IV (n= 9,2,0)	0	0	0	
Month 6 CI II (Baseline) to CI I (n=155,66,1249)	7	0	60	
Month 12 CI II (Baseline) to CI I (n=142,54,850)	6	0	50	
Month 18 CI II (Baseline) to CI I (n=123,47,611)	8	0	41	
Month 24 CI II (Baseline) to CI I (n=105,40,434)	8	0	31	
Month 30 CI II (Baseline) to CI I (n=64,23,291)	5	1	26	

Month 36 CI II (Baseline) to CI I (n=43,17,223)	3	0	19	
Month 42 CI II (Baseline) to CI I (n=31,8,163)	4	1	9	
Month 48 CI II (Baseline) to CI I (n=27,7,99)	2	1	2	
Month 54 CI II (Baseline) to CI I (n=18,4,44)	0	0	1	
Month 60 CI II (Baseline) to CI I (n= 9,2,0)	0	0	0	
Month 6 CI II (Baseline) to CI II (n=155,66,1249)	65	20	542	
Month 12 CI II (Baseline) to CI II (n=142,54,850)	63	16	371	
Month 18 CI II (Baseline) to CI II (n=123,47,611)	49	15	259	
Month 24 CI II (Baseline) to CI II (n=105,40,434)	49	12	191	
Month 30 CI II (Baseline) to CI II (n=64,23,291)	27	7	129	
Month 36 CI II (Baseline) to CI II (n= 43,17,223)	19	7	101	
Month 42 CI II (Baseline) to CI II (n=31,8,163)	14	4	77	
Month 48 CI II (Baseline) to CI II (n=27,7,99)	12	4	54	
Month 54 CI II (Baseline) to CI II (n=18,4,44)	7	3	22	
Month 60 CI II (Baseline) to CI II (n= 9,2,0)	4	0	0	
Month 6 CI II (Baseline) to CI III (n=155,66,1249)	11	2	100	
Month 12 CI II (Baseline) to CI III (n=142,54,850)	10	1	67	
Month 18 CI II (Baseline) to CI III (n=123,47,611)	9	1	61	
Month 24 CI II (Baseline) to CI III (n=105,40,434)	3	0	42	
Month 30 CI II (Baseline) to CI III (n=64,23,291)	2	1	24	
Month 36 CI II (Baseline) to CI III (n=43,17,223)	2	1	25	
Month 42 CI II (Baseline) to CI III (n=31,8,163)	2	0	16	
Month 48 CI II (Baseline) to CI III (n=27,7,99)	2	0	7	
Month 54 CI II (Baseline) to CI III (n=18,4,44)	2	0	6	
Month 60 CI II (Baseline) to CI III (n= 9,2,0)	2	0	0	
Month 6 CI II (Baseline) to CI IV (n=155,66,1249)	0	0	1	
Month 12 CI II (Baseline) to CI IV (n= 142,54,850)	1	0	1	
Month 18 CI II (Baseline) to CI IV (n= 123,47,611)	0	0	1	
Month 24 CI II (Baseline) to CI IV (n=105,40,434)	0	0	0	
Month 30 CI II (Baseline) to CI IV (n=64,23,291)	0	0	0	
Month 36 CI II (Baseline) to CI IV (n=43,17,223)	0	0	0	

Month 42 CI II (Baseline) to CI IV (n=31,8,163)	0	0	0	
Month 48 CI II (Baseline) to CI IV (n=27,7,99)	0	0	0	
Month 54 CI II (Baseline) to CI IV (n=18,4,44)	0	0	0	
Month 60 CI II (Baseline) to CI IV (n= 9,2,0)	0	0	0	
Month 6 CI III (Baseline) to CI I (n=155,66,1249)	1	0	4	
Month 12 CI III (Baseline) to CI I (n=142,54,850)	3	0	1	
Month 18 CI III (Baseline) to CI I (n=123,47,611)	2	0	5	
Month 24 CI III (Baseline) to CI I (n=105,40,434)	4	0	3	
Month 30 CI III (Baseline) to CI I (n=64,23,291)	4	0	2	
Month 36 CI III (Baseline) to CI I (n=43,17,223)	1	0	3	
Month 42 CI III (Baseline) to CI I (n=31,8,163)	1	0	1	
Month 48 CI III (Baseline) to CI I (n=27,7,99)	2	0	0	
Month 54 CI III (Baseline) to CI I (n=18,4,44)	3	0	0	
Month 60 CI III (Baseline) to CI I (n= 9,2,0)	1	0	0	
Month 6 CI III (Baseline) to CI II (n=155,66,1249)	17	9	88	
Month 12 CI III (Baseline) to CI II (n=142,54,850)	12	9	67	
Month 18 CI III (Baseline) to CI II (n=123,47,611)	19	6	57	
Month 24 CI III (Baseline) to CI II (n=105,40,434)	11	8	34	
Month 30 CI III (Baseline) to CI II (n=64,23,291)	14	4	22	
Month 36 CI III (Baseline) to CI II (n=43,17,223)	5	2	21	
Month 42 CI III (Baseline) to CI II (n=31,8,163)	3	1	20	
Month 48 CI III (Baseline) to CI II (n=27,7,99)	3	1	8	
Month 54 CI III (Baseline) to CI II (n=18,4,44)	3	1	4	
Month 60 CI III (Baseline) to CI II (n= 9,2,0)	1	2	0	
Month6 CI III(Baseline) to CI III (n=155,66,1249)	34	24	226	
Month12 CI III (Baseline) to CI III (n=142,54,850)	31	23	127	
Month18 CI III(Baseline) to CI III (n=123,47,611)	24	19	70	
Month24 CI III(Baseline) to CI III (n=105,40,434)	17	14	46	
Month30 CI III(Baseline) to CI III (n=64,23,291)	10	9	24	
Month36 CI III(Baseline) to CI III (n= 43,17,223)	7	4	14	
Month42CI III(Baseline) to CI III (n=31,8,163)	4	1	12	

Month48 CI III(Baseline) to CI III (n=27,7,99)	4	1	13	
Month54 CI III(Baseline) to CI III (n=18,4,44)	3	0	7	
Month60 CI III(Baseline) to CI III (n=9,2,0)	1	0	0	
Month6 CI III(Baseline) to CI IV (n=155,66,1249)	0	0	2	
Month12 CI III (Baseline) to CI IV (n=142,54,850)	0	0	0	
Month 18 CI III (Baseline) to CI IV (n=123,47,611)	0	0	0	
Month 24 CI III (Baseline) to CI IV (n=105,40,434)	0	0	0	
Month30 CI III(Baseline) to CI IV (n=64,23, 291)	0	0	0	
Month36 CI III(Baseline) to CI IV (n=43,17,223)	0	0	0	
Month42 CI III(Baseline) to CI IV (n=31,8,163)	0	0	0	
Month48 CI III(Baseline) to CI IV (n=27,7,99)	0	0	0	
Month54 CI III(Baseline) to CI IV (n=18,4,44)	0	0	0	
Month60 CI III(Baseline) to CI IV (n=9,2,0)	0	0	0	
Month 6 CI IV (Baseline) to CI I (n=155,66,1249)	0	0	1	
Month 12 CI IV (Baseline) to CI I (n=142,54,850)	0	0	0	
Month 18 CI IV (Baseline) to CI I (n=123,47,611)	2	0	0	
Month 24 CI IV (Baseline) to CI I (n=105,40,434)	0	0	0	
Month 30 CI IV (Baseline) to CI I (n=64,23,291)	0	0	0	
Month 36 CI IV (Baseline) to CI I (n=43,17,223)	0	0	0	
Month 42 CI IV (Baseline) to CI I (n=31,8,163)	0	0	0	
Month 48 CI IV (Baseline) to CI I (n=27,7,99)	0	0	0	
Month 54 CI IV (Baseline) to CI I (n=18,4,44)	0	0	0	
Month 60 CI IV (Baseline) to CI I (n=9,2,0)	0	0	0	
Month 6 CI IV (Baseline) to CI II (n=155,66,1249)	1	1	2	
Month 12 CI IV (Baseline) to CI II (n=142,54,850)	0	0	1	
Month 18 CI IV (Baseline) to CI II (n=123,47,611)	0	0	2	
Month 24 CI IV (Baseline) to CI II (n=105,40,434)	1	0	1	
Month 30 CI IV (Baseline) to CI II (n=64,23,291)	0	0	2	
Month 36 CI IV (Baseline) to CI II (n=43,17,223)	1	0	1	
Month 42 CI IV (Baseline) to CI II (n=31,8,163)	0	0	0	
Month 48 CI IV (Baseline) to CI II (n=27,7,99)	0	0	0	

Month 54 CI IV (Baseline) to CI II (n=18,4,44)	0	0	0	
Month 60 CI IV (Baseline) to CI II (n=9,2,0)	0	0	0	
Month 6 CI IV (Baseline) to CI III (n=155,66,1249)	1	3	10	
Month 12 CI IV (Baseline) to CI III (n=142,54,850)	0	1	7	
Month 18 CI IV (Baseline) to CI III (n=123,47,611)	2	2	3	
Month 24 CI IV (Baseline) to CI III (n=105,40,434)	2	0	4	
Month 30 CI IV (Baseline) to CI III (n=64,23,291)	0	0	2	
Month 36 CI IV (Baseline) to CI III (n=43,17,223)	0	1	0	
Month 42 CI IV (Baseline) to CI III (n=31,8,163)	0	0	0	
Month 48 CI IV (Baseline) to CI III (n=27,7,99)	0	0	1	
Month 54 CI IV (Baseline) to CI III (n=18,4,44)	0	0	0	
Month 60 CI IV (Baseline) to CI III (n=9,2,0)	0	0	0	
Month 6 CI IV (Baseline) to CI IV (n=155,66,1249)	1	1	3	
Month 12 CI IV (Baseline) to CI IV (n=142,54,850)	0	0	1	
Month 18 CI IV (Baseline) to CI IV (n=123,47,611)	0	0	0	
Month 24 CI IV (Baseline) to CI IV (n=105,40,434)	0	0	0	
Month 30 CI IV (Baseline) to CI IV (n=64,23,291)	0	0	0	
Month 36 CI IV (Baseline) to CI IV (n=43,17,223)	0	0	0	
Month 42 CI IV (Baseline) to CI IV (n=31,8,163)	0	0	0	
Month 48 CI IV (Baseline) to CI IV (n=27,7,99)	0	0	0	
Month 54 CI IV (Baseline) to CI IV (n=18,4,44)	0	0	0	
Month 60 CI IV (Baseline) to CI IV (n=9,2,0)	0	0	0	

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change From Baseline in Body Mass Index (BMI) at Months 6, 12, 18, 24, 30, 36, 42, 48, 54 and 60

End point title	Change From Baseline in Body Mass Index (BMI) at Months 6, 12, 18, 24, 30, 36, 42, 48, 54 and 60
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End point description:

BMI was calculated as: body weight in kilogram (kg) divided by (/) square of body height measurement in meters square (m²). Safety analysis population included all participants (Cohorts A and B) who were enrolled in this study and taken at least 1 dose of study medication. All participants reported under "Number of Participants Analyzed" contributed data to the table; however, may not have evaluable data

for every row. "n" signifies number of participants evaluable at specified time points.99999 indicates Arithmetic Mean and Standard Deviation was not estimable as there were no participants. Therefore, this analysis was based on the pooled dose groups, as per the SAP.

End point type	Other pre-specified
End point timeframe:	
B3461045: Baseline (Day 1, pre-dose), Months 6, 12, 18, 24, 30, 36, 42, 48, 54 and 60	

End point values	Cohort A: Tafamidis (Parent and Extension Study)	Cohort A: Placebo (Parent Study)/Tafamid is (Extension Study)	Cohort B: Tafamidis (Only in extension study)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	170	82	1476	
Units: kg/m^2				
arithmetic mean (standard deviation)				
Change at Month 6 (n= 155, 67, 1216)	-0.07 (± 0.873)	-0.27 (± 0.900)	-0.24 (± 1.234)	
Change at Month 12 (n= 141, 54, 800)	-0.21 (± 1.212)	-0.40 (± 1.440)	-0.20 (± 1.552)	
Change at Month 18 (n=122, 47, 555)	-0.38 (± 1.442)	-0.85 (± 1.502)	-0.30 (± 1.956)	
Change at Month 24 (n= 104, 40, 418)	-0.36 (± 1.407)	-0.78 (± 1.668)	-0.43 (± 1.747)	
Change at Month 30 (n= 62, 23, 287)	-0.71 (± 1.423)	-1.28 (± 1.814)	-0.41 (± 1.802)	
Change at Month 36 (n= 41, 16, 220)	-1.18 (± 2.200)	-0.49 (± 1.852)	-0.69 (± 1.730)	
Change at Month 42 (n=30, 8, 162)	-0.91 (± 1.402)	-0.11 (± 1.523)	-0.74 (± 1.827)	
Change at Month 48 (n= 27, 7, 100)	-1.14 (± 1.480)	-0.01 (± 1.927)	-0.83 (± 1.732)	
Change at Month 54 (n=18, 4, 44)	-1.03 (± 1.716)	-1.54 (± 0.528)	-1.24 (± 1.942)	
Change at Month 60 (n= 9, 2, 0)	-0.93 (± 2.102)	-1.62 (± 0.834)	99999 (± 99999)	

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change From Baseline in Modified Body Mass Index (mBMI) at Months 6, 12, 18, 24, 30, 36, 42, 48, 54 and 60

End point title	Change From Baseline in Modified Body Mass Index (mBMI) at Months 6, 12, 18, 24, 30, 36, 42, 48, 54 and 60
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End point description:

Modified (m)BMI of participants was calculated to determine if there was any gastrointestinal involvement in participants. The mBMI was calculated by multiplying BMI by serum albumin concentration gram/liter (g/L). Safety analysis population included all participants (Cohorts A and B) who were enrolled in this study and taken at least 1 dose of study medication. All participants reported under "Number of Participants Analyzed" contributed data to the table; however, may not have evaluable data for every row. "n" signifies number of participants evaluable at specified time points. Here, 88888 indicates Standard Deviation was not estimable as there was only one participant. 99999

indicates Arithmetic Mean and Standard Deviation was not estimable as there were no participants. This analysis (cohort A) was based on the pooled dose groups, as per the SAP.

End point type	Other pre-specified
End point timeframe:	
B3461045: Baseline (Day 1, pre-dose), Months 6, 12, 18, 24, 30, 36, 42, 48, 54 and 60	

End point values	Cohort A: Tafamidis (Parent and Extension Study)	Cohort A: Placebo (Parent Study)/Tafamid is (Extension Study)	Cohort B: Tafamidis (Only in extension study)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	170	82	1476	
Units: (kg/m ²) *(g/L)				
arithmetic mean (standard deviation)				
Change at Month 6 (n= 154, 64, 1037)	-2.96 (± 36.046)	-10.91 (± 36.338)	-8.51 (± 51.329)	
Change at Month 12 (n= 140, 51, 674)	-7.42 (± 49.840)	-16.09 (± 57.882)	-6.17 (± 66.094)	
Change at Month 18 (n= 121, 44, 455)	-15.46 (± 60.361)	-35.46 (± 63.390)	-10.08 (± 85.605)	
Change at Month 24 (n= 104, 38, 345)	-15.07 (± 58.706)	-32.33 (± 71.104)	-15.81 (± 74.009)	
Change at Month 30 (n= 62, 22, 234)	-29.31 (± 61.003)	-52.81 (± 78.705)	-15.70 (± 79.724)	
Change at Month 36 (n= 41, 15, 172)	-49.46 (± 98.257)	-17.81 (± 80.327)	-24.66 (± 74.366)	
Change at Month 42 (n= 30, 7, 135)	-36.32 (± 58.130)	1.59 (± 69.701)	-28.06 (± 78.987)	
Change at Month 48 (n= 27, 6, 87)	-46.43 (± 62.394)	14.05 (± 83.969)	-32.91 (± 71.745)	
Change at Month 54 (n= 18, 3, 36)	-41.98 (± 74.883)	-52.80 (± 14.562)	-51.15 (± 79.618)	
Change at Month 60 (n= 9, 1, 0)	-38.90 (± 92.253)	-41.20 (± 88888)	99999 (± 99999)	

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change From Baseline in Troponin I Concentration at Month 6, 12 , 18, 24, 30, 36, 42, 48, 54 and 60

End point title	Change From Baseline in Troponin I Concentration at Month 6, 12 , 18, 24, 30, 36, 42, 48, 54 and 60
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End point description:

NT-proBNP was a cardiac marker which had the prognostic value for participants with heart failure or left ventricular dysfunction. It was measure in nanogram per milliliter (ng/mL). Higher level of the marker was indicative of heart damage. Safety analysis population included all participants (Cohorts A and B) who were enrolled in this study and taken at least 1 dose of study medication. All participants reported under "Number of Participants Analyzed" contributed data to the table; however, may not have evaluable data for every row. "n" signifies number of participants evaluable at specified time points. Here, 88888 indicates Standard Deviation was not estimable as there was only one participant. 99999 indicates Arithmetic Mean and Standard Deviation was not estimable as there were no participants. This

analysis (cohort A) was based on the pooled dose groups, as per the SAP.

End point type	Other pre-specified
End point timeframe:	
B3461045: Baseline (Day 1, pre-dose), Months 6, 12, 18, 24, 30, 36, 42, 48, 54 and 60	

End point values	Cohort A: Tafamidis (Parent and Extension Study)	Cohort A: Placebo (Parent Study)/Tafamid is (Extension Study)	Cohort B: Tafamidis (Only in extension study)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	170	82	1476	
Units: ng/mL				
arithmetic mean (standard deviation)				
Change at Month 6 (n= 0, 0, 108)	99999 (± 99999)	99999 (± 99999)	0.012 (± 0.1706)	
Change at Month 12 (n= 165, 81, 99)	0.035 (± 0.3977)	0.037 (± 0.0853)	0.009 (± 0.0893)	
Change at Month 18 (n= 1, 0, 70)	0.040 (± 88888)	99999 (± 99999)	-0.007 (± 0.0786)	
Change at Month 24 (n= 2, 3, 64)	0.000 (± 0.0566)	0.033 (± 0.0306)	-0.031 (± 0.2031)	
Change at Month 30 (n= 168, 80, 64)	0.022 (± 0.1599)	0.100 (± 0.1728)	-0.033 (± 0.2055)	
Change at Month 36 (n= 27, 11, 64)	0.009 (± 0.0579)	0.018 (± 0.1057)	-0.034 (± 0.1913)	
Change at Month 42 (n= 26, 6, 24)	-0.002 (± 0.0795)	-0.047 (± 0.0755)	-0.021 (± 0.2484)	
Change at Month 48 (n= 26, 6, 2)	0.016 (± 0.0795)	-0.067 (± 0.2040)	-0.100 (± 0.0000)	
Change at Month 54 (n= 14, 3, 0)	-0.033 (± 0.0792)	-0.363 (± 0.6080)	99999 (± 99999)	
Change at Month 60 (n=8, 2, 0)	-0.040 (± 0.0414)	0.035 (± 0.0354)	99999 (± 99999)	

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change From Baseline in N-Terminal Prohormone Brain Natriuretic Peptide (NT-proBNP) Concentration at Month 6, 12, 18, 24, 30, 36, 42, 48, 54 and 60

End point title	Change From Baseline in N-Terminal Prohormone Brain Natriuretic Peptide (NT-proBNP) Concentration at Month 6, 12, 18, 24, 30, 36, 42, 48, 54 and 60
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End point description:

NT-proBNP was a cardiac marker which had the prognostic value for participants with heart failure or left ventricular dysfunction. It was measure in picomole per liter (pmole/L). Higher level of the marker was indicative of heart damage. Safety analysis population included all participants (Cohorts A and B) who were enrolled in this study and taken at least 1 dose of study medication. All participants reported under "Number of Participants Analyzed" contributed data to the table; however, may not have evaluable data for every row. "n" signifies number of participants evaluable at specified time points. Here, 88888 indicates Standard Deviation was not estimable as there was only one participant. 99999 indicates

Arithmetic Mean and Standard Deviation was not estimable as there were no participants. This analysis (cohort A) was based on the pooled dose groups, as per the SAP.

End point type	Other pre-specified
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End point timeframe:

B3461045: Baseline (Day 1, pre-dose), Months 6, 12, 18, 24, 30, 36, 42, 48, 54 and 60

End point values	Cohort A: Tafamidis (Parent and Extension Study)	Cohort A: Placebo (Parent Study)/Tafamidis (Extension Study)	Cohort B: Tafamidis (Only in extension study)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	170	82	1476	
Units: pmole/L				
arithmetic mean (standard deviation)				
Change at Month 6 (n= 0, 0, 108)	99999 (± 99999)	99999 (± 99999)	24.820 (± 171.2075)	
Change at Month 12 (n= 167, 80, 101)	31.117 (± 220.9279)	127.973 (± 226.7727)	32.686 (± 180.4921)	
Change at Month 18 (n= 1, 0, 79)	226.442 (± 88888)	99999 (± 99999)	71.582 (± 329.5411)	
Change at Month 24 (n= 2, 3, 69)	131.334 (± 119.5258)	256.442 (± 101.8073)	92.899 (± 320.6054)	
Change at Month 30 (n= 170, 81, 70)	159.596 (± 404.8483)	417.682 (± 597.9224)	149.049 (± 320.8814)	
Change at Month 36 (n= 29, 11, 63)	322.963 (± 215.1605)	420.196 (± 251.8446)	88.895 (± 227.7375)	
Change at Month 42 (n= 26, 6, 24)	419.034 (± 315.6436)	324.211 (± 173.6652)	191.318 (± 482.3582)	
Change at Month 48 (n= 26, 6, 2)	492.154 (± 387.4700)	400.571 (± 228.4343)	264.566 (± 78.7059)	
Change at Month 54 (n= 17, 3, 0)	405.887 (± 457.6349)	340.082 (± 190.6412)	99999 (± 99999)	
Change at Month 60 (n= 9, 2, 0)	392.363 (± 271.2883)	314.184 (± 274.6756)	99999 (± 99999)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

B3461045: From first dose of treatment up to 28 days post last dose of study treatment (approximately up to 61 months)

Adverse event reporting additional description:

Same event may appear as non-SAE & SAE, what is presented are distinct events. Event may be categorized as serious in 1 participant and as non-serious in another, or participant may have experienced both SAE & non-SAE. Safety analysis population consisted of all participants who were enrolled in this study & taken at least 1 dose of study medication.

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	26.1
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Reporting groups

Reporting group title	Cohort A: Tafamidis (Parent and Extension Study)
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Reporting group description:

Participants who received tafamidis 20 mg or 80 mg orally once daily in the parent study for 30 months (complete participation), after enrollment in the current extension study, continued to receive the same dose and later switched to tafamidis 61 mg (or 80 mg in regions where 61 mg tafamidis was unavailable), orally once daily along with standard of care for up to 60 months.

Reporting group title	Cohort B: Tafamidis (Only in extension study)
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Reporting group description:

Participants who did not participate in the parent study and received tafamidis at a dose of 61 mg (or 80 mg in regions where 61 mg tafamidis was unavailable), once daily along with standard of care for up to 60 months.

Reporting group title	Cohort A: Placebo (Parent Study)/Tafamidis (Extension Study)
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Reporting group description:

Participants who received placebo orally once daily in the parent study for 30 months (complete participation), after enrollment in the current extension study, received tafamidis 20 mg or 80 mg and later switched to tafamidis 61 mg (or 80 mg in regions where 61 mg tafamidis was unavailable), orally once daily along with standard of care for up to 60 months.

Serious adverse events	Cohort A: Tafamidis (Parent and Extension Study)	Cohort B: Tafamidis (Only in extension study)	Cohort A: Placebo (Parent Study)/Tafamidis (Extension Study)
Total subjects affected by serious adverse events			
subjects affected / exposed	132 / 170 (77.65%)	736 / 1476 (49.86%)	64 / 82 (78.05%)
number of deaths (all causes)	45	203	33
number of deaths resulting from adverse events	40	198	32
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma of colon			
subjects affected / exposed	1 / 170 (0.59%)	4 / 1476 (0.27%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Adrenal neoplasm			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Anal squamous cell carcinoma			
subjects affected / exposed	0 / 170 (0.00%)	0 / 1476 (0.00%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
B-cell lymphoma			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Basal cell carcinoma			
subjects affected / exposed	2 / 170 (1.18%)	9 / 1476 (0.61%)	2 / 82 (2.44%)
occurrences causally related to treatment / all	0 / 2	0 / 10	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bladder cancer			
subjects affected / exposed	1 / 170 (0.59%)	1 / 1476 (0.07%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bladder transitional cell carcinoma recurrent			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Bowen's disease			
subjects affected / exposed	0 / 170 (0.00%)	0 / 1476 (0.00%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung adenocarcinoma			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Cancer pain			

subjects affected / exposed	1 / 170 (0.59%)	0 / 1476 (0.00%)	0 / 82 (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
Central nervous system melanoma			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Chronic myelomonocytic leukaemia			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Colon neoplasm			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Diffuse large B-cell lymphoma			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Hormone-dependent prostate cancer			
subjects affected / exposed	1 / 170 (0.59%)	0 / 1476 (0.00%)	0 / 82 (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
Breast cancer			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung neoplasm			
subjects affected / exposed	1 / 170 (0.59%)	1 / 1476 (0.07%)	0 / 82 (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
Lung neoplasm malignant			

subjects affected / exposed	1 / 170 (0.59%)	0 / 1476 (0.00%)	0 / 82 (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
Malignant melanoma			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Metastases to lung			
subjects affected / exposed	0 / 170 (0.00%)	0 / 1476 (0.00%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myelodysplastic syndrome with excess blasts			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Neoplasm			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neuroendocrine carcinoma metastatic			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Neuroendocrine tumour			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Non-Hodgkin's lymphoma			
subjects affected / exposed	1 / 170 (0.59%)	0 / 1476 (0.00%)	0 / 82 (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
Non-small cell lung cancer stage IIIB			

subjects affected / exposed	1 / 170 (0.59%)	0 / 1476 (0.00%)	0 / 82 (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
Oesophageal squamous cell carcinoma			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Oncocytoma			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Pancreatic carcinoma			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Primary pulmonary melanoma			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostate cancer			
subjects affected / exposed	3 / 170 (1.76%)	5 / 1476 (0.34%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 5	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostate cancer metastatic			
subjects affected / exposed	1 / 170 (0.59%)	1 / 1476 (0.07%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Renal neoplasm			
subjects affected / exposed	0 / 170 (0.00%)	2 / 1476 (0.14%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Squamous cell carcinoma			

subjects affected / exposed	1 / 170 (0.59%)	6 / 1476 (0.41%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 6	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Squamous cell carcinoma of skin			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transitional cell carcinoma			
subjects affected / exposed	0 / 170 (0.00%)	4 / 1476 (0.27%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Distributive shock			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Circulatory collapse			
subjects affected / exposed	0 / 170 (0.00%)	2 / 1476 (0.14%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 2	0 / 0
Bleeding varicose vein			
subjects affected / exposed	0 / 170 (0.00%)	0 / 1476 (0.00%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Axillary vein thrombosis			
subjects affected / exposed	1 / 170 (0.59%)	0 / 1476 (0.00%)	0 / 82 (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
Arteriovenous fistula			
subjects affected / exposed	1 / 170 (0.59%)	0 / 1476 (0.00%)	0 / 82 (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
Aortic stenosis			

subjects affected / exposed	0 / 170 (0.00%)	10 / 1476 (0.68%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 0	0 / 11	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aortic dissection			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Embolism			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Hypertensive emergency			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Haemorrhage			
subjects affected / exposed	0 / 170 (0.00%)	0 / 1476 (0.00%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematoma			
subjects affected / exposed	2 / 170 (1.18%)	2 / 1476 (0.14%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Extremity necrosis			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Embolism venous			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Hypertensive urgency			

subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Hypotension			
subjects affected / exposed	2 / 170 (1.18%)	16 / 1476 (1.08%)	4 / 82 (4.88%)
occurrences causally related to treatment / all	0 / 2	0 / 16	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Peripheral venous disease			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Shock			
subjects affected / exposed	1 / 170 (0.59%)	1 / 1476 (0.07%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
Iliac artery stenosis			
subjects affected / exposed	1 / 170 (0.59%)	0 / 1476 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic limb pain			
subjects affected / exposed	1 / 170 (0.59%)	0 / 1476 (0.00%)	0 / 82 (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
Pelvic venous thrombosis			
subjects affected / exposed	1 / 170 (0.59%)	0 / 1476 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral arterial occlusive disease			
subjects affected / exposed	0 / 170 (0.00%)	2 / 1476 (0.14%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral artery occlusion			

subjects affected / exposed	0 / 170 (0.00%)	2 / 1476 (0.14%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Peripheral artery stenosis			
subjects affected / exposed	1 / 170 (0.59%)	1 / 1476 (0.07%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral embolism			
subjects affected / exposed	0 / 170 (0.00%)	3 / 1476 (0.20%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral ischaemia			
subjects affected / exposed	0 / 170 (0.00%)	2 / 1476 (0.14%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral vein stenosis			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Shock haemorrhagic			
subjects affected / exposed	1 / 170 (0.59%)	1 / 1476 (0.07%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Thrombosis			
subjects affected / exposed	1 / 170 (0.59%)	1 / 1476 (0.07%)	0 / 82 (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
Subclavian vein thrombosis			
subjects affected / exposed	1 / 170 (0.59%)	0 / 1476 (0.00%)	0 / 82 (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
Venous thrombosis limb			

subjects affected / exposed	1 / 170 (0.59%)	0 / 1476 (0.00%)	0 / 82 (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			
Therapy change			
subjects affected / exposed	0 / 170 (0.00%)	0 / 1476 (0.00%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac ablation			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Implantable defibrillator insertion			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Muscle electrostimulation therapy			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Wound treatment			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	2 / 170 (1.18%)	5 / 1476 (0.34%)	2 / 82 (2.44%)
occurrences causally related to treatment / all	0 / 2	0 / 5	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Chest pain			
subjects affected / exposed	4 / 170 (2.35%)	5 / 1476 (0.34%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 5	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Death			
subjects affected / exposed	0 / 170 (0.00%)	7 / 1476 (0.47%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 0	0 / 7	0 / 1
deaths causally related to treatment / all	0 / 0	7 / 7	1 / 1
Discomfort			
subjects affected / exposed	1 / 170 (0.59%)	0 / 1476 (0.00%)	0 / 82 (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
Inflammation			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Fatigue			
subjects affected / exposed	1 / 170 (0.59%)	3 / 1476 (0.20%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 1	2 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General physical health deterioration			
subjects affected / exposed	1 / 170 (0.59%)	11 / 1476 (0.75%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 1	0 / 13	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 4	0 / 1
Generalised oedema			
subjects affected / exposed	1 / 170 (0.59%)	3 / 1476 (0.20%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Hernia			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Hypothermia			
subjects affected / exposed	1 / 170 (0.59%)	0 / 1476 (0.00%)	0 / 82 (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
Implant site haematoma			

subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Disease progression			
subjects affected / exposed	4 / 170 (2.35%)	22 / 1476 (1.49%)	3 / 82 (3.66%)
occurrences causally related to treatment / all	0 / 4	0 / 22	0 / 3
deaths causally related to treatment / all	0 / 4	0 / 22	0 / 3
Multi-organ disorder			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Multiple organ dysfunction syndrome			
subjects affected / exposed	1 / 170 (0.59%)	1 / 1476 (0.07%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
Non-cardiac chest pain			
subjects affected / exposed	1 / 170 (0.59%)	0 / 1476 (0.00%)	0 / 82 (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
Oedema peripheral			
subjects affected / exposed	0 / 170 (0.00%)	6 / 1476 (0.41%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 9	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain			
subjects affected / exposed	0 / 170 (0.00%)	2 / 1476 (0.14%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral swelling			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			

subjects affected / exposed	0 / 170 (0.00%)	3 / 1476 (0.20%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sudden death			
subjects affected / exposed	0 / 170 (0.00%)	6 / 1476 (0.41%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 6	0 / 0
deaths causally related to treatment / all	0 / 0	6 / 6	0 / 0
Systemic inflammatory response syndrome			
subjects affected / exposed	2 / 170 (1.18%)	0 / 1476 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Acquired ATTR amyloidosis			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Amyloidosis			
subjects affected / exposed	0 / 170 (0.00%)	2 / 1476 (0.14%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Anaphylactic reaction			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Graft versus host disease			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Primary amyloidosis			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Reproductive system and breast disorders			

Breast pain			
subjects affected / exposed	1 / 170 (0.59%)	0 / 1476 (0.00%)	0 / 82 (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
Prostatitis			
subjects affected / exposed	0 / 170 (0.00%)	2 / 1476 (0.14%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostatomegaly			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Scrotal swelling			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Benign prostatic hyperplasia			
subjects affected / exposed	1 / 170 (0.59%)	5 / 1476 (0.34%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 5	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Atelectasis			
subjects affected / exposed	0 / 170 (0.00%)	3 / 1476 (0.20%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute respiratory distress syndrome			
subjects affected / exposed	2 / 170 (1.18%)	0 / 1476 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute respiratory failure			
subjects affected / exposed	3 / 170 (1.76%)	7 / 1476 (0.47%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 3	0 / 8	0 / 3
deaths causally related to treatment / all	0 / 2	0 / 1	0 / 0

Dyspnoea exertional			
subjects affected / exposed	1 / 170 (0.59%)	0 / 1476 (0.00%)	2 / 82 (2.44%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epistaxis			
subjects affected / exposed	2 / 170 (1.18%)	5 / 1476 (0.34%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 5	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemoptysis			
subjects affected / exposed	0 / 170 (0.00%)	3 / 1476 (0.20%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Hypercapnia			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Hypoxia			
subjects affected / exposed	0 / 170 (0.00%)	2 / 1476 (0.14%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Interstitial lung disease			
subjects affected / exposed	1 / 170 (0.59%)	2 / 1476 (0.14%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	3 / 170 (1.76%)	13 / 1476 (0.88%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 4	0 / 13	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	3 / 170 (1.76%)	10 / 1476 (0.68%)	4 / 82 (4.88%)
occurrences causally related to treatment / all	0 / 4	0 / 11	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonitis			

subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax			
subjects affected / exposed	0 / 170 (0.00%)	2 / 1476 (0.14%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary alveolar haemorrhage			
subjects affected / exposed	0 / 170 (0.00%)	3 / 1476 (0.20%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Chronic obstructive pulmonary disease			
subjects affected / exposed	1 / 170 (0.59%)	3 / 1476 (0.20%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Cough			
subjects affected / exposed	0 / 170 (0.00%)	2 / 1476 (0.14%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Organising pneumonia			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Pulmonary amyloidosis			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Pulmonary embolism			
subjects affected / exposed	0 / 170 (0.00%)	4 / 1476 (0.27%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary fibrosis			

subjects affected / exposed	1 / 170 (0.59%)	0 / 1476 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary haemorrhage			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Pulmonary hypertension			
subjects affected / exposed	0 / 170 (0.00%)	3 / 1476 (0.20%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary infarction			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Pulmonary toxicity			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory disorder			
subjects affected / exposed	1 / 170 (0.59%)	0 / 1476 (0.00%)	0 / 82 (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
Respiratory distress			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Respiratory failure			
subjects affected / exposed	1 / 170 (0.59%)	12 / 1476 (0.81%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 13	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 4	0 / 0
Pulmonary oedema			

subjects affected / exposed	1 / 170 (0.59%)	7 / 1476 (0.47%)	2 / 82 (2.44%)
occurrences causally related to treatment / all	0 / 1	0 / 7	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Psychiatric disorders			
Agitation			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Anxiety			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Completed suicide			
subjects affected / exposed	1 / 170 (0.59%)	0 / 1476 (0.00%)	0 / 82 (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
Confusional state			
subjects affected / exposed	0 / 170 (0.00%)	6 / 1476 (0.41%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 6	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Depressed mood			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Hallucination			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Major depression			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Mental status changes			

subjects affected / exposed	2 / 170 (1.18%)	4 / 1476 (0.27%)	2 / 82 (2.44%)
occurrences causally related to treatment / all	0 / 3	0 / 4	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mixed anxiety and depressive disorder			
subjects affected / exposed	1 / 170 (0.59%)	0 / 1476 (0.00%)	0 / 82 (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
Suicidal ideation			
subjects affected / exposed	0 / 170 (0.00%)	2 / 1476 (0.14%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Delirium			
subjects affected / exposed	0 / 170 (0.00%)	2 / 1476 (0.14%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Product issues			
Device loosening			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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 capturing issue			
subjects affected / exposed	1 / 170 (0.59%)	0 / 1476 (0.00%)	0 / 82 (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
Device dislocation			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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 failure			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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 inappropriate shock delivery			

subjects affected / exposed	1 / 170 (0.59%)	0 / 1476 (0.00%)	0 / 82 (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
Device malfunction			
subjects affected / exposed	2 / 170 (1.18%)	1 / 1476 (0.07%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device occlusion			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Biliary colic			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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 cirrhosis			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Cholangitis			
subjects affected / exposed	0 / 170 (0.00%)	2 / 1476 (0.14%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis acute			
subjects affected / exposed	0 / 170 (0.00%)	5 / 1476 (0.34%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 5	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Congestive hepatopathy			
subjects affected / exposed	1 / 170 (0.59%)	1 / 1476 (0.07%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic cirrhosis			

subjects affected / exposed	2 / 170 (1.18%)	1 / 1476 (0.07%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Hepatic failure			
subjects affected / exposed	0 / 170 (0.00%)	3 / 1476 (0.20%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Hepatic function abnormal			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatitis acute			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Hepatomegaly			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Ischaemic hepatitis			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Jaundice			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Investigations			
Blood potassium abnormal			
subjects affected / exposed	0 / 170 (0.00%)	0 / 1476 (0.00%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Activated partial thromboplastin time prolonged			

subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Anticoagulation drug level above therapeutic			
subjects affected / exposed	1 / 170 (0.59%)	0 / 1476 (0.00%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Apnoea test			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Blood bilirubin increased			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Blood urea increased			
subjects affected / exposed	0 / 170 (0.00%)	0 / 1476 (0.00%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchial aspiration procedure			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Ejection fraction			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Ejection fraction decreased			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Haemoglobin decreased			

subjects affected / exposed	0 / 170 (0.00%)	0 / 1476 (0.00%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Heart rate irregular			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Peritoneal fluid analysis			
subjects affected / exposed	0 / 170 (0.00%)	0 / 1476 (0.00%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SARS-CoV-2 test positive			
subjects affected / exposed	0 / 170 (0.00%)	4 / 1476 (0.27%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Troponin increased			
subjects affected / exposed	0 / 170 (0.00%)	3 / 1476 (0.20%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
International normalised ratio increased			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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			
Chest injury			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clavicle fracture			
subjects affected / exposed	1 / 170 (0.59%)	0 / 1476 (0.00%)	0 / 82 (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
Complications of transplanted kidney			

subjects affected / exposed	1 / 170 (0.59%)	0 / 1476 (0.00%)	0 / 82 (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
Cervical vertebral fracture			
subjects affected / exposed	0 / 170 (0.00%)	2 / 1476 (0.14%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acetabulum fracture			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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 procedure complication			
subjects affected / exposed	1 / 170 (0.59%)	0 / 1476 (0.00%)	0 / 82 (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
Contusion			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Craniocerebral injury			
subjects affected / exposed	1 / 170 (0.59%)	1 / 1476 (0.07%)	0 / 82 (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
Craniofacial fracture			
subjects affected / exposed	1 / 170 (0.59%)	1 / 1476 (0.07%)	0 / 82 (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
Fall			
subjects affected / exposed	10 / 170 (5.88%)	25 / 1476 (1.69%)	5 / 82 (6.10%)
occurrences causally related to treatment / all	0 / 10	0 / 26	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Fat embolism			

subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Femoral neck fracture			
subjects affected / exposed	1 / 170 (0.59%)	2 / 1476 (0.14%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Joint dislocation			
subjects affected / exposed	1 / 170 (0.59%)	0 / 1476 (0.00%)	0 / 82 (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
Foot fracture			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Head injury			
subjects affected / exposed	1 / 170 (0.59%)	3 / 1476 (0.20%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Hip fracture			
subjects affected / exposed	0 / 170 (0.00%)	9 / 1476 (0.61%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 10	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Humerus fracture			
subjects affected / exposed	0 / 170 (0.00%)	3 / 1476 (0.20%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ilium fracture			
subjects affected / exposed	0 / 170 (0.00%)	0 / 1476 (0.00%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury			

subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femur fracture			
subjects affected / exposed	2 / 170 (1.18%)	4 / 1476 (0.27%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 2	0 / 4	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Limb injury			
subjects affected / exposed	1 / 170 (0.59%)	3 / 1476 (0.20%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meniscus injury			
subjects affected / exposed	1 / 170 (0.59%)	0 / 1476 (0.00%)	0 / 82 (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
Muscle strain			
subjects affected / exposed	1 / 170 (0.59%)	0 / 1476 (0.00%)	0 / 82 (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
Nasal injury			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Overdose			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Pelvic fracture			
subjects affected / exposed	0 / 170 (0.00%)	4 / 1476 (0.27%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Periprosthetic fracture			

subjects affected / exposed	0 / 170 (0.00%)	0 / 1476 (0.00%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Periprosthetic osteolysis			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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 procedural constipation			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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 procedural haematoma			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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 procedural haematuria			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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 procedural haemorrhage			
subjects affected / exposed	1 / 170 (0.59%)	3 / 1476 (0.20%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Procedural complication			
subjects affected / exposed	1 / 170 (0.59%)	0 / 1476 (0.00%)	0 / 82 (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
Procedural pneumothorax			
subjects affected / exposed	1 / 170 (0.59%)	0 / 1476 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary contusion			

subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Thoracic vertebral fracture			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Rib fracture			
subjects affected / exposed	1 / 170 (0.59%)	4 / 1476 (0.27%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Road traffic accident			
subjects affected / exposed	0 / 170 (0.00%)	3 / 1476 (0.20%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seroma			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin abrasion			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin laceration			
subjects affected / exposed	0 / 170 (0.00%)	2 / 1476 (0.14%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal compression fracture			
subjects affected / exposed	3 / 170 (1.76%)	1 / 1476 (0.07%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal fracture			

subjects affected / exposed	0 / 170 (0.00%)	2 / 1476 (0.14%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Splenic injury			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Splenic rupture			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Sternal fracture			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Subdural haematoma			
subjects affected / exposed	1 / 170 (0.59%)	10 / 1476 (0.68%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 15	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Tendon rupture			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Radius fracture			
subjects affected / exposed	1 / 170 (0.59%)	0 / 1476 (0.00%)	0 / 82 (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
Toxicity to various agents			
subjects affected / exposed	1 / 170 (0.59%)	0 / 1476 (0.00%)	0 / 82 (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
Traumatic intracranial haemorrhage			

subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract stoma complication			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Vasoplegia syndrome			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Wound haemorrhage			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Wrist fracture			
subjects affected / exposed	0 / 170 (0.00%)	0 / 1476 (0.00%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound secretion			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Congenital, familial and genetic disorders			
Familial amyloidosis			
subjects affected / exposed	4 / 170 (2.35%)	10 / 1476 (0.68%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 4	0 / 10	0 / 2
deaths causally related to treatment / all	0 / 1	0 / 4	0 / 1
Hereditary neuropathic amyloidosis			
subjects affected / exposed	0 / 170 (0.00%)	2 / 1476 (0.14%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			

Acute coronary syndrome			
subjects affected / exposed	0 / 170 (0.00%)	2 / 1476 (0.14%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute left ventricular failure			
subjects affected / exposed	2 / 170 (1.18%)	7 / 1476 (0.47%)	3 / 82 (3.66%)
occurrences causally related to treatment / all	0 / 2	0 / 7	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bradyarrhythmia			
subjects affected / exposed	1 / 170 (0.59%)	1 / 1476 (0.07%)	0 / 82 (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
Bifascicular block			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Atrioventricular block complete			
subjects affected / exposed	1 / 170 (0.59%)	16 / 1476 (1.08%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 16	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrioventricular block			
subjects affected / exposed	4 / 170 (2.35%)	8 / 1476 (0.54%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 4	0 / 8	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial tachycardia			
subjects affected / exposed	0 / 170 (0.00%)	4 / 1476 (0.27%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 0	0 / 5	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial flutter			
subjects affected / exposed	4 / 170 (2.35%)	18 / 1476 (1.22%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 4	0 / 18	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			

subjects affected / exposed	11 / 170 (6.47%)	62 / 1476 (4.20%)	8 / 82 (9.76%)
occurrences causally related to treatment / all	0 / 11	0 / 79	0 / 11
deaths causally related to treatment / all	0 / 0	0 / 2	0 / 0
Arrhythmia supraventricular			
subjects affected / exposed	0 / 170 (0.00%)	2 / 1476 (0.14%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arrhythmia			
subjects affected / exposed	3 / 170 (1.76%)	2 / 1476 (0.14%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aortic valve stenosis			
subjects affected / exposed	0 / 170 (0.00%)	2 / 1476 (0.14%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina unstable			
subjects affected / exposed	1 / 170 (0.59%)	0 / 1476 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina pectoris			
subjects affected / exposed	2 / 170 (1.18%)	11 / 1476 (0.75%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 12	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bradycardia			
subjects affected / exposed	2 / 170 (1.18%)	11 / 1476 (0.75%)	2 / 82 (2.44%)
occurrences causally related to treatment / all	0 / 2	0 / 11	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute myocardial infarction			
subjects affected / exposed	2 / 170 (1.18%)	7 / 1476 (0.47%)	2 / 82 (2.44%)
occurrences causally related to treatment / all	0 / 2	0 / 7	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Bundle branch block bilateral			

subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Cardiomyopathy			
subjects affected / exposed	1 / 170 (0.59%)	0 / 1476 (0.00%)	0 / 82 (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
Cardiogenic shock			
subjects affected / exposed	3 / 170 (1.76%)	20 / 1476 (1.36%)	2 / 82 (2.44%)
occurrences causally related to treatment / all	0 / 3	0 / 22	0 / 2
deaths causally related to treatment / all	0 / 1	0 / 9	0 / 0
Cardio-respiratory distress			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Cardio-respiratory arrest			
subjects affected / exposed	0 / 170 (0.00%)	0 / 1476 (0.00%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Cardiac flutter			
subjects affected / exposed	1 / 170 (0.59%)	0 / 1476 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure congestive			
subjects affected / exposed	17 / 170 (10.00%)	52 / 1476 (3.52%)	14 / 82 (17.07%)
occurrences causally related to treatment / all	0 / 24	0 / 60	0 / 19
deaths causally related to treatment / all	0 / 4	0 / 6	0 / 6
Cardiac failure chronic			
subjects affected / exposed	1 / 170 (0.59%)	10 / 1476 (0.68%)	4 / 82 (4.88%)
occurrences causally related to treatment / all	0 / 1	0 / 12	0 / 4
deaths causally related to treatment / all	0 / 1	0 / 6	0 / 0
Cardiac failure acute			

subjects affected / exposed	13 / 170 (7.65%)	48 / 1476 (3.25%)	10 / 82 (12.20%)
occurrences causally related to treatment / all	0 / 21	0 / 60	0 / 11
deaths causally related to treatment / all	0 / 1	0 / 4	0 / 1
Cardiac failure			
subjects affected / exposed	30 / 170 (17.65%)	169 / 1476 (11.45%)	17 / 82 (20.73%)
occurrences causally related to treatment / all	0 / 55	1 / 255	0 / 30
deaths causally related to treatment / all	0 / 7	0 / 33	0 / 6
Cardiac arrest			
subjects affected / exposed	6 / 170 (3.53%)	14 / 1476 (0.95%)	3 / 82 (3.66%)
occurrences causally related to treatment / all	1 / 6	0 / 14	0 / 3
deaths causally related to treatment / all	1 / 2	0 / 13	0 / 2
Cardiac amyloidosis			
subjects affected / exposed	2 / 170 (1.18%)	16 / 1476 (1.08%)	2 / 82 (2.44%)
occurrences causally related to treatment / all	0 / 2	0 / 17	0 / 2
deaths causally related to treatment / all	0 / 2	0 / 12	0 / 2
Bundle branch block right			
subjects affected / exposed	0 / 170 (0.00%)	2 / 1476 (0.14%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bundle branch block left			
subjects affected / exposed	0 / 170 (0.00%)	4 / 1476 (0.27%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	1 / 170 (0.59%)	3 / 1476 (0.20%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mitral valve incompetence			
subjects affected / exposed	1 / 170 (0.59%)	0 / 1476 (0.00%)	0 / 82 (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
Low cardiac output syndrome			

subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Left ventricular failure			
subjects affected / exposed	1 / 170 (0.59%)	6 / 1476 (0.41%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 1	0 / 6	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Left ventricular dysfunction			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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 stenosis			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial ischaemia			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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	1 / 170 (0.59%)	1 / 1476 (0.07%)	0 / 82 (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
Conduction disorder			
subjects affected / exposed	0 / 170 (0.00%)	5 / 1476 (0.34%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 5	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic left ventricular failure			
subjects affected / exposed	1 / 170 (0.59%)	3 / 1476 (0.20%)	3 / 82 (3.66%)
occurrences causally related to treatment / all	0 / 1	0 / 4	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 2	0 / 1
Cardiovascular insufficiency			

subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Cardiorenal syndrome			
subjects affected / exposed	0 / 170 (0.00%)	3 / 1476 (0.20%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Cardiopulmonary failure			
subjects affected / exposed	0 / 170 (0.00%)	0 / 1476 (0.00%)	2 / 82 (2.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery embolism			
subjects affected / exposed	1 / 170 (0.59%)	0 / 1476 (0.00%)	0 / 82 (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
Sinoatrial block			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Sinus arrest			
subjects affected / exposed	1 / 170 (0.59%)	0 / 1476 (0.00%)	0 / 82 (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
Sinus node dysfunction			
subjects affected / exposed	1 / 170 (0.59%)	10 / 1476 (0.68%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 1	1 / 10	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Supraventricular tachycardia			
subjects affected / exposed	0 / 170 (0.00%)	7 / 1476 (0.47%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 7	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Nodal arrhythmia			

subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Nodal rhythm			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Palpitations			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Paroxysmal atrioventricular block			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Pericardial effusion			
subjects affected / exposed	3 / 170 (1.76%)	2 / 1476 (0.14%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 4	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericarditis			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Restrictive cardiomyopathy			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Right ventricular dysfunction			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Right ventricular failure			

subjects affected / exposed	0 / 170 (0.00%)	0 / 1476 (0.00%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tachyarrhythmia			
subjects affected / exposed	0 / 170 (0.00%)	0 / 1476 (0.00%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tachycardia			
subjects affected / exposed	1 / 170 (0.59%)	0 / 1476 (0.00%)	0 / 82 (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
Torsade de pointes			
subjects affected / exposed	0 / 170 (0.00%)	0 / 1476 (0.00%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tricuspid valve incompetence			
subjects affected / exposed	0 / 170 (0.00%)	2 / 1476 (0.14%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ventricular arrhythmia			
subjects affected / exposed	1 / 170 (0.59%)	0 / 1476 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ventricular dysfunction			
subjects affected / exposed	0 / 170 (0.00%)	4 / 1476 (0.27%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ventricular tachycardia			
subjects affected / exposed	3 / 170 (1.76%)	17 / 1476 (1.15%)	6 / 82 (7.32%)
occurrences causally related to treatment / all	0 / 6	0 / 18	0 / 7
deaths causally related to treatment / all	0 / 0	0 / 2	0 / 1
Ventricular fibrillation			

subjects affected / exposed	1 / 170 (0.59%)	1 / 1476 (0.07%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Nervous system disorders			
Cerebral ischaemia			
subjects affected / exposed	2 / 170 (1.18%)	0 / 1476 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Brain compression			
subjects affected / exposed	1 / 170 (0.59%)	0 / 1476 (0.00%)	0 / 82 (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
Brain injury			
subjects affected / exposed	2 / 170 (1.18%)	0 / 1476 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 2	0 / 0	0 / 0
Carpal tunnel syndrome			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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 artery embolism			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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 haemorrhage			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Cerebral infarction			
subjects affected / exposed	1 / 170 (0.59%)	0 / 1476 (0.00%)	0 / 82 (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
Ataxia			

subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Cerebrospinal fluid leakage			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular accident			
subjects affected / exposed	2 / 170 (1.18%)	17 / 1476 (1.15%)	3 / 82 (3.66%)
occurrences causally related to treatment / all	0 / 3	0 / 17	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cervical radiculopathy			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Cognitive disorder			
subjects affected / exposed	0 / 170 (0.00%)	6 / 1476 (0.41%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 6	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Coma			
subjects affected / exposed	1 / 170 (0.59%)	0 / 1476 (0.00%)	0 / 82 (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
Dementia			
subjects affected / exposed	3 / 170 (1.76%)	0 / 1476 (0.00%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Headache			
subjects affected / exposed	1 / 170 (0.59%)	0 / 1476 (0.00%)	0 / 82 (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
Dysarthria			

subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Embolitic stroke			
subjects affected / exposed	1 / 170 (0.59%)	0 / 1476 (0.00%)	0 / 82 (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	3 / 170 (1.76%)	3 / 1476 (0.20%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Epilepsy			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Haemorrhage intracranial			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Haemorrhagic transformation stroke			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Dizziness			
subjects affected / exposed	0 / 170 (0.00%)	5 / 1476 (0.34%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 5	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Loss of consciousness			
subjects affected / exposed	2 / 170 (1.18%)	1 / 1476 (0.07%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolic encephalopathy			

subjects affected / exposed	1 / 170 (0.59%)	1 / 1476 (0.07%)	0 / 82 (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
Neuralgia			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neuropathy peripheral			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Peripheral sensorimotor neuropathy			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Polyneuropathy			
subjects affected / exposed	1 / 170 (0.59%)	1 / 1476 (0.07%)	0 / 82 (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
Lethargy			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Radiculopathy			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Hemianopia			
subjects affected / exposed	1 / 170 (0.59%)	0 / 1476 (0.00%)	0 / 82 (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
Hemianopia homonymous			

subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Hepatic encephalopathy			
subjects affected / exposed	2 / 170 (1.18%)	1 / 1476 (0.07%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Ischaemic cerebral infarction			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Ischaemic stroke			
subjects affected / exposed	1 / 170 (0.59%)	11 / 1476 (0.75%)	3 / 82 (3.66%)
occurrences causally related to treatment / all	0 / 1	0 / 12	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 3	0 / 0
Presyncope			
subjects affected / exposed	0 / 170 (0.00%)	4 / 1476 (0.27%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seizure			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Somnolence			
subjects affected / exposed	1 / 170 (0.59%)	1 / 1476 (0.07%)	0 / 82 (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
Subarachnoid haemorrhage			
subjects affected / exposed	0 / 170 (0.00%)	0 / 1476 (0.00%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			

subjects affected / exposed	6 / 170 (3.53%)	42 / 1476 (2.85%)	2 / 82 (2.44%)
occurrences causally related to treatment / all	0 / 6	0 / 43	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient global amnesia			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Transient ischaemic attack			
subjects affected / exposed	0 / 170 (0.00%)	9 / 1476 (0.61%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 10	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Vascular dementia			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular encephalopathy			
subjects affected / exposed	0 / 170 (0.00%)	0 / 1476 (0.00%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uraemic encephalopathy			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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			
Anaemia			
subjects affected / exposed	2 / 170 (1.18%)	17 / 1476 (1.15%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 24	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			
subjects affected / exposed	1 / 170 (0.59%)	0 / 1476 (0.00%)	0 / 82 (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
Spontaneous haematoma			

subjects affected / exposed	1 / 170 (0.59%)	0 / 1476 (0.00%)	0 / 82 (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
Normochromic normocytic anaemia			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Leukocytosis			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Immune thrombocytopenia			
subjects affected / exposed	0 / 170 (0.00%)	2 / 1476 (0.14%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Deficiency anaemia			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Coagulopathy			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Blood loss anaemia			
subjects affected / exposed	1 / 170 (0.59%)	2 / 1476 (0.14%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aplastic anaemia			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Iron deficiency anaemia			

subjects affected / exposed	0 / 170 (0.00%)	2 / 1476 (0.14%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
Meniere's disease			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Vertigo			
subjects affected / exposed	1 / 170 (0.59%)	1 / 1476 (0.07%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Amaurosis fugax			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Blindness unilateral			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cataract			
subjects affected / exposed	1 / 170 (0.59%)	0 / 1476 (0.00%)	0 / 82 (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
Charles Bonnet syndrome			
subjects affected / exposed	1 / 170 (0.59%)	0 / 1476 (0.00%)	0 / 82 (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
Optic ischaemic neuropathy			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Orbital haematoma			

subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Retinal detachment			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Vitreous haemorrhage			
subjects affected / exposed	1 / 170 (0.59%)	0 / 1476 (0.00%)	0 / 82 (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
Vision blurred			
subjects affected / exposed	1 / 170 (0.59%)	0 / 1476 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	2 / 170 (1.18%)	0 / 1476 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal adhesions			
subjects affected / exposed	1 / 170 (0.59%)	0 / 1476 (0.00%)	0 / 82 (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
Abdominal discomfort			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Abdominal distension			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain			

subjects affected / exposed	0 / 170 (0.00%)	6 / 1476 (0.41%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 0	0 / 6	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain lower			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Acute abdomen			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Appendiceal mucocoele			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Ascites			
subjects affected / exposed	2 / 170 (1.18%)	8 / 1476 (0.54%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 4	0 / 10	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic gastritis			
subjects affected / exposed	1 / 170 (0.59%)	0 / 1476 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Colitis microscopic			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal haemorrhage			

subjects affected / exposed	4 / 170 (2.35%)	13 / 1476 (0.88%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 4	0 / 15	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	0 / 170 (0.00%)	2 / 1476 (0.14%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysphagia			
subjects affected / exposed	0 / 170 (0.00%)	2 / 1476 (0.14%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Faecaloma			
subjects affected / exposed	2 / 170 (1.18%)	0 / 1476 (0.00%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric ulcer			
subjects affected / exposed	1 / 170 (0.59%)	1 / 1476 (0.07%)	0 / 82 (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
Gastric ulcer haemorrhage			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Constipation			
subjects affected / exposed	2 / 170 (1.18%)	2 / 1476 (0.14%)	2 / 82 (2.44%)
occurrences causally related to treatment / all	0 / 2	0 / 2	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal ulcer haemorrhage			

subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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 vascular malformation haemorrhagic			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Haemorrhoids			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Ileus			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Impaired gastric emptying			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestine perforation			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Incarcerated umbilical hernia			
subjects affected / exposed	0 / 170 (0.00%)	0 / 1476 (0.00%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Inguinal hernia			

subjects affected / exposed	0 / 170 (0.00%)	4 / 1476 (0.27%)	2 / 82 (2.44%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Inguinal hernia strangulated			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal ischaemia			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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 / 170 (0.59%)	3 / 1476 (0.20%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 1	0 / 4	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intra-abdominal haemorrhage			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Incarcerated inguinal hernia			
subjects affected / exposed	1 / 170 (0.59%)	0 / 1476 (0.00%)	0 / 82 (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
Pancreatitis acute			
subjects affected / exposed	0 / 170 (0.00%)	2 / 1476 (0.14%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumoperitoneum			
subjects affected / exposed	1 / 170 (0.59%)	0 / 1476 (0.00%)	0 / 82 (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
Portal hypertensive gastropathy			

subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal haemorrhage			
subjects affected / exposed	3 / 170 (1.76%)	7 / 1476 (0.47%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 7	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			
subjects affected / exposed	1 / 170 (0.59%)	4 / 1476 (0.27%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 1	0 / 5	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Umbilical hernia			
subjects affected / exposed	1 / 170 (0.59%)	0 / 1476 (0.00%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis			
subjects affected / exposed	0 / 170 (0.00%)	2 / 1476 (0.14%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower gastrointestinal haemorrhage			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Melaena			
subjects affected / exposed	1 / 170 (0.59%)	4 / 1476 (0.27%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mesenteric vascular insufficiency			
subjects affected / exposed	1 / 170 (0.59%)	0 / 1476 (0.00%)	0 / 82 (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
Nausea			

subjects affected / exposed	0 / 170 (0.00%)	3 / 1476 (0.20%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophageal motility disorder			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Oesophageal ulcer			
subjects affected / exposed	1 / 170 (0.59%)	1 / 1476 (0.07%)	0 / 82 (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
Large intestine polyp			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Upper gastrointestinal haemorrhage			
subjects affected / exposed	1 / 170 (0.59%)	6 / 1476 (0.41%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 7	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	1 / 170 (0.59%)	4 / 1476 (0.27%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 1	0 / 4	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Cellulite			
subjects affected / exposed	0 / 170 (0.00%)	2 / 1476 (0.14%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Actinic keratosis			
subjects affected / exposed	2 / 170 (1.18%)	0 / 1476 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin ulcer			

subjects affected / exposed	0 / 170 (0.00%)	0 / 1476 (0.00%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin necrosis			
subjects affected / exposed	1 / 170 (0.59%)	0 / 1476 (0.00%)	0 / 82 (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
Rash papular			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rash maculo-papular			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Pruritus			
subjects affected / exposed	1 / 170 (0.59%)	0 / 1476 (0.00%)	0 / 82 (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
Hyperhidrosis			
subjects affected / exposed	0 / 170 (0.00%)	2 / 1476 (0.14%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Decubitus ulcer			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stasis dermatitis			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eczema			

subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	16 / 170 (9.41%)	34 / 1476 (2.30%)	13 / 82 (15.85%)
occurrences causally related to treatment / all	0 / 19	0 / 42	0 / 15
deaths causally related to treatment / all	0 / 3	0 / 1	0 / 1
Chronic kidney disease			
subjects affected / exposed	0 / 170 (0.00%)	7 / 1476 (0.47%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 8	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
End stage renal disease			
subjects affected / exposed	1 / 170 (0.59%)	3 / 1476 (0.20%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 5	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 2	0 / 0
Glomerulonephritis			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Haematuria			
subjects affected / exposed	3 / 170 (1.76%)	8 / 1476 (0.54%)	3 / 82 (3.66%)
occurrences causally related to treatment / all	0 / 5	0 / 12	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhage urinary tract			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal failure			
subjects affected / exposed	1 / 170 (0.59%)	5 / 1476 (0.34%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 5	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
Nephrolithiasis			

subjects affected / exposed	1 / 170 (0.59%)	1 / 1476 (0.07%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nephrotic syndrome			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Polyuria			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal disorder			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Hydronephrosis			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal impairment			
subjects affected / exposed	0 / 170 (0.00%)	7 / 1476 (0.47%)	2 / 82 (2.44%)
occurrences causally related to treatment / all	0 / 0	0 / 8	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Renal pseudoaneurysm			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Ureteric obstruction			
subjects affected / exposed	1 / 170 (0.59%)	0 / 1476 (0.00%)	0 / 82 (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
Ureterolithiasis			

subjects affected / exposed	0 / 170 (0.00%)	3 / 1476 (0.20%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary retention			
subjects affected / exposed	3 / 170 (1.76%)	7 / 1476 (0.47%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 7	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract obstruction			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	0 / 170 (0.00%)	2 / 1476 (0.14%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 170 (0.00%)	9 / 1476 (0.61%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 0	0 / 9	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthritis			
subjects affected / exposed	1 / 170 (0.59%)	1 / 1476 (0.07%)	0 / 82 (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
Back pain			
subjects affected / exposed	2 / 170 (1.18%)	4 / 1476 (0.27%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immunoglobulin G4 related disease			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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

Dupuytren's contracture			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Gouty arthritis			
subjects affected / exposed	0 / 170 (0.00%)	2 / 1476 (0.14%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Greater trochanteric pain syndrome			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Haemarthrosis			
subjects affected / exposed	0 / 170 (0.00%)	3 / 1476 (0.20%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematoma muscle			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Chondrocalcinosis			
subjects affected / exposed	0 / 170 (0.00%)	0 / 1476 (0.00%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lumbar spinal stenosis			
subjects affected / exposed	1 / 170 (0.59%)	4 / 1476 (0.27%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscle spasms			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal chest pain			

subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoarthritis			
subjects affected / exposed	2 / 170 (1.18%)	9 / 1476 (0.61%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 10	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tenosynovitis			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Pain in extremity			
subjects affected / exposed	0 / 170 (0.00%)	2 / 1476 (0.14%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pathological fracture			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Rheumatoid arthritis			
subjects affected / exposed	1 / 170 (0.59%)	0 / 1476 (0.00%)	0 / 82 (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
Rotator cuff syndrome			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Spinal stenosis			
subjects affected / exposed	0 / 170 (0.00%)	4 / 1476 (0.27%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tendonitis			

subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Osteonecrosis			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 170 (0.00%)	2 / 1476 (0.14%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abscess limb			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthritis bacterial			
subjects affected / exposed	1 / 170 (0.59%)	3 / 1476 (0.20%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthritis infective			
subjects affected / exposed	0 / 170 (0.00%)	2 / 1476 (0.14%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bacteraemia			
subjects affected / exposed	0 / 170 (0.00%)	4 / 1476 (0.27%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Bacterial pyelonephritis			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Beta haemolytic streptococcal infection			

subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Bronchitis			
subjects affected / exposed	0 / 170 (0.00%)	2 / 1476 (0.14%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device related infection			
subjects affected / exposed	1 / 170 (0.59%)	0 / 1476 (0.00%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bursitis infective			
subjects affected / exposed	0 / 170 (0.00%)	2 / 1476 (0.14%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19			
subjects affected / exposed	2 / 170 (1.18%)	16 / 1476 (1.08%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 2	0 / 16	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 3	0 / 0
COVID-19 pneumonia			
subjects affected / exposed	1 / 170 (0.59%)	9 / 1476 (0.61%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 1	0 / 9	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Cardiac infection			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Cellulitis			
subjects affected / exposed	8 / 170 (4.71%)	18 / 1476 (1.22%)	5 / 82 (6.10%)
occurrences causally related to treatment / all	0 / 10	0 / 20	0 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis staphylococcal			

subjects affected / exposed	1 / 170 (0.59%)	0 / 1476 (0.00%)	0 / 82 (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
Bronchitis viral			
subjects affected / exposed	1 / 170 (0.59%)	0 / 1476 (0.00%)	0 / 82 (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
Diverticulitis intestinal perforated			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Endocarditis			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Endophthalmitis			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Erysipelas			
subjects affected / exposed	1 / 170 (0.59%)	4 / 1476 (0.27%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 1	0 / 4	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 2	0 / 0
Escherichia sepsis			
subjects affected / exposed	2 / 170 (1.18%)	0 / 1476 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Extradural abscess			
subjects affected / exposed	0 / 170 (0.00%)	0 / 1476 (0.00%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Diverticulitis			

subjects affected / exposed	0 / 170 (0.00%)	5 / 1476 (0.34%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 5	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal viral infection			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Haematoma infection			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Hepatitis A			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Herpes zoster			
subjects affected / exposed	1 / 170 (0.59%)	0 / 1476 (0.00%)	0 / 82 (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
Herpes zoster meningoencephalitis			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Diabetic foot infection			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes zoster meningomyelitis			

subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Implant site infection			
subjects affected / exposed	1 / 170 (0.59%)	0 / 1476 (0.00%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infection			
subjects affected / exposed	0 / 170 (0.00%)	2 / 1476 (0.14%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infectious pleural effusion			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Infective exacerbation of chronic obstructive airways disease			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Influenza			
subjects affected / exposed	1 / 170 (0.59%)	2 / 1476 (0.14%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteomyelitis			
subjects affected / exposed	1 / 170 (0.59%)	0 / 1476 (0.00%)	0 / 82 (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
Localised infection			
subjects affected / exposed	0 / 170 (0.00%)	0 / 1476 (0.00%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower respiratory tract infection			

subjects affected / exposed	0 / 170 (0.00%)	2 / 1476 (0.14%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningitis			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningitis bacterial			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Necrotising fasciitis			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Oesophageal candidiasis			
subjects affected / exposed	0 / 170 (0.00%)	0 / 1476 (0.00%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Legionella infection			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Pericarditis infective			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Peritonitis			
subjects affected / exposed	0 / 170 (0.00%)	2 / 1476 (0.14%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Peritonsillar abscess			

subjects affected / exposed	1 / 170 (0.59%)	0 / 1476 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	12 / 170 (7.06%)	39 / 1476 (2.64%)	9 / 82 (10.98%)
occurrences causally related to treatment / all	0 / 14	0 / 49	0 / 11
deaths causally related to treatment / all	0 / 1	0 / 4	0 / 3
Pneumonia aspiration			
subjects affected / exposed	1 / 170 (0.59%)	5 / 1476 (0.34%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 1	0 / 5	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 2	0 / 0
Pneumonia bacterial			
subjects affected / exposed	1 / 170 (0.59%)	3 / 1476 (0.20%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 2	0 / 0
Pseudomonal sepsis			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Pneumonia pneumococcal			
subjects affected / exposed	2 / 170 (1.18%)	0 / 1476 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia staphylococcal			
subjects affected / exposed	1 / 170 (0.59%)	0 / 1476 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia streptococcal			
subjects affected / exposed	1 / 170 (0.59%)	0 / 1476 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia viral			

subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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 procedural sepsis			
subjects affected / exposed	0 / 170 (0.00%)	2 / 1476 (0.14%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia klebsiella			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Pulmonary sepsis			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Pyelonephritis			
subjects affected / exposed	1 / 170 (0.59%)	0 / 1476 (0.00%)	0 / 82 (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
Respiratory moniliasis			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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 tract infection			
subjects affected / exposed	0 / 170 (0.00%)	7 / 1476 (0.47%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 7	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory tract infection bacterial			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Scrotal cellulitis			

subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Streptococcal bacteraemia			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Septic shock			
subjects affected / exposed	1 / 170 (0.59%)	10 / 1476 (0.68%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 1	0 / 10	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 6	0 / 0
Sialoadenitis			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Spontaneous bacterial peritonitis			
subjects affected / exposed	0 / 170 (0.00%)	3 / 1476 (0.20%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal bacteraemia			
subjects affected / exposed	0 / 170 (0.00%)	3 / 1476 (0.20%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Staphylococcal infection			
subjects affected / exposed	1 / 170 (0.59%)	0 / 1476 (0.00%)	0 / 82 (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
Staphylococcal sepsis			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Sepsis			

subjects affected / exposed	8 / 170 (4.71%)	17 / 1476 (1.15%)	4 / 82 (4.88%)
occurrences causally related to treatment / all	0 / 10	0 / 17	0 / 4
deaths causally related to treatment / all	0 / 2	0 / 3	0 / 1
Streptococcal sepsis			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Superinfection fungal			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Tracheobronchitis			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	2 / 170 (1.18%)	17 / 1476 (1.15%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 2	1 / 17	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Urosepsis			
subjects affected / exposed	1 / 170 (0.59%)	5 / 1476 (0.34%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 1	0 / 5	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular device infection			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Viral infection			
subjects affected / exposed	1 / 170 (0.59%)	0 / 1476 (0.00%)	0 / 82 (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
Upper respiratory tract infection			

subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Metabolism and nutrition disorders			
Diabetes mellitus			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Cachexia			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Decreased appetite			
subjects affected / exposed	1 / 170 (0.59%)	2 / 1476 (0.14%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dehydration			
subjects affected / exposed	0 / 170 (0.00%)	7 / 1476 (0.47%)	5 / 82 (6.10%)
occurrences causally related to treatment / all	0 / 0	0 / 7	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetic metabolic decompensation			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Electrolyte imbalance			
subjects affected / exposed	0 / 170 (0.00%)	0 / 1476 (0.00%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Failure to thrive			
subjects affected / exposed	0 / 170 (0.00%)	4 / 1476 (0.27%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 2	0 / 0
Fluid retention			

subjects affected / exposed	0 / 170 (0.00%)	2 / 1476 (0.14%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gout			
subjects affected / exposed	1 / 170 (0.59%)	9 / 1476 (0.61%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 9	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperglycaemia			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Hyponatraemia			
subjects affected / exposed	3 / 170 (1.76%)	4 / 1476 (0.27%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 3	0 / 4	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperkalaemia			
subjects affected / exposed	2 / 170 (1.18%)	8 / 1476 (0.54%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 2	0 / 8	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypernatraemia			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Hypervolaemia			
subjects affected / exposed	0 / 170 (0.00%)	8 / 1476 (0.54%)	2 / 82 (2.44%)
occurrences causally related to treatment / all	0 / 0	0 / 9	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoglycaemia			
subjects affected / exposed	0 / 170 (0.00%)	2 / 1476 (0.14%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypokalaemia			

subjects affected / exposed	2 / 170 (1.18%)	9 / 1476 (0.61%)	2 / 82 (2.44%)
occurrences causally related to treatment / all	0 / 2	0 / 9	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperglycaemic hyperosmolar nonketotic syndrome			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Hypovolaemia			
subjects affected / exposed	0 / 170 (0.00%)	2 / 1476 (0.14%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malnutrition			
subjects affected / exposed	0 / 170 (0.00%)	1 / 1476 (0.07%)	0 / 82 (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
Metabolic alkalosis			
subjects affected / exposed	1 / 170 (0.59%)	0 / 1476 (0.00%)	0 / 82 (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

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

Non-serious adverse events	Cohort A: Tafamidis (Parent and Extension Study)	Cohort B: Tafamidis (Only in extension study)	Cohort A: Placebo (Parent Study)/Tafamidis (Extension Study)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	152 / 170 (89.41%)	1023 / 1476 (69.31%)	76 / 82 (92.68%)
Vascular disorders			
Hypotension			
subjects affected / exposed	14 / 170 (8.24%)	70 / 1476 (4.74%)	20 / 82 (24.39%)
occurrences (all)	16	81	24
General disorders and administration site conditions			
Gait disturbance			

subjects affected / exposed occurrences (all)	5 / 170 (2.94%) 6	10 / 1476 (0.68%) 11	6 / 82 (7.32%) 7
Asthenia subjects affected / exposed occurrences (all)	13 / 170 (7.65%) 16	54 / 1476 (3.66%) 59	12 / 82 (14.63%) 16
Fatigue subjects affected / exposed occurrences (all)	19 / 170 (11.18%) 22	78 / 1476 (5.28%) 82	15 / 82 (18.29%) 20
Oedema peripheral subjects affected / exposed occurrences (all)	26 / 170 (15.29%) 30	100 / 1476 (6.78%) 129	18 / 82 (21.95%) 27
Peripheral swelling subjects affected / exposed occurrences (all)	9 / 170 (5.29%) 14	22 / 1476 (1.49%) 23	5 / 82 (6.10%) 6
Pyrexia subjects affected / exposed occurrences (all)	6 / 170 (3.53%) 9	23 / 1476 (1.56%) 26	5 / 82 (6.10%) 6
Reproductive system and breast disorders Benign prostatic hyperplasia subjects affected / exposed occurrences (all)	3 / 170 (1.76%) 3	21 / 1476 (1.42%) 21	5 / 82 (6.10%) 5
Respiratory, thoracic and mediastinal disorders Epistaxis subjects affected / exposed occurrences (all)	13 / 170 (7.65%) 15	38 / 1476 (2.57%) 43	5 / 82 (6.10%) 6
Dyspnoea subjects affected / exposed occurrences (all)	31 / 170 (18.24%) 41	110 / 1476 (7.45%) 129	18 / 82 (21.95%) 30
Cough subjects affected / exposed occurrences (all)	29 / 170 (17.06%) 42	81 / 1476 (5.49%) 86	18 / 82 (21.95%) 24
Pulmonary hypertension subjects affected / exposed occurrences (all)	2 / 170 (1.18%) 2	8 / 1476 (0.54%) 8	5 / 82 (6.10%) 5
Pleural effusion			

subjects affected / exposed occurrences (all)	23 / 170 (13.53%) 30	58 / 1476 (3.93%) 72	24 / 82 (29.27%) 43
Orthopnoea subjects affected / exposed occurrences (all)	6 / 170 (3.53%) 6	11 / 1476 (0.75%) 11	5 / 82 (6.10%) 7
Psychiatric disorders			
Insomnia subjects affected / exposed occurrences (all)	13 / 170 (7.65%) 14	57 / 1476 (3.86%) 61	13 / 82 (15.85%) 15
Depression subjects affected / exposed occurrences (all)	8 / 170 (4.71%) 12	23 / 1476 (1.56%) 23	8 / 82 (9.76%) 9
Anxiety subjects affected / exposed occurrences (all)	7 / 170 (4.12%) 7	28 / 1476 (1.90%) 29	6 / 82 (7.32%) 6
Investigations			
Blood creatinine increased subjects affected / exposed occurrences (all)	2 / 170 (1.18%) 2	14 / 1476 (0.95%) 14	5 / 82 (6.10%) 5
Gamma-glutamyltransferase increased subjects affected / exposed occurrences (all)	3 / 170 (1.76%) 3	13 / 1476 (0.88%) 13	6 / 82 (7.32%) 6
Weight decreased subjects affected / exposed occurrences (all)	10 / 170 (5.88%) 11	32 / 1476 (2.17%) 41	8 / 82 (9.76%) 8
Injury, poisoning and procedural complications			
Contusion subjects affected / exposed occurrences (all)	13 / 170 (7.65%) 13	40 / 1476 (2.71%) 42	5 / 82 (6.10%) 6
Fall subjects affected / exposed occurrences (all)	41 / 170 (24.12%) 85	146 / 1476 (9.89%) 195	34 / 82 (41.46%) 48
Limb injury subjects affected / exposed occurrences (all)	7 / 170 (4.12%) 7	24 / 1476 (1.63%) 25	5 / 82 (6.10%) 6
Skin abrasion			

subjects affected / exposed occurrences (all)	11 / 170 (6.47%) 11	25 / 1476 (1.69%) 29	6 / 82 (7.32%) 8
Skin laceration subjects affected / exposed occurrences (all)	12 / 170 (7.06%) 19	46 / 1476 (3.12%) 56	13 / 82 (15.85%) 17
Wound subjects affected / exposed occurrences (all)	4 / 170 (2.35%) 6	13 / 1476 (0.88%) 13	5 / 82 (6.10%) 6
Cardiac disorders Atrial fibrillation subjects affected / exposed occurrences (all)	32 / 170 (18.82%) 37	150 / 1476 (10.16%) 172	17 / 82 (20.73%) 19
Cardiac failure subjects affected / exposed occurrences (all)	22 / 170 (12.94%) 28	167 / 1476 (11.31%) 222	9 / 82 (10.98%) 17
Pericardial effusion subjects affected / exposed occurrences (all)	6 / 170 (3.53%) 6	8 / 1476 (0.54%) 8	6 / 82 (7.32%) 6
Ventricular tachycardia subjects affected / exposed occurrences (all)	10 / 170 (5.88%) 12	20 / 1476 (1.36%) 24	9 / 82 (10.98%) 14
Nervous system disorders Dizziness subjects affected / exposed occurrences (all)	24 / 170 (14.12%) 37	97 / 1476 (6.57%) 104	11 / 82 (13.41%) 12
Balance disorder subjects affected / exposed occurrences (all)	11 / 170 (6.47%) 12	16 / 1476 (1.08%) 16	4 / 82 (4.88%) 6
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all)	14 / 170 (8.24%) 15	78 / 1476 (5.28%) 91	12 / 82 (14.63%) 12
Leukocytosis subjects affected / exposed occurrences (all)	1 / 170 (0.59%) 2	2 / 1476 (0.14%) 2	5 / 82 (6.10%) 6
Eye disorders			

Cataract subjects affected / exposed occurrences (all)	10 / 170 (5.88%) 12	24 / 1476 (1.63%) 30	1 / 82 (1.22%) 1
Gastrointestinal disorders			
Abdominal pain upper subjects affected / exposed occurrences (all)	5 / 170 (2.94%) 6	20 / 1476 (1.36%) 20	5 / 82 (6.10%) 6
Ascites subjects affected / exposed occurrences (all)	9 / 170 (5.29%) 11	19 / 1476 (1.29%) 24	4 / 82 (4.88%) 5
Constipation subjects affected / exposed occurrences (all)	18 / 170 (10.59%) 21	117 / 1476 (7.93%) 126	15 / 82 (18.29%) 16
Diarrhoea subjects affected / exposed occurrences (all)	15 / 170 (8.82%) 15	97 / 1476 (6.57%) 110	8 / 82 (9.76%) 13
Dysphagia subjects affected / exposed occurrences (all)	11 / 170 (6.47%) 11	29 / 1476 (1.96%) 31	7 / 82 (8.54%) 10
Nausea subjects affected / exposed occurrences (all)	17 / 170 (10.00%) 21	48 / 1476 (3.25%) 53	10 / 82 (12.20%) 11
Vomiting subjects affected / exposed occurrences (all)	10 / 170 (5.88%) 10	30 / 1476 (2.03%) 32	7 / 82 (8.54%) 8
Hepatobiliary disorders			
Congestive hepatopathy subjects affected / exposed occurrences (all)	1 / 170 (0.59%) 1	6 / 1476 (0.41%) 6	5 / 82 (6.10%) 5
Skin and subcutaneous tissue disorders			
Pruritus subjects affected / exposed occurrences (all)	17 / 170 (10.00%) 21	36 / 1476 (2.44%) 36	8 / 82 (9.76%) 9
Decubitus ulcer subjects affected / exposed occurrences (all)	3 / 170 (1.76%) 5	9 / 1476 (0.61%) 9	7 / 82 (8.54%) 8
Skin ulcer			

subjects affected / exposed occurrences (all)	10 / 170 (5.88%) 14	25 / 1476 (1.69%) 30	3 / 82 (3.66%) 5
Renal and urinary disorders			
Chronic kidney disease			
subjects affected / exposed	10 / 170 (5.88%)	20 / 1476 (1.36%)	13 / 82 (15.85%)
occurrences (all)	11	24	15
Acute kidney injury			
subjects affected / exposed	15 / 170 (8.82%)	54 / 1476 (3.66%)	15 / 82 (18.29%)
occurrences (all)	19	64	21
Renal failure			
subjects affected / exposed	11 / 170 (6.47%)	10 / 1476 (0.68%)	3 / 82 (3.66%)
occurrences (all)	11	10	3
Haematuria			
subjects affected / exposed	7 / 170 (4.12%)	47 / 1476 (3.18%)	11 / 82 (13.41%)
occurrences (all)	10	49	11
Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	24 / 170 (14.12%)	55 / 1476 (3.73%)	9 / 82 (10.98%)
occurrences (all)	41	68	17
Osteoarthritis			
subjects affected / exposed	12 / 170 (7.06%)	20 / 1476 (1.36%)	9 / 82 (10.98%)
occurrences (all)	18	21	13
Muscular weakness			
subjects affected / exposed	11 / 170 (6.47%)	19 / 1476 (1.29%)	7 / 82 (8.54%)
occurrences (all)	12	20	7
Muscle spasms			
subjects affected / exposed	14 / 170 (8.24%)	53 / 1476 (3.59%)	4 / 82 (4.88%)
occurrences (all)	16	55	4
Back pain			
subjects affected / exposed	18 / 170 (10.59%)	65 / 1476 (4.40%)	12 / 82 (14.63%)
occurrences (all)	23	72	12
Arthralgia			
subjects affected / exposed	29 / 170 (17.06%)	78 / 1476 (5.28%)	12 / 82 (14.63%)
occurrences (all)	39	91	14
Infections and infestations			

Bronchitis			
subjects affected / exposed	9 / 170 (5.29%)	38 / 1476 (2.57%)	6 / 82 (7.32%)
occurrences (all)	11	40	9
Cellulitis			
subjects affected / exposed	16 / 170 (9.41%)	51 / 1476 (3.46%)	8 / 82 (9.76%)
occurrences (all)	23	56	18
Nasopharyngitis			
subjects affected / exposed	9 / 170 (5.29%)	30 / 1476 (2.03%)	6 / 82 (7.32%)
occurrences (all)	11	31	7
Pneumonia			
subjects affected / exposed	10 / 170 (5.88%)	38 / 1476 (2.57%)	12 / 82 (14.63%)
occurrences (all)	15	43	14
Upper respiratory tract infection			
subjects affected / exposed	12 / 170 (7.06%)	53 / 1476 (3.59%)	2 / 82 (2.44%)
occurrences (all)	15	56	2
Urinary tract infection			
subjects affected / exposed	18 / 170 (10.59%)	75 / 1476 (5.08%)	16 / 82 (19.51%)
occurrences (all)	27	94	18
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	9 / 170 (5.29%)	50 / 1476 (3.39%)	8 / 82 (9.76%)
occurrences (all)	10	52	9
Dehydration			
subjects affected / exposed	9 / 170 (5.29%)	21 / 1476 (1.42%)	4 / 82 (4.88%)
occurrences (all)	12	25	7
Fluid retention			
subjects affected / exposed	9 / 170 (5.29%)	19 / 1476 (1.29%)	3 / 82 (3.66%)
occurrences (all)	11	23	4
Gout			
subjects affected / exposed	18 / 170 (10.59%)	113 / 1476 (7.66%)	10 / 82 (12.20%)
occurrences (all)	20	134	16
Hyperglycaemia			
subjects affected / exposed	2 / 170 (1.18%)	10 / 1476 (0.68%)	6 / 82 (7.32%)
occurrences (all)	2	10	7
Hyperkalaemia			

subjects affected / exposed	5 / 170 (2.94%)	35 / 1476 (2.37%)	5 / 82 (6.10%)
occurrences (all)	5	35	8
Hyperuricaemia			
subjects affected / exposed	9 / 170 (5.29%)	32 / 1476 (2.17%)	5 / 82 (6.10%)
occurrences (all)	9	33	5
Hypervolaemia			
subjects affected / exposed	10 / 170 (5.88%)	76 / 1476 (5.15%)	11 / 82 (13.41%)
occurrences (all)	12	80	17
Hypokalaemia			
subjects affected / exposed	23 / 170 (13.53%)	61 / 1476 (4.13%)	17 / 82 (20.73%)
occurrences (all)	24	75	27
Hyponatraemia			
subjects affected / exposed	11 / 170 (6.47%)	35 / 1476 (2.37%)	13 / 82 (15.85%)
occurrences (all)	13	41	17

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
20 July 2018	Addition of a second cohort to enroll ATTR-CM diagnosed subjects who did not participate in parent study B3461028. Transition of all subjects to open label 61 mg dose (where available).

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

Analyses based on CMA set for Cohort A of this study, data was combined from participants in study B3461028 (plus participants who died, discontinued) or not enrolled into the current study. Their data not included in other sections than endpoints.

Notes: