Clinical trial results:
A Phase 3 Randomized, Double-blind, Multi-dose, Placebo and Naproxen-Controlled Study to Evaluate the Efficacy and Safety of Fasinumab in Patients with Pain Due to Osteoarthritis of the Knee or Hip

Summary

EudraCT number	2016-005020-29
Trial protocol	BG LT GB DK PL HU ES RO
Global end of trial date	27 August 2021

Results information

Result version number	v1 (current)
This version publication date	10 September 2022
First version publication date	10 September 2022

Trial information

Trial identification

Sponsor protocol code	R475-OA-1611

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Regeneron Pharmaceuticals, Inc.
Sponsor organisation address	777 Old Saw Mill River Road, Tarrytown, NY, United States, 10591
Public contact	Clinical Trials Administrator, Regeneron Pharmaceuticals, Inc., 001 844-734-6643, clinicaltrials@regeneron.com
Scientific contact	Clinical Trials Administrator, Regeneron Pharmaceuticals, Inc., 001 844-734-6643, clinicaltrials@regeneron.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	27 August 2021
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	27 August 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective was to evaluate the efficacy of fasinumab compared with placebo, when administered for up to 16 weeks in participants with pain due to osteoarthritis (OA) of the knee or hip.

Protection of trial subjects:

It is the responsibility of both the sponsor and the investigator(s) to ensure that this clinical study is conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki, and that are consistent with the ICH guidelines for GCP and applicable regulatory requirements.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	17 August 2017
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	Bulgaria: 27
Country: Number of subjects enrolled	Denmark: 34
Country: Number of subjects enrolled	Germany: 11
Country: Number of subjects enrolled	Hungary: 120
Country: Number of subjects enrolled	Lithuania: 16
Country: Number of subjects enrolled	Poland: 444
Country: Number of subjects enrolled	South Africa: 1307
Country: Number of subjects enrolled	Romania: 91
Country: Number of subjects enrolled	Russian Federation: 109
Country: Number of subjects enrolled	Spain: 145
Country: Number of subjects enrolled	Ukraine: 100
Country: Number of subjects enrolled	United Kingdom: 294
Country: Number of subjects enrolled	United States: 609
Worldwide total number of subjects	3307
EEA total number of subjects	888

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)	1876
From 65 to 84 years	1409
85 years and over	22

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

9157 total participants were screened. 5850 were screen failures: 4681 did not meet criteria, 4 adverse events, 1 Death, 397 investigator/sponsor decision, 130 imaging, 18 lost to follow-up, 93 protocol noncompliance, 225 other, 301 withdrawal of consent. 3307 participants were randomized into the study and 28 were improperly randomized.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Fasinumab-matching placebo administered by subcutaneous (SC) injection, every 4 weeks (Q4W) and naproxen-matching placebo administered orally (PO), twice a day (BID)

Arm type	Placebo
Investigational medicinal product name	Fasinumab-matching placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Fasinumab-matching placebo administered subcutaneously

Investigational medicinal product name	Naproxen-matching placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Naproxen-matching placebo administered orally

Arm title	Naproxen

Arm description:

Fasinumab-matching placebo SC Q4W and naproxen 500 mg PO, BID

Arm type	Active comparator
Investigational medicinal product name	Naproxen
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

500 mg orally, given twice daily (BID)

Arm title	Fasinumab 1 mg SC Q8W

Arm description:	
Fasinumab 1 mg SC Q8W and naproxen-matching placebo, PO, BID	
Arm type	Experimental
Investigational medicinal product name	fasinumab
Investigational medicinal product code	REGN475
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use
Dosage and administration details:	
1 mg administered by subcutaneous injection every 8 weeks (Q8W)	
Arm title	Fasinumab 1 mg SC Q4W
Arm description:	
Fasinumab 1 mg SC Q4W and naproxen-matching placebo, PO, BID	
Arm type	Experimental
Investigational medicinal product name	fasinumab
Investigational medicinal product code	REGN475
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use
Dosage and administration details:	
1 mg administered by subcutaneous injection every 4 weeks (Q4W)	
Arm title	Fasinumab 3mg Q4W
Arm description:	
Fasinumab 3 mg SC Q4W and naproxen-matching placebo, PO, BID	
Arm type	Experimental
Investigational medicinal product name	fasinumab
Investigational medicinal product code	REGN475
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use
Dosage and administration details:	
3 mg administered by subcutaneous injection every 4 weeks (Q4W)	
Arm title	Fasinumab 6mg Q8W
Arm description:	
Fasinumab 6 mg SC Q8W and naproxen-matching placebo, PO, BID	
Arm type	Experimental
Investigational medicinal product name	fasinumab
Investigational medicinal product code	REGN475
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use
Dosage and administration details:	
6 mg administered by subcutaneous injection every 8 weeks (Q8W)	

Number of subjects in period 1	Placebo	Naproxen	Fasinumab 1 mg SC Q8W
Started	354	1063	551
Completed	299	919	465
Not completed	55	144	86
Adverse event, serious fatal	3	9	7
Consent withdrawn by subject	24	73	44
Physician decision	-	1	-
BLANK - Need a reason...	-	1	-
Adverse event, non-fatal	5	21	16
Lost to follow-up	3	12	4
Protocol deviation	11	14	6
Lack of efficacy	9	13	9

Number of subjects in period 1	Fasinumab 1 mg SC Q4W	Fasinumab 3mg Q4W	Fasinumab 6mg Q8W
Started	1054	145	140
Completed	867	102	99
Not completed	187	43	41
Adverse event, serious fatal	9	-	-
Consent withdrawn by subject	97	11	10
Physician decision	2	17	15
BLANK - Need a reason...	-	-	1
Adverse event, non-fatal	35	2	1
Lost to follow-up	7	8	13
Protocol deviation	13	1	-
Lack of efficacy	24	4	1

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Fasinumab-matching placebo administered by subcutaneous (SC) injection, every 4 weeks (Q4W) and naproxen-matching placebo administered orally (PO), twice a day (BID)	
Reporting group title	Naproxen
Reporting group description:	
Fasinumab-matching placebo SC Q4W and naproxen 500 mg PO, BID	
Reporting group title	Fasinumab 1 mg SC Q8W
Reporting group description:	
Fasinumab 1 mg SC Q8W and naproxen-matching placebo, PO, BID	
Reporting group title	Fasinumab 1 mg SC Q4W
Reporting group description:	
Fasinumab 1 mg SC Q4W and naproxen-matching placebo, PO, BID	
Reporting group title	Fasinumab 3mg Q4W
Reporting group description:	
Fasinumab 3 mg SC Q4W and naproxen-matching placebo, PO, BID	
Reporting group title	Fasinumab 6mg Q8W
Reporting group description:	
Fasinumab 6 mg SC Q8W and naproxen-matching placebo, PO, BID	

Reporting group values	Placebo	Naproxen	Fasinumab 1 mg SC Q8W
Number of subjects	354	1063	551
Age Categorical Units: Participants			
Between 18 and 65 years	212	608	300
<=18 years	0	0	0
>=65 years	142	455	251
Sex: Female, Male Units: Participants			
Female	265	807	419
Male	89	256	132
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	12	26	13
Not Hispanic or Latino	339	1032	537
Unknown or Not Reported	3	5	1
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	1	1
Asian	11	35	29
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	109	315	166
White	211	633	307
More than one race	0	0	0
Unknown or Not Reported	23	79	48

Reporting group values	Fasinumab 1 mg SC Q4W	Fasinumab 3mg Q4W	Fasinumab 6mg Q8W
Number of subjects	1054	145	140
Age Categorical Units: Participants			
Between 18 and 65 years	584	91	81
<=18 years	0	0	0
>=65 years	470	54	59
Sex: Female, Male Units: Participants			
Female	793	96	98
Male	261	49	42
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	38	6	6
Not Hispanic or Latino	1015	139	134
Unknown or Not Reported	1	0	0
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	37	3	1
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	308	47	47
White	630	89	86
More than one race	0	0	0
Unknown or Not Reported	79	6	6

Reporting group values	Total		
Number of subjects	3307		
Age Categorical Units: Participants			
Between 18 and 65 years	1876		
<=18 years	0		
>=65 years	1431		
Sex: Female, Male Units: Participants			
Female	2478		
Male	829		
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	101		
Not Hispanic or Latino	3196		
Unknown or Not Reported	10		
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	2		
Asian	116		
Native Hawaiian or Other Pacific Islander	0		
Black or African American	992		

White	1956		
More than one race	0		
Unknown or Not Reported	241		

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Fasinumab-matching placebo administered by subcutaneous (SC) injection, every 4 weeks (Q4W) and naproxen-matching placebo administered orally (PO), twice a day (BID)	
Reporting group title	Naproxen
Reporting group description:	
Fasinumab-matching placebo SC Q4W and naproxen 500 mg PO, BID	
Reporting group title	Fasinumab 1 mg SC Q8W
Reporting group description:	
Fasinumab 1 mg SC Q8W and naproxen-matching placebo, PO, BID	
Reporting group title	Fasinumab 1 mg SC Q4W
Reporting group description:	
Fasinumab 1 mg SC Q4W and naproxen-matching placebo, PO, BID	
Reporting group title	Fasinumab 3mg Q4W
Reporting group description:	
Fasinumab 3 mg SC Q4W and naproxen-matching placebo, PO, BID	
Reporting group title	Fasinumab 6mg Q8W
Reporting group description:	
Fasinumab 6 mg SC Q8W and naproxen-matching placebo, PO, BID	
Subject analysis set title	SAF Year 1 - Placebo
Subject analysis set type	Safety analysis
Subject analysis set description:	
As treated; Fasinumab-matching placebo administered by subcutaneous (SC) injection, every 4 weeks (Q4W) and naproxen-matching placebo orally (PO), twice a day (BID)	
Subject analysis set title	SAF Year 1 - Naproxen
Subject analysis set type	Safety analysis
Subject analysis set description:	
As treated; Fasinumab-matching placebo SC Q4W and naproxen 500 mg PO, BID	
Subject analysis set title	SAF Year 1 - 1mg Q8W
Subject analysis set type	Safety analysis
Subject analysis set description:	
As treated; Fasinumab 1 mg SC Q8W and naproxen-matching placebo, PO, BID	
Subject analysis set title	SAF Year 1 - 1mg Q4W
Subject analysis set type	Safety analysis
Subject analysis set description:	
As treated; Fasinumab 1 mg SC Q4W and naproxen-matching placebo, PO, BID	
Subject analysis set title	SAF Year 1 and Year 2 - Placebo
Subject analysis set type	Safety analysis
Subject analysis set description:	
As treated; Fasinumab-matching placebo administered by subcutaneous (SC) injection, every 4 weeks (Q4W) and naproxen-matching placebo orally (PO), twice a day (BID)	
Subject analysis set title	SAF Year 1 and Year 2 - Naproxen
Subject analysis set type	Safety analysis
Subject analysis set description:	
As treated; Fasinumab-matching placebo SC Q4W and naproxen 500 mg PO, BID	
Subject analysis set title	SAF Year 1 and Year 2 - 1mg Q8W
Subject analysis set type	Safety analysis

Subject analysis set description:

As treated; Fasinumab 1 mg SC Q8W and naproxen-matching placebo, PO, BID

Subject analysis set title	SAF Year 1 and Year 2 - 1mg Q4W
Subject analysis set type	Safety analysis

Subject analysis set description:

As treated; Fasinumab 1 mg SC Q4W and naproxen-matching placebo, PO, BID

Primary: Change in the WOMAC Pain Subscale Scores from Baseline to Week 16 in Participants Treated with Fasinumab 1mg SC Q4W Compared with that of Participants Treated with Placebo

End point title	Change in the WOMAC Pain Subscale Scores from Baseline to Week 16 in Participants Treated with Fasinumab 1mg SC Q4W Compared with that of Participants Treated with Placebo[1]

End point description:

The WOMAC index is comprised of 24 parameters grouped in 3 subscales (pain-5 questions, physical function -17 questions and stiffness - 2 questions), with 0-10 grading of each question. The scores for each subscale are summed up, divided by number of questions, and each subscale is reported using Numerical Rating Scale score of 0-10. In addition to subscales, a total score is provided as the sum of normalized subscale scores divided by three, and reported using a Numerical Rating Scale score of 0-10. Higher scores indicate worse pain, stiffness and functional limitations.

End point type	Primary

End point timeframe:

Baseline to Week 16

Notes:

[1] - 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: Endpoint applies to Placebo and Fasinumab 1 mg SC Q4W arms only.

End point values	Placebo	Fasinumab 1 mg SC Q4W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	155	522		
Units: Score on a scale				
least squares mean (standard error)	-1.82 (± 0.162)	-2.49 (± 0.098)		

Statistical analyses

Statistical analysis title	Placebo vs. fasinumab 1 mg SC Q4W
Comparison groups	Placebo v Fasinumab 1 mg SC Q4W
Number of subjects included in analysis	677
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0002
Method	Mixed models analysis
Parameter estimate	Least Squares Mean
Point estimate	-0.68
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.028
upper limit	-0.324

Variability estimate	Standard error of the mean
Dispersion value	0.18

Primary: Change in the WOMAC Pain Subscale Scores from Baseline to Week 16 in Participants Treated with Fasinumab 1mg SC Q8W Compared with that of Participants Treated with Placebo

End point title	Change in the WOMAC Pain Subscale Scores from Baseline to Week 16 in Participants Treated with Fasinumab 1mg SC Q8W Compared with that of Participants Treated with Placebo[2]

End point description:

The WOMAC index is comprised of 24 parameters grouped in 3 subscales (pain-5 questions, physical function -17 questions and stiffness - 2 questions), with 0-10 grading of each question. The scores for each subscale are summed up, divided by number of questions, and each subscale is reported using Numerical Rating Scale score of 0-10. In addition to subscales, a total score is provided as the sum of normalized subscale scores divided by three, and reported using a Numerical Rating Scale score of 0-10. Higher scores indicate worse pain, stiffness and functional limitations.

End point type	Primary

End point timeframe:

Baseline to Week 16

Notes:

[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: Endpoint applies to Placebo and Fasinumab 1 mg SC Q8W arms only.

End point values	Placebo	Fasinumab 1 mg SC Q8W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	80	254		
Units: Score on a scale				
least squares mean (standard error)	-2.09 (± 0.231)	-2.19 (± 0.144)		

Statistical analyses

Statistical analysis title	Placebo vs. fasinumab 1 mg SC Q8W
Comparison groups	Placebo v Fasinumab 1 mg SC Q8W
Number of subjects included in analysis	334
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.7036
Method	Mixed models analysis
Parameter estimate	Least Squares Mean
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.594
upper limit	0.401
Variability estimate	Standard error of the mean
Dispersion value	0.254

Primary: Change in the WOMAC Physical Function Subscale Scores from Baseline to Week 16 in Participants Treated with Fasinumab 1mg Q4W Compared with that of Participants Treated with Placebo

End point title	Change in the WOMAC Physical Function Subscale Scores from Baseline to Week 16 in Participants Treated with Fasinumab 1mg Q4W Compared with that of Participants Treated with Placebo[3]

End point description:

The WOMAC index is comprised of 24 parameters grouped in 3 subscales (pain-5 questions, physical function -17 questions and stiffness - 2 questions), with 0-10 grading of each question. The scores for each subscale are summed up, divided by number of questions, and each subscale is reported using Numerical Rating Scale score of 0-10. In addition to subscales, a total score is provided as the sum of normalized subscale scores divided by three, and reported using a Numerical Rating Scale score of 0-10. Higher scores indicate worse pain, stiffness and functional limitations.

End point type	Primary

End point timeframe:

Baseline to Week 16

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Endpoint applies to Placebo and Fasinumab 1 mg SC Q4W arms only.

End point values	Placebo	Fasinumab 1 mg SC Q4W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	155	521		
Units: Score on a scale				
least squares mean (standard error)	-1.71 (± 0.161)	-2.42 (± 0.096)		

Statistical analyses

Statistical analysis title	Placebo vs. fasinumab 1 mg SC Q4W
Comparison groups	Placebo v Fasinumab 1 mg SC Q4W
Number of subjects included in analysis	676
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Mixed models analysis
Parameter estimate	Least Squares Mean
Point estimate	-0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.046
upper limit	-0.346
Variability estimate	Standard error of the mean
Dispersion value	0.178

Primary: Change in the WOMAC Physical Function Subscale Scores from Baseline to Week 16 in Participants Treated with Fasinumab 1mg Q8W Compared with that of Participants Treated with Placebo

End point title	Change in the WOMAC Physical Function Subscale Scores from Baseline to Week 16 in Participants Treated with Fasinumab 1mg Q8W Compared with that of Participants Treated with Placebo[4]

End point description:

The WOMAC index is comprised of 24 parameters grouped in 3 subscales (pain-5 questions, physical function -17 questions and stiffness - 2 questions), with 0-10 grading of each question. The scores for each subscale are summed up, divided by number of questions, and each subscale is reported using Numerical Rating Scale score of 0-10. In addition to subscales, a total score is provided as the sum of normalized subscale scores divided by three, and reported using a Numerical Rating Scale score of 0-10. Higher scores indicate worse pain, stiffness and functional limitations.

End point type	Primary

End point timeframe:

Baseline to Week 16

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: Endpoint applies to Placebo and Fasinumab 1 mg SC Q8W arms only.

End point values	Placebo	Fasinumab 1 mg SC Q8W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	80	254		
Units: Score on a scale				
least squares mean (standard error)	-1.91 (± 0.223)	-2.09 (± 0.137)		

Statistical analyses

Statistical analysis title	Placebo vs. fasinumab 1 mg SC Q8W
Comparison groups	Placebo v Fasinumab 1 mg SC Q8W
Number of subjects included in analysis	334
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.4605
Method	Mixed models analysis
Parameter estimate	Least Squares Mean
Point estimate	-0.18
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.657
upper limit	0.297
Variability estimate	Standard error of the mean
Dispersion value	0.243

Secondary: Change in the Patient Global Assessment (PGA) Scores from Baseline to Week 16 in Participants Treated with Fasinumab 1mg Q4W Compared with That of Participants Treated with Placebo

End point title	Change in the Patient Global Assessment (PGA) Scores from Baseline to Week 16 in Participants Treated with Fasinumab 1mg Q4W Compared with That of Participants Treated with Placebo[5]

End point description:

The Patient Global Assessment of OA (PGA) is a patient-rated assessment of current disease state on a 5-point Likert scale (1 = very good; 2 = good; 3 = fair; 4 = poor; and 5 = very poor).

End point type	Secondary

End point timeframe:

Baseline to Week 16

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: Endpoint applies to Placebo and Fasinumab 1 mg SC Q4W arms only.

End point values	Placebo	Fasinumab 1 mg SC Q4W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	156	526		
Units: Score on a scale				
least squares mean (standard error)	-0.64 (± 0.064)	-0.92 (± 0.040)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in the PGA Scores from Baseline to Week 16 in Participants Treated with Fasinumab 1mg Q4W Compared with That of Participants Treated with Naproxen

End point title	Change in the PGA Scores from Baseline to Week 16 in Participants Treated with Fasinumab 1mg Q4W Compared with That of Participants Treated with Naproxen[6]

End point description:

PGA is a participant-rated assessment of current disease state on a 5-point Likert scale (1 = very good; 2 = good; 3 = fair; 4 = poor; and 5 = very poor).

End point type	Secondary

End point timeframe:

Baseline to Week 16

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: Endpoint applies to Naproxen and Fasinumab 1 mg SC Q4W arms only.

End point values	Naproxen	Fasinumab 1 mg SC Q4W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	492	526		
Units: Score on a scale				
least squares mean (standard error)	-0.78 (± 0.040)	-0.92 (± 0.040)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change In The PGA Scores From Baseline To Week 44 In Participants Treated With Fasinumab 1mg Q4W Compared With That Of Participants Treated With Placebo

End point title	Change In The PGA Scores From Baseline To Week 44 In Participants Treated With Fasinumab 1mg Q4W Compared With That Of Participants Treated With Placebo[7]

End point description:

PGA is a participant-rated assessment of current disease state on a 5-point Likert scale (1 = very good; 2 = good; 3 = fair; 4 = poor; and 5 = very poor).

End point type	Secondary

End point timeframe:

Baseline to Week 44

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: Endpoint applies to Placebo and Fasinumab 1 mg SC Q4W arms only.

End point values	Placebo	Fasinumab 1 mg SC Q4W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	123	394		
Units: Score on a scale				
least squares mean (standard error)	-0.60 (± 0.074)	-0.79 (± 0.043)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage Of Participants Treated With Fasinumab 1mg Q4W, Compared With That of Participants Treated With Placebo, Who Had A Response At Week 16, With Response Defined As An Improvement By ≥30% In The WOMAC Pain Subscale Scores

End point title	Percentage Of Participants Treated With Fasinumab 1mg Q4W, Compared With That of Participants Treated With Placebo, Who Had A Response At Week 16, With Response Defined As An Improvement By ≥30% In The WOMAC Pain Subscale Scores[8]

End point description:

The WOMAC index is comprised of 24 parameters grouped in 3 subscales (pain-5 questions, physical

function -17 questions and stiffness - 2 questions), with 0-10 grading of each question. The scores for each subscale are summed up, divided by number of questions, and each subscale is reported using Numerical Rating Scale score of 0-10. In addition to subscales, a total score is provided as the sum of normalized subscale scores divided by three, and reported using a Numerical Rating Scale score of 0-10. Higher scores indicate worse pain, stiffness and functional limitations.

End point type	Secondary

End point timeframe:

Baseline to Week 16

Notes:

[8] - 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: Endpoint applies to Placebo and Fasinumab 1 mg SC Q4W arms only.

End point values	Placebo	Fasinumab 1 mg SC Q4W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	214	639		
Units: Percentage of participants				
number (not applicable)	43.9	56.2		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Treated with Fasinumab 1mg Q4W, Compared with that of Participants Treated with Naproxen, Who Had A Response At Week 16, with Response Defined As An Improvement By ≥30% In The WOMAC Pain Subscale Scores

End point title	Percentage of Participants Treated with Fasinumab 1mg Q4W, Compared with that of Participants Treated with Naproxen, Who Had A Response At Week 16, with Response Defined As An Improvement By ≥30% In The WOMAC Pain Subscale Scores[9]

End point description:

The WOMAC index is comprised of 24 parameters grouped in 3 subscales (pain-5 questions, physical function -17 questions and stiffness - 2 questions), with 0-10 grading of each question. The scores for each subscale are summed up, divided by number of questions, and each subscale is reported using Numerical Rating Scale score of 0-10. In addition to subscales, a total score is provided as the sum of normalized subscale scores divided by three, and reported using a Numerical Rating Scale score of 0-10. Higher scores indicate worse pain, stiffness and functional limitations.

End point type	Secondary

End point timeframe:

Week 16

Notes:

[9] - 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: Endpoint applies to Naproxen and Fasinumab 1 mg SC Q4W arms only.

End point values	Naproxen	Fasinumab 1 mg SC Q4W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	644	639		
Units: Percentage of participants				
number (not applicable)	50.5	56.2		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in WOMAC Pain Subscale Scores from Baseline to Week 16 In Participants Treated with Fasinumab 1mg Q4W, Compared with That of Participants Treated with Naproxen

End point title	Change in WOMAC Pain Subscale Scores from Baseline to Week 16 In Participants Treated with Fasinumab 1mg Q4W, Compared with That of Participants Treated with Naproxen[10]

End point description:

The WOMAC index is comprised of 24 parameters grouped in 3 subscales (pain-5 questions, physical function -17 questions and stiffness - 2 questions), with 0-10 grading of each question. The scores for each subscale are summed up, divided by number of questions, and each subscale is reported using Numerical Rating Scale score of 0-10. In addition to subscales, a total score is provided as the sum of normalized subscale scores divided by three, and reported using a Numerical Rating Scale score of 0-10. Higher scores indicate worse pain, stiffness and functional limitations.

End point type	Secondary

End point timeframe:

Baseline to Week 16

Notes:

[10] - 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: Endpoint applies to Naproxen and Fasinumab 1 mg SC Q4W arms only.

End point values	Naproxen	Fasinumab 1 mg SC Q4W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	345	360		
Units: Score on a scale				
arithmetic mean (standard deviation)	-2.42 (± 2.095)	-2.88 (± 2.099)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in WOMAC Pain Subscale Scores from Baseline to Week 44 in Participants Treated with Fasinumab 1mg Q4W, Compared with that of Participants Treated with Placebo

End point title	Change in WOMAC Pain Subscale Scores from Baseline to Week 44 in Participants Treated with Fasinumab 1mg Q4W, Compared with that of Participants Treated with Placebo[11]

End point description:

The WOMAC index is comprised of 24 parameters grouped in 3 subscales (pain-5 questions, physical function -17 questions and stiffness - 2 questions), with 0-10 grading of each question. The scores for each subscale are summed up, divided by number of questions, and each subscale is reported using

Numerical Rating Scale score of 0-10. In addition to subscales, a total score is provided as the sum of normalized subscale scores divided by three, and reported using a Numerical Rating Scale score of 0-10. Higher scores indicate worse pain, stiffness and functional limitations.

End point type	Secondary

End point timeframe:

Baseline to Week 44

Notes:

[11] - 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: Endpoint applies to Placebo and Fasinumab 1 mg SC Q4W arms only.

End point values	Placebo	Fasinumab 1 mg SC Q4W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	122	391		
Units: Score on a scale				
least squares mean (standard error)	-1.69 (± 0.188)	-2.20 (± 0.114)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in WOMAC Pain Subscale Scores from Baseline to Week 44 in Participants Treated with Fasinumab 1 mg Q4W, Compared with that of Participants Treated with Naproxen

End point title	Change in WOMAC Pain Subscale Scores from Baseline to Week 44 in Participants Treated with Fasinumab 1 mg Q4W, Compared with that of Participants Treated with Naproxen[12]

End point description:

The WOMAC index is comprised of 24 parameters grouped in 3 subscales (pain-5 questions, physical function -17 questions and stiffness - 2 questions), with 0-10 grading of each question. The scores for each subscale are summed up, divided by number of questions, and each subscale is reported using Numerical Rating Scale score of 0-10. In addition to subscales, a total score is provided as the sum of normalized subscale scores divided by three, and reported using a Numerical Rating Scale score of 0-10. Higher scores indicate worse pain, stiffness and functional limitations.

End point type	Secondary

End point timeframe:

Baseline to Week 44

Notes:

[12] - 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: Endpoint applies to Naproxen and Fasinumab 1 mg SC Q4W arms only.

End point values	Naproxen	Fasinumab 1 mg SC Q4W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	381	391		
Units: Score on a scale				
least squares mean (standard error)	-2.15 (± 0.115)	-2.20 (± 0.114)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in WOMAC Physical Function Subscale Scores from Baseline to the Average Score Across Weeks 4, 8, 12 and 16, in Participants Treated with Fasinumab 1 mg Q4W Compared with that of Participants Treated with Placebo

End point title	Change in WOMAC Physical Function Subscale Scores from Baseline to the Average Score Across Weeks 4, 8, 12 and 16, in Participants Treated with Fasinumab 1 mg Q4W Compared with that of Participants Treated with Placebo[13]

End point description:

The WOMAC index is comprised of 24 parameters grouped in 3 subscales (pain-5 questions, physical function -17 questions and stiffness - 2 questions), with 0-10 grading of each question. The scores for each subscale are summed up, divided by number of questions, and each subscale is reported using Numerical Rating Scale score of 0-10. In addition to subscales, a total score is provided as the sum of normalized subscale scores divided by three, and reported using a Numerical Rating Scale score of 0-10. Higher scores indicate worse pain, stiffness and functional limitations.

End point type	Secondary

End point timeframe:

Baseline to average score across weeks 4, 8, 12 and 16

Notes:

[13] - 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: Endpoint applies to Placebo and Fasinumab 1 mg SC Q4W arms only.

End point values	Placebo	Fasinumab 1 mg SC Q4W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	192	595		
Units: Score on a scale				
least squares mean (standard error)	-1.37 (± 0.137)	-2.25 (± 0.088)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in WOMAC Physical Function Subscale Scores from Baseline to the Average Score Across Weeks 36, 40 and 44 in Participants Treated with Fasinumab 1mg Q4W Compared with that of Participants Treated with Placebo

End point title	Change in WOMAC Physical Function Subscale Scores from Baseline to the Average Score Across Weeks 36, 40 and 44 in Participants Treated with Fasinumab 1mg Q4W Compared with that of Participants Treated with Placebo[14]

End point description:

The WOMAC index is comprised of 24 parameters grouped in 3 subscales (pain-5 questions, physical

function -17 questions and stiffness - 2 questions), with 0-10 grading of each question. The scores for each subscale are summed up, divided by number of questions, and each subscale is reported using Numerical Rating Scale score of 0-10. In addition to subscales, a total score is provided as the sum of normalized subscale scores divided by three, and reported using a Numerical Rating Scale score of 0-10. Higher scores indicate worse pain, stiffness and functional limitations.

End point type	Secondary

End point timeframe:

Baseline to average score across weeks 36, 40 and 44

Notes:

[14] - 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: Endpoint applies to Placebo and Fasinumab 1 mg SC Q4W arms only.

End point values	Placebo	Fasinumab 1 mg SC Q4W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	133	426		
Units: Score on a scale				
least squares mean (standard error)	-1.50 (± 0.172)	-1.99 (± 0.113)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in WOMAC Physical Function Subscale Scores from Baseline to Week 16 in Participants Treated with Fasinumab 1mg Q4W, Compared with that of Participants Treated with Naproxen

End point title	Change in WOMAC Physical Function Subscale Scores from Baseline to Week 16 in Participants Treated with Fasinumab 1mg Q4W, Compared with that of Participants Treated with Naproxen[15]

End point description:

The WOMAC index is comprised of 24 parameters grouped in 3 subscales (pain-5 questions, physical function -17 questions and stiffness - 2 questions), with 0-10 grading of each question. The scores for each subscale are summed up, divided by number of questions, and each subscale is reported using Numerical Rating Scale score of 0-10. In addition to subscales, a total score is provided as the sum of normalized subscale scores divided by three, and reported using a Numerical Rating Scale score of 0-10. Higher scores indicate worse pain, stiffness and functional limitations.

End point type	Secondary

End point timeframe:

Baseline to Week 16

Notes:

[15] - 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: Endpoint applies to Naproxen and Fasinumab 1 mg SC Q4W arms only.

End point values	Naproxen	Fasinumab 1 mg SC Q4W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	485	521		
Units: Score on a scale				
least squares mean (standard error)	-1.98 (± 0.101)	-2.42 (± 0.096)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in WOMAC Physical Function Subscale Scores from Baseline to Week 44 in Participants Treated with Fasinumab 1mg Q4W, Compared with that of Participants Treated with Placebo

End point title	Change in WOMAC Physical Function Subscale Scores from Baseline to Week 44 in Participants Treated with Fasinumab 1mg Q4W, Compared with that of Participants Treated with Placebo[16]

End point description:

The WOMAC index is comprised of 24 parameters grouped in 3 subscales (pain-5 questions, physical function -17 questions and stiffness - 2 questions), with 0-10 grading of each question. The scores for each subscale are summed up, divided by number of questions, and each subscale is reported using Numerical Rating Scale score of 0-10. In addition to subscales, a total score is provided as the sum of normalized subscale scores divided by three, and reported using a Numerical Rating Scale score of 0-10. Higher scores indicate worse pain, stiffness and functional limitations.

End point type	Secondary

End point timeframe:

Baseline to Week 44

Notes:

[16] - 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: Endpoint applies to Placebo and Fasinumab 1 mg SC Q4W arms only.

End point values	Placebo	Fasinumab 1 mg SC Q4W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	122	390		
Units: Score on a scale				
least squares mean (standard error)	-1.60 (± 0.186)	-2.07 (± 0.109)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in WOMAC Physical Function Subscale Scores from Baseline to Week 44 in Participants Treated with Fasinumab 1mg Q4W, Compared with that of Participants Treated with Naproxen

End point title	Change in WOMAC Physical Function Subscale Scores from Baseline to Week 44 in Participants Treated with Fasinumab

	1mg Q4W, Compared with that of Participants Treated with Naproxen[17]

End point description:

The WOMAC index is comprised of 24 parameters grouped in 3 subscales (pain-5 questions, physical function -17 questions and stiffness - 2 questions), with 0-10 grading of each question. The scores for each subscale are summed up, divided by number of questions, and each subscale is reported using Numerical Rating Scale score of 0-10. In addition to subscales, a total score is provided as the sum of normalized subscale scores divided by three, and reported using a Numerical Rating Scale score of 0-10. Higher scores indicate worse pain, stiffness and functional limitations.

End point type	Secondary

End point timeframe:

Baseline to Week 44

Notes:

[17] - 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: Endpoint applies to Naproxenand Fasinumab 1 mg SC Q4W arms only.

End point values	Naproxen	Fasinumab 1 mg SC Q4W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	378	390		
Units: Score on a scale				
least squares mean (standard error)	-2.00 (± 0.113)	-2.07 (± 0.109)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change In WOMAC Pain Subscale Scores From Baseline To The Average Score Across Weeks 4, 8, 12 And 16, in Participants Treated With Fasinumab 1mg Q4W Compared With That of Participants Treated With Placebo

End point title	Change In WOMAC Pain Subscale Scores From Baseline To The Average Score Across Weeks 4, 8, 12 And 16, in Participants Treated With Fasinumab 1mg Q4W Compared With That of Participants Treated With Placebo[18]

End point description:

The WOMAC index is comprised of 24 parameters grouped in 3 subscales (pain-5 questions, physical function -17 questions and stiffness - 2 questions), with 0-10 grading of each question. The scores for each subscale are summed up, divided by number of questions, and each subscale is reported using Numerical Rating Scale score of 0-10. In addition to subscales, a total score is provided as the sum of normalized subscale scores divided by three, and reported using a Numerical Rating Scale score of 0-10. Higher scores indicate worse pain, stiffness and functional limitations.

End point type	Secondary

End point timeframe:

Baseline to average score across weeks 4, 8, 12 and 16

Notes:

[18] - 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: Endpoint applies to Placebo and Fasinumab 1 mg SC Q4W arms only.

End point values	Placebo	Fasinumab 1 mg SC Q4W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	192	596		
Units: Score on a scale				
least squares mean (standard error)	-1.46 (± 0.140)	-2.30 (± 0.090)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in WOMAC Pain Subscale Scores From Baseline To The Average Score Across Weeks 36, 40 And 44 In Participants Treated With Fasinumab 1mg Q4W Compared With That of Participants Treated With Placebo

End point title	Change in WOMAC Pain Subscale Scores From Baseline To The Average Score Across Weeks 36, 40 And 44 In Participants Treated With Fasinumab 1mg Q4W Compared With That of Participants Treated With Placebo[19]

End point description:

The WOMAC index is comprised of 24 parameters grouped in 3 subscales (pain-5 questions, physical function -17 questions and stiffness - 2 questions), with 0-10 grading of each question. The scores for each subscale are summed up, divided by number of questions, and each subscale is reported using Numerical Rating Scale score of 0-10. In addition to subscales, a total score is provided as the sum of normalized subscale scores divided by three, and reported using a Numerical Rating Scale score of 0-10. Higher scores indicate worse pain, stiffness and functional limitations.

End point type	Secondary

End point timeframe:

Baseline to average score across weeks 36, 40 and 44

Notes:

[19] - 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: Endpoint applies to Placebo and Fasinumab 1 mg SC Q4W arms only.

End point values	Placebo	Fasinumab 1 mg SC Q4W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	133	427		
Units: Score on a scale				
least squares mean (standard error)	-1.57 (± 0.184)	-2.06 (± 0.118)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in the PGA Scores from Baseline to Week 16 in Participants Treated with Fasinumab 1mg Q8W Compared with That of Participants Treated with Placebo

End point title	Change in the PGA Scores from Baseline to Week 16 in Participants Treated with Fasinumab 1mg Q8W Compared with

	That of Participants Treated with Placebo[20]

End point description:

PGA is a participant-rated assessment of current disease state on a 5-point Likert scale (1 = very good; 2 = good; 3 = fair; 4 = poor; and 5 = very poor).

End point type	Secondary

End point timeframe:

Baseline to Week 16

Notes:

[20] - 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: Endpoint applies to Placebo and Fasinumab 1 mg SC Q8W arms only.

End point values	Placebo	Fasinumab 1 mg SC Q8W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	80	257		
Units: Score on a scale				
least squares mean (standard error)	-0.79 (± 0.094)	-0.77 (± 0.057)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in the PGA Scores from Baseline to Week 16 in Participants Treated with Fasinumab 1 mg Q8W Compared with That of Participants Treated with Naproxen

End point title	Change in the PGA Scores from Baseline to Week 16 in Participants Treated with Fasinumab 1 mg Q8W Compared with That of Participants Treated with Naproxen[21]

End point description:

PGA is a participant-rated assessment of current disease state on a 5-point Likert scale (1 = very good; 2 = good; 3 = fair; 4 = poor; and 5 = very poor).

End point type	Secondary

End point timeframe:

Baseline to Week 16

Notes:

[21] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Endpoint applies to Naproxen and Fasinumab 1 mg SC Q8W arms only.

End point values	Naproxen	Fasinumab 1 mg SC Q8W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	245	257		
Units: Score on a scale				
least squares mean (standard error)	-0.82 (± 0.057)	-0.77 (± 0.057)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change In The PGA Scores From Baseline To Week 44 In Participants Treated With Fasinumab 1mg Q8W Compared With That Of Participants Treated With Placebo

End point title	Change In The PGA Scores From Baseline To Week 44 In Participants Treated With Fasinumab 1mg Q8W Compared With That Of Participants Treated With Placebo[22]

End point description:

PGA is a participant-rated assessment of current disease state on a 5-point Likert scale (1 = very good; 2 = good; 3 = fair; 4 = poor; and 5 = very poor).

End point type	Secondary

End point timeframe:

Baseline to Week 44

Notes:

[22] - 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: Endpoint applies to Placebo and Fasinumab 1 mg SC Q8W arms only.

End point values	Placebo	Fasinumab 1 mg SC Q4W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	62	193		
Units: Score on a scale				
least squares mean (standard error)	-0.74 (± 0.1115)	-0.75 (± 0.064)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage Of Participants Treated With Fasinumab 1mg Q8W, Compared With That of Participants Treated With Placebo, Who Had A Response At Week 16, With Response Defined As An Improvement By ≥30% In The WOMAC Pain Subscale Scores

End point title	Percentage Of Participants Treated With Fasinumab 1mg Q8W, Compared With That of Participants Treated With Placebo, Who Had A Response At Week 16, With Response Defined As An Improvement By ≥30% In The WOMAC Pain Subscale Scores[23]

End point description:

The WOMAC index is comprised of 24 parameters grouped in 3 subscales (pain-5 questions, physical function -17 questions and stiffness - 2 questions), with 0-10 grading of each question. The scores for each subscale are summed up, divided by number of questions, and each subscale is reported using Numerical Rating Scale score of 0-10. In addition to subscales, a total score is provided as the sum of normalized subscale scores divided by three, and reported using a Numerical Rating Scale score of 0-10. Higher scores indicate worse pain, stiffness and functional limitations.

End point type	Secondary

End point timeframe:

Baseline to Week 16

Notes:

[23] - 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: Endpoint applies to Placebo and Fasinumab 1 mg SC Q8W arms only.

End point values	Placebo	Fasinumab 1 mg SC Q8W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	102	304		
Units: Percentage of participants				
number (not applicable)	53.9	52.3		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in WOMAC Pain Subscale Scores from Baseline to Week 16 In Participants Treated with Fasinumab 1mg Q8W, Compared with That of Participants Treated with Naproxen

End point title	Change in WOMAC Pain Subscale Scores from Baseline to Week 16 In Participants Treated with Fasinumab 1mg Q8W, Compared with That of Participants Treated with Naproxen[24]

End point description:

The WOMAC index is comprised of 24 parameters grouped in 3 subscales (pain-5 questions, physical function -17 questions and stiffness - 2 questions), with 0-10 grading of each question. The scores for each subscale are summed up, divided by number of questions, and each subscale is reported using Numerical Rating Scale score of 0-10. In addition to subscales, a total score is provided as the sum of normalized subscale scores divided by three, and reported using a Numerical Rating Scale score of 0-10. Higher scores indicate worse pain, stiffness and functional limitations.

End point type	Secondary

End point timeframe:

Baseline to Week 16

Notes:

[24] - 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: Endpoint applies to Naproxen and Fasinumab 1 mg SC Q8W arms only.

End point values	Naproxen	Fasinumab 1 mg SC Q8W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	170	171		
Units: Score on a scale				
least squares mean (standard error)	-2.41 (± 0.155)	-2.53 (± 0.154)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in WOMAC Pain Subscale Scores from Baseline to Week 44 in Participants Treated with Fasinumab 1mg Q8W, Compared with that of Participants Treated with Placebo

End point title	Change in WOMAC Pain Subscale Scores from Baseline to Week 44 in Participants Treated with Fasinumab 1mg Q8W, Compared with that of Participants Treated with Placebo[25]

End point description:

The WOMAC index is comprised of 24 parameters grouped in 3 subscales (pain-5 questions, physical function -17 questions and stiffness - 2 questions), with 0-10 grading of each question. The scores for each subscale are summed up, divided by number of questions, and each subscale is reported using Numerical Rating Scale score of 0-10. In addition to subscales, a total score is provided as the sum of normalized subscale scores divided by three, and reported using a Numerical Rating Scale score of 0-10. Higher scores indicate worse pain, stiffness and functional limitations.

End point type	Secondary

End point timeframe:

Baseline to Week 44

Notes:

[25] - 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: Endpoint applies to Placebo and Fasinumab 1 mg SC Q8W arms only.

End point values	Placebo	Fasinumab 1 mg SC Q8W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	62	189		
Units: Score on a scale				
least squares mean (standard error)	-1.77 (± 0.276)	-1.99 (± 0.163)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in WOMAC Physical Function Subscale Scores from Baseline to the Average Score Across Weeks 4, 8, 12 and 16, in Participants Treated with Fasinumab 1 mg Q8W Compared with that of Participants Treated with Placebo

End point title	Change in WOMAC Physical Function Subscale Scores from Baseline to the Average Score Across Weeks 4, 8, 12 and 16, in Participants Treated with Fasinumab 1 mg Q8W Compared with that of Participants Treated with Placebo[26]

End point description:

The WOMAC index is comprised of 24 parameters grouped in 3 subscales (pain-5 questions, physical function -17 questions and stiffness - 2 questions), with 0-10 grading of each question. The scores for each subscale are summed up, divided by number of questions, and each subscale is reported using Numerical Rating Scale score of 0-10. In addition to subscales, a total score is provided as the sum of normalized subscale scores divided by three, and reported using a Numerical Rating Scale score of 0-10. Higher scores indicate worse pain, stiffness and functional limitations.

End point type	Secondary

End point timeframe:

Baseline to average score across weeks 4, 8, 12 and 16

Notes:

[26] - 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: Endpoint applies to Placebo and Fasinumab 1 mg SC Q8W arms only.

End point values	Placebo	Fasinumab 1 mg SC Q8W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	94	291		
Units: Score on a scale				
least squares mean (standard error)	-1.61 (± 0.196)	-2.04 (± 0.127)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in WOMAC Physical Function Subscale Scores from Baseline to the Average Score Across Weeks 36, 40 and 44 in Participants Treated with Fasinumab 1mg Q8W Compared with that of Participants Treated with Placebo

End point title	Change in WOMAC Physical Function Subscale Scores from Baseline to the Average Score Across Weeks 36, 40 and 44 in Participants Treated with Fasinumab 1mg Q8W Compared with that of Participants Treated with Placebo[27]

End point description:

The WOMAC index is comprised of 24 parameters grouped in 3 subscales (pain-5 questions, physical function -17 questions and stiffness - 2 questions), with 0-10 grading of each question. The scores for each subscale are summed up, divided by number of questions, and each subscale is reported using Numerical Rating Scale score of 0-10. In addition to subscales, a total score is provided as the sum of normalized subscale scores divided by three, and reported using a Numerical Rating Scale score of 0-10. Higher scores indicate worse pain, stiffness and functional limitations.

End point type	Secondary

End point timeframe:

Baseline to average score across weeks 36, 40 and 44

Notes:

[27] - 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: Endpoint applies to Placebo and Fasinumab 1 mg SC Q8W arms only.

End point values	Placebo	Fasinumab 1 mg SC Q8W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	69	210		
Units: Score on a scale				
least squares mean (standard error)	-1.62 (± 0.261)	-1.69 (± 0.166)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in WOMAC Physical Function Subscale Scores from Baseline to Week 16 in Participants Treated with Fasinumab 1mg Q8W, Compared with that of Participants Treated with Naproxen

End point title	Change in WOMAC Physical Function Subscale Scores from Baseline to Week 16 in Participants Treated with Fasinumab

	1mg Q8W, Compared with that of Participants Treated with Naproxen[28]

End point description:

The WOMAC index is comprised of 24 parameters grouped in 3 subscales (pain-5 questions, physical function -17 questions and stiffness - 2 questions), with 0-10 grading of each question. The scores for each subscale are summed up, divided by number of questions, and each subscale is reported using Numerical Rating Scale score of 0-10. In addition to subscales, a total score is provided as the sum of normalized subscale scores divided by three, and reported using a Numerical Rating Scale score of 0-10. Higher scores indicate worse pain, stiffness and functional limitations.

End point type	Secondary

End point timeframe:

Baseline to Week 16

Notes:

[28] - 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: Endpoint applies to Naproxen and Fasinumab 1 mg SC Q8W arms only.

End point values	Naproxen	Fasinumab 1 mg SC Q8W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	241	254		
Units: Score on a scale				
least squares mean (standard error)	-2.04 (± 0.140)	-2.09 (± 0.137)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in WOMAC Physical Function Subscale Scores from Baseline to Week 44 in Participants Treated with Fasinumab 1mg Q8W, Compared with that of Participants Treated with Placebo

End point title	Change in WOMAC Physical Function Subscale Scores from Baseline to Week 44 in Participants Treated with Fasinumab 1mg Q8W, Compared with that of Participants Treated with Placebo[29]

End point description:

The WOMAC index is comprised of 24 parameters grouped in 3 subscales (pain-5 questions, physical function -17 questions and stiffness - 2 questions), with 0-10 grading of each question. The scores for each subscale are summed up, divided by number of questions, and each subscale is reported using Numerical Rating Scale score of 0-10. In addition to subscales, a total score is provided as the sum of normalized subscale scores divided by three, and reported using a Numerical Rating Scale score of 0-10. Higher scores indicate worse pain, stiffness and functional limitations.

End point type	Secondary

End point timeframe:

Baseline to Week 44

Notes:

[29] - 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: Endpoint applies to Placebo and Fasinumab 1 mg SC Q8W arms only.

End point values	Placebo	Fasinumab 1 mg SC Q8W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	62	189		
Units: Score on a scale				
least squares mean (standard error)	-1.76 (± 0.262)	-1.90 (± 0.157)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change In WOMAC Pain Subscale Scores From Baseline To The Average Score Across Weeks 4, 8, 12 And 16, in Participants Treated With Fasinumab 1mg Q8W Compared With That of Participants Treated With Placebo

End point title	Change In WOMAC Pain Subscale Scores From Baseline To The Average Score Across Weeks 4, 8, 12 And 16, in Participants Treated With Fasinumab 1mg Q8W Compared With That of Participants Treated With Placebo[30]

End point description:

The WOMAC index is comprised of 24 parameters grouped in 3 subscales (pain-5 questions, physical function -17 questions and stiffness - 2 questions), with 0-10 grading of each question. The scores for each subscale are summed up, divided by number of questions, and each subscale is reported using Numerical Rating Scale score of 0-10. In addition to subscales, a total score is provided as the sum of normalized subscale scores divided by three, and reported using a Numerical Rating Scale score of 0-10. Higher scores indicate worse pain, stiffness and functional limitations.

End point type	Secondary

End point timeframe:

Baseline to average score across weeks 4, 8, 12 and 16

Notes:

[30] - 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: Endpoint applies to Placebo and Fasinumab 1 mg SC Q8W arms only.

End point values	Placebo	Fasinumab 1 mg SC Q8W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	94	291		
Units: Score on a scale				
least squares mean (standard error)	-1.73 (± 0.202)	-2.11 (± 0.131)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in WOMAC Pain Subscale Scores From Baseline To The Average Score Across Weeks 36, 40 And 44 In Participants Treated With Fasinumab 1mg Q8W Compared With That of Participants Treated With Placebo

End point title	Change in WOMAC Pain Subscale Scores From Baseline To The Average Score Across Weeks 36, 40 And 44 In Participants

	Treated With Fasinumab 1mg Q8W Compared With That of Participants Treated With Placebo[31]

End point description:

The WOMAC index is comprised of 24 parameters grouped in 3 subscales (pain-5 questions, physical function -17 questions and stiffness - 2 questions), with 0-10 grading of each question. The scores for each subscale are summed up, divided by number of questions, and each subscale is reported using Numerical Rating Scale score of 0-10. In addition to subscales, a total score is provided as the sum of normalized subscale scores divided by three, and reported using a Numerical Rating Scale score of 0-10. Higher scores indicate worse pain, stiffness and functional limitations.

End point type	Secondary

End point timeframe:

Baseline to average score across weeks 36, 40 and 44

Notes:

[31] - 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: Endpoint applies to Placebo and Fasinumab 1 mg SC Q8W arms only.

End point values	Placebo	Fasinumab 1 mg SC Q8W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	69	210		
Units: Score on a scale				
least squares mean (standard error)	-1.69 (± 0.271)	-1.80 (± 0.169)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Adjudicated Arthropathy (AA) (as confirmed by adjudication) - Year 1

End point title	Number of Participants with Adjudicated Arthropathy (AA) (as confirmed by adjudication) - Year 1

End point description:

End point type	Secondary

End point timeframe:

Baseline to Week 52

End point values	SAF Year 1 - Placebo	SAF Year 1 - Naproxen	SAF Year 1 - 1mg Q8W	SAF Year 1 - 1mg Q4W
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	352	1056	554	1052
Units: Participants	4	27	40	102

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with AA (as confirmed by adjudication) - Year 2

End point title	Number of Participants with AA (as confirmed by adjudication) - Year 2[32]

End point description:

End point type	Secondary

End point timeframe:

First dose of study drug in Year 2 through week 104E

Notes:

[32] - 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: Endpoint did not apply to the 3mg and 6mg dosing arms as those were discontinued.

End point values	Placebo	Naproxen	Fasinumab 1 mg SC Q8W	Fasinumab 1 mg SC Q4W
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	137	402	193	371
Units: Participants	2	7	11	53

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with AA (as confirmed by adjudication) - Year 1 and Year 2

End point title	Number of Participants with AA (as confirmed by adjudication) - Year 1 and Year 2

End point description:

End point type	Secondary

End point timeframe:

Day 1 through week 104E (Extension)

End point values	SAF Year 1 and Year 2 - Placebo	SAF Year 1 and Year 2 - Naproxen	SAF Year 1 and Year 2 - 1mg Q8W	SAF Year 1 and Year 2 - 1mg Q4W
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	353	1056	553	1052
Units: Participants	6	33	50	152

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Destructive Arthropathy (DA) (as confirmed by adjudication) - Year 1

End point title	Number of Participants with Destructive Arthropathy (DA) (as confirmed by adjudication) - Year 1

End point description:

End point type	Secondary

End point timeframe:

Baseline to Week 52

End point values	SAF Year 1 - Placebo	SAF Year 1 - Naproxen	SAF Year 1 - 1mg Q8W	SAF Year 1 - 1mg Q4W
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	352	1056	554	1052
Units: Participants	0	1	2	7

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with DA (as confirmed by adjudication) - Year 2

End point title	Number of Participants with DA (as confirmed by adjudication) - Year 2[33]

End point description:

End point type	Secondary

End point timeframe:

First dose of study drug in Year 2 through week 104E

Notes:

[33] - 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: Endpoint did not apply to the 3mg and 6mg dosing arms as those were discontinued.

End point values	Placebo	Naproxen	Fasinumab 1 mg SC Q8W	Fasinumab 1 mg SC Q4W
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	137	402	193	371
Units: Participants	0	0	0	4

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with DA (as confirmed by adjudication) - Year 1 and Year 2

End point title	Number of Participants with DA (as confirmed by adjudication) - Year 1 and Year 2

End point description:

End point type	Secondary

End point timeframe:

Day 1 through week 104E

End point values	SAF Year 1 and Year 2 - Placebo	SAF Year 1 and Year 2 - Naproxen	SAF Year 1 and Year 2 - 1mg Q8W	SAF Year 1 and Year 2 - 1mg Q4W
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	353	1056	553	1052
Units: Participants	0	1	2	11

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Treatment Emergent Adverse Events (TEAEs) - Year 1

End point title	Number of Treatment Emergent Adverse Events (TEAEs) - Year 1

End point description:

End point type	Secondary

End point timeframe:

Baseline to Week 52

End point values	SAF Year 1 - Placebo	SAF Year 1 - Naproxen	SAF Year 1 - 1mg Q8W	SAF Year 1 - 1mg Q4W
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	352	1056	554	1052
Units: Events	1063	3641	1985	3901

Statistical analyses

No statistical analyses for this end point

Secondary: Number of TEAEs - Year 2

End point title	Number of TEAEs - Year 2[34]

End point description:

End point type	Secondary

End point timeframe:

First dose of study drug in Year 2 through week 104E

Notes:

[34] - 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: Endpoint did not apply to the 3mg and 6mg dosing arms as those were discontinued.

End point values	Naproxen	Fasinumab 1 mg SC Q8W	Fasinumab 1 mg SC Q4W	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	554	190	385	
Units: Events	973	277	808	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of TEAEs - Year 1 and Year 2

End point title	Number of TEAEs - Year 1 and Year 2

End point description:

End point type	Secondary

End point timeframe:

Day 1 through week 104E

End point values	SAF Year 1 and Year 2 - Placebo	SAF Year 1 and Year 2 - Naproxen	SAF Year 1 and Year 2 - 1mg Q8W	SAF Year 1 and Year 2 - 1mg Q4W
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	353	1056	553	1052
Units: Events	1317	4348	2271	4712

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with at Least 1 Sympathetic Nervous System (SNS) Dysfunction Adverse Event of Special Interest (AESI) - Year 1

End point title	Number of Participants with at Least 1 Sympathetic Nervous System (SNS) Dysfunction Adverse Event of Special Interest (AESI) - Year 1

End point description:

End point type	Secondary

End point timeframe:

Baseline to Week 52

End point values	SAF Year 1 - Placebo	SAF Year 1 - Naproxen	SAF Year 1 - 1mg Q8W	SAF Year 1 - 1mg Q4W
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	352	1056	554	1052
Units: Participants	1	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with at Least 1 Sympathetic Nervous System (SNS) Dysfunction Adverse Event of Special Interest (AESI) - Year 2

End point title	Number of Participants with at Least 1 Sympathetic Nervous System (SNS) Dysfunction Adverse Event of Special Interest (AESI) - Year 2[35]

End point description:

End point type	Secondary

End point timeframe:

First dose of study drug in Year 2 through week 104E

Notes:

[35] - 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: Endpoint did not apply to the 3mg and 6mg dosing arms as those were discontinued.

End point values	Naproxen	Fasinumab 1 mg SC Q8W	Fasinumab 1 mg SC Q4W	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	554	190	385	
Units: Participants	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with at Least 1 Sympathetic Nervous System (SNS) Dysfunction Adverse Event of Special Interest (AESI) - Year 1 and Year 2

End point title	Number of Participants with at Least 1 Sympathetic Nervous System (SNS) Dysfunction Adverse Event of Special Interest (AESI) - Year 1 and Year 2

End point description:

End point type	Secondary

End point timeframe:

Day 1 through week 104E

End point values	SAF Year 1 and Year 2 - Placebo	SAF Year 1 and Year 2 - Naproxen	SAF Year 1 and Year 2 - 1mg Q8W	SAF Year 1 and Year 2 - 1mg Q4W
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	353	1056	553	1052
Units: Participants	1	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with at Least 1 Peripheral Sensory Neuropathy AESI That Require a Neurology or Other Specialty Consultation - Year 1

End point title	Number of Participants with at Least 1 Peripheral Sensory Neuropathy AESI That Require a Neurology or Other Specialty Consultation - Year 1

End point description:

End point type	Secondary

End point timeframe:

Baseline to Week 52

End point values	SAF Year 1 - Placebo	SAF Year 1 - Naproxen	SAF Year 1 - 1mg Q8W	SAF Year 1 - 1mg Q4W
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	352	1056	554	1052
Units: Participants	18	43	29	70

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with at Least 1 Peripheral Sensory Neuropathy AESI That Require a Neurology or Other Specialty Consultation - Year 2

End point title	Number of Participants with at Least 1 Peripheral Sensory Neuropathy AESI That Require a Neurology or Other Specialty Consultation - Year 2[36]

End point description:

End point type	Secondary

End point timeframe:

First dose of study drug in Year 2 through week 104E

Notes:

[36] - 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: Endpoint did not apply to the 3mg and 6mg dosing arms as those were discontinued.

End point values	Naproxen	Fasinumab 1 mg SC Q8W	Fasinumab 1 mg SC Q4W	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	554	190	385	
Units: Participants	16	6	12	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with at Least 1 Peripheral Sensory Neuropathy AESI That Require a Neurology or Other Specialty Consultation - Year 1 and Year 2

End point title	Number of Participants with at Least 1 Peripheral Sensory Neuropathy AESI That Require a Neurology or Other Specialty Consultation - Year 1 and Year 2

End point description:

End point type	Secondary

End point timeframe:

Day 1 through week 104E

End point values	SAF Year 1 and Year 2 - Placebo	SAF Year 1 and Year 2 - Naproxen	SAF Year 1 and Year 2 - 1mg Q8W	SAF Year 1 and Year 2 - 1mg Q4W
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	353	1056	553	1052
Units: Participants	23	51	35	82

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Any Type of All-Cause Joint Replacement (JR) in Year 1

End point title	Number of Participants with Any Type of All-Cause Joint Replacement (JR) in Year 1

End point description:

End point type	Secondary

End point timeframe:

Baseline to Week 52

End point values	SAF Year 1 - Placebo	SAF Year 1 - Naproxen	SAF Year 1 - 1mg Q8W	SAF Year 1 - 1mg Q4W
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	352	1056	554	1052
Units: Participants	12	33	31	67

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Any Type of All-Cause JR in Year 2

End point title	Number of Participants with Any Type of All-Cause JR in Year

End point description:

End point type	Secondary

End point timeframe:

First dose of study drug in Year 2 through week 104E

Notes:

[37] - 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: Endpoint did not apply to the 3mg and 6mg dosing arms as those were discontinued.

End point values	Naproxen	Fasinumab 1 mg SC Q8W	Fasinumab 1 mg SC Q4W	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	554	190	385	
Units: Participants	22	12	33	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Any Type of All-Cause JR - Year 1 and Year 2

End point title	Number of Participants with Any Type of All-Cause JR - Year 1 and Year 2

End point description:

End point type	Secondary

End point timeframe:

Day 1 through week 104E

End point values	SAF Year 1 and Year 2 - Placebo	SAF Year 1 and Year 2 - Naproxen	SAF Year 1 and Year 2 - 1mg Q8W	SAF Year 1 and Year 2 - 1mg Q4W
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	353	1056	553	1052
Units: Participants	19	47	44	100

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From first dose up to week 124	
Adverse event reporting additional description:	
As treated population	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	23.1

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Fasinumab-matching placebo administered by subcutaneous (SC) injection, every 4 weeks (Q4W) and naproxen-matching placebo administered orally (PO), twice a day (BID)	
Reporting group title	Naproxen
Reporting group description:	
Fasinumab-matching placebo SC Q4W and naproxen 500 mg PO, BID	
Reporting group title	Fasinumab 1mg Q8W
Reporting group description:	
Fasinumab 1 mg SC Q8W and naproxen-matching placebo, PO, BID	
Reporting group title	Fasinumab 1mg Q4W
Reporting group description:	
Fasinumab 1 mg SC Q4W and naproxen-matching placebo, PO, BID	
Reporting group title	Fasinumab 3mg Q4W
Reporting group description:	
Fasinumab 3 mg SC Q4W and naproxen-matching placebo, PO, BID	
Reporting group title	Fasinumab 6mg Q8W
Reporting group description:	
Fasinumab 6 mg SC Q8W and naproxen-matching placebo, PO, BID	

Serious adverse events	Placebo	Naproxen	Fasinumab 1mg Q8W
Total subjects affected by serious adverse events			
subjects affected / exposed	49 / 352 (13.92%)	103 / 1056 (9.75%)	81 / 554 (14.62%)
number of deaths (all causes)	5	13	12
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Bladder cancer			
subjects affected / exposed	0 / 352 (0.00%)	1 / 1056 (0.09%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bladder neoplasm			

subjects affected / exposed	0 / 352 (0.00%)	1 / 1056 (0.09%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bladder transitional cell carcinoma			
subjects affected / exposed	0 / 352 (0.00%)	1 / 1056 (0.09%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Breast cancer			
subjects affected / exposed	0 / 352 (0.00%)	1 / 1056 (0.09%)	2 / 554 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic myeloid leukaemia			
subjects affected / exposed	0 / 352 (0.00%)	1 / 1056 (0.09%)	0 / 554 (0.00%)
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 cancer metastatic			
subjects affected / exposed	0 / 352 (0.00%)	1 / 1056 (0.09%)	0 / 554 (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
Lung cancer metastatic			
subjects affected / exposed	0 / 352 (0.00%)	1 / 1056 (0.09%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteosarcoma			
subjects affected / exposed	0 / 352 (0.00%)	1 / 1056 (0.09%)	0 / 554 (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
Prostate cancer metastatic			
subjects affected / exposed	0 / 352 (0.00%)	1 / 1056 (0.09%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Basal cell carcinoma			

subjects affected / exposed	0 / 352 (0.00%)	0 / 1056 (0.00%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Benign ovarian tumour			
subjects affected / exposed	0 / 352 (0.00%)	0 / 1056 (0.00%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Benign soft tissue neoplasm			
subjects affected / exposed	0 / 352 (0.00%)	0 / 1056 (0.00%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Breast cancer recurrent			
subjects affected / exposed	0 / 352 (0.00%)	0 / 1056 (0.00%)	1 / 554 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic neoplasm			
subjects affected / exposed	0 / 352 (0.00%)	0 / 1056 (0.00%)	1 / 554 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intraductal proliferative breast lesion			
subjects affected / exposed	0 / 352 (0.00%)	0 / 1056 (0.00%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Invasive ductal breast carcinoma			
subjects affected / exposed	1 / 352 (0.28%)	0 / 1056 (0.00%)	0 / 554 (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
Lung neoplasm malignant			
subjects affected / exposed	0 / 352 (0.00%)	0 / 1056 (0.00%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningioma			

subjects affected / exposed	0 / 352 (0.00%)	0 / 1056 (0.00%)	1 / 554 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastases to bone			
subjects affected / exposed	0 / 352 (0.00%)	0 / 1056 (0.00%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neoplasm malignant			
subjects affected / exposed	0 / 352 (0.00%)	0 / 1056 (0.00%)	1 / 554 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Non-small cell lung cancer metastatic			
subjects affected / exposed	0 / 352 (0.00%)	0 / 1056 (0.00%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophageal carcinoma			
subjects affected / exposed	0 / 352 (0.00%)	0 / 1056 (0.00%)	1 / 554 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Pancreatic carcinoma metastatic			
subjects affected / exposed	1 / 352 (0.28%)	0 / 1056 (0.00%)	0 / 554 (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
Pancreatic neoplasm			
subjects affected / exposed	0 / 352 (0.00%)	0 / 1056 (0.00%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal hamartoma			
subjects affected / exposed	0 / 352 (0.00%)	0 / 1056 (0.00%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Retroperitoneal neoplasm			

subjects affected / exposed	1 / 352 (0.28%)	0 / 1056 (0.00%)	0 / 554 (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
Squamous cell carcinoma of lung			
subjects affected / exposed	0 / 352 (0.00%)	0 / 1056 (0.00%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uterine cancer			
subjects affected / exposed	0 / 352 (0.00%)	0 / 1056 (0.00%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Aortic stenosis			
subjects affected / exposed	0 / 352 (0.00%)	1 / 1056 (0.09%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral artery occlusion			
subjects affected / exposed	0 / 352 (0.00%)	1 / 1056 (0.09%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aortic dissection			
subjects affected / exposed	0 / 352 (0.00%)	0 / 1056 (0.00%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Deep vein thrombosis			
subjects affected / exposed	0 / 352 (0.00%)	0 / 1056 (0.00%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertension			
subjects affected / exposed	1 / 352 (0.28%)	0 / 1056 (0.00%)	1 / 554 (0.18%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertensive urgency			

subjects affected / exposed	0 / 352 (0.00%)	0 / 1056 (0.00%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Knee arthroplasty			
subjects affected / exposed	7 / 352 (1.99%)	7 / 1056 (0.66%)	4 / 554 (0.72%)
occurrences causally related to treatment / all	0 / 7	1 / 7	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hip arthroplasty			
subjects affected / exposed	0 / 352 (0.00%)	5 / 1056 (0.47%)	5 / 554 (0.90%)
occurrences causally related to treatment / all	0 / 0	0 / 6	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Joint arthroplasty			
subjects affected / exposed	2 / 352 (0.57%)	3 / 1056 (0.28%)	4 / 554 (0.72%)
occurrences causally related to treatment / all	0 / 2	1 / 3	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Joint resurfacing surgery			
subjects affected / exposed	0 / 352 (0.00%)	0 / 1056 (0.00%)	1 / 554 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Knee operation			
subjects affected / exposed	0 / 352 (0.00%)	0 / 1056 (0.00%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Sudden death			
subjects affected / exposed	1 / 352 (0.28%)	3 / 1056 (0.28%)	1 / 554 (0.18%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 3	0 / 1
Death			
subjects affected / exposed	2 / 352 (0.57%)	2 / 1056 (0.19%)	1 / 554 (0.18%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 2	0 / 2	0 / 1

Adverse drug reaction			
subjects affected / exposed	0 / 352 (0.00%)	0 / 1056 (0.00%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chest pain			
subjects affected / exposed	1 / 352 (0.28%)	0 / 1056 (0.00%)	0 / 554 (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 / 352 (0.00%)	0 / 1056 (0.00%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	0 / 352 (0.00%)	1 / 1056 (0.09%)	0 / 554 (0.00%)
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			
Benign prostatic hyperplasia			
subjects affected / exposed	0 / 352 (0.00%)	0 / 1056 (0.00%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cervical polyp			
subjects affected / exposed	0 / 352 (0.00%)	0 / 1056 (0.00%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endometrial hyperplasia			
subjects affected / exposed	0 / 352 (0.00%)	0 / 1056 (0.00%)	1 / 554 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ovarian cyst			
subjects affected / exposed	0 / 352 (0.00%)	0 / 1056 (0.00%)	1 / 554 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 352 (0.00%)	1 / 1056 (0.09%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Apnoea			
subjects affected / exposed	1 / 352 (0.28%)	0 / 1056 (0.00%)	0 / 554 (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
Asthma			
subjects affected / exposed	0 / 352 (0.00%)	0 / 1056 (0.00%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	1 / 352 (0.28%)	0 / 1056 (0.00%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 352 (0.00%)	0 / 1056 (0.00%)	2 / 554 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary oedema			
subjects affected / exposed	0 / 352 (0.00%)	0 / 1056 (0.00%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Psychotic disorder			
subjects affected / exposed	0 / 352 (0.00%)	1 / 1056 (0.09%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Substance abuse			

subjects affected / exposed	0 / 352 (0.00%)	1 / 1056 (0.09%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pseudodementia			
subjects affected / exposed	1 / 352 (0.28%)	0 / 1056 (0.00%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Product issues			
Device dislocation			
subjects affected / exposed	0 / 352 (0.00%)	1 / 1056 (0.09%)	0 / 554 (0.00%)
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 loosening			
subjects affected / exposed	0 / 352 (0.00%)	0 / 1056 (0.00%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Gun shot wound			
subjects affected / exposed	0 / 352 (0.00%)	1 / 1056 (0.09%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hip fracture			
subjects affected / exposed	0 / 352 (0.00%)	1 / 1056 (0.09%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Joint dislocation			
subjects affected / exposed	1 / 352 (0.28%)	1 / 1056 (0.09%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Limb injury			
subjects affected / exposed	0 / 352 (0.00%)	1 / 1056 (0.09%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Lower limb fracture			
subjects affected / exposed	0 / 352 (0.00%)	1 / 1056 (0.09%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meniscus injury			
subjects affected / exposed	0 / 352 (0.00%)	1 / 1056 (0.09%)	1 / 554 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Radius fracture			
subjects affected / exposed	1 / 352 (0.28%)	1 / 1056 (0.09%)	1 / 554 (0.18%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Road traffic accident			
subjects affected / exposed	0 / 352 (0.00%)	1 / 1056 (0.09%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Soft tissue injury			
subjects affected / exposed	0 / 352 (0.00%)	1 / 1056 (0.09%)	0 / 554 (0.00%)
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 / 352 (0.00%)	1 / 1056 (0.09%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ankle fracture			
subjects affected / exposed	1 / 352 (0.28%)	0 / 1056 (0.00%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Deep vein thrombosis postoperative			
subjects affected / exposed	1 / 352 (0.28%)	0 / 1056 (0.00%)	0 / 554 (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
Femoral neck fracture			

subjects affected / exposed	0 / 352 (0.00%)	0 / 1056 (0.00%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femur fracture			
subjects affected / exposed	0 / 352 (0.00%)	0 / 1056 (0.00%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Foot fracture			
subjects affected / exposed	0 / 352 (0.00%)	0 / 1056 (0.00%)	1 / 554 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fractured sacrum			
subjects affected / exposed	0 / 352 (0.00%)	0 / 1056 (0.00%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Humerus fracture			
subjects affected / exposed	0 / 352 (0.00%)	0 / 1056 (0.00%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Joint injury			
subjects affected / exposed	0 / 352 (0.00%)	0 / 1056 (0.00%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ligament rupture			
subjects affected / exposed	1 / 352 (0.28%)	0 / 1056 (0.00%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pelvic fracture			
subjects affected / exposed	0 / 352 (0.00%)	0 / 1056 (0.00%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Postoperative wound complication			

subjects affected / exposed	0 / 352 (0.00%)	0 / 1056 (0.00%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal compression fracture			
subjects affected / exposed	1 / 352 (0.28%)	0 / 1056 (0.00%)	0 / 554 (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
Spinal fracture			
subjects affected / exposed	1 / 352 (0.28%)	0 / 1056 (0.00%)	0 / 554 (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
Tendon injury			
subjects affected / exposed	0 / 352 (0.00%)	0 / 1056 (0.00%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tendon rupture			
subjects affected / exposed	0 / 352 (0.00%)	0 / 1056 (0.00%)	1 / 554 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper limb fracture			
subjects affected / exposed	0 / 352 (0.00%)	0 / 1056 (0.00%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wrist fracture			
subjects affected / exposed	0 / 352 (0.00%)	0 / 1056 (0.00%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Congenital, familial and genetic disorders			
Hydrocele			
subjects affected / exposed	0 / 352 (0.00%)	0 / 1056 (0.00%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			

Acute coronary syndrome			
subjects affected / exposed	0 / 352 (0.00%)	2 / 1056 (0.19%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery disease			
subjects affected / exposed	1 / 352 (0.28%)	2 / 1056 (0.19%)	0 / 554 (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
Myocardial infarction			
subjects affected / exposed	1 / 352 (0.28%)	2 / 1056 (0.19%)	2 / 554 (0.36%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 3
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
Atrial fibrillation			
subjects affected / exposed	1 / 352 (0.28%)	1 / 1056 (0.09%)	0 / 554 (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
Cardiovascular disorder			
subjects affected / exposed	0 / 352 (0.00%)	1 / 1056 (0.09%)	0 / 554 (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
Myocardial ischaemia			
subjects affected / exposed	0 / 352 (0.00%)	1 / 1056 (0.09%)	0 / 554 (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
Acute myocardial infarction			
subjects affected / exposed	1 / 352 (0.28%)	0 / 1056 (0.00%)	0 / 554 (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 unstable			
subjects affected / exposed	0 / 352 (0.00%)	0 / 1056 (0.00%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial tachycardia			

subjects affected / exposed	0 / 352 (0.00%)	0 / 1056 (0.00%)	1 / 554 (0.18%)
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 arrest			
subjects affected / exposed	0 / 352 (0.00%)	0 / 1056 (0.00%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure			
subjects affected / exposed	0 / 352 (0.00%)	0 / 1056 (0.00%)	1 / 554 (0.18%)
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 failure congestive			
subjects affected / exposed	1 / 352 (0.28%)	0 / 1056 (0.00%)	2 / 554 (0.36%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Cardiac tamponade			
subjects affected / exposed	0 / 352 (0.00%)	0 / 1056 (0.00%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Extrasystoles			
subjects affected / exposed	0 / 352 (0.00%)	0 / 1056 (0.00%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Carotid artery aneurysm			
subjects affected / exposed	0 / 352 (0.00%)	1 / 1056 (0.09%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular accident			
subjects affected / exposed	0 / 352 (0.00%)	1 / 1056 (0.09%)	2 / 554 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 1	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1
Guillain-Barre syndrome			

subjects affected / exposed	0 / 352 (0.00%)	1 / 1056 (0.09%)	0 / 554 (0.00%)
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	0 / 352 (0.00%)	1 / 1056 (0.09%)	0 / 554 (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
Transient ischaemic attack			
subjects affected / exposed	0 / 352 (0.00%)	1 / 1056 (0.09%)	0 / 554 (0.00%)
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	1 / 352 (0.28%)	1 / 1056 (0.09%)	1 / 554 (0.18%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Carpal tunnel syndrome			
subjects affected / exposed	0 / 352 (0.00%)	0 / 1056 (0.00%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral infarction			
subjects affected / exposed	0 / 352 (0.00%)	0 / 1056 (0.00%)	1 / 554 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrospinal fistula			
subjects affected / exposed	0 / 352 (0.00%)	0 / 1056 (0.00%)	1 / 554 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hemiplegic migraine			
subjects affected / exposed	0 / 352 (0.00%)	0 / 1056 (0.00%)	1 / 554 (0.18%)
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 radiculopathy			

subjects affected / exposed	0 / 352 (0.00%)	0 / 1056 (0.00%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscle tone disorder			
subjects affected / exposed	0 / 352 (0.00%)	0 / 1056 (0.00%)	1 / 554 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myelopathy			
subjects affected / exposed	0 / 352 (0.00%)	0 / 1056 (0.00%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Radiculopathy			
subjects affected / exposed	0 / 352 (0.00%)	0 / 1056 (0.00%)	1 / 554 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sciatica			
subjects affected / exposed	0 / 352 (0.00%)	0 / 1056 (0.00%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 352 (0.00%)	0 / 1056 (0.00%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 352 (0.57%)	4 / 1056 (0.38%)	2 / 554 (0.36%)
occurrences causally related to treatment / all	0 / 4	2 / 4	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Cataract			
subjects affected / exposed	0 / 352 (0.00%)	1 / 1056 (0.09%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eyelid ptosis			

subjects affected / exposed	1 / 352 (0.28%)	0 / 1056 (0.00%)	0 / 554 (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			
Hiatus hernia			
subjects affected / exposed	0 / 352 (0.00%)	2 / 1056 (0.19%)	0 / 554 (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 hernia			
subjects affected / exposed	1 / 352 (0.28%)	1 / 1056 (0.09%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	0 / 352 (0.00%)	1 / 1056 (0.09%)	0 / 554 (0.00%)
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 / 352 (0.00%)	1 / 1056 (0.09%)	0 / 554 (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
Intestinal obstruction			
subjects affected / exposed	0 / 352 (0.00%)	1 / 1056 (0.09%)	1 / 554 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Nausea			
subjects affected / exposed	0 / 352 (0.00%)	1 / 1056 (0.09%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oedematous pancreatitis			
subjects affected / exposed	0 / 352 (0.00%)	1 / 1056 (0.09%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peptic ulcer			

subjects affected / exposed	0 / 352 (0.00%)	1 / 1056 (0.09%)	0 / 554 (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
Small intestinal obstruction			
subjects affected / exposed	1 / 352 (0.28%)	1 / 1056 (0.09%)	0 / 554 (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
Vomiting			
subjects affected / exposed	0 / 352 (0.00%)	1 / 1056 (0.09%)	1 / 554 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain			
subjects affected / exposed	0 / 352 (0.00%)	0 / 1056 (0.00%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anal fissure			
subjects affected / exposed	0 / 352 (0.00%)	0 / 1056 (0.00%)	1 / 554 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Food poisoning			
subjects affected / exposed	0 / 352 (0.00%)	0 / 1056 (0.00%)	1 / 554 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Gastrointestinal inflammation			
subjects affected / exposed	1 / 352 (0.28%)	0 / 1056 (0.00%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Inguinal hernia			
subjects affected / exposed	1 / 352 (0.28%)	0 / 1056 (0.00%)	1 / 554 (0.18%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal haemorrhage			

subjects affected / exposed	1 / 352 (0.28%)	0 / 1056 (0.00%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal perforation			
subjects affected / exposed	0 / 352 (0.00%)	0 / 1056 (0.00%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis acute			
subjects affected / exposed	1 / 352 (0.28%)	0 / 1056 (0.00%)	0 / 554 (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
Volvulus of small bowel			
subjects affected / exposed	0 / 352 (0.00%)	0 / 1056 (0.00%)	1 / 554 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 352 (0.00%)	2 / 1056 (0.19%)	0 / 554 (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
Cholangitis			
subjects affected / exposed	0 / 352 (0.00%)	1 / 1056 (0.09%)	0 / 554 (0.00%)
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 alcoholic			
subjects affected / exposed	0 / 352 (0.00%)	1 / 1056 (0.09%)	0 / 554 (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
Bile duct stone			
subjects affected / exposed	0 / 352 (0.00%)	0 / 1056 (0.00%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholangitis acute			

subjects affected / exposed	0 / 352 (0.00%)	0 / 1056 (0.00%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis chronic			
subjects affected / exposed	0 / 352 (0.00%)	0 / 1056 (0.00%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholelithiasis			
subjects affected / exposed	0 / 352 (0.00%)	0 / 1056 (0.00%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	1 / 352 (0.28%)	2 / 1056 (0.19%)	0 / 554 (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
Acute kidney injury			
subjects affected / exposed	0 / 352 (0.00%)	0 / 1056 (0.00%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bladder prolapse			
subjects affected / exposed	1 / 352 (0.28%)	0 / 1056 (0.00%)	0 / 554 (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
Diabetic nephropathy			
subjects affected / exposed	1 / 352 (0.28%)	0 / 1056 (0.00%)	0 / 554 (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
Prerenal failure			
subjects affected / exposed	0 / 352 (0.00%)	0 / 1056 (0.00%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal failure			

subjects affected / exposed	0 / 352 (0.00%)	0 / 1056 (0.00%)	1 / 554 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Renal impairment			
subjects affected / exposed	0 / 352 (0.00%)	0 / 1056 (0.00%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	4 / 352 (1.14%)	11 / 1056 (1.04%)	10 / 554 (1.81%)
occurrences causally related to treatment / all	1 / 4	2 / 11	0 / 11
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rapidly progressive osteoarthritis			
subjects affected / exposed	1 / 352 (0.28%)	4 / 1056 (0.38%)	13 / 554 (2.35%)
occurrences causally related to treatment / all	1 / 1	5 / 7	7 / 13
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoarthritis			
subjects affected / exposed	3 / 352 (0.85%)	3 / 1056 (0.28%)	3 / 554 (0.54%)
occurrences causally related to treatment / all	0 / 3	0 / 3	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Back pain			
subjects affected / exposed	0 / 352 (0.00%)	1 / 1056 (0.09%)	2 / 554 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cervical spinal stenosis			
subjects affected / exposed	0 / 352 (0.00%)	1 / 1056 (0.09%)	0 / 554 (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
Haemarthrosis			
subjects affected / exposed	0 / 352 (0.00%)	1 / 1056 (0.09%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lumbar spinal stenosis			

subjects affected / exposed	0 / 352 (0.00%)	1 / 1056 (0.09%)	0 / 554 (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
Osteonecrosis			
subjects affected / exposed	0 / 352 (0.00%)	1 / 1056 (0.09%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rotator cuff syndrome			
subjects affected / exposed	0 / 352 (0.00%)	1 / 1056 (0.09%)	1 / 554 (0.18%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal stenosis			
subjects affected / exposed	0 / 352 (0.00%)	1 / 1056 (0.09%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthritis			
subjects affected / exposed	0 / 352 (0.00%)	0 / 1056 (0.00%)	1 / 554 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bursitis			
subjects affected / exposed	0 / 352 (0.00%)	0 / 1056 (0.00%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Exostosis			
subjects affected / exposed	1 / 352 (0.28%)	0 / 1056 (0.00%)	0 / 554 (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
Intervertebral disc protrusion			
subjects affected / exposed	0 / 352 (0.00%)	0 / 1056 (0.00%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Joint effusion			

subjects affected / exposed	0 / 352 (0.00%)	0 / 1056 (0.00%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Limb mass			
subjects affected / exposed	0 / 352 (0.00%)	0 / 1056 (0.00%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal osteoarthritis			
subjects affected / exposed	0 / 352 (0.00%)	0 / 1056 (0.00%)	1 / 554 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal synovial cyst			
subjects affected / exposed	0 / 352 (0.00%)	0 / 1056 (0.00%)	1 / 554 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subchondral insufficiency fracture			
subjects affected / exposed	0 / 352 (0.00%)	0 / 1056 (0.00%)	1 / 554 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vertebral foraminal stenosis			
subjects affected / exposed	0 / 352 (0.00%)	0 / 1056 (0.00%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
COVID-19 pneumonia			
subjects affected / exposed	2 / 352 (0.57%)	3 / 1056 (0.28%)	1 / 554 (0.18%)
occurrences causally related to treatment / all	0 / 2	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
COVID-19			
subjects affected / exposed	0 / 352 (0.00%)	2 / 1056 (0.19%)	2 / 554 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 2
Cellulitis			

subjects affected / exposed	1 / 352 (0.28%)	2 / 1056 (0.19%)	0 / 554 (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
Gastroenteritis			
subjects affected / exposed	0 / 352 (0.00%)	2 / 1056 (0.19%)	2 / 554 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 352 (0.00%)	2 / 1056 (0.19%)	0 / 554 (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
Arthritis infective			
subjects affected / exposed	0 / 352 (0.00%)	1 / 1056 (0.09%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis			
subjects affected / exposed	0 / 352 (0.00%)	1 / 1056 (0.09%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Empyema			
subjects affected / exposed	0 / 352 (0.00%)	1 / 1056 (0.09%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric ulcer helicobacter			
subjects affected / exposed	0 / 352 (0.00%)	1 / 1056 (0.09%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infectious pleural effusion			
subjects affected / exposed	0 / 352 (0.00%)	1 / 1056 (0.09%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peritonsillar abscess			

subjects affected / exposed	0 / 352 (0.00%)	1 / 1056 (0.09%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	1 / 352 (0.28%)	1 / 1056 (0.09%)	1 / 554 (0.18%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia klebsiella			
subjects affected / exposed	0 / 352 (0.00%)	1 / 1056 (0.09%)	0 / 554 (0.00%)
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 infection			
subjects affected / exposed	0 / 352 (0.00%)	1 / 1056 (0.09%)	0 / 554 (0.00%)
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	1 / 352 (0.28%)	1 / 1056 (0.09%)	0 / 554 (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
Appendicitis			
subjects affected / exposed	0 / 352 (0.00%)	0 / 1056 (0.00%)	1 / 554 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Erysipelas			
subjects affected / exposed	0 / 352 (0.00%)	0 / 1056 (0.00%)	1 / 554 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia urinary tract infection			
subjects affected / exposed	0 / 352 (0.00%)	0 / 1056 (0.00%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infected bite			

subjects affected / exposed	0 / 352 (0.00%)	0 / 1056 (0.00%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower respiratory tract infection			
subjects affected / exposed	0 / 352 (0.00%)	0 / 1056 (0.00%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung abscess			
subjects affected / exposed	0 / 352 (0.00%)	0 / 1056 (0.00%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningitis			
subjects affected / exposed	0 / 352 (0.00%)	0 / 1056 (0.00%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningitis pneumococcal			
subjects affected / exposed	0 / 352 (0.00%)	0 / 1056 (0.00%)	1 / 554 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia bacterial			
subjects affected / exposed	0 / 352 (0.00%)	0 / 1056 (0.00%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural cellulitis			
subjects affected / exposed	0 / 352 (0.00%)	0 / 1056 (0.00%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	0 / 352 (0.00%)	0 / 1056 (0.00%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tuberculosis			

subjects affected / exposed	0 / 352 (0.00%)	0 / 1056 (0.00%)	1 / 554 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Wound infection staphylococcal			
subjects affected / exposed	0 / 352 (0.00%)	0 / 1056 (0.00%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Diabetes mellitus			
subjects affected / exposed	0 / 352 (0.00%)	1 / 1056 (0.09%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperkalaemia			
subjects affected / exposed	0 / 352 (0.00%)	1 / 1056 (0.09%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dehydration			
subjects affected / exposed	0 / 352 (0.00%)	0 / 1056 (0.00%)	1 / 554 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoglycaemia			
subjects affected / exposed	1 / 352 (0.28%)	0 / 1056 (0.00%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Fasinumab 1mg Q4W	Fasinumab 3mg Q4W	Fasinumab 6mg Q8W
Total subjects affected by serious adverse events			
subjects affected / exposed	175 / 1052 (16.63%)	7 / 145 (4.83%)	6 / 139 (4.32%)
number of deaths (all causes)	13	0	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Bladder cancer			

subjects affected / exposed	0 / 1052 (0.00%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bladder neoplasm			
subjects affected / exposed	0 / 1052 (0.00%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bladder transitional cell carcinoma			
subjects affected / exposed	0 / 1052 (0.00%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Breast cancer			
subjects affected / exposed	0 / 1052 (0.00%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic myeloid leukaemia			
subjects affected / exposed	0 / 1052 (0.00%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic cancer metastatic			
subjects affected / exposed	0 / 1052 (0.00%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung cancer metastatic			
subjects affected / exposed	0 / 1052 (0.00%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteosarcoma			
subjects affected / exposed	0 / 1052 (0.00%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostate cancer metastatic			

subjects affected / exposed	0 / 1052 (0.00%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Basal cell carcinoma			
subjects affected / exposed	2 / 1052 (0.19%)	0 / 145 (0.00%)	0 / 139 (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
Benign ovarian tumour			
subjects affected / exposed	1 / 1052 (0.10%)	0 / 145 (0.00%)	0 / 139 (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
Benign soft tissue neoplasm			
subjects affected / exposed	1 / 1052 (0.10%)	0 / 145 (0.00%)	0 / 139 (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 recurrent			
subjects affected / exposed	0 / 1052 (0.00%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic neoplasm			
subjects affected / exposed	0 / 1052 (0.00%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intraductal proliferative breast lesion			
subjects affected / exposed	1 / 1052 (0.10%)	0 / 145 (0.00%)	0 / 139 (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
Invasive ductal breast carcinoma			
subjects affected / exposed	0 / 1052 (0.00%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung neoplasm malignant			

subjects affected / exposed	1 / 1052 (0.10%)	0 / 145 (0.00%)	0 / 139 (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
Meningioma			
subjects affected / exposed	0 / 1052 (0.00%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastases to bone			
subjects affected / exposed	1 / 1052 (0.10%)	0 / 145 (0.00%)	0 / 139 (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
Neoplasm malignant			
subjects affected / exposed	0 / 1052 (0.00%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Non-small cell lung cancer metastatic			
subjects affected / exposed	1 / 1052 (0.10%)	0 / 145 (0.00%)	0 / 139 (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 carcinoma			
subjects affected / exposed	0 / 1052 (0.00%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatic carcinoma metastatic			
subjects affected / exposed	0 / 1052 (0.00%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatic neoplasm			
subjects affected / exposed	1 / 1052 (0.10%)	0 / 145 (0.00%)	0 / 139 (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
Renal hamartoma			

subjects affected / exposed	1 / 1052 (0.10%)	0 / 145 (0.00%)	0 / 139 (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
Retroperitoneal neoplasm			
subjects affected / exposed	0 / 1052 (0.00%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Squamous cell carcinoma of lung			
subjects affected / exposed	1 / 1052 (0.10%)	0 / 145 (0.00%)	0 / 139 (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
Uterine cancer			
subjects affected / exposed	1 / 1052 (0.10%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Aortic stenosis			
subjects affected / exposed	0 / 1052 (0.00%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral artery occlusion			
subjects affected / exposed	0 / 1052 (0.00%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aortic dissection			
subjects affected / exposed	1 / 1052 (0.10%)	0 / 145 (0.00%)	0 / 139 (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
Deep vein thrombosis			
subjects affected / exposed	2 / 1052 (0.19%)	1 / 145 (0.69%)	0 / 139 (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
Hypertension			

subjects affected / exposed	3 / 1052 (0.29%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertensive urgency			
subjects affected / exposed	1 / 1052 (0.10%)	0 / 145 (0.00%)	0 / 139 (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			
Knee arthroplasty			
subjects affected / exposed	17 / 1052 (1.62%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	4 / 20	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hip arthroplasty			
subjects affected / exposed	3 / 1052 (0.29%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Joint arthroplasty			
subjects affected / exposed	8 / 1052 (0.76%)	0 / 145 (0.00%)	1 / 139 (0.72%)
occurrences causally related to treatment / all	0 / 8	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Joint resurfacing surgery			
subjects affected / exposed	0 / 1052 (0.00%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Knee operation			
subjects affected / exposed	1 / 1052 (0.10%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Sudden death			
subjects affected / exposed	3 / 1052 (0.29%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 3	0 / 0	0 / 0

Death			
subjects affected / exposed	2 / 1052 (0.19%)	0 / 145 (0.00%)	0 / 139 (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
Adverse drug reaction			
subjects affected / exposed	1 / 1052 (0.10%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chest pain			
subjects affected / exposed	1 / 1052 (0.10%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oedema peripheral			
subjects affected / exposed	1 / 1052 (0.10%)	0 / 145 (0.00%)	0 / 139 (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
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	0 / 1052 (0.00%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	1 / 1052 (0.10%)	0 / 145 (0.00%)	0 / 139 (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 polyp			
subjects affected / exposed	1 / 1052 (0.10%)	0 / 145 (0.00%)	0 / 139 (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
Endometrial hyperplasia			
subjects affected / exposed	1 / 1052 (0.10%)	0 / 145 (0.00%)	0 / 139 (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

Ovarian cyst			
subjects affected / exposed	0 / 1052 (0.00%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 1052 (0.00%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Apnoea			
subjects affected / exposed	0 / 1052 (0.00%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Asthma			
subjects affected / exposed	2 / 1052 (0.19%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	2 / 1052 (0.19%)	0 / 145 (0.00%)	0 / 139 (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
Pulmonary embolism			
subjects affected / exposed	2 / 1052 (0.19%)	0 / 145 (0.00%)	0 / 139 (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
Pulmonary oedema			
subjects affected / exposed	1 / 1052 (0.10%)	0 / 145 (0.00%)	0 / 139 (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
Psychiatric disorders			
Psychotic disorder			

subjects affected / exposed	0 / 1052 (0.00%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Substance abuse			
subjects affected / exposed	0 / 1052 (0.00%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pseudodementia			
subjects affected / exposed	0 / 1052 (0.00%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Product issues			
Device dislocation			
subjects affected / exposed	0 / 1052 (0.00%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device loosening			
subjects affected / exposed	1 / 1052 (0.10%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Gun shot wound			
subjects affected / exposed	0 / 1052 (0.00%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hip fracture			
subjects affected / exposed	1 / 1052 (0.10%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Joint dislocation			
subjects affected / exposed	0 / 1052 (0.00%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Limb injury			
subjects affected / exposed	0 / 1052 (0.00%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower limb fracture			
subjects affected / exposed	1 / 1052 (0.10%)	0 / 145 (0.00%)	0 / 139 (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
Meniscus injury			
subjects affected / exposed	0 / 1052 (0.00%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Radius fracture			
subjects affected / exposed	2 / 1052 (0.19%)	0 / 145 (0.00%)	0 / 139 (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
Road traffic accident			
subjects affected / exposed	1 / 1052 (0.10%)	0 / 145 (0.00%)	0 / 139 (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
Soft tissue injury			
subjects affected / exposed	1 / 1052 (0.10%)	0 / 145 (0.00%)	0 / 139 (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
Thoracic vertebral fracture			
subjects affected / exposed	0 / 1052 (0.00%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ankle fracture			
subjects affected / exposed	1 / 1052 (0.10%)	0 / 145 (0.00%)	0 / 139 (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
Deep vein thrombosis postoperative			

subjects affected / exposed	0 / 1052 (0.00%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femoral neck fracture			
subjects affected / exposed	1 / 1052 (0.10%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femur fracture			
subjects affected / exposed	1 / 1052 (0.10%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Foot fracture			
subjects affected / exposed	0 / 1052 (0.00%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fractured sacrum			
subjects affected / exposed	1 / 1052 (0.10%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Humerus fracture			
subjects affected / exposed	1 / 1052 (0.10%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Joint injury			
subjects affected / exposed	2 / 1052 (0.19%)	0 / 145 (0.00%)	0 / 139 (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
Ligament rupture			
subjects affected / exposed	0 / 1052 (0.00%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pelvic fracture			

subjects affected / exposed	1 / 1052 (0.10%)	0 / 145 (0.00%)	0 / 139 (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
Postoperative wound complication			
subjects affected / exposed	1 / 1052 (0.10%)	0 / 145 (0.00%)	0 / 139 (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
Spinal compression fracture			
subjects affected / exposed	0 / 1052 (0.00%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal fracture			
subjects affected / exposed	0 / 1052 (0.00%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tendon injury			
subjects affected / exposed	1 / 1052 (0.10%)	0 / 145 (0.00%)	0 / 139 (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
Tendon rupture			
subjects affected / exposed	0 / 1052 (0.00%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper limb fracture			
subjects affected / exposed	1 / 1052 (0.10%)	0 / 145 (0.00%)	0 / 139 (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
Wrist fracture			
subjects affected / exposed	1 / 1052 (0.10%)	0 / 145 (0.00%)	0 / 139 (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
Congenital, familial and genetic disorders			
Hydrocele			

subjects affected / exposed	1 / 1052 (0.10%)	0 / 145 (0.00%)	0 / 139 (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 disorders			
Acute coronary syndrome			
subjects affected / exposed	0 / 1052 (0.00%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery disease			
subjects affected / exposed	1 / 1052 (0.10%)	0 / 145 (0.00%)	0 / 139 (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
Myocardial infarction			
subjects affected / exposed	1 / 1052 (0.10%)	0 / 145 (0.00%)	0 / 139 (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
Atrial fibrillation			
subjects affected / exposed	0 / 1052 (0.00%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiovascular disorder			
subjects affected / exposed	0 / 1052 (0.00%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial ischaemia			
subjects affected / exposed	1 / 1052 (0.10%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute myocardial infarction			
subjects affected / exposed	0 / 1052 (0.00%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina unstable			

subjects affected / exposed	4 / 1052 (0.38%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	1 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial tachycardia			
subjects affected / exposed	0 / 1052 (0.00%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac arrest			
subjects affected / exposed	1 / 1052 (0.10%)	0 / 145 (0.00%)	0 / 139 (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
Cardiac failure			
subjects affected / exposed	0 / 1052 (0.00%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure congestive			
subjects affected / exposed	3 / 1052 (0.29%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac tamponade			
subjects affected / exposed	1 / 1052 (0.10%)	0 / 145 (0.00%)	0 / 139 (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
Extrasystoles			
subjects affected / exposed	1 / 1052 (0.10%)	0 / 145 (0.00%)	0 / 139 (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
Nervous system disorders			
Carotid artery aneurysm			
subjects affected / exposed	0 / 1052 (0.00%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular accident			

subjects affected / exposed	5 / 1052 (0.48%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 5	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 2	0 / 0	0 / 0
Guillain-Barre syndrome			
subjects affected / exposed	0 / 1052 (0.00%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic stroke			
subjects affected / exposed	0 / 1052 (0.00%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			
subjects affected / exposed	0 / 1052 (0.00%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular encephalopathy			
subjects affected / exposed	0 / 1052 (0.00%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Carpal tunnel syndrome			
subjects affected / exposed	2 / 1052 (0.19%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral infarction			
subjects affected / exposed	0 / 1052 (0.00%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrospinal fistula			
subjects affected / exposed	0 / 1052 (0.00%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hemiplegic migraine			

subjects affected / exposed	0 / 1052 (0.00%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lumbar radiculopathy			
subjects affected / exposed	1 / 1052 (0.10%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscle tone disorder			
subjects affected / exposed	0 / 1052 (0.00%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myelopathy			
subjects affected / exposed	1 / 1052 (0.10%)	0 / 145 (0.00%)	0 / 139 (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
Radiculopathy			
subjects affected / exposed	0 / 1052 (0.00%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sciatica			
subjects affected / exposed	1 / 1052 (0.10%)	0 / 145 (0.00%)	0 / 139 (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
Syncope			
subjects affected / exposed	1 / 1052 (0.10%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 1052 (0.00%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			

Cataract			
subjects affected / exposed	0 / 1052 (0.00%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eyelid ptosis			
subjects affected / exposed	0 / 1052 (0.00%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Hiatus hernia			
subjects affected / exposed	0 / 1052 (0.00%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal hernia			
subjects affected / exposed	0 / 1052 (0.00%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	0 / 1052 (0.00%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhoids			
subjects affected / exposed	0 / 1052 (0.00%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal obstruction			
subjects affected / exposed	0 / 1052 (0.00%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	0 / 1052 (0.00%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oedematous pancreatitis			

subjects affected / exposed	0 / 1052 (0.00%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peptic ulcer			
subjects affected / exposed	0 / 1052 (0.00%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			
subjects affected / exposed	0 / 1052 (0.00%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 1052 (0.00%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain			
subjects affected / exposed	2 / 1052 (0.19%)	0 / 145 (0.00%)	0 / 139 (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
Anal fissure			
subjects affected / exposed	0 / 1052 (0.00%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Food poisoning			
subjects affected / exposed	0 / 1052 (0.00%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal inflammation			
subjects affected / exposed	0 / 1052 (0.00%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Inguinal hernia			

subjects affected / exposed	1 / 1052 (0.10%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal haemorrhage			
subjects affected / exposed	0 / 1052 (0.00%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal perforation			
subjects affected / exposed	1 / 1052 (0.10%)	0 / 145 (0.00%)	0 / 139 (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 / 1052 (0.00%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Volvulus of small bowel			
subjects affected / exposed	0 / 1052 (0.00%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	1 / 1052 (0.10%)	0 / 145 (0.00%)	0 / 139 (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
Cholangitis			
subjects affected / exposed	0 / 1052 (0.00%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatitis alcoholic			
subjects affected / exposed	0 / 1052 (0.00%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bile duct stone			

subjects affected / exposed	1 / 1052 (0.10%)	0 / 145 (0.00%)	0 / 139 (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
Cholangitis acute			
subjects affected / exposed	1 / 1052 (0.10%)	0 / 145 (0.00%)	0 / 139 (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
Cholecystitis chronic			
subjects affected / exposed	1 / 1052 (0.10%)	0 / 145 (0.00%)	0 / 139 (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
Cholelithiasis			
subjects affected / exposed	3 / 1052 (0.29%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	0 / 1052 (0.00%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute kidney injury			
subjects affected / exposed	1 / 1052 (0.10%)	0 / 145 (0.00%)	0 / 139 (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
Bladder prolapse			
subjects affected / exposed	0 / 1052 (0.00%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetic nephropathy			
subjects affected / exposed	0 / 1052 (0.00%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prerenal failure			

subjects affected / exposed	1 / 1052 (0.10%)	0 / 145 (0.00%)	0 / 139 (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
Renal failure			
subjects affected / exposed	0 / 1052 (0.00%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal impairment			
subjects affected / exposed	1 / 1052 (0.10%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	8 / 1052 (0.76%)	1 / 145 (0.69%)	2 / 139 (1.44%)
occurrences causally related to treatment / all	1 / 9	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rapidly progressive osteoarthritis			
subjects affected / exposed	44 / 1052 (4.18%)	1 / 145 (0.69%)	1 / 139 (0.72%)
occurrences causally related to treatment / all	39 / 53	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoarthritis			
subjects affected / exposed	6 / 1052 (0.57%)	1 / 145 (0.69%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 6	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Back pain			
subjects affected / exposed	1 / 1052 (0.10%)	0 / 145 (0.00%)	0 / 139 (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 spinal stenosis			
subjects affected / exposed	0 / 1052 (0.00%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemarthrosis			

subjects affected / exposed	0 / 1052 (0.00%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lumbar spinal stenosis			
subjects affected / exposed	0 / 1052 (0.00%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteonecrosis			
subjects affected / exposed	1 / 1052 (0.10%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rotator cuff syndrome			
subjects affected / exposed	0 / 1052 (0.00%)	0 / 145 (0.00%)	1 / 139 (0.72%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal stenosis			
subjects affected / exposed	0 / 1052 (0.00%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthritis			
subjects affected / exposed	0 / 1052 (0.00%)	1 / 145 (0.69%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bursitis			
subjects affected / exposed	1 / 1052 (0.10%)	0 / 145 (0.00%)	0 / 139 (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
Exostosis			
subjects affected / exposed	0 / 1052 (0.00%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intervertebral disc protrusion			

subjects affected / exposed	1 / 1052 (0.10%)	0 / 145 (0.00%)	0 / 139 (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
Joint effusion			
subjects affected / exposed	1 / 1052 (0.10%)	0 / 145 (0.00%)	0 / 139 (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
Limb mass			
subjects affected / exposed	1 / 1052 (0.10%)	0 / 145 (0.00%)	0 / 139 (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
Spinal osteoarthritis			
subjects affected / exposed	2 / 1052 (0.19%)	0 / 145 (0.00%)	1 / 139 (0.72%)
occurrences causally related to treatment / all	0 / 2	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal synovial cyst			
subjects affected / exposed	0 / 1052 (0.00%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subchondral insufficiency fracture			
subjects affected / exposed	1 / 1052 (0.10%)	1 / 145 (0.69%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vertebral foraminal stenosis			
subjects affected / exposed	1 / 1052 (0.10%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
COVID-19 pneumonia			
subjects affected / exposed	0 / 1052 (0.00%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19			

subjects affected / exposed	3 / 1052 (0.29%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	1 / 1052 (0.10%)	0 / 145 (0.00%)	0 / 139 (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
Gastroenteritis			
subjects affected / exposed	1 / 1052 (0.10%)	1 / 145 (0.69%)	0 / 139 (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
Sepsis			
subjects affected / exposed	0 / 1052 (0.00%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthritis infective			
subjects affected / exposed	0 / 1052 (0.00%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis			
subjects affected / exposed	0 / 1052 (0.00%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Empyema			
subjects affected / exposed	0 / 1052 (0.00%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric ulcer helicobacter			
subjects affected / exposed	0 / 1052 (0.00%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infectious pleural effusion			

subjects affected / exposed	0 / 1052 (0.00%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peritonsillar abscess			
subjects affected / exposed	0 / 1052 (0.00%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	3 / 1052 (0.29%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Pneumonia klebsiella			
subjects affected / exposed	0 / 1052 (0.00%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural infection			
subjects affected / exposed	0 / 1052 (0.00%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	2 / 1052 (0.19%)	0 / 145 (0.00%)	0 / 139 (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
Appendicitis			
subjects affected / exposed	1 / 1052 (0.10%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Erysipelas			
subjects affected / exposed	0 / 1052 (0.00%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia urinary tract infection			

subjects affected / exposed	1 / 1052 (0.10%)	0 / 145 (0.00%)	0 / 139 (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
Infected bite			
subjects affected / exposed	1 / 1052 (0.10%)	0 / 145 (0.00%)	0 / 139 (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
Lower respiratory tract infection			
subjects affected / exposed	2 / 1052 (0.19%)	0 / 145 (0.00%)	0 / 139 (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
Lung abscess			
subjects affected / exposed	1 / 1052 (0.10%)	0 / 145 (0.00%)	0 / 139 (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
Meningitis			
subjects affected / exposed	1 / 1052 (0.10%)	0 / 145 (0.00%)	0 / 139 (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
Meningitis pneumococcal			
subjects affected / exposed	0 / 1052 (0.00%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia bacterial			
subjects affected / exposed	1 / 1052 (0.10%)	0 / 145 (0.00%)	0 / 139 (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
Post procedural cellulitis			
subjects affected / exposed	0 / 1052 (0.00%)	1 / 145 (0.69%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			

subjects affected / exposed	1 / 1052 (0.10%)	0 / 145 (0.00%)	0 / 139 (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
Tuberculosis			
subjects affected / exposed	0 / 1052 (0.00%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound infection staphylococcal			
subjects affected / exposed	1 / 1052 (0.10%)	0 / 145 (0.00%)	0 / 139 (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
Metabolism and nutrition disorders			
Diabetes mellitus			
subjects affected / exposed	0 / 1052 (0.00%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperkalaemia			
subjects affected / exposed	0 / 1052 (0.00%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dehydration			
subjects affected / exposed	0 / 1052 (0.00%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoglycaemia			
subjects affected / exposed	0 / 1052 (0.00%)	0 / 145 (0.00%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Placebo	Naproxen	Fasinumab 1mg Q8W
Total subjects affected by non-serious adverse events			
subjects affected / exposed	215 / 352 (61.08%)	687 / 1056 (65.06%)	382 / 554 (68.95%)
Vascular disorders			
Hypertension			
subjects affected / exposed	31 / 352 (8.81%)	77 / 1056 (7.29%)	36 / 554 (6.50%)
occurrences (all)	34	88	41
Nervous system disorders			
Headache			
subjects affected / exposed	67 / 352 (19.03%)	216 / 1056 (20.45%)	127 / 554 (22.92%)
occurrences (all)	109	548	308
Carpal tunnel syndrome			
subjects affected / exposed	15 / 352 (4.26%)	20 / 1056 (1.89%)	26 / 554 (4.69%)
occurrences (all)	16	23	32
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	8 / 352 (2.27%)	65 / 1056 (6.16%)	12 / 554 (2.17%)
occurrences (all)	8	75	12
Gastritis			
subjects affected / exposed	12 / 352 (3.41%)	54 / 1056 (5.11%)	27 / 554 (4.87%)
occurrences (all)	12	72	35
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	76 / 352 (21.59%)	232 / 1056 (21.97%)	152 / 554 (27.44%)
occurrences (all)	117	357	228
Back pain			
subjects affected / exposed	39 / 352 (11.08%)	117 / 1056 (11.08%)	83 / 554 (14.98%)
occurrences (all)	51	160	112
Pain in extremity			
subjects affected / exposed	20 / 352 (5.68%)	62 / 1056 (5.87%)	34 / 554 (6.14%)
occurrences (all)	27	82	41
Osteoarthritis			
subjects affected / exposed	18 / 352 (5.11%)	34 / 1056 (3.22%)	22 / 554 (3.97%)
occurrences (all)	23	41	29
Rapidly progressive osteoarthritis			

subjects affected / exposed	5 / 352 (1.42%)	27 / 1056 (2.56%)	38 / 554 (6.86%)
occurrences (all)	6	28	45
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	28 / 352 (7.95%)	92 / 1056 (8.71%)	54 / 554 (9.75%)
occurrences (all)	37	122	64
Upper respiratory tract infection			
subjects affected / exposed	25 / 352 (7.10%)	90 / 1056 (8.52%)	41 / 554 (7.40%)
occurrences (all)	27	106	51
Urinary tract infection			
subjects affected / exposed	24 / 352 (6.82%)	86 / 1056 (8.14%)	41 / 554 (7.40%)
occurrences (all)	29	105	45
Influenza			
subjects affected / exposed	24 / 352 (6.82%)	55 / 1056 (5.21%)	31 / 554 (5.60%)
occurrences (all)	30	70	41
Bronchitis			
subjects affected / exposed	19 / 352 (5.40%)	50 / 1056 (4.73%)	30 / 554 (5.42%)
occurrences (all)	20	61	34

Non-serious adverse events	Fasinumab 1mg Q4W	Fasinumab 3mg Q4W	Fasinumab 6mg Q8W
Total subjects affected by non-serious adverse events			
subjects affected / exposed	727 / 1052 (69.11%)	41 / 145 (28.28%)	58 / 139 (41.73%)
Vascular disorders			
Hypertension			
subjects affected / exposed	55 / 1052 (5.23%)	2 / 145 (1.38%)	1 / 139 (0.72%)
occurrences (all)	59	2	1
Nervous system disorders			
Headache			
subjects affected / exposed	236 / 1052 (22.43%)	13 / 145 (8.97%)	8 / 139 (5.76%)
occurrences (all)	588	21	10
Carpal tunnel syndrome			
subjects affected / exposed	58 / 1052 (5.51%)	4 / 145 (2.76%)	5 / 139 (3.60%)
occurrences (all)	69	6	5
Gastrointestinal disorders			
Constipation			

subjects affected / exposed	22 / 1052 (2.09%)	2 / 145 (1.38%)	2 / 139 (1.44%)
occurrences (all)	23	2	2
Gastritis			
subjects affected / exposed	33 / 1052 (3.14%)	0 / 145 (0.00%)	1 / 139 (0.72%)
occurrences (all)	41	0	1
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	284 / 1052 (27.00%)	13 / 145 (8.97%)	30 / 139 (21.58%)
occurrences (all)	467	16	42
Back pain			
subjects affected / exposed	124 / 1052 (11.79%)	4 / 145 (2.76%)	4 / 139 (2.88%)
occurrences (all)	155	5	5
Pain in extremity			
subjects affected / exposed	65 / 1052 (6.18%)	2 / 145 (1.38%)	3 / 139 (2.16%)
occurrences (all)	88	2	4
Osteoarthritis			
subjects affected / exposed	47 / 1052 (4.47%)	1 / 145 (0.69%)	2 / 139 (1.44%)
occurrences (all)	57	1	3
Rapidly progressive osteoarthritis			
subjects affected / exposed	109 / 1052 (10.36%)	3 / 145 (2.07%)	8 / 139 (5.76%)
occurrences (all)	126	3	8
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	95 / 1052 (9.03%)	5 / 145 (3.45%)	2 / 139 (1.44%)
occurrences (all)	125	5	3
Upper respiratory tract infection			
subjects affected / exposed	92 / 1052 (8.75%)	5 / 145 (3.45%)	6 / 139 (4.32%)
occurrences (all)	111	5	6
Urinary tract infection			
subjects affected / exposed	79 / 1052 (7.51%)	4 / 145 (2.76%)	5 / 139 (3.60%)
occurrences (all)	101	4	5
Influenza			
subjects affected / exposed	70 / 1052 (6.65%)	1 / 145 (0.69%)	2 / 139 (1.44%)
occurrences (all)	85	1	2
Bronchitis			

subjects affected / exposed occurrences (all)	41 / 1052 (3.90%) 46	1 / 145 (0.69%) 1	1 / 139 (0.72%) 1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
26 September 2017	Amendment 1: Incorporated health authority (HA) feedback, ensured consistency across the program, made minor corrections and provided clarifications.
07 October 2017	Amendment 1VHP: Incorporated HA feedback.
20 October 2017	Amendment 2VHP: Incorporated health authority (HA) feedback, ensured consistency across the program, made minor corrections and provided clarifications.
27 April 2018	Amendment 3 (obsolete): Updated exclusion criteria for participant safety, made updates to ensure consistency across the program, make minor corrections and provided clarifications. (Amendment not implemented)
24 May 2018	Amendment 4: Incorporated urgent safety measure, which required discontinuing the 3 mg every 4 weeks (Q4W) and 6 mg every 8 weeks (Q8W) dose regimens.
11 July 2018	Amendment 5: Updated exclusion criteria to improve participants safety and to include an additional fasinumab dose group of 1 mg every 8 weeks (Q8W). Additional changes made to ensure consistency across the program, made minor corrections and provided clarification.
05 March 2019	Amendment 6: Updated so that first and second 52-week periods noted as Year 1 and Year 2 respectively and made minor corrections.
23 April 2020	Amendment 7: Added statement to address impact of COVID-19; updated to note that Year 2 enrollment to be stopped; updated timeframe for secondary efficacy endpoints to week 44 from week 52; and added secondary and exploratory endpoints and associated objectives and analyses.
01 July 2020	Amendment 8: Modification made to the primary and secondary efficacy analysis set.
26 August 2020	Amendment 9: Updated to reflect permanently discontinued all participants in the Year 2 Treatment Period from study drug and to complete the End of Treatment study visit for impacted participants.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported