Clinical trial results:
A Phase 3 Randomized, Double-Blind, Multi-Dose, Placebo and NSAID-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	2017-001702-15
Trial protocol	DK DE EE GB RO
Global end of trial date	09 November 2020

Results information

Result version number	v1 (current)
This version publication date	24 November 2021
First version publication date	24 November 2021

Trial information

Trial identification

Sponsor protocol code	R475-OA-1688

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03304379
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Regeneron Pharmaceuticals, Inc.
Sponsor organisation address	777 Old Saw Mill River Rd., Tarrytown, United States, 10591
Public contact	Clinical Trial Administrator, Regeneron Pharmaceuticals, Inc., 001 844-734-6643, clinicaltrials@regeneron.com
Scientific contact	Clinical Trial 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	09 November 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	09 November 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of this study was to evaluate the efficacy of Fasinumab compared to placebo and non-steroidal anti-inflammatory drug (NSAIDs) when administered for up to 24 weeks in subjects with pain due to osteoarthritis (OA) of the knee or hip.

Protection of trial subjects:

This study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with the International Conference on Harmonisation (ICH) guidelines for Good Clinical Practice (GCP) and applicable regulatory requirements.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	26 October 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	United States: 737
Country: Number of subjects enrolled	Canada: 17
Country: Number of subjects enrolled	Estonia: 17
Country: Number of subjects enrolled	Germany: 92
Country: Number of subjects enrolled	Poland: 331
Country: Number of subjects enrolled	South Africa: 329
Country: Number of subjects enrolled	Romania: 54
Country: Number of subjects enrolled	United Kingdom: 73
Worldwide total number of subjects	1650
EEA total number of subjects	494

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	0

months)	
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	1005
From 65 to 84 years	637
85 years and over	8

Subject disposition

Recruitment

Recruitment details:

A total of 4531 subjects were screened, of which 1650 subjects were randomised.

Pre-assignment

Screening details:

The study consisted of a screening period of up to 30 days, a 7-10-day pre-randomisation/washout period (7 days +3 day window), a 24-week treatment period (with last Q4W dose of study drug administered at week 20), a 20-week follow-up period, and a final phone call approximately 52 weeks after the last subcutaneous (SC) dose of study drug.

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	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Subjects who received subcutaneous (SC) injection of placebo matched to Fasinumab every 4 weeks (Q4W) or every 8 weeks (Q8W) alternatively or oral placebo matched to NSAID twice daily (BID) up to 24 weeks.

Arm type	Placebo
Investigational medicinal product name	Placebo matched to NSAIDs
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Subjects received oral dose of placebo matched to NSAID BID up to 24 weeks.

Investigational medicinal product name	Placebo matched to Fasinumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects received SC injections of placebo matched to Fasinumab in the abdomen, thigh or upper arm up to 24 weeks.

Arm title	NSAIDs

Arm description:

Subjects received oral capsule of Diclofenac at a dose of 75 mg BID or oral capsule of Celecoxib at a dose of 200 mg once daily (QD) up to 24 weeks.

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

Dosage and administration details:	
Subjects received 75 mg of Diclofenac BID up to 24 weeks.	
Investigational medicinal product name	Celecoxib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use
Dosage and administration details:	
Subjects received 200 mg of Celecoxib QD up to 24 weeks.	
Arm title	Fasinumab 1 mg
Arm description:	
Subjects received SC injection of Fasinumab at a dose of 1 mg Q4W up to 24 weeks and NSAID-matching placebo oral, 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:	
Subjects received SC injection of Fasinumab at a dose of 1 mg Q4W up to 24 weeks.	
Arm title	Fasinumab 3 mg
Arm description:	
Subjects received SC injection of Fasinumab at a dose of 3 mg Q4W up to 24 weeks and NSAID-matching placebo oral, 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:	
Subjects received SC injection of Fasinumab at a dose of 3 mg Q4W up to 24 weeks.	
Arm title	Fasinumab 6 mg
Arm description:	
Subjects received SC injection of Fasinumab at a dose of 6 mg Q8W up to 24 weeks, alternating with Q8W placebo injections. Subjects received placebo injections at the Q4W study visits where study drug was not administered and NSAID-matching placebo oral, 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:	
Subjects received SC injection of Fasinumab at a dose of 6 mg Q8W up to 24 weeks.	

Number of subjects in period 1	Placebo	NSAIDs	Fasinumab 1 mg
Started	308	612	612
Completed	238	471	463
Not completed	70	141	149
Physician decision	6	10	6
Consent withdrawn by subject	26	58	66
Adverse event, non-fatal	4	20	17
Death	1	2	-
Lost to follow-up	8	24	35
Protocol deviation	8	10	5
Lack of efficacy	17	16	20
Other Unspecified	-	1	-

Number of subjects in period 1	Fasinumab 3 mg	Fasinumab 6 mg
Started	59	59
Completed	42	42
Not completed	17	17
Physician decision	9	10
Consent withdrawn by subject	3	5
Adverse event, non-fatal	1	-
Death	-	-
Lost to follow-up	4	-
Protocol deviation	-	2
Lack of efficacy	-	-
Other Unspecified	-	-

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Subjects who received subcutaneous (SC) injection of placebo matched to Fasinumab every 4 weeks (Q4W) or every 8 weeks (Q8W) alternatively or oral placebo matched to NSAID twice daily (BID) up to 24 weeks.	
Reporting group title	NSAIDs
Reporting group description:	
Subjects received oral capsule of Diclofenac at a dose of 75 mg BID or oral capsule of Celecoxib at a dose of 200 mg once daily (QD) up to 24 weeks.	
Reporting group title	Fasinumab 1 mg
Reporting group description:	
Subjects received SC injection of Fasinumab at a dose of 1 mg Q4W up to 24 weeks and NSAID-matching placebo oral, BID	
Reporting group title	Fasinumab 3 mg
Reporting group description:	
Subjects received SC injection of Fasinumab at a dose of 3 mg Q4W up to 24 weeks and NSAID-matching placebo oral, BID	
Reporting group title	Fasinumab 6 mg
Reporting group description:	
Subjects received SC injection of Fasinumab at a dose of 6 mg Q8W up to 24 weeks, alternating with Q8W placebo injections. Subjects received placebo injections at the Q4W study visits where study drug was not administered and NSAID-matching placebo oral, BID	

Reporting group values	Placebo	NSAIDs	Fasinumab 1 mg
Number of subjects	308	612	612
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	62.0	62.3	62.1
standard deviation	± 9.30	± 9.41	± 9.13
Gender categorical Units: Subjects			
Female	222	418	436
Male	86	194	176
Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) Pain Subscale Score			
WOMAC pain subscale was a 5-item questionnaire used to assess the amount of pain experienced due to osteoarthritis in the index joint (knee or hip) in the past 48 hours. It was calculated as the mean of the scores from the 5 individual questions scored on a numerical rating scale (NRS) of 0 (no pain) to 10 (higher pain), where higher scores indicated higher pain.			
Units: Score on a Scale			
arithmetic mean	6.4	6.4	6.5
standard deviation	± 1.39	± 1.34	± 1.32
WOMAC Physical Function Subscale Scores			
WOMAC physical function subscale:17-item questionnaire used to assess degree of difficulty experienced due to OA in index joint during past 48 hours. It was calculated as mean of scores from 17 individual			

questions scored on a NRS of 0 (minimum difficulty) to 10 (maximum difficulty), where higher scores indicated maximum difficulty.			
Units: Score on a Scale			
arithmetic mean	6.40	6.32	6.39
standard deviation	± 1.495	± 1.418	± 1.462

Reporting group values	Fasinumab 3 mg	Fasinumab 6 mg	Total
Number of subjects	59	59	1650
Age categorical			
Units: Subjects			
Age continuous			
Units: years			
arithmetic mean	62.8	61.5	
standard deviation	± 9.38	± 9.55	-
Gender categorical			
Units: Subjects			
Female	36	34	1146
Male	23	25	504
Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) Pain Subscale Score			
WOMAC pain subscale was a 5-item questionnaire used to assess the amount of pain experienced due to osteoarthritis in the index joint (knee or hip) in the past 48 hours. It was calculated as the mean of the scores from the 5 individual questions scored on a numerical rating scale (NRS) of 0 (no pain) to 10 (higher pain), where higher scores indicated higher pain.			
Units: Score on a Scale			
arithmetic mean	6.4	6.5	
standard deviation	± 1.40	± 1.28	-
WOMAC Physical Function Subscale Scores			
WOMAC physical function subscale:17-item questionnaire used to assess degree of difficulty experienced due to OA in index joint during past 48 hours. It was calculated as mean of scores from 17 individual questions scored on a NRS of 0 (minimum difficulty) to 10 (maximum difficulty), where higher scores indicated maximum difficulty.			
Units: Score on a Scale			
arithmetic mean	6.50	6.34	
standard deviation	± 1.350	± 1.392	-

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Subjects who received subcutaneous (SC) injection of placebo matched to Fasinumab every 4 weeks (Q4W) or every 8 weeks (Q8W) alternatively or oral placebo matched to NSAID twice daily (BID) up to 24 weeks.	
Reporting group title	NSAIDs
Reporting group description:	
Subjects received oral capsule of Diclofenac at a dose of 75 mg BID or oral capsule of Celecoxib at a dose of 200 mg once daily (QD) up to 24 weeks.	
Reporting group title	Fasinumab 1 mg
Reporting group description:	
Subjects received SC injection of Fasinumab at a dose of 1 mg Q4W up to 24 weeks and NSAID-matching placebo oral, BID	
Reporting group title	Fasinumab 3 mg
Reporting group description:	
Subjects received SC injection of Fasinumab at a dose of 3 mg Q4W up to 24 weeks and NSAID-matching placebo oral, BID	
Reporting group title	Fasinumab 6 mg
Reporting group description:	
Subjects received SC injection of Fasinumab at a dose of 6 mg Q8W up to 24 weeks, alternating with Q8W placebo injections. Subjects received placebo injections at the Q4W study visits where study drug was not administered and NSAID-matching placebo oral, BID	

Primary: Change From Baseline in the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) Pain Subscale Scores up to Week 24 in Subjects Treated With Fasinumab Compared to Placebo

End point title	Change From Baseline in the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) Pain Subscale Scores up to Week 24 in Subjects Treated With Fasinumab Compared to Placebo[1]
End point description:	
WOMAC pain subscale was a 5-item questionnaire used to assess the amount of pain experienced due to osteoarthritis in the index joint (knee or hip) in past 48 hours. It was calculated as the mean of the scores from the 5 individual questions scored on a numerical rating scale (NRS) of 0 (no pain) to 10 (higher pain), where higher scores indicated higher pain. Here, "Number of Subjects Analysed" signifies those subjects who were evaluable for this endpoint. The modified full analysis set (mFAS) includes all randomized subjects in the FAS but excludes subjects from four sites for which there were potential concerns regarding data quality, identified prior to database lock.	
End point type	Primary
End point timeframe:	
Baseline up to Week 24	

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: Only fasinumab 1 mg and placebo were evaluated in this endpoint. The fasinumab 3 mg and 6 mg arms were not evaluated as they were discontinued early in the study.

End point values	Placebo	Fasinumab 1 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	208	439		
Units: Score on a Scale				
least squares mean (standard error)				
FAS (n=208, 439)	-2.21 (± 0.165)	-2.84 (± 0.127)		
mFAS (n=173, 372)	-2.01 (± 0.182)	-2.78 (± 0.141)		

Statistical analyses

Statistical analysis title	Pooled Placebo vs Fasinumab 1 mg

Statistical analysis description:

Analyses were based on a multiple imputation approach using an Mixed-Effect Model With Repeated Measure (MMRM) model with baseline randomization strata, baseline, treatment, visit and treatment by-visit interaction.

Comparison groups	Placebo v Fasinumab 1 mg
Number of subjects included in analysis	647
Analysis specification	Pre-specified
Analysis type	superiority[2]
P-value	= 0.0003 [3]
Method	MMRM
Parameter estimate	Least Square (LS) Mean Difference
Point estimate	-0.63
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.971
upper limit	-0.286

Notes:

[2] - FAS

[3] - Threshold for significance at 0.05 level.

Statistical analysis title	Pooled Placebo vs Fasinumab 1 mg (mFAS)

Statistical analysis description:

Analyses were based on a multiple imputation approach using a MMRM model with baseline, randomization strata, baseline, treatment, visit and treatment by-visit interaction

Comparison groups	Placebo v Fasinumab 1 mg
Number of subjects included in analysis	647
Analysis specification	Pre-specified
Analysis type	superiority[4]
P-value	> 0.0001 [5]
Method	MMRM
Parameter estimate	Least Square (LS) Mean Difference
Point estimate	-0.77

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.154
upper limit	-0.383

Notes:

[4] - Subjects in mFAS analysis = 545

[5] - Threshold for significance at 0.05 level.

Primary: Change From Baseline in WOMAC Physical Function Subscale Scores up to Week 24 in Subjects Treated With Fasinumab Compared to Placebo

End point title	Change From Baseline in WOMAC Physical Function Subscale Scores up to Week 24 in Subjects Treated With Fasinumab Compared to Placebo[6]

End point description:

Physical function referred to subject's ability to move around and perform usual activities of daily living. The WOMAC physical function subscale was a 17-item questionnaire used to assess the degree of difficulty experienced due to osteoarthritis in index joint (knee or hip) during past 48 hours. It was calculated as mean of the scores from 17 individual questions scored on a NRS of 0 (minimum difficulty) to 10 (maximum difficulty), where higher scores indicated maximum difficulty. Here, "Number of Subjects Analysed" signifies those subjects who were evaluable for this endpoint. The modified full analysis set (mFAS) includes all randomized subjects in the FAS but excludes subjects from four sites for which there were potential concerns regarding data quality, identified prior to database lock.

End point type	Primary

End point timeframe:

Baseline up to Week 24

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: The fasinumab 3 mg and 6 mg arms were not evaluated as they were discontinued early in the study.

End point values	Placebo	Fasinumab 1 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	207	439		
Units: Score on a Scale				
least squares mean (standard error)				
FAS (n=208, 439)	-2.02 (± 0.164)	-2.65 (± 0.125)		
mFAS (n=173, 372)	-1.80 (± 0.180)	-2.62 (± 0.138)		

Statistical analyses

Statistical analysis title	Pooled Placebo vs Fasinumab 1 mg

Statistical analysis description:

Analyses were based on a multiple imputation approach using an Mixed-Effect Model With Repeated Measure (MMRM) model with baseline randomization strata, baseline, treatment, visit and treatment by-visit interaction.

Comparison groups	Placebo v Fasinumab 1 mg

Number of subjects included in analysis	646
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0003 [7]
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-0.64
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.981
upper limit	-0.29

Notes:

[7] - Threshold for significance at 0.05 level.

Statistical analysis title	Pooled Placebo vs Fasinumab 1 mg (mFAS)

Statistical analysis description:

Analyses were based on a multiple imputation approach using an Mixed-Effect Model With Repeated Measure (MMRM) model with baseline randomization strata, baseline, treatment, visit and treatment by-visit interaction.

Comparison groups	Placebo v Fasinumab 1 mg
Number of subjects included in analysis	646
Analysis specification	Pre-specified
Analysis type	superiority[8]
P-value	< 0.0001 [9]
Method	MMRM
Parameter estimate	Least Square (LS) Mean Difference
Point estimate	-0.82
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.198
upper limit	-0.443

Notes:

[8] - Subjects in mFAS analysis = 545

[9] - Threshold for significance at 0.05 level

Secondary: Percentage of Subjects With Greater Than or Equal to (≥) 30 Percent (%) Reduction From Baseline up to Week 24 in WOMAC Pain Subscale Score in Subjects Treated With Fasinumab Compared to Placebo

End point title	Percentage of Subjects With Greater Than or Equal to (≥) 30 Percent (%) Reduction From Baseline up to Week 24 in WOMAC Pain Subscale Score in Subjects Treated With Fasinumab Compared to Placebo[10]

End point description:

WOMAC pain subscale was a 5-item questionnaire used to assess the amount of pain experienced due to osteoarthritis in the index knee during past 48 hours. It was calculated as mean of the scores from 5 individual questions scored on a NRS of 0 (minimum pain) to 10 (maximum pain), where higher scores indicate more pain.

End point type	Secondary

End point timeframe:

Baseline up to Week 24

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: The fasinumab 3 mg and 6 mg arms were not evaluated as they were discontinued early in the study.

End point values	Placebo	Fasinumab 1 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	308	612		
Units: Percentage of Subjects				
number (not applicable)	48.7	59.8		

Statistical analyses

Statistical analysis title	Pooled Placebo vs Fasinumab 1 mg

Statistical analysis description:

A hierarchical testing procedure was used to control type I error and handle multiple secondary endpoint analyses. Testing was then performed sequentially in the order the endpoints are reported. The hierarchical testing sequence continued only when the previous endpoint was statistically significant at 0.05 level. Analyses are based on Cochran-Mantel-Haenszel model.

Comparison groups	Fasinumab 1 mg v Placebo
Number of subjects included in analysis	920
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0013 [11]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	1.581
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.195
upper limit	2.092

Notes:

[11] - Threshold for significance at 0.05 level.

Secondary: Change From Baseline in Patient Global Assessment (PGA) Score up to Week 24 in Subjects Treated With Fasinumab Compared to Placebo

End point title	Change From Baseline in Patient Global Assessment (PGA) Score up to Week 24 in Subjects Treated With Fasinumab Compared to Placebo[12]

End point description:

The PGA was a patient-rated assessment of current disease state on a 5-point Likert scale where 1 = very good (asymptomatic and no limitation of normal activities), 2 = good (mild symptoms and no limitation of normal activities), 3 = fair (moderate symptoms and limitation of some normal activities), 4 = poor (Severe symptoms and inability to carry out most normal activities) and, 5 =very poor (Very severe symptoms which were intolerable and inability to carry out all normal activities). Higher score indicated severe condition. Here, "Number of Subjects Analysed" signifies those subjects who were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline up to Week 24

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: Only fasinumab 1 mg and placebo were evaluated in this endpoint. The fasinumab 3 mg and 6 mg arms were not evaluated as they were discontinued early in the study.

End point values	Placebo	Fasinumab 1 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	214	440		
Units: Score on a Scale				
least squares mean (standard error)	-0.66 (± 0.063)	-0.81 (± 0.047)		

Statistical analyses

Statistical analysis title	Pooled Placebo vs Fasinumab 1 mg

Statistical analysis description:

A hierarchical testing procedure was used to control type I error and handle multiple secondary endpoint analyses. Testing was then performed sequentially in the order the endpoints are reported. The hierarchical testing sequence continued only when the previous endpoint was statistically significant at 0.05 level. Analyses are based on a multiple imputation approach using Mixed-Effect Model With Repeated Measure (MMRM) model.

Comparison groups	Placebo v Fasinumab 1 mg
Number of subjects included in analysis	654
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0365 [13]
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-0.14
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.28
upper limit	-0.009

Notes:

[13] - Threshold for significance at 0.05 level.

Secondary: Change From Baseline in WOMAC Pain Subscale Scores up to Week 24 in Subjects Treated With Fasinumab Compared to Subjects Treated With NSAIDs

End point title	Change From Baseline in WOMAC Pain Subscale Scores up to Week 24 in Subjects Treated With Fasinumab Compared to Subjects Treated With NSAIDs[14]

End point description:

WOMAC pain subscale is a 5-item questionnaire used to assess the amount of pain experienced due to osteoarthritis in the index joint (knee or hip) in the past 48 hours. It is calculated as the mean of the scores from the 5 individual questions scored on a NRS of 0 (no pain) to 10 (higher pain), where higher scores indicated higher pain. Here, "Number of Subjects Analysed" signifies those subjects who were evaluable for this endpoint. The modified full analysis set (mFAS) includes all randomized subjects in the FAS but excludes subjects from four sites for which there were potential concerns regarding data

quality, identified prior to database lock.

End point type	Secondary

End point timeframe:

Baseline up to Week 24

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: Only fasinumab 1 mg and NSAIDs were evaluated in this endpoint. The fasinumab 3 mg and 6 mg arms were not evaluated as they were discontinued early in the study.

End point values	NSAIDs	Fasinumab 1 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	426	439		
Units: Score on a Scale				
least squares mean (standard error)				
FAS (n=426, 439)	-2.60 (± 0.128)	-2.84 (± 0.127)		
mFAS (n=363, 372)	-2.48 (± 0.140)	-2.78 (± 0.141)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in WOMAC Physical Function Subscale Scores up to Week 24 in Subjects Treated With Fasinumab Compared to Subjects Treated With NSAIDs

End point title	Change From Baseline in WOMAC Physical Function Subscale Scores up to Week 24 in Subjects Treated With Fasinumab Compared to Subjects Treated With NSAIDs[15]

End point description:

Physical function referred to subject's ability to move around and perform usual activities of daily living. The WOMAC physical function subscale was a 17-item questionnaire used to assess the degree of difficulty experienced due to osteoarthritis in index joint (knee or hip) during past 48 hours. It was calculated as mean of the scores from 17 individual questions scored on a NRS of 0 (minimum difficulty) to 10 (maximum difficulty), where higher scores indicated maximum difficulty. Here, "Number of Subjects Analysed" signifies those subjects who were evaluable for this endpoint. The modified full analysis set (mFAS) includes all randomized subjects in the FAS but excludes subjects from four sites for which there were potential concerns regarding data quality, identified prior to database lock.

End point type	Secondary

End point timeframe:

Baseline up to Week 24

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: Only fasinumab 1 mg and NSAIDs were evaluated in this endpoint. The fasinumab 3 mg and 6 mg arms were not evaluated as they were discontinued early in the study.

End point values	NSAIDs	Fasinumab 1 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	426	439		
Units: Score on a Scale				
least squares mean (standard error)				
FAS (n=426, 439)	-2.33 (± 0.127)	-2.65 (± 0.125)		
mFAS (n=364, 372)	-2.26 (± 0.140)	-2.62 (± 0.138)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in PGA Score up to Week 24 in Subjects Treated With Fasinumab Compared to Subjects Treated With NSAIDs

End point title	Change From Baseline in PGA Score up to Week 24 in Subjects Treated With Fasinumab Compared to Subjects Treated With NSAIDs[16]

End point description:

The PGA was a patient-rated assessment of current disease state on a 5-point Likert scale where 1 = very good (asymptomatic and no limitation of normal activities), 2 = good (mild symptoms and no limitation of normal activities), 3 = fair (moderate symptoms and limitation of some normal activities), 4 = poor (Severe symptoms and inability to carry out most normal activities) and, 5 =very poor (Very severe symptoms which were intolerable and inability to carry out all normal activities). Higher score indicated severe condition. Here, "Number of Subjects Analysed" signifies those subjects who were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline up to Week 24

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: Only fasinumab 1 mg and NSAIDs were evaluated in this endpoint. The fasinumab 3 mg and 6 mg arms were not evaluated as they were discontinued early in the study.

End point values	NSAIDs	Fasinumab 1 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	427	440		
Units: Score on a Scale				
least squares mean (standard error)	-0.75 (± 0.048)	-0.81 (± 0.047)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Weekly Average Walking Index Joint Pain Score up to Week 24 by Using the Numeric Rating Scale (NRS) Pain Scale

End point title	Change From Baseline in Weekly Average Walking Index Joint Pain Score up to Week 24 by Using the Numeric Rating Scale (NRS) Pain Scale[17]

End point description:

Subjects reported weekly average walking index joint pain based on NRS. The NRS was nationally recognized numeric scale from 0 to 10, where 0 would demonstrate no pain, 1 to 3 would demonstrate mild pain, 4 to 6 would be moderate pain, 7 to 9 would be severe pain and 10 would be the worst pain possible. Higher score indicated greater pain. Here, "Number of Subjects Analysed" signifies those subjects who were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline up to Week 24

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: The fasinumab 3 mg and 6 mg arms were not evaluated as they were discontinued early in the study.

End point values	Placebo	NSAIDs	Fasinumab 1 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	231	449	470	
Units: Score on a Scale				
least squares mean (standard error)	-1.85 (± 0.130)	-2.13 (± 0.101)	-2.51 (± 0.100)	

Statistical analyses

No statistical analyses for this end point

Secondary: Serum Concentrations of Functional Fasinumab

End point title	Serum Concentrations of Functional Fasinumab[18]

End point description:

Serum concentrations of functional Fasinumab were reported. Pharmacokinetic (PK) analysis set included all treated subjects who received any study drug and who had at least 1 non-missing drug concentration result following the first study dose. Here, Number of Subjects Analysed" = subjects who were evaluable for this endpoint and "n = subjects who were evaluable at specified time points.

End point type	Secondary

End point timeframe:

At Weeks 0, 4, 8, 16, 24 and 44

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: Only fasinumab 1 mg was evaluated in this endpoint and the fasinumab 3 mg and 6 mg arms were not evaluated as they were discontinued early in the study.

End point values	Fasinumab 1 mg			
Subject group type	Reporting group			
Number of subjects analysed	586			
Units: Milligrams per Liter (mg/L)				
arithmetic mean (standard deviation)				

Week 0: (n = 586)	0.000155 (± 0.002)			
Week 4: (n = 570)	0.0469 (± 0.0179)			
Week 8: (n = 543)	0.0644 (± 0.0275)			
Week 16: (n = 502)	0.0738 (± 0.0380)			
Week 24: (n = 465)	0.0713 (± 0.0379)			
Week 44: (n = 186)	0.000349 (± 0.00476)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With At-least One Positive Anti-Drug Antibody (ADA) Development

End point title	Number of Subjects With At-least One Positive Anti-Drug Antibody (ADA) Development[19]

End point description:

Immunogenicity was characterized by ADA responses & titers. Responses categories: Pre-existing immunoreactivity - ADA positive response at baseline with all post first dose negative results or positive response at baseline with all post first dose ADA responses < 9-fold over baseline titer levels; Treatment-boosted response - positive response in the assay post first dose, ≥ 9-fold over baseline titer levels, when baseline results are positive; Treatment-emergent response - ADA positive response post first dose when baseline results = negative or missing. ADA analysis set included all subjects who received any study drug and had at least 1 non-missing ADA result following the first dose of study drug.

End point type	Secondary

End point timeframe:

Baseline up to follow-up period (Week 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: The fasinumab 3 mg and 6 mg arms were not evaluated as they were discontinued early in the study.

End point values	Placebo	NSAIDs	Fasinumab 1 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	291	568	569	
Units: Subjects				
Pre-Existing Immunoreactivity	10	9	15	
Treatment-Boosted Response	0	0	0	
Treatment-Emergent Response	3	1	4	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Baseline up to week 72	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	23.1

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Subjects received SC injection of placebo matched to Fasinumab Q4W or Q8W or oral placebo matched to NSAID BID up to 24 weeks. At time of dosing, two subjects from NSAID cohort received placebo.	
Reporting group title	NSAIDs
Reporting group description:	
Subjects received oral capsule of Diclofenac at a dose of 75 mg BID or oral capsule of Celecoxib at a dose of 200 mg once daily (QD) up to 24 weeks.	
Reporting group title	Fasinumab 1mg Q4W
Reporting group description:	
Subjects received SC injection of Fasinumab at a dose of 1 mg Q4W up to 24 weeks and NSAID-matching placebo oral, BID	
Reporting group title	Fasinumab 3mg Q4W
Reporting group description:	
Subjects received SC injection of Fasinumab at a dose of 3 mg Q4W up to 24 weeks and NSAID-matching placebo oral, BID	
Reporting group title	Fasinumab 6mg Q8W
Reporting group description:	
Subjects received SC injection of Fasinumab at a dose of 6 mg Q8W up to 24 weeks, alternating with Q8W placebo injections. Subjects received placebo injections at the Q4W study visits where study drug was not administered and NSAID-matching placebo oral, BID	

Serious adverse events	Placebo	NSAIDs	Fasinumab 1mg Q4W
Total subjects affected by serious adverse events			
subjects affected / exposed	20 / 309 (6.47%)	45 / 609 (7.39%)	35 / 609 (5.75%)
number of deaths (all causes)	0	3	1
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Prostate cancer			
subjects affected / exposed	0 / 309 (0.00%)	2 / 609 (0.33%)	1 / 609 (0.16%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Invasive papillary breast carcinoma			

subjects affected / exposed	0 / 309 (0.00%)	1 / 609 (0.16%)	0 / 609 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Arteriosclerosis			
subjects affected / exposed	1 / 309 (0.32%)	0 / 609 (0.00%)	0 / 609 (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
Hypertensive crisis			
subjects affected / exposed	1 / 309 (0.32%)	0 / 609 (0.00%)	1 / 609 (0.16%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Varicose vein			
subjects affected / exposed	0 / 309 (0.00%)	1 / 609 (0.16%)	0 / 609 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertension			
subjects affected / exposed	0 / 309 (0.00%)	0 / 609 (0.00%)	1 / 609 (0.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Joint arthroplasty			
subjects affected / exposed	1 / 309 (0.32%)	3 / 609 (0.49%)	1 / 609 (0.16%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Knee arthroplasty			
subjects affected / exposed	1 / 309 (0.32%)	4 / 609 (0.66%)	2 / 609 (0.33%)
occurrences causally related to treatment / all	0 / 1	0 / 4	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hip arthroplasty			
subjects affected / exposed	1 / 309 (0.32%)	3 / 609 (0.49%)	1 / 609 (0.16%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration			

site conditions			
Impaired healing			
subjects affected / exposed	0 / 309 (0.00%)	0 / 609 (0.00%)	1 / 609 (0.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Endometrial hyperplasia			
subjects affected / exposed	0 / 309 (0.00%)	1 / 609 (0.16%)	0 / 609 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uterine prolapse			
subjects affected / exposed	0 / 309 (0.00%)	1 / 609 (0.16%)	0 / 609 (0.00%)
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 cyst			
subjects affected / exposed	0 / 309 (0.00%)	0 / 609 (0.00%)	1 / 609 (0.16%)
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			
Dyspnoea			
subjects affected / exposed	1 / 309 (0.32%)	0 / 609 (0.00%)	0 / 609 (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 / 309 (0.00%)	1 / 609 (0.16%)	0 / 609 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Depressed mood			
subjects affected / exposed	1 / 309 (0.32%)	0 / 609 (0.00%)	0 / 609 (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 loosening			

subjects affected / exposed	1 / 309 (0.32%)	0 / 609 (0.00%)	0 / 609 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device dislocation			
subjects affected / exposed	0 / 309 (0.00%)	0 / 609 (0.00%)	1 / 609 (0.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Concussion			
subjects affected / exposed	0 / 309 (0.00%)	0 / 609 (0.00%)	1 / 609 (0.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femur fracture			
subjects affected / exposed	1 / 309 (0.32%)	0 / 609 (0.00%)	1 / 609 (0.16%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fractured sacrum			
subjects affected / exposed	0 / 309 (0.00%)	1 / 609 (0.16%)	0 / 609 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Multiple injuries			
subjects affected / exposed	0 / 309 (0.00%)	1 / 609 (0.16%)	0 / 609 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Radius fracture			
subjects affected / exposed	0 / 309 (0.00%)	1 / 609 (0.16%)	0 / 609 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Accidental overdose			
subjects affected / exposed	0 / 309 (0.00%)	0 / 609 (0.00%)	1 / 609 (0.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hip fracture			

subjects affected / exposed	1 / 309 (0.32%)	0 / 609 (0.00%)	0 / 609 (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 / 309 (0.00%)	1 / 609 (0.16%)	0 / 609 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tendon rupture			
subjects affected / exposed	0 / 309 (0.00%)	1 / 609 (0.16%)	0 / 609 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Arteriosclerosis coronary artery			
subjects affected / exposed	0 / 309 (0.00%)	0 / 609 (0.00%)	1 / 609 (0.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			
subjects affected / exposed	1 / 309 (0.32%)	2 / 609 (0.33%)	0 / 609 (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
Cardiac failure			
subjects affected / exposed	0 / 309 (0.00%)	1 / 609 (0.16%)	0 / 609 (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
Acute myocardial infarction			
subjects affected / exposed	1 / 309 (0.32%)	1 / 609 (0.16%)	0 / 609 (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
Atrioventricular block complete			
subjects affected / exposed	0 / 309 (0.00%)	0 / 609 (0.00%)	0 / 609 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac arrest			

subjects affected / exposed	0 / 309 (0.00%)	0 / 609 (0.00%)	1 / 609 (0.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Nervous system disorders			
Amnesia			
subjects affected / exposed	0 / 309 (0.00%)	1 / 609 (0.16%)	0 / 609 (0.00%)
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 / 309 (0.00%)	2 / 609 (0.33%)	0 / 609 (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
Dizziness			
subjects affected / exposed	1 / 309 (0.32%)	0 / 609 (0.00%)	0 / 609 (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
Presyncope			
subjects affected / exposed	0 / 309 (0.00%)	0 / 609 (0.00%)	1 / 609 (0.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Trigeminal neuralgia			
subjects affected / exposed	0 / 309 (0.00%)	0 / 609 (0.00%)	1 / 609 (0.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pseudostroke			
subjects affected / exposed	0 / 309 (0.00%)	0 / 609 (0.00%)	1 / 609 (0.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
Vertigo positional			
subjects affected / exposed	0 / 309 (0.00%)	0 / 609 (0.00%)	1 / 609 (0.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			

Retinal detachment			
subjects affected / exposed	1 / 309 (0.32%)	0 / 609 (0.00%)	0 / 609 (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			
Gastritis			
subjects affected / exposed	0 / 309 (0.00%)	1 / 609 (0.16%)	0 / 609 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 309 (0.00%)	0 / 609 (0.00%)	2 / 609 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hiatus hernia			
subjects affected / exposed	0 / 309 (0.00%)	1 / 609 (0.16%)	0 / 609 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis acute			
subjects affected / exposed	0 / 309 (0.00%)	0 / 609 (0.00%)	1 / 609 (0.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulum intestinal haemorrhagic			
subjects affected / exposed	0 / 309 (0.00%)	1 / 609 (0.16%)	0 / 609 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestine polyp			
subjects affected / exposed	0 / 309 (0.00%)	1 / 609 (0.16%)	0 / 609 (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
Rectal haemorrhage			
subjects affected / exposed	0 / 309 (0.00%)	0 / 609 (0.00%)	1 / 609 (0.16%)
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 acute			
subjects affected / exposed	1 / 309 (0.32%)	0 / 609 (0.00%)	0 / 609 (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	0 / 309 (0.00%)	1 / 609 (0.16%)	0 / 609 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	1 / 309 (0.32%)	0 / 609 (0.00%)	0 / 609 (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	0 / 309 (0.00%)	1 / 609 (0.16%)	0 / 609 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intervertebral disc protrusion			
subjects affected / exposed	0 / 309 (0.00%)	0 / 609 (0.00%)	1 / 609 (0.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoarthritis			
subjects affected / exposed	3 / 309 (0.97%)	6 / 609 (0.99%)	1 / 609 (0.16%)
occurrences causally related to treatment / all	0 / 3	0 / 6	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoporotic fracture			
subjects affected / exposed	0 / 309 (0.00%)	1 / 609 (0.16%)	0 / 609 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rapidly progressive osteoarthritis			
subjects affected / exposed	2 / 309 (0.65%)	0 / 609 (0.00%)	8 / 609 (1.31%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 9
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Rotator cuff syndrome			
subjects affected / exposed	0 / 309 (0.00%)	2 / 609 (0.33%)	0 / 609 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal synovial cyst			
subjects affected / exposed	0 / 309 (0.00%)	0 / 609 (0.00%)	1 / 609 (0.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tendonitis			
subjects affected / exposed	0 / 309 (0.00%)	1 / 609 (0.16%)	0 / 609 (0.00%)
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 / 309 (0.00%)	0 / 609 (0.00%)	1 / 609 (0.16%)
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 / 309 (0.00%)	1 / 609 (0.16%)	0 / 609 (0.00%)
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 range of motion decreased			
subjects affected / exposed	0 / 309 (0.00%)	1 / 609 (0.16%)	0 / 609 (0.00%)
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 / 309 (0.00%)	0 / 609 (0.00%)	1 / 609 (0.16%)
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 osteoarthritis			
subjects affected / exposed	0 / 309 (0.00%)	0 / 609 (0.00%)	1 / 609 (0.16%)
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 stenosis			

subjects affected / exposed	0 / 309 (0.00%)	1 / 609 (0.16%)	0 / 609 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subchondral insufficiency fracture			
subjects affected / exposed	0 / 309 (0.00%)	0 / 609 (0.00%)	0 / 609 (0.00%)
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			
Cellulitis			
subjects affected / exposed	0 / 309 (0.00%)	2 / 609 (0.33%)	0 / 609 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 309 (0.00%)	1 / 609 (0.16%)	0 / 609 (0.00%)
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 / 309 (0.00%)	1 / 609 (0.16%)	0 / 609 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound infection staphylococcal			
subjects affected / exposed	0 / 309 (0.00%)	1 / 609 (0.16%)	0 / 609 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atypical pneumonia			
subjects affected / exposed	0 / 309 (0.00%)	0 / 609 (0.00%)	1 / 609 (0.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19 pneumonia			
subjects affected / exposed	0 / 309 (0.00%)	1 / 609 (0.16%)	0 / 609 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			

subjects affected / exposed	0 / 309 (0.00%)	1 / 609 (0.16%)	0 / 609 (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
Lower respiratory tract infection			
subjects affected / exposed	1 / 309 (0.32%)	0 / 609 (0.00%)	0 / 609 (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 viral			
subjects affected / exposed	0 / 309 (0.00%)	0 / 609 (0.00%)	1 / 609 (0.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hyperkalaemia			
subjects affected / exposed	0 / 309 (0.00%)	1 / 609 (0.16%)	0 / 609 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			
subjects affected / exposed	0 / 309 (0.00%)	1 / 609 (0.16%)	1 / 609 (0.16%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Fasinumab 3mg Q4W	Fasinumab 6mg Q8W	
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 58 (8.62%)	2 / 59 (3.39%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Prostate cancer			
subjects affected / exposed	0 / 58 (0.00%)	0 / 59 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Invasive papillary breast carcinoma			

subjects affected / exposed	0 / 58 (0.00%)	0 / 59 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Arteriosclerosis			
subjects affected / exposed	0 / 58 (0.00%)	0 / 59 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertensive crisis			
subjects affected / exposed	0 / 58 (0.00%)	0 / 59 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Varicose vein			
subjects affected / exposed	0 / 58 (0.00%)	0 / 59 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertension			
subjects affected / exposed	0 / 58 (0.00%)	0 / 59 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Joint arthroplasty			
subjects affected / exposed	0 / 58 (0.00%)	0 / 59 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Knee arthroplasty			
subjects affected / exposed	1 / 58 (1.72%)	0 / 59 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hip arthroplasty			
subjects affected / exposed	0 / 58 (0.00%)	0 / 59 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration			

site conditions			
Impaired healing			
subjects affected / exposed	0 / 58 (0.00%)	0 / 59 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Endometrial hyperplasia			
subjects affected / exposed	0 / 58 (0.00%)	0 / 59 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine prolapse			
subjects affected / exposed	0 / 58 (0.00%)	0 / 59 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast cyst			
subjects affected / exposed	0 / 58 (0.00%)	0 / 59 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 58 (0.00%)	0 / 59 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	0 / 58 (0.00%)	0 / 59 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Depressed mood			
subjects affected / exposed	0 / 58 (0.00%)	0 / 59 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Product issues			
Device loosening			

subjects affected / exposed	0 / 58 (0.00%)	0 / 59 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device dislocation			
subjects affected / exposed	0 / 58 (0.00%)	0 / 59 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Concussion			
subjects affected / exposed	0 / 58 (0.00%)	0 / 59 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femur fracture			
subjects affected / exposed	0 / 58 (0.00%)	0 / 59 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fractured sacrum			
subjects affected / exposed	0 / 58 (0.00%)	0 / 59 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple injuries			
subjects affected / exposed	0 / 58 (0.00%)	0 / 59 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radius fracture			
subjects affected / exposed	0 / 58 (0.00%)	0 / 59 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Accidental overdose			
subjects affected / exposed	0 / 58 (0.00%)	0 / 59 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hip fracture			

subjects affected / exposed	0 / 58 (0.00%)	0 / 59 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tendon injury			
subjects affected / exposed	0 / 58 (0.00%)	0 / 59 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tendon rupture			
subjects affected / exposed	0 / 58 (0.00%)	0 / 59 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Arteriosclerosis coronary artery			
subjects affected / exposed	0 / 58 (0.00%)	0 / 59 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	0 / 58 (0.00%)	0 / 59 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure			
subjects affected / exposed	0 / 58 (0.00%)	0 / 59 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute myocardial infarction			
subjects affected / exposed	0 / 58 (0.00%)	0 / 59 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrioventricular block complete			
subjects affected / exposed	1 / 58 (1.72%)	0 / 59 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac arrest			

subjects affected / exposed	0 / 58 (0.00%)	0 / 59 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Amnesia			
subjects affected / exposed	0 / 58 (0.00%)	0 / 59 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular accident			
subjects affected / exposed	0 / 58 (0.00%)	0 / 59 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dizziness			
subjects affected / exposed	0 / 58 (0.00%)	0 / 59 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Presyncope			
subjects affected / exposed	0 / 58 (0.00%)	0 / 59 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Trigeminal neuralgia			
subjects affected / exposed	0 / 58 (0.00%)	0 / 59 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pseudostroke			
subjects affected / exposed	0 / 58 (0.00%)	0 / 59 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Vertigo positional			
subjects affected / exposed	0 / 58 (0.00%)	0 / 59 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			

Retinal detachment			
subjects affected / exposed	0 / 58 (0.00%)	0 / 59 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Gastritis			
subjects affected / exposed	0 / 58 (0.00%)	0 / 59 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 58 (0.00%)	0 / 59 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hiatus hernia			
subjects affected / exposed	0 / 58 (0.00%)	0 / 59 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis acute			
subjects affected / exposed	0 / 58 (0.00%)	0 / 59 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulum intestinal haemorrhagic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 59 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestine polyp			
subjects affected / exposed	0 / 58 (0.00%)	0 / 59 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal haemorrhage			
subjects affected / exposed	0 / 58 (0.00%)	0 / 59 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			

Cholecystitis acute			
subjects affected / exposed	0 / 58 (0.00%)	0 / 59 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholelithiasis			
subjects affected / exposed	0 / 58 (0.00%)	0 / 59 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	0 / 58 (0.00%)	0 / 59 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 58 (1.72%)	0 / 59 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral disc protrusion			
subjects affected / exposed	0 / 58 (0.00%)	0 / 59 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoarthritis			
subjects affected / exposed	1 / 58 (1.72%)	0 / 59 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoporotic fracture			
subjects affected / exposed	0 / 58 (0.00%)	0 / 59 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rapidly progressive osteoarthritis			
subjects affected / exposed	2 / 58 (3.45%)	2 / 59 (3.39%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

Rotator cuff syndrome			
subjects affected / exposed	0 / 58 (0.00%)	0 / 59 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal synovial cyst			
subjects affected / exposed	0 / 58 (0.00%)	0 / 59 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tendonitis			
subjects affected / exposed	0 / 58 (0.00%)	0 / 59 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthritis			
subjects affected / exposed	0 / 58 (0.00%)	0 / 59 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bursitis			
subjects affected / exposed	0 / 58 (0.00%)	0 / 59 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint range of motion decreased			
subjects affected / exposed	0 / 58 (0.00%)	0 / 59 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lumbar spinal stenosis			
subjects affected / exposed	0 / 58 (0.00%)	0 / 59 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal osteoarthritis			
subjects affected / exposed	0 / 58 (0.00%)	0 / 59 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal stenosis			

subjects affected / exposed	0 / 58 (0.00%)	0 / 59 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subchondral insufficiency fracture			
subjects affected / exposed	1 / 58 (1.72%)	0 / 59 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Cellulitis			
subjects affected / exposed	0 / 58 (0.00%)	0 / 59 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	0 / 58 (0.00%)	0 / 59 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritonsillar abscess			
subjects affected / exposed	0 / 58 (0.00%)	0 / 59 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound infection staphylococcal			
subjects affected / exposed	0 / 58 (0.00%)	0 / 59 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atypical pneumonia			
subjects affected / exposed	0 / 58 (0.00%)	0 / 59 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19 pneumonia			
subjects affected / exposed	0 / 58 (0.00%)	0 / 59 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			

subjects affected / exposed	0 / 58 (0.00%)	0 / 59 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection			
subjects affected / exposed	0 / 58 (0.00%)	0 / 59 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningitis viral			
subjects affected / exposed	0 / 58 (0.00%)	0 / 59 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hyperkalaemia			
subjects affected / exposed	0 / 58 (0.00%)	0 / 59 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatraemia			
subjects affected / exposed	0 / 58 (0.00%)	0 / 59 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Placebo	NSAIDs	Fasinumab 1mg Q4W
Total subjects affected by non-serious adverse events			
subjects affected / exposed	121 / 309 (39.16%)	263 / 609 (43.19%)	261 / 609 (42.86%)
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	3 / 309 (0.97%)	5 / 609 (0.82%)	5 / 609 (0.82%)
occurrences (all)	3	5	5
Injury, poisoning and procedural complications			
Ligament sprain			
subjects affected / exposed	2 / 309 (0.65%)	4 / 609 (0.66%)	5 / 609 (0.82%)
occurrences (all)	2	4	5

Muscle strain			
subjects affected / exposed	0 / 309 (0.00%)	4 / 609 (0.66%)	6 / 609 (0.99%)
occurrences (all)	0	5	7
Nervous system disorders			
Headache			
subjects affected / exposed	48 / 309 (15.53%)	107 / 609 (17.57%)	95 / 609 (15.60%)
occurrences (all)	113	210	224
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	36 / 309 (11.65%)	78 / 609 (12.81%)	82 / 609 (13.46%)
occurrences (all)	53	102	109
Back pain			
subjects affected / exposed	17 / 309 (5.50%)	44 / 609 (7.22%)	46 / 609 (7.55%)
occurrences (all)	17	60	51
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	25 / 309 (8.09%)	35 / 609 (5.75%)	50 / 609 (8.21%)
occurrences (all)	29	39	57
Nasopharyngitis			
subjects affected / exposed	22 / 309 (7.12%)	38 / 609 (6.24%)	29 / 609 (4.76%)
occurrences (all)	26	44	35
Upper respiratory tract infection			
subjects affected / exposed	15 / 309 (4.85%)	30 / 609 (4.93%)	30 / 609 (4.93%)
occurrences (all)	18	31	33

Non-serious adverse events	Fasinumab 3mg Q4W	Fasinumab 6mg Q8W	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	17 / 58 (29.31%)	15 / 59 (25.42%)	
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	3 / 58 (5.17%)	3 / 59 (5.08%)	
occurrences (all)	3	3	
Injury, poisoning and procedural complications			
Ligament sprain			
subjects affected / exposed	0 / 58 (0.00%)	3 / 59 (5.08%)	
occurrences (all)	0	3	

Muscle strain			
subjects affected / exposed	3 / 58 (5.17%)	1 / 59 (1.69%)	
occurrences (all)	3	1	
Nervous system disorders			
Headache			
subjects affected / exposed	2 / 58 (3.45%)	2 / 59 (3.39%)	
occurrences (all)	2	2	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	4 / 58 (6.90%)	3 / 59 (5.08%)	
occurrences (all)	7	3	
Back pain			
subjects affected / exposed	1 / 58 (1.72%)	1 / 59 (1.69%)	
occurrences (all)	1	1	
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	1 / 58 (1.72%)	2 / 59 (3.39%)	
occurrences (all)	1	2	
Nasopharyngitis			
subjects affected / exposed	2 / 58 (3.45%)	1 / 59 (1.69%)	
occurrences (all)	2	1	
Upper respiratory tract infection			
subjects affected / exposed	3 / 58 (5.17%)	1 / 59 (1.69%)	
occurrences (all)	3	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
24 May 2018	To incorporate an urgent safety measure, which requires discontinuing the 3 mg Q4W and 6 mg Q8W dose regimens. The recommendation by the independent Data Monitoring Committee (DMC) to discontinue these dose regimens was made following a review of unblinded data from an ongoing study in the fasinumab phase 3 osteoarthritis program (R475-PN-1523) and was based on an imbalance in clinically relevant adverse events including time to total joint replacement, peripheral edema, arthralgia and a trend towards early fractures in the 6 mg Q8W group. Based on the independent DMC review, study of lower dose levels (eg, 1 mg Q4W) may continue to be evaluated in this population. With this amendment, subjects randomised to the 3 mg Q4W or 6 mg Q8W dose regimens will be permanently discontinued from study drug but encouraged to otherwise complete all remaining study visits and study procedures in the follow up period and the end of study phone call.
11 July 2018	Updated reasons for permanent discontinuation of study drug to ensure subjects enrolled under earlier protocol version were immediately discontinued from study drug and moved to follow-up period if they met updated exclusion criteria or were taking newly added prohibited medications.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

5/2018: Urgent safety measure to stop dosing Fasinumab 3 & 6mg, to prevent further randomisation to these regimens across Fasinumab program. Subjects randomised to fasinumab 3 & 6mg discontinued from study drug & moved directly into follow-up period.

Notes: