Clinical trial results:
A Randomized, Double-Blind, Placebo-Controlled, Multicenter Study to Evaluate the Effects of Fasinumab on Peripheral Nerve Function in Patients with Pain Due to Osteoarthritis of the Hip or Knee

Summary

EudraCT number	2017-004921-33
Trial protocol	GB PL
Global end of trial date	07 January 2021

Results information

Result version number	v1 (current)
This version publication date	22 January 2022
First version publication date	22 January 2022

Trial information

Trial identification

Sponsor protocol code	R475-OA-1758

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03691974
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Regeneron Pharmaceuticals, Inc.
Sponsor organisation address	777 Old Saw Mill River Rd., Tarrytown, NY, 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	07 January 2021
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	07 January 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study was to evaluate the effect of fasinumab compared to placebo on peripheral nerves in subjects with pain due to Osteoarthritis (OA) of the hip or knee.

The secondary objectives of the study were to:
- Evaluate the efficacy of fasinumab compared to placebo in subjects with pain due to OA of the hip or knee
- Evaluate the safety and tolerability of fasinumab compared to placebo in subjects with pain due to OA of the hip or knee
- Characterize the concentrations of fasinumab in serum in subjects with pain due to OA of the hip or knee
- Evaluate the immunogenicity of fasinumab in subjects with pain due to OA of the hip or knee

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	15 October 2018
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 Kingdom: 63
Country: Number of subjects enrolled	United States: 55
Country: Number of subjects enrolled	Poland: 62
Worldwide total number of subjects	180
EEA total number of subjects	62

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)	102
From 65 to 84 years	78
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 1604 subjects were screened, out of which 180 were randomized into the study.

Pre-assignment

Screening details:

Subjects who met the eligibility criteria were randomized in a 1:1 ratio to receive either fasinumab or fasinumab-matching placebo.

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, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Fasinumab-matching Placebo

Arm description:

Subjects received Fasinumab-matching placebo subcutaneously (SC) every 4 weeks (Q4W) from Day 1 through Week 12 of the 16-week treatment period.

Arm type	Placebo
Investigational medicinal product name	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:

Subjects received SC injection of Fasinumab-matching placebo in the abdomen, thigh, or upper arm.

Arm title	Fasinumab 1 mg SC Q4W

Arm description:

Subjects received Fasinumab 1 milligram (mg) SC Q4W from Day 1 through Week 12 of the 16-week treatment period.

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 in the abdomen, thigh, or upper arm.

Number of subjects in period 1	Fasinumab-matching Placebo	Fasinumab 1 mg SC Q4W
Started	89	91
Completed	67	75
Not completed	22	16
Physician decision	1	-
Consent withdrawn by subject	11	9
Noncompliance with protocol by subject	1	-
Adverse event, non-fatal	1	-
Lost to follow-up	8	7

Baseline characteristics

Reporting groups	
Reporting group title	Fasinumab-matching Placebo
Reporting group description:	
Subjects received Fasinumab-matching placebo subcutaneously (SC) every 4 weeks (Q4W) from Day 1 through Week 12 of the 16-week treatment period.	
Reporting group title	Fasinumab 1 mg SC Q4W
Reporting group description:	
Subjects received Fasinumab 1 milligram (mg) SC Q4W from Day 1 through Week 12 of the 16-week treatment period.	

Reporting group values	Fasinumab-matching Placebo	Fasinumab 1 mg SC Q4W	Total
Number of subjects	89	91	180
Age categorical			
Units: Subjects			
Age continuous			
Units: years			
arithmetic mean	62.4	62.9	
standard deviation	± 7.9	± 9.1	-
Gender categorical			
Units: Subjects			
Female	63	59	122
Male	26	32	58
Peroneal Motor Nerve Conduction Velocity			
Peroneal motor nerve conduction velocity was evaluated by electrical stimulation of the nerve and recorded the compound muscle action potential from surface electrodes overlying a muscle supplied by the nerve. The safety analysis set (SAF) included all randomized subjects who received any study drug and was based on the treatment received (as treated). In the SAF, 'N' = 88 in the placebo group as one subject did not meet eligibility criteria but was randomized. The subject did not receive study drug and was therefore excluded from the placebo group in the SAF.			
Units: Meters per Second (m/s)			
arithmetic mean	46.864	46.803	
standard deviation	± 4.174	± 3.880	-
Peroneal Motor Nerve Action Potential Amplitude - Ankle			
Peroneal motor nerve action potential amplitude was evaluated at ankle by electrical stimulation of the nerve and recorded the compound muscle action potential from surface electrodes overlying a muscle supplied by the nerve. SAF included all randomized subjects who received any study drug and was based on the treatment received (as treated). In the SAF, 'N' = 88 in the placebo group as one subject did not meet eligibility criteria but was randomized. The subject did not receive study drug and was therefore excluded from the placebo group in the SAF.			
Units: Millivolts (mV)			
arithmetic mean	4.75	4.67	
standard deviation	± 2.01	± 1.70	-
Sural Sensory Nerve Conduction Velocity			
Sural sensory nerve conduction velocity was evaluated by electrically stimulating sensory fibers and recorded the nerve action potential at a point further along that nerve. SAF included all randomized subjects who received any study drug and was based on the treatment received (as treated). In the SAF, 'N' = 88 in the placebo group as one subject did not meet eligibility criteria but was randomized. The subject did not receive study drug and was therefore excluded from the placebo group in the SAF.			

Units: Meters per Second (m/s)			
arithmetic mean	52.349	52.488	
standard deviation	± 8.519	± 8.276	-
Sural Sensory Nerve Action Potential Amplitude			
Sural sensory nerve action potential amplitude was evaluated by electrically stimulating sensory fibers and recorded the nerve action potential at a point further along that nerve. SAF included all randomized subjects who received any study drug and was based on the treatment received (as treated). In the SAF, 'N' = 88 in the placebo group as one subject did not meet eligibility criteria but was randomized. The subject did not receive study drug and was therefore excluded from the placebo group in the SAF.			
Units: Microvolts (µV)			
arithmetic mean	9.67	9.95	
standard deviation	± 4.79	± 5.67	-
Ulnar Sensory Nerve Conduction Velocity			
Ulnar sensory nerve conduction velocity was evaluated by electrically stimulating sensory fibers and recorded the nerve action potential at a point further along that nerve. SAF included all randomized subjects who received any study drug and was based on the treatment received (as treated). In the SAF, 'N' = 88 in the placebo group as one subject did not meet eligibility criteria but was randomized. The subject did not receive study drug and was therefore excluded from the placebo group in the SAF.			
Units: Meters per Second (m/s)			
arithmetic mean	56.033	56.238	
standard deviation	± 6.584	± 7.452	-
Ulnar Sensory Nerve Action Potential Amplitude			
Ulnar sensory nerve action potential amplitude was evaluated by electrically stimulating sensory fibers and recorded the nerve action potential at a point further along that nerve. SAF included all randomized subjects who received any study drug and was based on the treatment received (as treated). In the SAF, 'N' = 88 in the placebo group as one subject did not meet eligibility criteria but was randomized. The subject did not receive study drug and was therefore excluded from the placebo group in the SAF.			
Units: Microvolts (µV)			
arithmetic mean	19.18	18.47	
standard deviation	± 9.68	± 10.20	-

End points

End points reporting groups

Reporting group title	Fasinumab-matching Placebo
Reporting group description:	
Subjects received Fasinumab-matching placebo subcutaneously (SC) every 4 weeks (Q4W) from Day 1 through Week 12 of the 16-week treatment period.	
Reporting group title	Fasinumab 1 mg SC Q4W
Reporting group description:	
Subjects received Fasinumab 1 milligram (mg) SC Q4W from Day 1 through Week 12 of the 16-week treatment period.	

Primary: Change From Baseline in Peroneal Motor Nerve Conduction Velocity at Week 16

End point title	Change From Baseline in Peroneal Motor Nerve Conduction Velocity at Week 16
End point description:	
Peroneal motor nerve conduction velocity was evaluated by electrical stimulation of the nerve and recorded the compound muscle action potential from surface electrodes overlying a muscle supplied by the nerve. Change from baseline in peroneal motor nerve conduction velocity at Week 16 was reported. Safety analysis set (SAF) included all randomized subjects who received any study drug and was based on the treatment received (as treated).	
End point type	Primary
End point timeframe:	
Week 16	

End point values	Fasinumab-matching Placebo	Fasinumab 1 mg SC Q4W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	69	84		
Units: Meters per Second (m/s)				
least squares mean (standard error)	-0.2 (± 0.46)	0.2 (± 0.42)		

Statistical analyses

Statistical analysis title	Placebo vs Fasinumab 1 mg SC Q4W
Comparison groups	Fasinumab 1 mg SC Q4W v Fasinumab-matching Placebo
Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4192 [1]
Method	Mixed Model for Repeated Measures (MMRM)
Parameter estimate	Least Square (LS) Mean Difference
Point estimate	0.4

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.55
upper limit	1.32

Notes:

[1] - Analyses are based on Mixed Model for Repeated Measures (MMRM) model with terms for baseline nerve conduction test score, treatment, screening Kellgren-Lawrence score, index joint, visit, and treatment by visit interaction.

Primary: Change From Baseline in Peroneal Motor Nerve Action Potential Amplitude at Week 16

End point title	Change From Baseline in Peroneal Motor Nerve Action Potential Amplitude at Week 16

End point description:

Peroneal motor nerve action potential amplitude was evaluated at ankle by electrical stimulation of the nerve and recorded the compound muscle action potential from surface electrodes overlying a muscle supplied by the nerve. Change from baseline in peroneal motor nerve action potential amplitude at Week 16 was reported. SAF included all randomized subjects who received any study drug and was based on the treatment received (as treated).

End point type	Primary

End point timeframe:

Week 16

End point values	Fasinumab-matching Placebo	Fasinumab 1 mg SC Q4W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	69	84		
Units: Millivolts (mV)				
least squares mean (standard error)	-0.2 (± 0.20)	0.2 (± 0.19)		

Statistical analyses

Statistical analysis title	Placebo vs Fasinumab 1 mg SC Q4W
Comparison groups	Fasinumab 1 mg SC Q4W v Fasinumab-matching Placebo
Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0521 [2]
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	0.8

Notes:

[2] - Analyses are based on MMRM model with terms for baseline nerve conduction test score, treatment, screening Kellgren-Lawrence score, index joint, visit, and treatment by visit interaction.

Primary: Change From Baseline in Sural Sensory Nerve Conduction Velocity at Week 16

End point title	Change From Baseline in Sural Sensory Nerve Conduction Velocity at Week 16

End point description:

Sural sensory nerve conduction velocity was evaluated by electrically stimulating sensory fibers and recorded the nerve action potential at a point further along that nerve. Change from baseline in sural sensory nerve conduction velocity at Week 16 was reported. SAF included all randomized subjects who received any study drug and was based on the treatment received (as treated).

End point type	Primary

End point timeframe:

Week 16

End point values	Fasinumab-matching Placebo	Fasinumab 1 mg SC Q4W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	69	84		
Units: Meters per Second (m/s)				
least squares mean (standard error)	-2.9 (± 0.90)	-1.6 (± 0.83)		

Statistical analyses

Statistical analysis title	Placebo vs Fasinumab 1 mg SC Q4W
Comparison groups	Fasinumab-matching Placebo v Fasinumab 1 mg SC Q4W
Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	superiority[3]
P-value	= 0.1593
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	1.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.52
upper limit	3.15

Notes:

[3] - Analyses are based on MMRM model with terms for baseline nerve conduction test score, treatment, screening Kellgren-Lawrence score, index joint, visit, and treatment by visit interaction.

Primary: Change From Baseline in Sural Sensory Nerve Action Potential Amplitude at Week 16

End point title	Change From Baseline in Sural Sensory Nerve Action Potential Amplitude at Week 16

End point description:

Sural sensory nerve action potential amplitude was evaluated by electrically stimulating sensory fibers and recorded the nerve action potential at a point further along that nerve. Change from baseline in sural sensory nerve action potential amplitude at Week 16 was reported. SAF included all randomized subjects who received any study drug and was based on the treatment received (as treated).

End point type	Primary

End point timeframe:

Week 16

End point values	Fasinumab-matching Placebo	Fasinumab 1 mg SC Q4W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	69	84		
Units: Microvolts (µV)				
least squares mean (standard error)	0.5 (± 0.69)	0.3 (± 0.64)		

Statistical analyses

Statistical analysis title	Placebo vs Fasinumab 1 mg SC Q4W
Comparison groups	Fasinumab-matching Placebo v Fasinumab 1 mg SC Q4W
Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7757 [4]
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.59
upper limit	1.19

Notes:

[4] - Analyses are based on MMRM model with terms for baseline nerve conduction test score, treatment, screening Kellgren-Lawrence score, index joint, visit, and treatment by visit interaction

Primary: Change From Baseline in Ulnar Sensory Nerve Conduction Velocity at Week 16

End point title	Change From Baseline in Ulnar Sensory Nerve Conduction Velocity at Week 16

End point description:

Ulnar sensory nerve conduction velocity was evaluated by electrically stimulating sensory fibers and recorded the nerve action potential at a point further along that nerve. Change from baseline in ulnar sensory nerve conduction velocity at Week 16 was reported. SAF included all randomized subjects who received any study drug and was based on the treatment received (as treated).

End point type	Primary

End point timeframe:

Week 16

End point values	Fasinumab-matching Placebo	Fasinumab 1 mg SC Q4W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	69	84		
Units: Meters per Second (m/s)				
least squares mean (standard error)	-0.7 (± 0.74)	-1.1 (± 0.68)		

Statistical analyses

Statistical analysis title	Placebo vs Fasinumab 1 mg SC Q4W
Comparison groups	Fasinumab-matching Placebo v Fasinumab 1 mg SC Q4W
Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6063 [5]
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.87
upper limit	1.09

Notes:

[5] - Analyses are based on MMRM model with terms for baseline nerve conduction test score, treatment, screening Kellgren-Lawrence score, index joint, visit, and treatment by visit interaction.

Primary: Change From Baseline in Ulnar Sensory Nerve Action Potential Amplitude at Week 16

End point title	Change From Baseline in Ulnar Sensory Nerve Action Potential Amplitude at Week 16

End point description:

Ulnar sensory nerve action potential amplitude was evaluated by electrically stimulating sensory fibers and recorded the nerve action potential at a point further along that nerve. Change from baseline ulnar sensory nerve action potential amplitude at Week 16 was reported. SAF included all randomized subjects who received any study drug and was based on the treatment received (as treated).

End point type	Primary

End point timeframe:

Week 16

End point values	Fasinumab-matching Placebo	Fasinumab 1 mg SC Q4W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	69	84		
Units: Microvolts (µV)				
least squares mean (standard error)	2.4 (± 1.21)	1.4 (± 1.12)		

Statistical analyses

Statistical analysis title	Placebo vs Fasinumab 1 mg SC Q4W
Comparison groups	Fasinumab-matching Placebo v Fasinumab 1 mg SC Q4W
Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4203 [6]
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.3
upper limit	1.39

Notes:

[6] - Analyses are based on MMRM model with terms for baseline nerve conduction test score, treatment, screening Kellgren-Lawrence score, index joint, visit, and treatment by visit interaction.

Secondary: Change From Baseline in Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) Pain Subscale Score at Week 16

End point title	Change From Baseline in Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) Pain Subscale Score at Week 16

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. Total score range for WOMAC pain subscale score is 0 to 10, where higher scores indicate higher pain. A negative change from baseline indicated improvement. The FAS included all randomized subjects and was based on the treatment allocated (as randomized). Change from Baseline in WOMAC Pain subscale score at Week 16 was reported.

End point type	Secondary

End point timeframe:

Week 16

End point values	Fasinumab-matching Placebo	Fasinumab 1 mg SC Q4W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	54	67		
Units: Score on a Scale				
least squares mean (standard error)	-1.19 (± 0.359)	-2.52 (± 0.335)		

Statistical analyses

Statistical analysis title	Placebo vs Fasinumab 1 mg SC Q4W
Comparison groups	Fasinumab-matching Placebo v Fasinumab 1 mg SC Q4W
Number of subjects included in analysis	121
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.001 [7]
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-1.33
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.123
upper limit	-0.538

Notes:

[7] - Analyses are based on multiple imputation with MMRM model with terms for baseline WOMAC subscale score, treatment, screening Kellgren-Lawrence score, index joint, visit, and treatment by visit interaction.

Secondary: Change From Baseline in WOMAC Physical Function Subscale Score at Week 16

End point title	Change From Baseline in WOMAC Physical Function Subscale Score at Week 16

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 (no difficulty) to 10 (extreme difficulty), where higher scores indicated worse function. Total score range for WOMAC physical function subscale score is 0 (no difficulty) to 10 (extreme difficulty), where higher scores indicate worse function. A negative change from baseline indicated improvement. FAS included all randomized subjects and was based on the treatment allocated (as randomized). Change from Baseline in WOMAC physical function subscale score at Week 16 was reported.

End point type	Secondary

End point timeframe:

Week 16

End point values	Fasinumab-matching Placebo	Fasinumab 1 mg SC Q4W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	54	66		
Units: Score on a Scale				
least squares mean (standard error)	-0.83 (± 0.366)	-2.24 (± 0.341)		

Statistical analyses

Statistical analysis title	Placebo vs Fasinumab 1 mg SC Q4W
Comparison groups	Fasinumab-matching Placebo v Fasinumab 1 mg SC Q4W
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0005 [8]
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-1.42
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.212
upper limit	-0.625

Notes:

[8] - Analyses are based on multiple imputation with MMRM model with terms for baseline WOMAC subscale score, treatment, screening Kellgren-Lawrence score, index joint, visit, and treatment by visit interaction.

Secondary: Serum Concentration of Functional Fasinumab

End point title	Serum Concentration of Functional Fasinumab[9]

End point description:

Serum concentrations of functional Fasinumab were reported. The 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 dose of study drug. Here, 'n' signifies those subjects who were evaluable at specified time points.

End point type	Secondary

End point timeframe:

Baseline, Week 1, 2, 4, 8, 12, 16, and 36

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 Fasinumab 1 mg SC Q4W arm only.

End point values	Fasinumab 1 mg SC Q4W			
Subject group type	Reporting group			
Number of subjects analysed	91			
Units: Milligrams per Liter (mg/L)				
arithmetic mean (standard deviation)				
Baseline: n = 91	0 (± 0)			

Week 1: n = 84	0.0864 (± 0.0299)			
Week 2: n = 87	0.0820 (± 0.0252)			
Week 4: n = 85	0.0525 (± 0.0181)			
Week 8: n = 84	0.0780 (± 0.0326)			
Week 12: n = 81	0.0802 (± 0.0400)			
Week 16: n = 76	0.0824 (± 0.0497)			
Week 36: n = 11	0 (± 0)			

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

ADA analysis set included all treated subjects who received any amount of study drug (active or placebo [safety analysis set]) and had at least one non-missing anti-fasinumab antibody result following the first dose of study drug or placebo.

End point type	Secondary

End point timeframe:

Baseline up to Week 36

End point values	Fasinumab-matching Placebo	Fasinumab 1 mg SC Q4W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	80	87		
Units: Subjects				
Negative	79	87		
Pre-Existing Immunoreactivity	1	0		
Treatment-Boosted Response	0	0		
Treatment-Emergent Response	0	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From the first dose of study drug up to 24 weeks post the last dose of study drug (up to Week 36)

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.1

Reporting groups

Reporting group title	Fasinumab 1 mg SC Q4W

Reporting group description:

Subjects received Fasinumab 1 milligram (mg) SC Q4W from Day 1 through Week 12 of the 16-week treatment period.

Reporting group title	Fasinumab-matching Placebo

Reporting group description:

Subjects received Fasinumab-matching placebo subcutaneously (SC) every 4 weeks (Q4W) from Day 1 through Week 12 of the 16-week treatment period.

Serious adverse events	Fasinumab 1 mg SC Q4W	Fasinumab-matching Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 91 (3.30%)	6 / 88 (6.82%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lung squamous cell carcinoma metastatic			
subjects affected / exposed	0 / 91 (0.00%)	1 / 88 (1.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Multiple injuries			
subjects affected / exposed	0 / 91 (0.00%)	1 / 88 (1.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Humerus fracture			
subjects affected / exposed	0 / 91 (0.00%)	1 / 88 (1.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Limb traumatic amputation			
subjects affected / exposed	1 / 91 (1.10%)	0 / 88 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Patella fracture			
subjects affected / exposed	0 / 91 (0.00%)	1 / 88 (1.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Supraventricular tachycardia			
subjects affected / exposed	0 / 91 (0.00%)	1 / 88 (1.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Knee arthroplasty			
subjects affected / exposed	0 / 91 (0.00%)	1 / 88 (1.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 91 (1.10%)	1 / 88 (1.14%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rapidly progressive osteoarthritis			
subjects affected / exposed	1 / 91 (1.10%)	0 / 88 (0.00%)	
occurrences causally related to treatment / all	0 / 1	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	Fasinumab 1 mg SC Q4W	Fasinumab-matching Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	55 / 91 (60.44%)	49 / 88 (55.68%)	
Investigations			

Nerve conduction studies abnormal			
subjects affected / exposed	10 / 91 (10.99%)	17 / 88 (19.32%)	
occurrences (all)	13	17	
Nervous system disorders			
Headache			
subjects affected / exposed	13 / 91 (14.29%)	15 / 88 (17.05%)	
occurrences (all)	22	26	
Dizziness			
subjects affected / exposed	5 / 91 (5.49%)	3 / 88 (3.41%)	
occurrences (all)	5	3	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	5 / 91 (5.49%)	3 / 88 (3.41%)	
occurrences (all)	6	3	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	24 / 91 (26.37%)	19 / 88 (21.59%)	
occurrences (all)	44	27	
Myalgia			
subjects affected / exposed	0 / 91 (0.00%)	5 / 88 (5.68%)	
occurrences (all)	0	5	
Pain in extremity			
subjects affected / exposed	6 / 91 (6.59%)	5 / 88 (5.68%)	
occurrences (all)	7	8	
Back pain			
subjects affected / exposed	5 / 91 (5.49%)	5 / 88 (5.68%)	
occurrences (all)	5	5	
Osteoarthritis			
subjects affected / exposed	5 / 91 (5.49%)	1 / 88 (1.14%)	
occurrences (all)	6	1	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	8 / 91 (8.79%)	6 / 88 (6.82%)	
occurrences (all)	10	8	
Upper respiratory tract infection			

subjects affected / exposed	5 / 91 (5.49%)	5 / 88 (5.68%)	
occurrences (all)	5	6	
Urinary tract infection			
subjects affected / exposed	7 / 91 (7.69%)	4 / 88 (4.55%)	
occurrences (all)	8	5	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
16 July 2018	The purpose of this amendment was to change the fasinumab 3 mg Q4W dose regimen to a 1 mg Q4W dose regimen because the 3 mg Q4W dose regimen is no longer being evaluated in the osteoarthritis (OA) pain program. The 1 mg Q4W dose regimen is now the highest dose being evaluated in this patient population.
19 February 2019	The purpose of this amendment was to revise the criterion for detecting a change in nerve conduction velocity that would be considered not to be within established parameters, in order to reduce false-positive findings.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported