Clinical trial results:
A Phase 3, Randomized, Double-Blind, Placebo-Controlled Study to Evaluate the Efficacy and Safety of Fasinumab in Patients with Moderate to-Severe Chronic Low Back Pain and Osteoarthritis of the Hip or Knee

Summary

EudraCT number	2017-001943-12
Trial protocol	GB HU ES
Global end of trial date	03 May 2019

Results information

Result version number	v2 (current)
This version publication date	17 October 2021
First version publication date	15 May 2020
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	R475-PN-1612

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03285646
WHO universal trial number (UTN)	-
Other trial identifiers	Acronym: FACT CLBP 1

Notes:

Sponsors

Sponsor organisation name	Regeneron Pharmaceuticals, Inc.
Sponsor organisation address	777 Old Saw Mill River Rd., Tarrytown, United States, 10591
Public contact	Study Director, Regeneron Pharmaceuticals, Inc., clinicaltrials@regeneron.com
Scientific contact	Study Director, Regeneron Pharmaceuticals, Inc., 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	05 June 2019
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	03 May 2019
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of fasinumab in relieving chronic low back pain (CLBP) as compared to placebo in subjects with a clinical diagnosis of moderate-to-severe non-radicular CLBP and osteoarthritis (OA) of the knee or hip when treated for up to 16 weeks.

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	30 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: 63
Worldwide total number of subjects	63
EEA total number of subjects	0

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)	45
From 65 to 84 years	18
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects were screened for study eligibility across the United States. Of the 377 subjects screened, 63 met eligibility criteria. The most frequently reported reason for non-randomization was inclusion criteria not met and/or exclusion criteria met (224 subjects):139 did not meet inclusion criteria, 86 subjects met exclusion criteria.

Pre-assignment

Screening details:

The study consisted of a screening period of up to 30 days and a 7 (+3 day) day pre-randomization period during which all pain medication except study-provided rescue medication was discontinued.

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, Carer, Data analyst, 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. Subjects were permitted to use only acetaminophen/paracetamol as rescue medication. The treatment period included both study visits and a phone contact on day 8 (±1 day) up to 16 weeks.

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 were administered SC injection of placebo matched to fasinumab Q4W into abdomen, thigh or upper arm

Arm title	Fasinumab 3 mg SC Q4W

Arm description:

Subjects received fasinumab 3 milligrams (mg) subcutaneously (SC) every 4 weeks (Q4W) from day 1 through week 12 of the 16 week treatment period. Subjects were permitted to use only acetaminophen/paracetamol as rescue medication. The treatment period included both study visits and a phone contact on day 8 (±1 day) up to 16 weeks.

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 were administered 3 mg SC injection of fasinumab Q4W into abdomen, thigh or upper arm

Number of subjects in period 1	Fasinumab-matching Placebo	Fasinumab 3 mg SC Q4W
Started	32	31
Completed	19	27
Not completed	13	4
Consent withdrawn by subject	10	2
Investigator/Sponsor Decision	-	1
Adverse event, non-fatal	1	-
Lost to follow-up	2	1

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. Subjects were permitted to use only acetaminophen/paracetamol as rescue medication. The treatment period included both study visits and a phone contact on day 8 (±1 day) up to 16 weeks.	
Reporting group title	Fasinumab 3 mg SC Q4W
Reporting group description:	
Subjects received fasinumab 3 milligrams (mg) subcutaneously (SC) every 4 weeks (Q4W) from day 1 through week 12 of the 16 week treatment period. Subjects were permitted to use only acetaminophen/paracetamol as rescue medication. The treatment period included both study visits and a phone contact on day 8 (±1 day) up to 16 weeks.	

Reporting group values	Fasinumab-matching Placebo	Fasinumab 3 mg SC Q4W	Total
Number of subjects	32	31	63
Age categorical Units: Subjects			
Adults <65 years of age	24	21	45
Adults >=65 years of age	8	10	18
Age Continuous Units: years			
arithmetic mean	57.7	60.0	
standard deviation	± 9.88	± 10.52	-
Sex: Female, Male Units:			
Female	21	18	39
Male	11	13	24
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	1	3	4
Not Hispanic or Latino	31	28	59
Unknown or Not Reported	0	0	0
Race/Ethnicity, Customized Units: Subjects			
White	15	17	32
Black or African American	15	14	29
American Indian or Alaskan	1	0	1
Native Hawaiian or Other Pacific Islander	1	0	1
Average Daily Low Back Pain Intensity (LBPI) Numerical Rating Scale (NRS) Score			
Average daily low back pain (LBP) was assessed on an 11-point numeric rating scale (NRS) and was defined as the average of the non-missing daily LBPI NRS scores for the 7 days before and including nominal visit. Subjects described their average low back pain during the past 24 hours on a scale ranging from 0 (no pain) to 10 (worst possible pain), where higher scores indicate higher pain.			
Units: Score on a Scale			
arithmetic mean	6.66	6.81	
standard deviation	± 1.475	± 1.338	-

Roland Morris Disability Questionnaire (RMDQ) Total Score			
The RMDQ is a self-administered, health status measure for lower back pain (LBP). It measures pain and function, using 24 items describing limitations to everyday life that can be caused by LBP. The score of the RMDQ is the total number of items checked from a minimum of 0 (no disability) to a maximum of 24 (maximum disability), where lower scores are indicative of better function.			
Units: Score on a Scale			
arithmetic mean	11.03	10.90	
standard deviation	± 5.445	± 5.492	-

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. Subjects were permitted to use only acetaminophen/paracetamol as rescue medication. The treatment period included both study visits and a phone contact on day 8 (±1 day) up to 16 weeks.

Reporting group title	Fasinumab 3 mg SC Q4W

Reporting group description:

Subjects received fasinumab 3 milligrams (mg) subcutaneously (SC) every 4 weeks (Q4W) from day 1 through week 12 of the 16 week treatment period. Subjects were permitted to use only acetaminophen/paracetamol as rescue medication. The treatment period included both study visits and a phone contact on day 8 (±1 day) up to 16 weeks.

Primary: Change from Baseline to Week 16 in the Average Daily Low Back Pain Intensity (LBPI) Numeric Rating Scale (NRS) Score

End point title	Change from Baseline to Week 16 in the Average Daily Low Back Pain Intensity (LBPI) Numeric Rating Scale (NRS) Score[1]

End point description:

Average daily low back pain (LBP) was assessed on an 11-point numeric rating scale (NRS) and was defined as the average of the non-missing daily LBPI NRS scores for the 7 days before and including nominal visit. Subjects described their average low back pain during the past 24 hours on a scale ranging from 0 (no pain) to 10 (worst possible pain), where higher scores indicate higher pain.

End point type	Primary

End point timeframe:

Week 1, Week 2, Week 4, Week 8, Week 12, Week 16

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Placebo subjects were not included in the concentration analysis

End point values	Fasinumab-matching Placebo	Fasinumab 3 mg SC Q4W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	31		
Units: Score on a Scale				
arithmetic mean (standard deviation)				
Change from Baseline to Week 1 (n=32,31)	-0.73 (± 1.424)	-1.62 (± 2.037)		
Change from Baseline to Week 2 (n=29,31)	-0.98 (± 1.588)	-2.15 (± 2.067)		
Change from Baseline to Week 4 (n=28,29)	-1.28 (± 1.878)	-2.64 (± 2.038)		
Change from Baseline to Week 8 (n=20,21)	-1.21 (± 1.568)	-2.82 (± 1.963)		
Change from Baseline to Week 12 (n=9,13)	-2.12 (± 1.582)	-3.18 (± 2.046)		
Change from Baseline to Week 16 (n=2,7)	-0.77 (± 1.943)	-2.32 (± 1.367)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Week 16 in the Roland Morris Disability Questionnaire (RMDQ) Total Score

End point title	Change from Baseline to Week 16 in the Roland Morris Disability Questionnaire (RMDQ) Total Score

End point description:

The RMDQ is a self-administered, health status measure for lower back pain (LBP). It measures pain and function, using 24 items describing limitations to everyday life that can be caused by LBP. The score of the RMDQ is the total number of items checked from a minimum of 0 (no disability) to a maximum of 24 (maximum disability), where lower scores are indicative of better function.

End point type	Secondary

End point timeframe:

Week 2, Week 4, Week 8, Week 12, Week 16

End point values	Fasinumab-matching Placebo	Fasinumab 3 mg SC Q4W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	31		
Units: Score on a Scale				
arithmetic mean (standard deviation)				
Change from Baseline to Week 2 (n=27,24)	-2.70 (± 5.120)	-2.54 (± 4.836)		
Change from Baseline to Week 4 (n=24,23)	-1.92 (± 4.529)	-3.09 (± 3.884)		
Change from Baseline to Week 8 (n=19,17)	0.37 (± 4.487)	-4.18 (± 5.015)		
Change from Baseline to Week 12 (n=6,9)	0.83 (± 3.061)	-3.33 (± 4.301)		
Change from Baseline to Week 16 (n=1,4)	-1.00 (± 99999)	-5.75 (± 3.948)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Week 16 in Patient Global Assessment (PGA) of Low Back Pain (LBP) Score

End point title	Change from Baseline to Week 16 in Patient Global Assessment (PGA) of Low Back Pain (LBP) Score

End point description:

The PGA of LBP is a subject assessed 5 point Likert scale of LBP ranging from 1-5 where 1 = very well; 2 = well; 3 = fair; 4 = poor; and 5 = very poor.

End point type	Secondary

End point timeframe:

Week 2, Week 4, Week 8, Week 12, Week 16

End point values	Fasinumab-matching Placebo	Fasinumab 3 mg SC Q4W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	31		
Units: Score on a Scale				
arithmetic mean (standard deviation)				
Change from Baseline to Week 2 (n=27,29)	-0.44 (± 0.751)	-0.76 (± 0.786)		
Change from Baseline to Week 4 (n=25,25)	-0.60 (± 0.957)	-1.04 (± 0.676)		
Change from Baseline to Week 8 (n=20,20)	-0.55 (± 0.945)	-1.10 (± 1.021)		
Change from Baseline to Week 12 (n=7,10)	-0.57 (± 1.134)	-1.00 (± 1.333)		
Change from Baseline to Week 16 (n=1,4)	0.00 (± 99999)	-0.75 (± 0.500)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Week 16 in the Brief Pain Inventory-Short Form (BPI-sf) Pain Interference Score

End point title	Change from Baseline to Week 16 in the Brief Pain Inventory-Short Form (BPI-sf) Pain Interference Score

End point description:

The BPI-sf is a self-administered questionnaire for subjects to rate the severity of their pain and the degree to which their pain interferes with common dimensions of feeling and function. With a recall period of 24 hours, the questionnaire contains the front and back body diagrams, the 4 pain severity items and 7 pain interference items rated on 0-10 scale; total interference score ranges from 0-10 (0, does not interfere; 10 completely interferes), and the question about percentage of pain relief by analgesics. The BPI pain interference is typically scored as the mean of the 7 interference items.

End point type	Secondary

End point timeframe:

Week 2, Week 4, Week 8, Week 12, Week 16

End point values	Fasinumab-matching Placebo	Fasinumab 3 mg SC Q4W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	31		
Units: Score on a Scale				
arithmetic mean (standard deviation)				
Change from Baseline to Week 2 (n=27,29)	-1.55 (± 2.306)	-1.94 (± 2.255)		
Change from Baseline to Week 4 (n=25,25)	-1.49 (± 2.390)	-2.15 (± 2.157)		
Change from Baseline to Week 8 (n=20,20)	-1.31 (± 2.119)	-2.70 (± 2.774)		
Change from Baseline to Week 12 (n=7,10)	-1.63 (± 2.096)	-1.84 (± 1.978)		
Change from Baseline to Week 16 (n=1,4)	-1.14 (± 99999)	-1.29 (± 3.017)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects Achieving ≥30% Reduction from Baseline to Week 16 in Average Daily LBPI NRS Score

End point title	Number of Subjects Achieving ≥30% Reduction from Baseline to Week 16 in Average Daily LBPI NRS Score

End point description:

Average daily low back pain (LBP) was assessed on an 11-point numeric rating scale (NRS) and was defined as the average of the non-missing daily LBPI NRS scores for the 7 days before and including nominal visit. Subjects described their average low back pain during the past 24 hours on a scale ranging from 0 (no pain) to 10 (worst possible pain), where higher scores indicate higher pain.

End point type	Secondary

End point timeframe:

Week 16

End point values	Fasinumab-matching Placebo	Fasinumab 3 mg SC Q4W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	31		
Units: Subjects	12	21		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Adjudicated Arthropathy (AA) Events

End point title	Number of Adjudicated Arthropathy (AA) Events

End point description:

Adjudicated arthropathy (AA) is a composite term that encompasses the following conditions: Rapidly progressive OA type 1 and 2, Subchondral insufficiency fractures, and Primary Osteonecrosis. AAs were also evaluated to determine if they met Destructive Arthropathy criteria.

End point type	Secondary

End point timeframe:

Up to Week 36

End point values	Fasinumab-matching Placebo	Fasinumab 3 mg SC Q4W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	31		
Units: Adjudicated Arthropathy (AA) Events	0	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Adjudicated Arthropathy (AA) Events meeting Destructive Arthropathy (DA) Criteria

End point title	Number of Adjudicated Arthropathy (AA) Events meeting Destructive Arthropathy (DA) Criteria

End point description:

Destructive arthropathy (DA) is a unique clinical form of rapidly destructive arthropathy over and above that seen in the normal progression of OA. DA criteria can be associated with Rapidly Progressive Osteoarthritis type 2, Subchondral Insufficiency fracture, and Primary Osteonecrosis.

End point type	Secondary

End point timeframe:

Up to Week 36

End point values	Fasinumab-matching Placebo	Fasinumab 3 mg SC Q4W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	31		
Units: Destructive Arthropathy (DA) Events	0	0		

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

Treatment-emergent adverse events are defined as those that are not present at baseline or represent the exacerbation of a pre-existing condition during the on-treatment period.

End point type	Secondary

End point timeframe:

Up to Week 16

End point values	Fasinumab-matching Placebo	Fasinumab 3 mg SC Q4W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	31		
Units: Treatment-Emergent Adverse Events	33	14		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Sympathetic Nervous System (SNS) Dysfunction Events

End point title	Number of Sympathetic Nervous System (SNS) Dysfunction Events

End point description:

Potential events of sympathetic nervous system (SNS) dysfunction were monitored throughout the study through physical examination, AE reporting, assessment of orthostatic hypotension, and the Survey of Autonomic Symptoms. Sympathetic nervous system dysfunction was diagnosed after consultation with an appropriate specialist, such as a neurologist and/or cardiologist.

End point type	Secondary

End point timeframe:

Up to Week 36

End point values	Fasinumab-matching Placebo	Fasinumab 3 mg SC Q4W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	31		
Units: Sympathetic NS Dysfunction Events	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Peripheral Sensory Adverse Events (AEs) that Require a Neurology Consultation

End point title	Number of Peripheral Sensory Adverse Events (AEs) that Require a Neurology Consultation

End point description:

Any peripheral sensory AE (eg, paraesthesia and hypoaesthesia) that required a neurology consultation.

End point type	Secondary

End point timeframe:

Up to Week 36

End point values	Fasinumab-matching Placebo	Fasinumab 3 mg SC Q4W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	31		
Units: Peripheral Sensory Adverse Events (AEs)				
Hypoaesthesia events	1	0		
Paraesthesia events	1	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of All-Cause Joint Replacement (JR) Surgery Events

End point title	Number of All-Cause Joint Replacement (JR) Surgery Events

End point description:

All joint replacement surgery events regardless of cause.

End point type	Secondary

End point timeframe:

Up to Week 36

End point values	Fasinumab-matching Placebo	Fasinumab 3 mg SC Q4W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	31		
Units: Joint Replacement (JR) Surgery Events	2	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Joint Replacement (JR) Surgery Events Reported at Telephone Survey After Last Dose of Study Drug

End point title	Number of Joint Replacement (JR) Surgery Events Reported at Telephone Survey After Last Dose of Study Drug

End point description:

An end of study phone contact was conducted approximately 52 weeks following the last dose of study drug (week 12) to evaluate the number of participants who had undergone or were scheduled for JR surgery.

End point type	Secondary

End point timeframe:

Up to Week 64

End point values	Fasinumab-matching Placebo	Fasinumab 3 mg SC Q4W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	31		
Units: Joint Replacement (JR) Surgery Events	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With at Least One Positive Anti-Drug Antibody (ADA) Assay

End point title	Number of Subjects With at Least One Positive Anti-Drug Antibody (ADA) Assay

End point description:

Samples for Anti-Drug Antibody (ADA) evaluation were collected at baseline and at subsequent study visits. ADA variables include ADA status (+ or -) and titer as follows: Total subjects negative in the ADA assay at all time points analyzed. Pre-existing immunoreactivity - positive response at baseline with all post-dose results negative, or a positive response at baseline with all post-dose responses less than 9-fold over baseline titer levels. Treatment emergent - post-dose positive result when baseline results were negative. Persistent - A positive result detected in at least 2 consecutive post baseline samples separated by at least a 16-week post baseline period, with no negative results in-between. Indeterminate - A positive result at the last collection time point analyzed only. Transient - Not persistent or indeterminate regardless of any missing samples. Treatment boosted - any post-dose positive result at least 9-fold over the baseline level when baseline is positive.

End point type	Secondary

End point timeframe:

16 Weeks

End point values	Fasinumab-matching Placebo	Fasinumab 3 mg SC Q4W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	31		
Units: Subjects				
Negative/Pre-Existing	31	31		
Treatment Boosted	0	0		
Treatment-Emergent	0	0		
Treatment-Emergent: Persistent	0	0		
Treatment-Emergent: Transient	0	0		
Treatment-Emergent: Indeterminate	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Serum Concentration of Functional Fasinumab Over Time

End point title	Serum Concentration of Functional Fasinumab Over Time[2]

End point description:

Summary of mean concentration of functional fasinumab are presented by nominal time point.

End point type	Secondary

End point timeframe:

Baseline, Week 2, Week 4, Week 8, Week 16

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Placebo subjects were not included in the concentration analysis

End point values	Fasinumab 3 mg SC Q4W			
Subject group type	Reporting group			
Number of subjects analysed	31			
Units: Milligram per Liter (mg/L)				
arithmetic mean (standard deviation)				
Baseline (n=31)	0 (± 0)			
Week 2 (n=23)	0.262 (± 0.0992)			
Week 4 (n=25)	0.176 (± 0.0679)			
Week 8 (n=18)	0.247 (± 0.130)			
Week 16 (n=3)	0.192 (± 0.0932)			

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)

Adverse event reporting additional description:

Reported adverse events (AEs) are AEs that developed/worsened from the time of the first administration of study drug until the end of the follow up period (week 36)

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	22.0

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. Subjects were permitted to use only acetaminophen/paracetamol as rescue medication. The treatment period included both study visits and a phone contact on day 8 (±1 day) up to 16 weeks.

Reporting group title	Fasinumab 3 mg SC Q4W

Reporting group description:

Subjects received fasinumab 3 milligrams (mg) subcutaneously (SC) every 4 weeks (Q4W) from day 1 through week 12 of the 16 week treatment period. Subjects were permitted to use only acetaminophen/paracetamol as rescue medication. The treatment period included both study visits and a phone contact on day 8 (±1 day) up to 16 weeks.

Serious adverse events	Fasinumab-matching Placebo	Fasinumab 3 mg SC Q4W	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 32 (3.13%)	2 / 31 (6.45%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer stage IV			
subjects affected / exposed	0 / 32 (0.00%)	1 / 31 (3.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 32 (0.00%)	1 / 31 (3.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			

Dyspnoea			
subjects affected / exposed	0 / 32 (0.00%)	1 / 31 (3.23%)	
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			
Osteoarthritis			
subjects affected / exposed	1 / 32 (3.13%)	0 / 31 (0.00%)	
occurrences causally related to treatment / all	0 / 2	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-matching Placebo	Fasinumab 3 mg SC Q4W	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	14 / 32 (43.75%)	4 / 31 (12.90%)	
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	3 / 32 (9.38%)	1 / 31 (3.23%)	
occurrences (all)	3	1	
General disorders and administration site conditions			
Peripheral swelling			
subjects affected / exposed	2 / 32 (6.25%)	0 / 31 (0.00%)	
occurrences (all)	2	0	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 32 (6.25%)	0 / 31 (0.00%)	
occurrences (all)	2	0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	4 / 32 (12.50%)	3 / 31 (9.68%)	
occurrences (all)	7	4	
Back pain			
subjects affected / exposed	5 / 32 (15.63%)	0 / 31 (0.00%)	
occurrences (all)	5	0	

Neck pain subjects affected / exposed occurrences (all)	2 / 32 (6.25%) 2	1 / 31 (3.23%) 1	
Infections and infestations Upper respiratory tract infection subjects affected / exposed occurrences (all)	4 / 32 (12.50%) 4	1 / 31 (3.23%) 1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
03 May 2018	In May 2018, the sponsor implemented an urgent safety measure. As a result, enrollment into R475-PN-1612 was stopped on 03 May 2018; subjects already enrolled in the study immediately discontinued study drug and entered the 20-week follow-up period.	-

Notes:

Limitations and caveats

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

As a result of an urgent safety measure and discontinuation of study drug, the small number of subjects enrolled in this study limited the interpretability of the efficacy results.

Notes: