Clinical trial results:
Randomized, 16-Week, Multi-Phase, Double-Blind, Placebo-Controlled Study to Evaluate the Efficacy, Safety, and Tolerability of Fulranumab as Monotherapy in Subjects with Signs and Symptoms of Osteoarthritis of the Hip or Knee

Summary

EudraCT number	2014-003879-37
Trial protocol	GB ES
Global end of trial date	15 September 2016

Results information

Result version number	v1 (current)
This version publication date	14 October 2017
First version publication date	14 October 2017

Trial information

Trial identification

Sponsor protocol code	42160443PAI3002

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02336698
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Janssen Research & Development LLC
Sponsor organisation address	Archimedesweg 29, Leiden, Netherlands, 2333CM
Public contact	Clinical Registry group, Janssen Research & Development LLC, ClinicalTrialsEU@its.jnj.com
Scientific contact	Clinical Registry group, Janssen Research & Development LLC, ClinicalTrialsEU@its.jnj.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	15 September 2016
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	15 September 2016
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to demonstrate the efficacy (as measured by the changes from baseline to the end of Week 16 in the Western Ontario and McMaster University Osteoarthritis Index [WOMAC] pain and physical function subscale scores), safety, and tolerability of fulranumab subcutaneous (SC) injections as monotherapy compared with placebo SC injections in subjects who had signs and symptoms of osteoarthritis (OA) of the hip or knee that were not adequately controlled by their current pain therapy and who were planning a joint replacement surgery.

Protection of trial subjects:

Safety was evaluated throughout the study and included monitoring of adverse event (AE), clinical laboratory testing, vital sign collection (including orthostatic testing), neurologic evaluation (abbreviated neurologic examination including an assessment of pupillary light reflex and signs consistent with carpal tunnel syndrome, Total Neuropathy Score-nurse [TNSn], Mini Mental State Examination [MMSE], autonomic nervous system dysfunction history, and carpal tunnel syndrome questionnaire), joint-related event evaluations (joint examinations and radiographs), numerical rating scale (NRS) for nonstudy joint pain, electrocardiograms (ECGs), physical examinations, and injection-site reactions. This study was conducted in accordance with the ethical principles that have their origin in the declaration of Helsinki and that are consistent with Good Clinical Practice (GCP) and applicable regulatory requirements.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	16 July 2015
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	12 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Spain: 5
Country: Number of subjects enrolled	United States: 12
Worldwide total number of subjects	17
EEA total number of subjects	5

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37	0

wk	
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)	6
From 65 to 84 years	11
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 17 subjects were randomized: 5 in placebo group, 25 in fulranumab (FUL) 1 milligram (mg) every 4 weeks (Q4wk) group, and 5 in FUL 3 mg Q4wk group. The intent-to-treat (ITT) and safety analysis sets included all 17 subjects.

Period 1

Period 1 title	Double Blind
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Subjects received 4 placebo subcutaneous (SC) injections (one injection every 4 weeks) for 16 weeks during the double-blind treatment phase.

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 4 placebo SC injections (one injection every 4 weeks) for 16 weeks during the double-blind treatment phase.

Arm title	Fulranumab 1 mg

Arm description:

Subjects received 4 SC injections (one injection every 4 weeks) of fulranumab 1 mg during the double-blind treatment phase.

Arm type	Experimental
Investigational medicinal product name	Fulranumab 1 mg
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 fulranumab 1 mg injection every 4 weeks for 16 weeks during the double-blind treatment phase.

Arm title	Fulranumab 3 mg

Arm description:

Subjects received 4 SC injections (one injection every 4 weeks) of fulranumab 3 mg during the double-blind treatment phase.

Arm type	Experimental

Investigational medicinal product name	Fulranumab 3 mg
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 fulranumab 3 mg injection every 4 weeks for 16 weeks during the double-blind treatment phase.

Number of subjects in period 1	Placebo	Fulranumab 1 mg	Fulranumab 3 mg
Started	5	7	5
Completed	0	0	1
Not completed	5	7	4
Consent withdrawn by subject	-	1	1
Withdrawn by sponsor due to positive thc results	-	1	-
Study terminated by sponsor	5	5	3

Period 2

Period 2 title	24 Week Follow-up Phase
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	No
Arm title	Placebo

Arm description:

Subjects who received placebo in treatment phase were followed for 24 weeks in this period.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Arm title	Fulranumab 1 mg

Arm description:

Subjects who received fulranumab 1 mg in treatment phase were followed for 24 weeks in this period.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Arm title	Fulranumab 3 mg

Arm description:

Subjects who received fulranumab 3 mg in treatment phase were followed for 24 weeks in this period.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Number of subjects in period 2	Placebo	Fulranumab 1 mg	Fulranumab 3 mg
Started	4	2	5
Completed	2	2	1
Not completed	2	0	4
Consent withdrawn by subject	-	-	1
Study terminated by sponsor	2	-	3

Period 3	
Period 3 title	Limited Safety Follow-up (LSFU)
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	No
Arm title	Placebo

Arm description:

Subjects who received placebo in treatment phase were followed for up to 24 weeks after the last injection of study drug in the limited safety follow-up phase. Subjects who discontinued from the 24-week follow-up phase were asked to enter the LSFU phase.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Arm title	Fulranumab 1 mg

Arm description:

Subjects who received fulranumab 1 mg in treatment phase were followed for up to 24 weeks after the last injection of study drug in this follow-up phase. Subjects who discontinued from the 24- week follow-up phase were asked to enter the LSFU phase.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Arm title	Fulranumab 3 mg

Arm description:

Subjects who received fulranumab 3 mg in treatment phase were followed for up to 24 weeks after the last injection of study drug in this follow-up phase. Subjects who discontinued from the 24- week follow-up phase were asked to enter the LSFU phase.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Number of subjects in period 3	Placebo	Fulranumab 1 mg	Fulranumab 3 mg
Started	1	2	2
Completed	1	1	2
Not completed	0	1	0
Study terminated by sponsor	-	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Subjects received 4 placebo subcutaneous (SC) injections (one injection every 4 weeks) for 16 weeks during the double-blind treatment phase.	
Reporting group title	Fulranumab 1 mg
Reporting group description:	
Subjects received 4 SC injections (one injection every 4 weeks) of fulranumab 1 mg during the double-blind treatment phase.	
Reporting group title	Fulranumab 3 mg
Reporting group description:	
Subjects received 4 SC injections (one injection every 4 weeks) of fulranumab 3 mg during the double-blind treatment phase.	

Reporting group values	Placebo	Fulranumab 1 mg	Fulranumab 3 mg
Number of subjects	5	7	5
Title for AgeCategorical			
Units: subjects			
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	2	2	2
From 65 to 84 years	3	5	3
85 years and over	0	0	0
Title for AgeContinuous			
Units: years			
median	70	70	65
full range (min-max)	62 to 78	57 to 79	58 to 72
Title for Gender			
Units: subjects			
Female	3	6	4
Male	2	1	1

Reporting group values	Total		
Number of subjects	17		
Title for AgeCategorical			
Units: subjects			
Children (2-11 years)	0		
Adolescents (12-17 years)	0		
Adults (18-64 years)	6		
From 65 to 84 years	11		
85 years and over	0		
Title for AgeContinuous			
Units: years			
median			
full range (min-max)	-		

Title for Gender Units: subjects			
Female	13		
Male	4		

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Subjects received 4 placebo subcutaneous (SC) injections (one injection every 4 weeks) for 16 weeks during the double-blind treatment phase.	
Reporting group title	Fulranumab 1 mg
Reporting group description:	
Subjects received 4 SC injections (one injection every 4 weeks) of fulranumab 1 mg during the double-blind treatment phase.	
Reporting group title	Fulranumab 3 mg
Reporting group description:	
Subjects received 4 SC injections (one injection every 4 weeks) of fulranumab 3 mg during the double-blind treatment phase.	
Reporting group title	Placebo
Reporting group description:	
Subjects who received placebo in treatment phase were followed for 24 weeks in this period.	
Reporting group title	Fulranumab 1 mg
Reporting group description:	
Subjects who received fulranumab 1 mg in treatment phase were followed for 24 weeks in this period.	
Reporting group title	Fulranumab 3 mg
Reporting group description:	
Subjects who received fulranumab 3 mg in treatment phase were followed for 24 weeks in this period.	
Reporting group title	Placebo
Reporting group description:	
Subjects who received placebo in treatment phase were followed for up to 24 weeks after the last injection of study drug in the limited safety follow-up phase. Subjects who discontinued from the 24-week follow-up phase were asked to enter the LSFU phase.	
Reporting group title	Fulranumab 1 mg
Reporting group description:	
Subjects who received fulranumab 1 mg in treatment phase were followed for up to 24 weeks after the last injection of study drug in this follow-up phase. Subjects who discontinued from the 24- week follow-up phase were asked to enter the LSFU phase.	
Reporting group title	Fulranumab 3 mg
Reporting group description:	
Subjects who received fulranumab 3 mg in treatment phase were followed for up to 24 weeks after the last injection of study drug in this follow-up phase. Subjects who discontinued from the 24- week follow-up phase were asked to enter the LSFU phase.	

Primary: Change from Baseline to DB-LOCF in Patient Global Assessment (PGA) Score

End point title	Change from Baseline to DB-LOCF in Patient Global Assessment (PGA) Score[1]
End point description:	
The PGA is a single item that the patient completes to indicate their perception of their osteoarthritis status, on an 11-point numerical rating scale from 0 (Very Good) to 10 (Very Bad).The intent-to-treat (ITT) analysis set was defined as all randomized subjects who received at least 1 dose of study drug. Here 'n' signifies number of subjects who were evaluable for this outcome measure at specific timepoint. Here "99999" signifies that no subject was evaluable at specified time points Week 13 and 17 (Placebo group); Standard Deviation could not be calculated as only 1 subject was evaluable at specific time points Week 13 and 17 (Fulranumab 1 mg and 3 mg groups).	
End point type	Primary

End point timeframe:

Baseline, Weeks 5, 9, 13, 17 and DB-LOCF

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: Only descriptive statistical analysis was performed for this outcome measure due to the small number of subjects subsequent to premature closure of the study.

End point values	Placebo	Fulranumab 1 mg	Fulranumab 3 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	5	7	5	
Units: units on Scale				
arithmetic mean (standard deviation)				
Baseline (n=5,7,5)	7.8 (± 0.84)	8.1 (± 1.35)	8 (± 1.58)	
Change at Week 5 (n=4,4,3)	-1.3 (± 0.5)	-2 (± 1.41)	-3.3 (± 2.52)	
Change at Week 9 (n=2,2,2)	-1 (± 0)	-3.5 (± 0.71)	-4.5 (± 0.71)	
Change at Week 13 (n=0,1,1)	99999 (± 99999)	-2 (± 99999)	-7 (± 99999)	
Change at Week 17 (n=0,1,1)	99999 (± 99999)	-2 (± 99999)	-7 (± 99999)	
Change at DB-LOCF (n=4,4,3)	-1.3 (± 0.5)	-2.3 (± 1.71)	-4.7 (± 2.08)	

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Treatment-Emergent Adverse Events as a Measure of Safety and Tolerability

End point title	Number of Subjects With Treatment-Emergent Adverse Events as a Measure of Safety and Tolerability[2]

End point description:

An adverse event is any untoward medical event that occurs in a participant administered an investigational product, and it does not necessarily indicate only events with clear causal relationship with the relevant investigational product.

End point type	Primary

End point timeframe:

Baseline Up to 16 Weeks

Notes:

[2] - 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: Only descriptive statistical analysis was performed for this outcome measure due to the small number of subjects subsequent to premature closure of the study.

End point values	Placebo	Fulranumab 1 mg	Fulranumab 3 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	5	7	5	
Units: subjects	2	1	2	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Double-Blind Phase, Last Observation Carried Forward (DB-LOCF) in Western Ontario and McMaster University Arthritis Index (WOMAC) Pain Subscale Score

End point title	Change from Baseline to Double-Blind Phase, Last Observation Carried Forward (DB-LOCF) in Western Ontario and McMaster University Arthritis Index (WOMAC) Pain Subscale Score

End point description:

The WOMAC 3.1 is a multi-dimensional, osteoarthritis (OA) specific self-administered questionnaire using 24 questions with a 48-hour recall that are grouped into 3 subscales (pain, stiffness, and physical function) associated with hip or knee OA. Pain, stiffness, and physical function are rated on a scale of 0-10, where 0=no pain to 10=extreme pain in the WOMAC pain subscale score. The intent-to-treat (ITT) analysis set was defined as all randomized subjects who received at least 1 dose of study drug. Here 'n' signifies number of subjects who were evaluable for this outcome measure at specific timepoint. Here "99999" signifies that no subject was evaluable at specified time points Week 13 and 17 (Placebo group); Standard Deviation (SD) could not be calculated as only 1 subject was evaluable at specific time points Week 13 and 17 (Fulranumab 1 mg and 3 mg groups).

End point type	Secondary

End point timeframe:

Baseline, Weeks 5, 9, 13, 17 and DB-LOCF

End point values	Placebo	Fulranumab 1 mg	Fulranumab 3 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	5	7	5	
Units: units on Scale				
arithmetic mean (standard deviation)				
Baseline (n=5,7,5)	7.24 (± 0.921)	8.03 (± 1.023)	8 (± 1.356)	
Change at Week 5 (n=4,4,3)	-1.35 (± 1.399)	-2.6 (± 1.575)	-3.53 (± 1.137)	
Change at Week 9 (n=2,2,2)	-0.9 (± 1.556)	-2.1 (± 0.424)	-3.1 (± 1.556)	
Change at Week 13 (n=0,1,1)	99999 (± 99999)	-0.2 (± 99999)	-6.8 (± 99999)	
Change at Week 17 (n=0,1,1)	99999 (± 99999)	-2.4 (± 99999)	-6.8 (± 99999)	
Change at DB-LOCF (n=4,4,3)	-1.55 (± 1.427)	-2.7 (± 1.428)	-3.8 (± 2.615)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Double-Blind Phase, Last Observation Carried Forward (DB-LOCF) in Western Ontario and McMaster University Arthritis Index (WOMAC) Physical Function Subscale Score

End point title	Change from Baseline to Double-Blind Phase, Last Observation Carried Forward (DB-LOCF) in Western Ontario and McMaster University Arthritis Index (WOMAC) Physical Function Subscale Score

End point description:

The WOMAC 3.1 is a multi-dimensional, osteoarthritis (OA) specific self-administered questionnaire using 24 questions with a 48-hour recall that are grouped into 3 subscales (pain, stiffness, and physical function) associated with hip or knee OA. Pain, stiffness, and physical function is rated on a scale of 0-10, where 0=no difficulty to 10=extreme difficulty in performing daily activities in the WOMAC physical function subscale score. The ITT analysis set was defined as all randomized subjects who received at least 1 dose of study drug. Here 'n' signifies number of subjects who were evaluable for this outcome measure at specific timepoint. Here "99999" signifies that no subject was evaluable at specified time points Week 13 and 17 (Placebo group); Standard Deviation (SD) could not be calculated as only 1 subject was evaluable at specific time points Week 13 and 17 (Fulranumab 1 mg and 3 mg groups).

End point type	Secondary

End point timeframe:

Baseline, Weeks 5, 9, 13, 17 and DB-LOCF

End point values	Placebo	Fulranumab 1 mg	Fulranumab 3 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	5	7	5	
Units: units on Scale				
arithmetic mean (standard deviation)				
Baseline (n=5,7,5)	7.0588 (± 0.72879)	7.6471 (± 1.35932)	7.8235 (± 1.47646)	
Change at Week 5 (n=4,4,3)	-0.75 (± 0.49536)	-1.6618 (± 1.5896)	-3.4706 (± 1.5328)	
Change at Week 9 (n=2,2,2)	-0.8824 (± 0.33276)	-3.2353 (± 1.58059)	-5.0882 (± 0.12478)	
Change at Week 13 (n=0,1,1)	99999 (± 99999)	-0.7059 (± 99999)	-6.5882 (± 99999)	
Change at Week 17 (n=0,1,1)	99999 (± 99999)	-2.2353 (± 99999)	-6.5882 (± 99999)	
Change at DB-LOCF (n=4,4,3)	-0.9412 (± 0.43492)	-2.4853 (± 1.90451)	-4.6863 (± 2.07667)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline Through Week 20 in Daily Numerical Rating Scale (NRS) Score

End point title	Change From Baseline Through Week 20 in Daily Numerical Rating Scale (NRS) Score

End point description:

The numerical rating scale (NRS) uses an 11-point scale to assess OA pain ranging from 0 to 10 with high scores representing greater symptom severity (0=no pain and 10=pain as bad as you can imagine). The ITT analysis set was defined as all randomized subjects who received at least 1 dose of study drug. Here 'n' signifies number of subjects who were evaluable for this outcome measure at specific timepoint. Here "99999" signifies that no subject was evaluable at specified time points Week 13-16 and 17-20 (Placebo group); Standard Deviation (SD) could not be calculated as only 1 subject was evaluable at specified time points Week 9-12 (Placebo and Fulranumab 1 mg groups), Week 13-16 and 17-20 (Fulranumab 1 mg and 3 mg groups).

End point type	Secondary

End point timeframe:

Baseline, Weeks 1-4, 5-8, 9-12, 13-16 and 17-20

End point values	Placebo	Fulranumab 1 mg	Fulranumab 3 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	5	7	5	
Units: units on Scale				
arithmetic mean (standard deviation)				
Baseline (n=5,7,5)	7.4667 (± 1.30384)	7.5524 (± 1.35508)	8.09 (± 1.01514)	
Change at Week 1-4 (n=5,7,5)	-0.7524 (± 1.02362)	-0.7565 (± 1.02343)	-2.3186 (± 1.938)	
Change at Week 5-8 (n=3,3,3)	-2.2619 (± 1.55566)	-1.0714 (± 0.70991)	-2.4562 (± 0.79051)	
Change at Week 9-12 (n=1,1,2)	-4 (± 99999)	-1.119 (± 99999)	-4.2143 (± 3.83858)	
Change at Week 13-16 (n=0,1,1)	99999 (± 99999)	-1.3333 (± 99999)	-7.5 (± 99999)	
Change at Week 17-20 (n=0,1,1)	99999 (± 99999)	-1.3333 (± 99999)	-7.5 (± 99999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline to DB-LOCF in WOMAC Stiffness Subscale Score

End point title	Change From Baseline to DB-LOCF in WOMAC Stiffness Subscale Score

End point description:

The WOMAC 3.1 is a multi-dimensional, osteoarthritis (OA) specific self-administered questionnaire using 24 questions with a 48-hour recall that are grouped into 3 subscales (pain, stiffness, and physical function) associated with hip or knee OA. Pain, stiffness, and physical function is rated on a scale of 0-10, where 0=no stiffness to 10=extreme stiffness in the WOMAC stiffness subscale score. The ITT analysis set was defined as all randomized subjects who received at least 1 dose of study drug. Here 'n' signifies number of subjects who were evaluable for this outcome measure at specific timepoint. Here "99999" indicates that no subject was evaluable at Week 13 and Week 17 for placebo group. Here"99999" indicates that Standard deviation (SD) was not calculated for Fulranumab 1 mg and 3 mg groups as there was only 1 subject who was evaluable in the arms at a given timepoint.

End point type	Secondary

End point timeframe:

Baseline, Weeks 5, 9, 13, 17 and DB-LOCF

End point values	Placebo	Fulranumab 1 mg	Fulranumab 3 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	5	7	5	
Units: units on Scale				
arithmetic mean (standard deviation)				
Baseline (n=5,7,5)	6.6 (± 1.084)	7.5 (± 1.354)	7.7 (± 1.718)	
Change at Week 5 (n=4,4,3)	-0.63 (± 1.315)	-1.5 (± 1.472)	-3.33 (± 1.528)	
Change at Week 9 (n=2,2,2)	-1 (± 0)	-2 (± 0.707)	-4.5 (± 3.536)	
Change at Week 13 (0,1,1)	99999 (± 99999)	-2 (± 99999)	-7 (± 99999)	
Change at Week 17 (n=0,1,1)	99999 (± 99999)	-4 (± 99999)	-7 (± 99999)	
Change at DB-LOCF (n=4,4,3)	-1.13 (± 1.031)	-2 (± 1.958)	-4 (± 2.646)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline Through Double-blind Phase in Medical Outcomes Study (MOS) Sleep Subscale Scores

End point title	Change from Baseline Through Double-blind Phase in Medical Outcomes Study (MOS) Sleep Subscale Scores

End point description:

The MOS Sleep Scale (acute version) contains 12 items that address aspects of sleep. Six subscale scores may be calculated including: daytime somnolence, sleep disturbances, snoring, shortness of breath or headache upon awaking, adequacy of sleep and amount of sleep plus a summary index of sleep disturbances. A higher score indicates worse sleep in most domains, but the amount of sleep and adequacy of sleep are scored in the opposite direction. The primary subscale of interest in this study is daytime somnolence.

End point type	Secondary

End point timeframe:

Baseline through Double-blind Phase

End point values	Placebo	Fulranumab 1 mg	Fulranumab 3 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[3]	0[4]	0[5]	
Units: units on Scale				
arithmetic mean (standard deviation)	()	()	()	

Notes:

[3] - Analysis of this endpoint was not done because the program was terminated.

[4] - Analysis of this endpoint was not done because the program was terminated.

[5] - Analysis of this endpoint was not done because the program was terminated.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline Through Double Blind Phase in Short-Form-36 Health Survey (SF-36) Subscale Score

End point title	Change From Baseline Through Double Blind Phase in Short-Form-36 Health Survey (SF-36) Subscale Score

End point description:

The Short Form-36 (SF-36) is a self-administered, generic, 36-item questionnaire designed to evaluate 8 domains of functional health and well being: physical and social functioning, physical and emotional role (rolephysical, role-emotional) limitations, bodily pain, general health, vitality, mental health. The score for a section is an average of the individual question scores, which are scaled 0-100 (100=highest level of functioning).

End point type	Secondary

End point timeframe:

Baseline through Double-Blind Phase

End point values	Placebo	Fulranumab 1 mg	Fulranumab 3 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[6]	0[7]	0[8]	
Units: units on Scale				
arithmetic mean (standard deviation)	()	()	()	

Notes:

[6] - Analysis of this endpoint was not done because the program was terminated.

[7] - Analysis of this endpoint was not done because the program was terminated.

[8] - Analysis of this endpoint was not done because the program was terminated.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Additional Analgesics Medication Use Through Double-blind Phase

End point title	Number of Subjects With Additional Analgesics Medication Use Through Double-blind Phase

End point description:

Use other OA pain medication was recorded weekly during the study. The ITT analysis set was defined as all randomized subjects who received at least 1 dose of study drug.

End point type	Secondary

End point timeframe:

Up to 67 weeks

End point values	Placebo	Fulranumab 1 mg	Fulranumab 3 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[9]	0[10]	0[11]	
Units: Subjects				

Notes:

[9] - Analysis of this endpoint was not done because the program was terminated.

[10] - Analysis of this endpoint was not done because the program was terminated.

[11] - Analysis of this endpoint was not done because the program was terminated.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects who Developed Antibodies to Fulranumab

End point title	Number of Subjects who Developed Antibodies to Fulranumab

End point description:

Number of subjects who developed antibodies to fulranumab were assessed.

End point type	Secondary

End point timeframe:

Baseline Up to 67 weeks

End point values	Placebo	Fulranumab 1 mg	Fulranumab 3 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	5	7	5	
Units: subjects	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma Concentrations for Fulranumab

End point title	Plasma Concentrations for Fulranumab

End point description:

Plasma Concentrations for Fulranumab were assessed.

End point type	Secondary

End point timeframe:

Up to 67 weeks

End point values	Placebo	Fulranumab 1 mg	Fulranumab 3 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[12]	0[13]	0[14]	
Units: nanogram/milliliter (ng/mL)				
arithmetic mean (standard deviation)	()	()	()	

Notes:

[12] - Due to less number of subjects treated, only few samples were collected. No PK analyses was done.

[13] - Due to less number of subjects treated, only few samples were collected. No PK analyses was done.

[14] - Due to less number of subjects treated, only few samples were collected. No PK analyses was done.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 67 weeks

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19

Reporting groups

Reporting group title	Placebo

Reporting group description:

Subjects received 4 placebo subcutaneous (SC) injection (one injection every 4 week) for 16 weeks during double blind treatment phase (Period 1) and were followed-up for 24 weeks in follow-up phase (Period 2). Subjects who received placebo and discontinued from the double-blind phase and did not enter the post-treatment follow-up phase were followed-up for up to 24 weeks in LSFU phase (Period 3). Subjects who discontinued from the post-treatment follow-up phase were also followed-up for 24 weeks in LSFU (Period 3).

Reporting group title	Fulranumab 1 mg

Reporting group description:

Subjects received fulranumab 1 mg injection every 4 weeks for 16 weeks during double-blind treatment phase and were followed-up for 24 weeks in follow-up phase (Period 2). Subjects who received Fulranumab 1 mg and discontinued from the double-blind phase and did not enter the post-treatment follow-up phase were followed-up for up to 24 weeks in LSFU phase (Period 3). Subjects who discontinued from the post-treatment follow-up phase were also followed-up for 24 weeks in LSFU (Period 3).

Reporting group title	Fulranumab 3 mg

Reporting group description:

Subjects received fulranumab 3 mg injection every 4 weeks for 16 weeks during double-blind treatment phase and were followed-up for 24 weeks in follow-up phase (Period 2). Subjects who received Fulranumab 3 mg and discontinued from the double-blind phase and did not enter the post-treatment follow-up phase were followed-up for up to 24 weeks in LSFU phase (Period 3). Subjects who discontinued from the post-treatment follow-up phase were also followed-up for 24 weeks in LSFU (Period 3).

Serious adverse events	Placebo	Fulranumab 1 mg	Fulranumab 3 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 5 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Placebo	Fulranumab 1 mg	Fulranumab 3 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 5 (40.00%)	2 / 7 (28.57%)	2 / 5 (40.00%)
Investigations			
Blood Pressure Diastolic Decreased			
subjects affected / exposed	1 / 5 (20.00%)	1 / 7 (14.29%)	2 / 5 (40.00%)
occurrences (all)	1	1	2
Blood Pressure Systolic Decreased			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	2 / 5 (40.00%)
occurrences (all)	0	1	2
Gamma-Glutamyltransferase Increased			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Heart Rate Decreased			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
Carpal Tunnel Syndrome			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Eye disorders			
Retinal Haemorrhage			
subjects affected / exposed	1 / 5 (20.00%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Retinal Vein Occlusion			
subjects affected / exposed	1 / 5 (20.00%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
Sleep Apnoea Syndrome			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			

Muscle Spasms subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	1 / 7 (14.29%) 1	0 / 5 (0.00%) 0
Infections and infestations Conjunctivitis subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	1 / 7 (14.29%) 1	0 / 5 (0.00%) 0
Metabolism and nutrition disorders Vitamin D Deficiency subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 7 (0.00%) 0	1 / 5 (20.00%) 1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
17 February 2015	Amendment INT-1 included the: Response to regulatory authority requests and improve the overall study design and conduct.
18 February 2015	Amendment INT-2 included the following changes: Addition of criteria to be used to alert the IDMC to review events of interest (neurologic) and reference to criteria to be used by the IDMC for decisions related to the further conduct of the study based on prespecified safety based criteria (for joint replacement, neurologic, sympathetic, hepatic and renal events of interest, ie, stopping criteria); clarification to improve performance of assessments and conduct of study and minor errors were noted.
15 July 2015	Amendment INT-3 included the following changes: Changes requested by ethics committees and health authorities to clarify study conduct and/or subject safety; and changes to clarify study conduct.
14 December 2015	Amendment INT-4 included the following changes: Respond to regulatory authority request to prohibit resumption of dosing for subjects who develop joint events of interest; respond to regulatory authority requests to include an assessment for carpal tunnel syndrome (CTS), at each clinic visit during the treatment periods, and at dedicated clinic visits during the safety follow-up period; clarification of what is acceptable as opioid failure in U.S. and Canada as per FDA request. clarification that a medication that is contraindicated will qualify as a failure due to intolerability; and clarify that fasting serum and urine samples are preferred for biomarker analysis; and minor errors were noted.

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.

Due to discontinuation of fulranumab program by sponsor for strategic reasons, the study was closed to enrollment before being fully enrolled. Hence, the study results are limited to descriptive summaries of all safety data and select efficacy data.

Notes: