Clinical trial results:
A Three Arm Double blind, Randomised Multicentre Study to Investigate the Non-Inferiority of a Soft Gel Capsule of Ibuprofen Lipid Formulation (total daily dose 1200 mg) versus a Standard Soft Gel Ibuprofen Capsule (total daily dose 1200 mg and 2400 mg) in the Treatment of Patients with Episodic Knee Arthralgia/Flaring Knee Pain.

Summary

EudraCT number	2014-004254-33
Trial protocol	NL GB
Global end of trial date	10 August 2016

Results information

Result version number	v2 (current)
This version publication date	25 May 2022
First version publication date	18 April 2022
Version creation reason	• Correction of full data set Non-serious adverse event occurrence data updated.

Trial information

Trial identification

Sponsor protocol code	IFH-2014-002

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Infirst+ HEALTHCARE Ltd
Sponsor organisation address	45 Beech Street, London, United Kingdom, EC2Y 8AD
Public contact	Director of Regulatory Affairs, Infirst+ HEALTHCARE Ltd, medinfo@infirst.co.uk
Scientific contact	Director of Regulatory Affairs, Infirst+ HEALTHCARE Ltd, medinfo@infirst.co.uk

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	21 March 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	10 August 2016
Global end of trial reached?	Yes
Global end of trial date	10 August 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine if a 5 day treatment course of 1200 mg/day of ibuprofen in lipid formulation is non inferior to standard ibuprofen capsules (either 1200 mg /day or 2400 mg/day) for the pain subscale of the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) in patients suffering from episodic knee arthralgia/knee flare pain.

Protection of trial subjects:

The study was conducted in accordance with the principles of Good Clinical Practice (GCP), the Declaration of Helsinki and applicable European clinical trials directives and local regulatory requirements.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	02 March 2015
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Netherlands: 135
Country: Number of subjects enrolled	United Kingdom: 329
Worldwide total number of subjects	464
EEA total number of subjects	135

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)	370
From 65 to 84 years	94

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study was conducted at 20 centres in the UK and 7 centres in The Netherlands. Recruitment was stopped early after 464 patients had been randomised into the study, of which 462 patients received study drug. Randomisation ranged between 107 patients (of which 106 patients were treated) at one centre to 1 patient each at others.

Pre-assignment

Screening details:

For patients identified by the Healthcare Professional, the Healthcare Professional eliminated any patient who did not meet the study inclusion/exclusion criteria, which specifically excluded patients with other risk factors for gastric bleeding, in particular in the 60-70 years age group.

Period 1

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

Blinding implementation details:

This was a double-blind study. The IMP, comparator product, and placebo were blinded. They were identical in size and shape and their appearance was that of soft, white gelatin capsules.

Arms

Are arms mutually exclusive?	Yes
Arm title	Lipid 1200 group

Arm description:

5-day treatment course of 200 mg soft gel capsule of ibuprofen lipid formulation.

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

Dosage and administration details:

5-day treatment course of 200 mg soft gel capsule of ibuprofen lipid formulation (2 capsules to be taken 3 times a day, 6 hours apart [morning, afternoon, and evening]).

Arm title	Soft Gel 1200 group

Arm description:

5-day treatment course of one 400 mg soft gel capsule ibuprofen plus placebo capsule.

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

Dosage and administration details:

5-day treatment course of one 400 mg soft gel capsule ibuprofen plus placebo capsule (1 of each - total 2 capsules - to be taken 3 times a day, 6 hours apart [morning, afternoon, and evening]).

Investigational medicinal product name	Ibuprofen
Investigational medicinal product code	
Other name	

Pharmaceutical forms	Capsule, soft
Routes of administration	Oral use

Dosage and administration details:

5-day treatment course of one 400 mg soft gel capsule ibuprofen plus placebo capsule (1 of each - total 2 capsules - to be taken 3 times a day, 6 hours apart [morning, afternoon, and evening]).

Arm title	Soft Gel 2400 group

Arm description:

5-day treatment course of 400 mg soft gel capsule ibuprofen.

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

Dosage and administration details:

5-day treatment course of 400 mg soft gel capsule ibuprofen (2 capsules to be taken 3 times a day, 6 hours apart [morning, afternoon, and evening]).

Number of subjects in period 1	Lipid 1200 group	Soft Gel 1200 group	Soft Gel 2400 group
Started	150	155	159
Completed	142	149	150
Not completed	8	6	9
Adverse event, non-fatal	2	2	5
Other	2	-	-
Lost to follow-up	2	-	-
most frequent- patients attended the clinic early	-	4	4
Protocol deviation	2	-	-

Baseline characteristics

Reporting groups	
Reporting group title	Lipid 1200 group
Reporting group description:	
5-day treatment course of 200 mg soft gel capsule of ibuprofen lipid formulation.	
Reporting group title	Soft Gel 1200 group
Reporting group description:	
5-day treatment course of one 400 mg soft gel capsule ibuprofen plus placebo capsule.	
Reporting group title	Soft Gel 2400 group
Reporting group description:	
5-day treatment course of 400 mg soft gel capsule ibuprofen.	

Reporting group values	Lipid 1200 group	Soft Gel 1200 group	Soft Gel 2400 group
Number of subjects	150	155	159
Age categorical Units: Subjects			
<65 years	114	130	124
≥65 years	34	25	35
Not recorded	2	0	0
Gender categorical Units: Subjects			
Female	61	64	65
Male	87	91	94
Not recorded	2	0	0
Ethnicity Units: Subjects			
Asian	5	5	3
Black	6	5	2
White	131	142	152
Other	6	3	2
Not recorded	2	0	0
Index knee Units: Subjects			
Left	75	84	88
Right	73	71	71
Not recorded	2	0	0
Number of patients with at least 1 medical history Units: Subjects			
Number of patients with at least 1 medical history	141	147	148
Number of patients with no medical history	7	8	11
Not recorded	2	0	0
Surgical and medical procedures			
Surgical and medical procedures (N/group)*: - Appendicectomy: 4 / 5 / 4 - Meniscus removal: 4 / 4 / 3 - Hysterectomy: 4 / 3 / 3			

* Medical History Reported for >2% of Patients. Subjects can appear in more than preferred term.			
Units: Subjects			
Surgical and medical procedures	35	36	40
No surgical and medical procedures	113	119	119
Not recorded	2	0	0
Gastrointestinal disorders			
Gastrointestinal disorders (N/group)*: - Dyspepsia: 10 / 13 / 14 - Gastrooesophageal reflux disease: 6 / 5 / 11 - Irritable bowel syndrome: 4 / 6 / 4 * Medical History Reported for >2% of Patients. Subjects can appear in more than preferred term.			
Units: Subjects			
Gastrointestinal disorders	31	37	38
No gastrointestinal disorders	117	118	121
Not recorded	2	0	0
Vascular disorders			
Vascular disorders (N/group)*: - Hypertension: 28 / 30 / 26 - Essential hypertension: 4 / 5 / 4 * Medical History Reported for >2% of Patients. Subjects can appear in more than preferred term.			
Units: Subjects			
Vascular disorders	35	38	33
No vascular disorders	113	117	126
Not recorded	2	0	0
Metabolism and nutrition disorders			
Metabolism and nutrition disorders (N/group)*: - Type 2 diabetes mellitus: 11 / 17 / 14 - Hypercholesterolaemia: 9 / 16 / 12			
Units: Subjects			
Metabolism and nutrition disorders	21	37	29
No metabolism and nutrition disorders	127	118	130
Not recorded	2	0	0
Respiratory, thoracic and mediastinal disorders			
Respiratory, thoracic and mediastinal disorders (N/group)*: - Asthma: 10 / 12 / 12 * Medical History Reported for >2% of Patients.			
Units: Subjects			
Respiratory, thoracic and mediastinal disorders	20	18	19
No respiratory, thoracic and mediastinal disorders	128	137	140
Not recorded	2	0	0
Skin and subcutaneous tissue disorders			
Skin and subcutaneous tissue disorders (N/group)*: - Eczema: 3 / 5 / 3 * Medical History Reported for >2% of Patients.			
Units: Subjects			
Skin and subcutaneous tissue disorders	25	20	10
No skin and subcutaneous tissue disorders	123	135	149
Not recorded	2	0	0

Investigations			
Investigations (N/group)*: - Arthroscopy: 11 / 9 / 7 - Blood cholesterol increased: 7 / 3 / 6 * Medical History Reported for >2% of Patients. Subjects can appear in more than preferred term.			
Units: Subjects			
Investigations	19	16	18
No Investigations	129	139	141
Not recorded	2	0	0
Injury, poisoning and procedural complications			
Injury, poisoning and procedural complications (N/group)*: - Meniscus injury: 4 / 4 / 3 * Medical History Reported for >2% of Patients.			
Units: Subjects			
Injury, poisoning and procedural complications	20	18	14
No injury, poisoning and procedural complications	128	137	145
Not recorded	2	0	0
Infections and infestations			
Units: Subjects			
Infections and infestations	16	15	15
No infections and infestations	132	140	144
Not recorded	2	0	0
Psychiatric disorders			
Psychiatric disorders (N/group)*: - Depression: 11 / 6 / 10 * Medical History Reported for >2% of Patients.			
Units: Subjects			
Psychiatric disorders	18	9	13
No psychiatric disorders	130	146	146
Not recorded	2	0	0
Nervous system disorders			
Units: Subjects			
Nervous system disorders	14	10	13
No nervous system disorders	134	145	146
Not recorded	2	0	0
Reproductive system and breast disorders			
Reproductive system and breast disorders (N/group)*: - Erectile dysfunction: 3 / 4 / 5 * Medical History Reported for >2% of Patients.			
Units: Subjects			
Reproductive system and breast disorders	7	15	13
No reproductive system and breast disorders	141	140	146
Not recorded	2	0	0
Immune system disorders			
Immune system disorders (N/group)*: - Seasonal allergy: 4 / 2 / 8			

* Medical History Reported for >2% of Patients.			
Units: Subjects			
Immune system disorders	5	3	14
No immune system disorders	143	152	145
Not recorded	2	0	0
Endocrine disorders			
Endocrine disorders (N/group)*: - Hypothyroidism: 7 / 6 / 4 * Medical History Reported for >2% of Patients.			
Units: Subjects			
Endocrine disorders	9	6	6
No endocrine disorders	139	149	153
Not recorded	2	0	0
Eye disorders Units: Subjects			
Eye disorders	9	7	4
No eye disorders	139	148	155
Not recorded	2	0	0
Neoplasms benign, malignant and unspecified (incl. cysts and polyps) Units: Subjects			
Neoplasms benign, malignant and unspecified	7	4	9
No neoplasms benign, malignant and unspecified	141	151	150
Not recorded	2	0	0
Cardiac disorders Units: Subjects			
Cardiac disorders	8	5	6
No cardiac disorders	140	150	153
Not recorded	2	0	0
Ear and labyrinth disorders Units: Subjects			
Ear and labyrinth disorders	5	6	8
No ear and labyrinth disorders	143	149	151
Not recorded	2	0	0
General disorders and administration site conditions Units: Subjects			
General disorders and admin. site conditiions	3	2	6
No general disorders and admin. site conditiions	145	153	153
Not recorded	2	0	0
Renal and urinary disorders Units: Subjects			
Renal and urinary disorders	1	4	6
No renal and urinary disorders	147	151	153
Not recorded	2	0	0
Musculoskeletal and connective tissue disorders			
Musculoskeletal and connective tissue disorders (N/group)*: - Osteoarthritis: 59 / 63 / 65 - Arthralgia: 38 / 40 / 44			

- Back pain: 9 / 7 / 12 * Medical History Reported for >2% of Patients. Subjects can appear in more than preferred term.			
Units: Subjects			
Musculoskeletal and connective tissue disorders	98	112	114
No musculoskeletal and connective tissue disorders	50	43	45
Not recorded	2	0	0
WOMAC total score			
WOMAC: Western Ontario and McMaster Universities Osteoarthritis Index WOMAC scores range from 0 (best outcome) to 10 (worst outcome). Number of patients analysed per group was 144, 152 and 154, respectively.			
Units: Score			
arithmetic mean	5.44	5.49	5.45
standard deviation	± 1.74	± 1.62	± 1.70
WOMAC stiffness score			
WOMAC: Western Ontario and McMaster Universities Osteoarthritis Index WOMAC scores range from 0 (best outcome) to 10 (worst outcome). Number of patients analysed per group was 144, 152 and 154, respectively.			
Units: Score			
arithmetic mean	6.38	6.06	6.15
standard deviation	± 1.91	± 1.96	± 2.03
WOMAC function score			
WOMAC: Western Ontario and McMaster Universities Osteoarthritis Index WOMAC scores range from 0 (best outcome) to 10 (worst outcome). Number of patients analysed per group was 144, 152 and 154, respectively.			
Units: Score			
arithmetic mean	5.25	5.39	5.32
standard deviation	± 1.92	± 1.71	± 1.82
WOMAC pain scale score			
WOMAC scores range from 0 (best outcome) to 10 (worst outcome). Number of patients analysed per group was 145, 152 and 155, respectively.			
Units: Score			
arithmetic mean	5.72	5.60	5.61
standard deviation	± 1.64	± 1.69	± 1.64
GSRS total score			
GSRS: Gastrointestinal Symptom Rating Scale Number of patients analysed per group was 145, 149 and 154, respectively.			
Units: Score			
arithmetic mean	1.30	1.36	1.34
standard deviation	± 0.53	± 0.55	± 0.47
GSRS Dimension Score - Abdominal pain score			
GSRS: Gastrointestinal Symptom Rating Scale Number of patients analysed per group was 145, 151 and 155, respectively.			
Units: Score			
arithmetic mean	1.28	1.26	1.26
standard deviation	± 0.58	± 0.52	± 0.52
GSRS Dimension Score - Constipation score			
GSRS: Gastrointestinal Symptom Rating Scale			

Number of patients analysed per group was 145, 151 and 155, respectively.			
Units: Score			
arithmetic mean	1.26	1.36	1.26
standard deviation	± 0.63	± 0.78	± 0.56
GSRS Dimension Score - Diarrhoea score			
GSRS: Gastrointestinal Symptom Rating Scale Number of patients analysed per group was 145, 151 and 154, respectively.			
Units: Score			
arithmetic mean	1.21	1.30	1.31
standard deviation	± 0.69	± 0.64	± 0.66
GSRS Dimension Score - Indigestion score			
GSRS: Gastrointestinal Symptom Rating Scale Number of patients analysed per group was 145, 150 and 155, respectively.			
Units: Score			
arithmetic mean	1.44	1.53	1.48
standard deviation	± 0.76	± 0.80	± 0.69
GSRS Dimension Score - Reflux score			
GSRS: Gastrointestinal Symptom Rating Scale Number of patients analysed per group was 145, 150 and 155, respectively.			
Units: Score			
arithmetic mean	1.21	1.25	1.32
standard deviation	± 0.72	± 0.76	± 0.63
NRS score - Pain			
NRS: Numerical Rating Score Pain scores range from 0 (best outcome) to 10 (worst outcome). Number of patients analysed per group was 145, 152 and 155, respectively.			
Units: Score			
arithmetic mean	7.0	6.8	6.7
standard deviation	± 1.1	± 1.2	± 1.2
NRS score - Stiffness			
NRS: Numerical Rating Score Stiffness scores range from 0 (best outcome) to 10 (worst outcome). Number of patients analysed per group was 145, 152 and 155, respectively.			
Units: Score			
arithmetic mean	6.6	6.1	6.2
standard deviation	± 2.0	± 2.3	± 2.2
NRS score - Patient-nominated activity performance			
NRS: Numerical Rating Score Patient-nominated activity performance scores range from 0 (best outcome) to 10 (worst outcome). Number of patients analysed per group was 145, 152 and 155, respectively.			
Units: Score			
arithmetic mean	6.9	6.8	6.8
standard deviation	± 1.8	± 1.6	± 1.8
NRS score - Swelling			
NRS: Numerical Rating Score Swelling scores range from 0 (best outcome) to 10 (worst outcome). Number of patients analysed per group was 145, 152 and 155, respectively.			

Units: Score			
arithmetic mean	3.9	3.6	3.9
standard deviation	± 3.0	± 2.7	± 2.9
Global Assessment NRS			
NRS: Numerical Rating Score Global assessment scores range from 0 (very well) to 10 (very poorly). Number of patients analysed per group was 145, 149 and 155, respectively.			
Units: Score			
arithmetic mean	6.5	6.5	6.4
standard deviation	± 1.6	± 1.7	± 1.7

Reporting group values	Total		
Number of subjects	464		
Age categorical Units: Subjects			
<65 years	368		
≥65 years	94		
Not recorded	2		
Gender categorical Units: Subjects			
Female	190		
Male	272		
Not recorded	2		
Ethnicity Units: Subjects			
Asian	13		
Black	13		
White	425		
Other	11		
Not recorded	2		
Index knee Units: Subjects			
Left	247		
Right	215		
Not recorded	2		
Number of patients with at least 1 medical history Units: Subjects			
Number of patients with at least 1 medical history	436		
Number of patients with no medical history	26		
Not recorded	2		
Surgical and medical procedures			
Surgical and medical procedures (N/group)*: - Appendicectomy: 4 / 5 / 4 - Meniscus removal: 4 / 4 / 3 - Hysterectomy: 4 / 3 / 3 * Medical History Reported for >2% of Patients. Subjects can appear in more than preferred term.			
Units: Subjects			
Surgical and medical procedures	111		
No surgical and medical procedures	351		
Not recorded	2		

Gastrointestinal disorders			
Gastrointestinal disorders (N/group)*: - Dyspepsia: 10 / 13 / 14 - Gastrooesophageal reflux disease: 6 / 5 / 11 - Irritable bowel syndrome: 4 / 6 / 4 * Medical History Reported for >2% of Patients. Subjects can appear in more than preferred term.			
Units: Subjects			
Gastrointestinal disorders	106		
No gastrointestinal disorders	356		
Not recorded	2		
Vascular disorders			
Vascular disorders (N/group)*: - Hypertension: 28 / 30 / 26 - Essential hypertension: 4 / 5 / 4 * Medical History Reported for >2% of Patients. Subjects can appear in more than preferred term.			
Units: Subjects			
Vascular disorders	106		
No vascular disorders	356		
Not recorded	2		
Metabolism and nutrition disorders			
Metabolism and nutrition disorders (N/group)*: - Type 2 diabetes mellitus: 11 / 17 / 14 - Hypercholesterolaemia: 9 / 16 / 12			
Units: Subjects			
Metabolism and nutrition disorders	87		
No metabolism and nutrition disorders	375		
Not recorded	2		
Respiratory, thoracic and mediastinal disorders			
Respiratory, thoracic and mediastinal disorders (N/group)*: - Asthma: 10 / 12 / 12 * Medical History Reported for >2% of Patients.			
Units: Subjects			
Respiratory, thoracic and mediastinal disorders	57		
No respiratory, thoracic and mediastinal disorders	405		
Not recorded	2		
Skin and subcutaneous tissue disorders			
Skin and subcutaneous tissue disorders (N/group)*: - Eczema: 3 / 5 / 3 * Medical History Reported for >2% of Patients.			
Units: Subjects			
Skin and subcutaneous tissue disorders	55		
No skin and subcutaneous tissue disorders	407		
Not recorded	2		
Investigations			
Investigations (N/group)*: - Arthroscopy: 11 / 9 / 7 - Blood cholesterol increased: 7 / 3 / 6 * Medical History Reported for >2% of Patients. Subjects can appear in more than preferred term.			

Units: Subjects			
Investigations	53		
No Investigations	409		
Not recorded	2		
Injury, poisoning and procedural complications			
Injury, poisoning and procedural complications (N/group)*: - Meniscus injury: 4 / 4 / 3 * Medical History Reported for >2% of Patients.			
Units: Subjects			
Injury, poisoning and procedural complications	52		
No injury, poisoning and procedural complications	410		
Not recorded	2		
Infections and infestations			
Units: Subjects			
Infections and infestations	46		
No infections and infestations	416		
Not recorded	2		
Psychiatric disorders			
Psychiatric disorders (N/group)*: - Depression: 11 / 6 / 10 * Medical History Reported for >2% of Patients.			
Units: Subjects			
Psychiatric disorders	40		
No psychiatric disorders	422		
Not recorded	2		
Nervous system disorders			
Units: Subjects			
Nervous system disorders	37		
No nervous system disorders	425		
Not recorded	2		
Reproductive system and breast disorders			
Reproductive system and breast disorders (N/group)*: - Erectile dysfunction: 3 / 4 / 5 * Medical History Reported for >2% of Patients.			
Units: Subjects			
Reproductive system and breast disorders	35		
No reproductive system and breast disorders	427		
Not recorded	2		
Immune system disorders			
Immune system disorders (N/group)*: - Seasonal allergy: 4 / 2 / 8 * Medical History Reported for >2% of Patients.			
Units: Subjects			
Immune system disorders	22		
No immune system disorders	440		
Not recorded	2		

Endocrine disorders			
Endocrine disorders (N/group)*: - Hypothyroidism: 7 / 6 / 4 * Medical History Reported for >2% of Patients.			
Units: Subjects			
Endocrine disorders	21		
No endocrine disorders	441		
Not recorded	2		
Eye disorders Units: Subjects			
Eye disorders	20		
No eye disorders	442		
Not recorded	2		
Neoplasms benign, malignant and unspecified (incl. cysts and polyps) Units: Subjects			
Neoplasms benign, malignant and unspecified	20		
No neoplasms benign, malignant and unspecified	442		
Not recorded	2		
Cardiac disorders Units: Subjects			
Cardiac disorders	19		
No cardiac disorders	443		
Not recorded	2		
Ear and labyrinth disorders Units: Subjects			
Ear and labyrinth disorders	19		
No ear and labyrinth disorders	443		
Not recorded	2		
General disorders and administration site conditions Units: Subjects			
General disorders and admin. site conditiions	11		
No general disorders and admin. site conditiions	451		
Not recorded	2		
Renal and urinary disorders Units: Subjects			
Renal and urinary disorders	11		
No renal and urinary disorders	451		
Not recorded	2		
Musculoskeletal and connective tissue disorders			
Musculoskeletal and connective tissue disorders (N/group)*: - Osteoarthritis: 59 / 63 / 65 - Arthralgia: 38 / 40 / 44 - Back pain: 9 / 7 / 12 * Medical History Reported for >2% of Patients. Subjects can appear in more than preferred term.			
Units: Subjects			
Musculoskeletal and connective tissue disorders	324		

No musculoskeletal and connective tissue disorders	138		
Not recorded	2		

WOMAC total score			
WOMAC: Western Ontario and McMaster Universities Osteoarthritis Index WOMAC scores range from 0 (best outcome) to 10 (worst outcome). Number of patients analysed per group was 144, 152 and 154, respectively.			
Units: Score arithmetic mean standard deviation	- -		
WOMAC stiffness score			
WOMAC: Western Ontario and McMaster Universities Osteoarthritis Index WOMAC scores range from 0 (best outcome) to 10 (worst outcome). Number of patients analysed per group was 144, 152 and 154, respectively.			
Units: Score arithmetic mean standard deviation	- -		
WOMAC function score			
WOMAC: Western Ontario and McMaster Universities Osteoarthritis Index WOMAC scores range from 0 (best outcome) to 10 (worst outcome). Number of patients analysed per group was 144, 152 and 154, respectively.			
Units: Score arithmetic mean standard deviation	- -		
WOMAC pain scale score			
WOMAC scores range from 0 (best outcome) to 10 (worst outcome). Number of patients analysed per group was 145, 152 and 155, respectively.			
Units: Score arithmetic mean standard deviation	- -		
GSRS total score			
GSRS: Gastrointestinal Symptom Rating Scale Number of patients analysed per group was 145, 149 and 154, respectively.			
Units: Score arithmetic mean standard deviation	- -		
GSRS Dimension Score - Abdominal pain score			
GSRS: Gastrointestinal Symptom Rating Scale Number of patients analysed per group was 145, 151 and 155, respectively.			
Units: Score arithmetic mean standard deviation	- -		
GSRS Dimension Score - Constipation score			
GSRS: Gastrointestinal Symptom Rating Scale Number of patients analysed per group was 145, 151 and 155, respectively.			
Units: Score arithmetic mean standard deviation	- -		
GSRS Dimension Score - Diarrhoea			

score			
GSRS: Gastrointestinal Symptom Rating Scale Number of patients analysed per group was 145, 151 and 154, respectively.			
Units: Score arithmetic mean standard deviation	- -		
GSRS Dimension Score - Indigestion score			
GSRS: Gastrointestinal Symptom Rating Scale Number of patients analysed per group was 145, 150 and 155, respectively.			
Units: Score arithmetic mean standard deviation	- -		
GSRS Dimension Score - Reflux score			
GSRS: Gastrointestinal Symptom Rating Scale Number of patients analysed per group was 145, 150 and 155, respectively.			
Units: Score arithmetic mean standard deviation	- -		
NRS score - Pain			
NRS: Numerical Rating Score Pain scores range from 0 (best outcome) to 10 (worst outcome). Number of patients analysed per group was 145, 152 and 155, respectively.			
Units: Score arithmetic mean standard deviation	- -		
NRS score - Stiffness			
NRS: Numerical Rating Score Stiffness scores range from 0 (best outcome) to 10 (worst outcome). Number of patients analysed per group was 145, 152 and 155, respectively.			
Units: Score arithmetic mean standard deviation	- -		
NRS score - Patient-nominated activity performance			
NRS: Numerical Rating Score Patient-nominated activity performance scores range from 0 (best outcome) to 10 (worst outcome). Number of patients analysed per group was 145, 152 and 155, respectively.			
Units: Score arithmetic mean standard deviation	- -		
NRS score - Swelling			
NRS: Numerical Rating Score Swelling scores range from 0 (best outcome) to 10 (worst outcome). Number of patients analysed per group was 145, 152 and 155, respectively.			
Units: Score arithmetic mean standard deviation	- -		
Global Assessment NRS			
NRS: Numerical Rating Score			

Global assessment scores range from 0 (very well) to 10 (very poorly). Number of patients analysed per group was 145, 149 and 155, respectively.			
Units: Score arithmetic mean standard deviation	- 		

End points

End points reporting groups	
Reporting group title	Lipid 1200 group
Reporting group description:	
5-day treatment course of 200 mg soft gel capsule of ibuprofen lipid formulation.	
Reporting group title	Soft Gel 1200 group
Reporting group description:	
5-day treatment course of one 400 mg soft gel capsule ibuprofen plus placebo capsule.	
Reporting group title	Soft Gel 2400 group
Reporting group description:	
5-day treatment course of 400 mg soft gel capsule ibuprofen.	

Primary: Change from baseline after 5 days of treatment in the WOMAC pain scale score	
End point title	Change from baseline after 5 days of treatment in the WOMAC pain scale score
End point description:	
WOMAC: Western Ontario and McMaster Universities Osteoarthritis Index	
End point type	Primary
End point timeframe:	
Day 5	

End point values	Lipid 1200 group	Soft Gel 1200 group	Soft Gel 2400 group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	145	152	155	
Units: Change from baseline				
least squares mean (confidence interval 95%)	-2.42 (-2.76 to -2.09)	-2.16 (-2.49 to -1.84)	-2.61 (-2.94 to -2.29)	

Statistical analyses

Statistical analysis title	Lipid 1200 vs Soft Gel 1200
Comparison groups	Soft Gel 1200 group v Lipid 1200 group
Number of subjects included in analysis	297
Analysis specification	Pre-specified
Analysis type	superiority[1]
P-value	= 0.2327
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.26

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.69
upper limit	0.17
Variability estimate	Standard error of the mean
Dispersion value	0.22

Notes:

[1] - n in analysis = 297 (Lipid 1200=145, soft gel 1200=152)

Statistical analysis title	Lipid 1200 vs Soft Gel 2400
Comparison groups	Lipid 1200 group v Soft Gel 2400 group
Number of subjects included in analysis	300
Analysis specification	Pre-specified
Analysis type	superiority[2]
P-value	= 0.3799
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	0.19
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.24
upper limit	0.62
Variability estimate	Standard error of the mean
Dispersion value	0.22

Notes:

[2] - n in analysis = 300 (Lipid 1200=145, soft gel 2400=155)

Secondary: Change from baseline after 5 days of treatment in the GSRS total score

End point title	Change from baseline after 5 days of treatment in the GSRS total score

End point description:

GSRS: Gastrointestinal Symptom Rating Scale

End point type	Secondary

End point timeframe:

Day 5

End point values	Lipid 1200 group	Soft Gel 1200 group	Soft Gel 2400 group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	145	152[3]	155[4]	
Units: Change from baseline				
least squares mean (confidence interval 95%)	0.08 (-0.00 to 0.16)	0.05 (-0.03 to 0.14)	0.13 (0.05 to 0.21)	

Notes:

[3] - 149 included in analysis

[4] - 154 included in analysis

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline after 5 days of treatment in the WOMAC total, stiffness, and function scale scores

End point title	Change from baseline after 5 days of treatment in the WOMAC total, stiffness, and function scale scores

End point description:

WOMAC: Western Ontario and McMaster Universities Osteoarthritis Index

End point type	Secondary

End point timeframe:

Day 5

End point values	Lipid 1200 group	Soft Gel 1200 group	Soft Gel 2400 group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	145[5]	152[6]	155[7]	
Units: Change from baseline				
least squares mean (confidence interval 95%)				
Total score	-2.32 (-2.63 to -2.01)	-2.18 (-2.49 to -1.87)	-2.53 (-2.84 to -2.23)	
Stiffness score	-2.78 (-3.16 to -2.40)	-2.38 (-2.75 to -2.02)	-2.80 (-3.17 to -2.43)	
Function score	-2.26 (-2.57 to -1.95)	-2.14 (-2.44 to -1.83)	-2.46 (-2.77 to -2.16)	

Notes:

[5] - Number of patients in analysis: Total score =144, Stiffness score =144, Function score =145

[6] - Number of patients in analysis: Total score=149, Stiffness score=152, Function score=149

[7] - Number of patients in analysis: Total score=154, Stiffness score=154, Function score=155

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline after 5 days of treatment in the GSRS dimension scores

End point title	Change from baseline after 5 days of treatment in the GSRS dimension scores

End point description:

Change from baseline after 5 days of treatment in the GSRS dimension scores of diarrhoea, indigestion, constipation, abdominal pain and reflux syndromes.

GSRS: Gastrointestinal Symptom Rating Scale

End point type	Secondary

End point timeframe:

Day 5

End point values	Lipid 1200 group	Soft Gel 1200 group	Soft Gel 2400 group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	145	152[8]	155[9]	
Units: Change from baseline				
least squares mean (confidence interval 95%)				
Abdominal pain score	0.11 (0.00 to 0.22)	0.14 (0.04 to 0.25)	0.18 (0.08 to 0.29)	
Constipation score	0.11 (0.00 to 0.22)	0.06 (-0.05 to 0.17)	0.06 (-0.04 to 0.17)	
Diarrhoea score	0.08 (-0.04 to 0.19)	0.01 (-0.11 to 0.12)	0.12 (0.01 to 0.23)	
Indigestion score	0.03 (-0.09 to 0.15)	0.02 (-0.09 to 0.14)	0.12 (0.00 to 0.23)	
Reflux score	0.07 (-0.08 to 0.21)	0.08 (-0.06 to 0.23)	0.21 (0.07 to 0.36)	

Notes:

[8] - n in analysis: Abdominal=151, Constipation=151, Diarrhoea=151, Indigestion=150, Reflux=150

[9] - n in analysis: Abdominal=155, Constipation=155, Diarrhoea=154, Indigestion=155, Reflux=155

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline after each day of study treatment in the NRS scores of pain, stiffness, patient-nominated activity performance and swelling

End point title	Change from baseline after each day of study treatment in the NRS scores of pain, stiffness, patient-nominated activity performance and swelling

End point description:

Change from baseline after each day of study treatment in the NRS scores of pain, stiffness, patient-nominated activity performance and swelling.

End point type	Secondary

End point timeframe:

Day 6

End point values	Lipid 1200 group	Soft Gel 1200 group	Soft Gel 2400 group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	145	152	155	
Units: Change from baseline				
least squares mean (confidence interval 95%)				
Pain	-3.4 (-3.8 to -3.0)	-3.1 (-3.4 to -2.7)	-3.6 (-3.9 to -3.2)	

Stiffness	-3.2 (-3.6 to -2.8)	-3.0 (-3.4 to -2.6)	-3.4 (-3.8 to -3.1)	
Patient-Nominated Activity	-3.3 (-3.7 to -2.9)	-3.0 (-3.4 to -2.6)	-3.5 (-3.9 to -3.1)	
Swelling	-1.7 (-2.0 to -1.3)	-1.2 (-1.5 to -0.9)	-1.7 (-2.0 to -1.4)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in Global Assessment NRS after 5 days of treatment

End point title	Change from baseline in Global Assessment NRS after 5 days of treatment
End point description: NRS: Numerical Rating Score	
End point type	Secondary
End point timeframe: Day 5	

End point values	Lipid 1200 group	Soft Gel 1200 group	Soft Gel 2400 group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	145	152[10]	155	
Units: Change from baseline				
least squares mean (confidence interval 95%)	-2.8 (-3.2 to -2.4)	-2.6 (-3.0 to -2.3)	-3.1 (-3.5 to -2.7)	

Notes:

[10] - 149 included in analysis

Statistical analyses

No statistical analyses for this end point

Secondary: OMERACT-OARSI response after 5 days of treatment

End point title	OMERACT-OARSI response after 5 days of treatment
End point description: OMERACT: Outcome Measures in Rheumatology OARSI: Osteoarthritis Research Society International Response defined as improvement in WOMAC pain or function of ≥ 50% with change of ≥ 2, or improvement in at least 2 of: 1) pain ≥ 20% with change of ≥ 1, 2) function ≥ 20% with change of ≥ 1, 3) global assessment ≥ 20% with change of ≥ 1.	
End point type	Secondary
End point timeframe: Day 5	

End point values	Lipid 1200 group	Soft Gel 1200 group	Soft Gel 2400 group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	145	152	155	
Units: Percentage of responders				
number (confidence interval 95%)	73.1 (65.1 to 80.1)	69.7 (61.8 to 76.9)	76.1 (68.6 to 82.6)	

Statistical analyses

No statistical analyses for this end point

Secondary: Knee flare category

End point title	Knee flare category

End point description:

Percentage of responders after 5 days of treatment. Knee Flare Response Categories were: 'Fully controlled' , 'Under control' , 'Partially controlled' , 'Not under control'.
Response defined as knee flare category of 'Fully controlled' or 'Under control'.

End point type	Secondary

End point timeframe:

Day 5

End point values	Lipid 1200 group	Soft Gel 1200 group	Soft Gel 2400 group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	145	152	155	
Units: Percentage of responders				
number (confidence interval 95%)	55.9 (47.4 to 64.1)	49.3 (41.1 to 57.6)	59.4 (51.2 to 67.2)	

Statistical analyses

No statistical analyses for this end point

Secondary: Resolution of knee flare

End point title	Resolution of knee flare

End point description:

Resolution of knee flare was a calculated term defined as the first occurrence of 2 consecutive days with pain NRS score <4, or knee flare under control at end of the course and pain NRS score <4

End point type	Secondary

End point timeframe:

Day 5

End point values	Lipid 1200 group	Soft Gel 1200 group	Soft Gel 2400 group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	145	152	155	
Units: Percentage of patients with resolution				
number (not applicable)	44.8	41.4	53.5	

Statistical analyses

No statistical analyses for this end point

Secondary: Summary of Adverse Events

End point title	Summary of Adverse Events

End point description:

End point type	Secondary

End point timeframe:

Day 5

End point values	Lipid 1200 group	Soft Gel 1200 group	Soft Gel 2400 group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	148	155	159	
Units: Subjects				
number (not applicable)				
Patients with at least 1 AE	54	53	65	
Worst severity of AE - Mild	38	33	45	
Worst severity of AE - Moderate	14	18	18	
Worst severity of AE - Severe	2	2	2	
Patients with at least 1 drug-related AE	28	37	50	
Patients with at least 1 AE leading to discont.	2	2	5	
Patients with at least 1 SAE	0	0	1	

Statistical analyses

No statistical analyses for this end point

Secondary: Vital Signs at Baseline and End of Treatment

End point title	Vital Signs at Baseline and End of Treatment

End point description:

SBP = Systolic blood pressure
DBP = Diastolic blood pressure

BMI = Body mass index

End point type	Secondary

End point timeframe:

Day 5

End point values	Lipid 1200 group	Soft Gel 1200 group	Soft Gel 2400 group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	148	155	159	
Units: Specified for each category				
arithmetic mean (standard deviation)				
SBP-baseline (mmHg)	133.6 (± 15.4)	132.1 (± 15.3)	134.3 (± 16.3)	
SBP-change from baseline (mmHg)	-0.7 (± 12.2)	1.6 (± 11.1)	1.3 (± 11.6)	
DBP-baseline (mmHg)	78.5 (± 9.8)	77.9 (± 10.5)	78.9 (± 9.7)	
DBP-change from baseline (mmHg)	0.4 (± 7.0)	0.4 (± 8.3)	1.0 (± 8.1)	
Pulse Rate-baseline (bpm)	71.2 (± 10.2)	70.1 (± 10.3)	72.4 (± 10.0)	
Pulse Rate-change from baseline (bpm)	-0.2 (± 8.2)	-0.8 (± 8.6)	-1.5 (± 8.4)	
BMI-baseline (kg/sq.metre)	28.39 (± 4.68)	28.66 (± 4.53)	28.60 (± 4.54)	
BMI-change from baseline (kg/sq.metre))	0.13 (± 0.33)	0.09 (± 0.51)	0.06 (± 0.31)	
Temperature-baseline (degrees C)	36.52 (± 0.37)	36.44 (± 0.40)	36.51 (± 0.39)	
Temperature-change from baseline (degrees C)	-0.09 (± 0.41)	-0.02 (± 0.39)	-0.06 (± 0.40)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

The Investigator instructed the patient to report any new AE that occurred within 30 days of completing their last study treatment, for possible assessment and follow-up.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18.0

Reporting groups

Reporting group title	Lipid 1200 group
Reporting group description: -	
Reporting group title	Soft Gel 1200 group
Reporting group description: -	
Reporting group title	Soft Gel 2400 group
Reporting group description: -	

Serious adverse events	Lipid 1200 group	Soft Gel 1200 group	Soft Gel 2400 group
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 148 (0.00%)	0 / 155 (0.00%)	1 / 159 (0.63%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Reproductive system and breast disorders			
Endometriosis			
subjects affected / exposed	0 / 148 (0.00%)	0 / 155 (0.00%)	1 / 159 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	Lipid 1200 group	Soft Gel 1200 group	Soft Gel 2400 group
Total subjects affected by non-serious adverse events			
subjects affected / exposed	54 / 148 (36.49%)	53 / 155 (34.19%)	65 / 159 (40.88%)
Investigations			
Investigations			
subjects affected / exposed	0 / 148 (0.00%)	1 / 155 (0.65%)	2 / 159 (1.26%)
occurrences (all)	0	1	2
Blood pressure increased			

subjects affected / exposed	0 / 148 (0.00%)	1 / 155 (0.65%)	2 / 159 (1.26%)
occurrences (all)	0	1	2
Vascular disorders			
Vascular disorders			
subjects affected / exposed	2 / 148 (1.35%)	1 / 155 (0.65%)	1 / 159 (0.63%)
occurrences (all)	2	1	1
Hypertension			
subjects affected / exposed	2 / 148 (1.35%)	1 / 155 (0.65%)	1 / 159 (0.63%)
occurrences (all)	2	1	1
Nervous system disorders			
Nervous system disorders			
subjects affected / exposed	5 / 148 (3.38%)	4 / 155 (2.58%)	3 / 159 (1.89%)
occurrences (all)	5	5	3
Headache			
subjects affected / exposed	2 / 148 (1.35%)	3 / 155 (1.94%)	1 / 159 (0.63%)
occurrences (all)	2	3	1
Dizziness			
subjects affected / exposed	2 / 148 (1.35%)	0 / 155 (0.00%)	2 / 159 (1.26%)
occurrences (all)	2	0	2
General disorders and administration site conditions			
General disorders and administration site conditions			
subjects affected / exposed	6 / 148 (4.05%)	3 / 155 (1.94%)	5 / 159 (3.14%)
occurrences (all)	6	3	5
Fatigue			
subjects affected / exposed	2 / 148 (1.35%)	0 / 155 (0.00%)	2 / 159 (1.26%)
occurrences (all)	2	0	2
Gastrointestinal disorders			
Gastrointestinal disorders			
subjects affected / exposed	39 / 148 (26.35%)	47 / 155 (30.32%)	53 / 159 (33.33%)
occurrences (all)	83	99	129
Diarrhoea			
subjects affected / exposed	10 / 148 (6.76%)	12 / 155 (7.74%)	9 / 159 (5.66%)
occurrences (all)	12	15	13
Nausea			
subjects affected / exposed	10 / 148 (6.76%)	8 / 155 (5.16%)	9 / 159 (5.66%)
occurrences (all)	10	9	9

Abdominal discomfort			
subjects affected / exposed	8 / 148 (5.41%)	5 / 155 (3.23%)	12 / 159 (7.55%)
occurrences (all)	8	5	14
Abdominal distension			
subjects affected / exposed	6 / 148 (4.05%)	5 / 155 (3.23%)	15 / 159 (9.43%)
occurrences (all)	6	5	15
Dyspepsia			
subjects affected / exposed	5 / 148 (3.38%)	8 / 155 (5.16%)	12 / 159 (7.55%)
occurrences (all)	5	8	14
Constipation			
subjects affected / exposed	8 / 148 (5.41%)	7 / 155 (4.52%)	9 / 159 (5.66%)
occurrences (all)	9	7	9
Flatulence			
subjects affected / exposed	5 / 148 (3.38%)	8 / 155 (5.16%)	6 / 159 (3.77%)
occurrences (all)	5	8	6
Abdominal pain upper			
subjects affected / exposed	4 / 148 (2.70%)	8 / 155 (5.16%)	6 / 159 (3.77%)
occurrences (all)	5	8	6
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 148 (0.68%)	6 / 155 (3.87%)	8 / 159 (5.03%)
occurrences (all)	1	6	8
Eructation			
subjects affected / exposed	4 / 148 (2.70%)	4 / 155 (2.58%)	6 / 159 (3.77%)
occurrences (all)	4	4	6
Gastrointestinal motility disorder			
subjects affected / exposed	2 / 148 (1.35%)	6 / 155 (3.87%)	5 / 159 (3.14%)
occurrences (all)	2	6	5
Abdominal pain			
subjects affected / exposed	3 / 148 (2.03%)	3 / 155 (1.94%)	6 / 159 (3.77%)
occurrences (all)	4	3	6
Gastrointestinal sounds abnormal			
subjects affected / exposed	3 / 148 (2.03%)	5 / 155 (3.23%)	4 / 159 (2.52%)
occurrences (all)	3	5	4
Defaecation urgency			
subjects affected / exposed	3 / 148 (2.03%)	2 / 155 (1.29%)	5 / 159 (3.14%)
occurrences (all)	3	2	5

Abdominal pain lower			
subjects affected / exposed	0 / 148 (0.00%)	0 / 155 (0.00%)	2 / 159 (1.26%)
occurrences (all)	0	0	2
Faeces hard			
subjects affected / exposed	1 / 148 (0.68%)	4 / 155 (2.58%)	3 / 159 (1.89%)
occurrences (all)	1	4	3
Abdominal tenderness			
subjects affected / exposed	1 / 148 (0.68%)	0 / 155 (0.00%)	2 / 159 (1.26%)
occurrences (all)	1	0	2
Respiratory, thoracic and mediastinal disorders			
Respiratory, thoracic and mediastinal disorders			
subjects affected / exposed	1 / 148 (0.68%)	1 / 155 (0.65%)	2 / 159 (1.26%)
occurrences (all)	2	2	2
Musculoskeletal and connective tissue disorders			
Musculoskeletal and connective tissue disorders			
subjects affected / exposed	1 / 148 (0.68%)	2 / 155 (1.29%)	1 / 159 (0.63%)
occurrences (all)	1	2	1
Infections and infestations			
Infections and infestations			
subjects affected / exposed	4 / 148 (2.70%)	1 / 155 (0.65%)	4 / 159 (2.52%)
occurrences (all)	4	1	4
Gastroenteritis			
subjects affected / exposed	2 / 148 (1.35%)	0 / 155 (0.00%)	1 / 159 (0.63%)
occurrences (all)	2	0	1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
08 October 2015	The qualifying number of knee flare pain episodes in the previous 12 months was reduced from 2 to 1 (note this change was not expected to alter the study population because the severity of the current knee flare was still assessed in the same way, i.e. an NRS score of 5 or above at baseline).
08 October 2015	The method of identifying prospective study patients was changed from using a keyword search of the GP database to approach by a HCP. Patients were then referred to the study centre for informed consent and enrolment. The relationship between the patient's GP and the investigative site was clarified.
08 October 2015	The required duration of contraceptive use for female patients of childbearing potential was reduced from 90 days to 30 days.
08 October 2015	The exclusion criteria concerning concomitant use of medications for chronic pain was revised to clarify the difference between pain medications that were taken regularly (and so were excluded if they had been taken within 4 weeks prior to baseline visit) and pain medication that was taken on an intermittent basis (which were permitted as long as a dose has not been taken within 7 days prior to the baseline visit).

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported