# 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<br>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<br>Units: Subjects | | | |
| <65 years | 114 | 130 | 124 |
| ≥65 years | 34 | 25 | 35 |
| Not recorded | 2 | 0 | 0 |
| Gender categorical<br>Units: Subjects | | | |
| Female | 61 | 64 | 65 |
| Male | 87 | 91 | 94 |
| Not recorded | 2 | 0 | 0 |
| Ethnicity<br>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<br>Units: Subjects | | | |
| Left | 75 | 84 | 88 |
| Right | 73 | 71 | 71 |
| Not recorded | 2 | 0 | 0 |
| Number of patients with at least 1 medical history<br>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)*:<br>- Appendicectomy: 4 / 5 / 4<br>- Meniscus removal: 4 / 4 / 3<br>- 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)*:<br>- Dyspepsia: 10 / 13 / 14<br>- Gastrooesophageal reflux disease: 6 / 5 / 11<br>- Irritable bowel syndrome: 4 / 6 / 4<br><br>* 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)*:<br>- Hypertension: 28 / 30 / 26<br>- Essential hypertension: 4 / 5 / 4<br><br>* 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)*:<br>- Type 2 diabetes mellitus: 11 / 17 / 14<br>- 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)*:<br>- Asthma: 10 / 12 / 12<br><br>* 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)*:<br>- Eczema: 3 / 5 / 3<br><br>* 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)*:<br>- Arthroscopy: 11 / 9 / 7<br>- Blood cholesterol increased: 7 / 3 / 6<br><br>* 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)*:<br>- Meniscus injury: 4 / 4 / 3<br><br>* 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)*:<br>- Depression: 11 / 6 / 10<br><br>* 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)*:<br>- Erectile dysfunction: 3 / 4 / 5<br><br>* 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)*:<br>- 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)*:<br>- Hypothyroidism: 7 / 6 / 4<br><br>* 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<br>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)<br>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<br>Units: Subjects | | | |
| Cardiac disorders | 8 | 5 | 6 |
| No cardiac disorders | 140 | 150 | 153 |
| Not recorded | 2 | 0 | 0 |
| Ear and labyrinth disorders<br>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<br>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<br>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)*:<br>- Osteoarthritis: 59 / 63 / 65<br>- Arthralgia: 38 / 40 / 44 | | | |

| | | | |
|---|---|---|---|
| - Back pain: 9 / 7 / 12<br><br>* 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<br><br>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<br><br>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<br><br>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<br><br>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<br><br>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<br><br>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<br><br>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<br><br>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<br><br>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<br><br>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<br><br>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<br><br>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<br><br>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<br>Units: Subjects | | | |
| <65 years | 368 | | |
| ≥65 years | 94 | | |
| Not recorded | 2 | | |
| Gender categorical<br>Units: Subjects | | | |
| Female | 190 | | |
| Male | 272 | | |
| Not recorded | 2 | | |
| Ethnicity<br>Units: Subjects | | | |
| Asian | 13 | | |
| Black | 13 | | |
| White | 425 | | |
| Other | 11 | | |
| Not recorded | 2 | | |
| Index knee<br>Units: Subjects | | | |
| Left | 247 | | |
| Right | 215 | | |
| Not recorded | 2 | | |
| Number of patients with at least 1 medical history<br>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)*:<br>- Appendicectomy: 4 / 5 / 4<br>- Meniscus removal: 4 / 4 / 3<br>- Hysterectomy: 4 / 3 / 3<br><br>* 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)*:<br>- Dyspepsia: 10 / 13 / 14<br>- Gastrooesophageal reflux disease: 6 / 5 / 11<br>- Irritable bowel syndrome: 4 / 6 / 4<br><br>* 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)*:<br>- Hypertension: 28 / 30 / 26<br>- Essential hypertension: 4 / 5 / 4<br><br>* 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)*:<br>- Type 2 diabetes mellitus: 11 / 17 / 14<br>- 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)*:<br>- Asthma: 10 / 12 / 12<br><br>* 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)*:<br>- Eczema: 3 / 5 / 3<br><br>* 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)*:<br>- Arthroscopy: 11 / 9 / 7<br>- Blood cholesterol increased: 7 / 3 / 6<br><br>* 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)*:<br>- Meniscus injury: 4 / 4 / 3<br><br>* 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)*:<br>- Depression: 11 / 6 / 10<br><br>* 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)*:<br>- Erectile dysfunction: 3 / 4 / 5<br><br>* 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)*:<br>- Seasonal allergy: 4 / 2 / 8<br><br>* 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)*:<br>- Hypothyroidism: 7 / 6 / 4<br><br>* Medical History Reported for >2% of Patients. | | | |
| Units: Subjects | | | |
| Endocrine disorders | 21 | | |
| No endocrine disorders | 441 | | |
| Not recorded | 2 | | |
| Eye disorders<br>Units: Subjects | | | |
| Eye disorders | 20 | | |
| No eye disorders | 442 | | |
| Not recorded | 2 | | |
| Neoplasms benign, malignant and unspecified (incl. cysts and polyps)<br>Units: Subjects | | | |
| Neoplasms benign, malignant and unspecified | 20 | | |
| No neoplasms benign, malignant and unspecified | 442 | | |
| Not recorded | 2 | | |
| Cardiac disorders<br>Units: Subjects | | | |
| Cardiac disorders | 19 | | |
| No cardiac disorders | 443 | | |
| Not recorded | 2 | | |
| Ear and labyrinth disorders<br>Units: Subjects | | | |
| Ear and labyrinth disorders | 19 | | |
| No ear and labyrinth disorders | 443 | | |
| Not recorded | 2 | | |
| General disorders and administration site conditions<br>Units: Subjects | | | |
| General disorders and admin. site conditiions | 11 | | |
| No general disorders and admin. site conditiions | 451 | | |
| Not recorded | 2 | | |
| Renal and urinary disorders<br>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)*:<br>- Osteoarthritis: 59 / 63 / 65<br>- Arthralgia: 38 / 40 / 44<br>- Back pain: 9 / 7 / 12<br><br>* 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<br><br>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<br>arithmetic mean<br>standard deviation | -<br>- | | |
| WOMAC stiffness score | | | |
| WOMAC: Western Ontario and McMaster Universities Osteoarthritis Index<br><br>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<br>arithmetic mean<br>standard deviation | -<br>- | | |
| WOMAC function score | | | |
| WOMAC: Western Ontario and McMaster Universities Osteoarthritis Index<br><br>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<br>arithmetic mean<br>standard deviation | -<br>- | | |
| 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<br>arithmetic mean<br>standard deviation | -<br>- | | |
| GSRS total score | | | |
| GSRS: Gastrointestinal Symptom Rating Scale<br><br>Number of patients analysed per group was 145, 149 and 154, respectively. | | | |
| Units: Score<br>arithmetic mean<br>standard deviation | -<br>- | | |
| GSRS Dimension Score - Abdominal pain score | | | |
| GSRS: Gastrointestinal Symptom Rating Scale<br><br>Number of patients analysed per group was 145, 151 and 155, respectively. | | | |
| Units: Score<br>arithmetic mean<br>standard deviation | -<br>- | | |
| GSRS Dimension Score - Constipation score | | | |
| GSRS: Gastrointestinal Symptom Rating Scale<br><br>Number of patients analysed per group was 145, 151 and 155, respectively. | | | |
| Units: Score<br>arithmetic mean<br>standard deviation | -<br>- | | |
| GSRS Dimension Score - Diarrhoea | | | |

| | | | |
|---|---|---|---|
| score | | | |
| GSRS: Gastrointestinal Symptom Rating Scale<br><br>Number of patients analysed per group was 145, 151 and 154, respectively. | | | |
| Units: Score<br>arithmetic mean<br>standard deviation | -<br>- | | |
| GSRS Dimension Score - Indigestion score | | | |
| GSRS: Gastrointestinal Symptom Rating Scale<br><br>Number of patients analysed per group was 145, 150 and 155, respectively. | | | |
| Units: Score<br>arithmetic mean<br>standard deviation | -<br>- | | |
| GSRS Dimension Score - Reflux score | | | |
| GSRS: Gastrointestinal Symptom Rating Scale<br><br>Number of patients analysed per group was 145, 150 and 155, respectively. | | | |
| Units: Score<br>arithmetic mean<br>standard deviation | -<br>- | | |
| NRS score - Pain | | | |
| NRS: Numerical Rating Score<br><br>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<br>arithmetic mean<br>standard deviation | -<br>- | | |
| NRS score - Stiffness | | | |
| NRS: Numerical Rating Score<br><br>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<br>arithmetic mean<br>standard deviation | -<br>- | | |
| NRS score - Patient-nominated activity performance | | | |
| NRS: Numerical Rating Score<br><br>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<br>arithmetic mean<br>standard deviation | -<br>- | | |
| NRS score - Swelling | | | |
| NRS: Numerical Rating Score<br><br>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<br>arithmetic mean<br>standard deviation | -<br>- | | |
| 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<br>arithmetic mean<br>standard deviation | -<br> | | |

## 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<br>OARSI: Osteoarthritis Research Society International<br><br>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