



Clinical trial results:

A Phase III, Two-Part, Randomized, Double-Blind, Placebo-Controlled, Multicenter Clinical Trial to Assess the Relative Efficacy and Tolerability of Two Doses of MK-0663/Etoricoxib in Patients with Rheumatoid Arthritis (MK-0663-107)

Summary

| | |
|--------------------------|-------------------------|
| EudraCT number | 2010-019871-31 |
| Trial protocol | FI BE AT LT GB DE SK CZ |
| Global end of trial date | 29 July 2014 |

Results information

| | |
|--------------------------------|---------------|
| Result version number | v2 (current) |
| This version publication date | 19 March 2016 |
| First version publication date | 03 June 2015 |
| Version creation reason | |

Trial information

Trial identification

| | |
|-----------------------|----------|
| Sponsor protocol code | 0663-107 |
|-----------------------|----------|

Additional study identifiers

| | |
|------------------------------------|------------------------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01208181 |
| WHO universal trial number (UTN) | - |
| Other trial identifiers | Protocol number: MK-0663-107 |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | Merck Sharp & Dohme Corp. |
| Sponsor organisation address | 2000 Galloping Hill Road, Kenilworth, NJ, United States, 07033 |
| Public contact | Clinical Trials Disclosure, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.com |
| Scientific contact | Clinical Trials Disclosure, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.com |

Notes:

Paediatric regulatory details

| | |
|--|----|
| Is trial part of an agreed paediatric investigation plan (PIP) | No |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | No |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | No |

Notes:

Results analysis stage

| | |
|--|--------------|
| Analysis stage | Final |
| Date of interim/final analysis | 29 July 2014 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 29 July 2014 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

This is a 2-part (6 weeks duration for each part), randomized, double-blind, placebo-controlled study in participants with rheumatoid arthritis. The hypothesis is that etoricoxib (60 mg and 90 mg) administration will demonstrate superior efficacy compared to placebo after 6 weeks of treatment, as measured by the greater mean improvement from baseline in the Disease Activity Score C-Reactive Protein (DAS-28 CRP), and by the greater mean improvement in Patient Global Assessment of Pain (PGAP) from baseline over 6 weeks of treatment. Additionally, the added benefit of increasing the dose of etoricoxib from 60 mg to 90 mg will be assessed in the second part of the study.

Protection of trial subjects:

This study was conducted in conformance with Good Clinical Practice standards and applicable country and/or local statutes and regulations regarding ethical committee review, informed consent, and the protection of human subjects participating in biomedical research.

Background therapy: -

Evidence for comparator: -

| | |
|---|-------------------|
| Actual start date of recruitment | 27 September 2010 |
| 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 | Poland: 216 |
| Country: Number of subjects enrolled | Slovakia: 6 |
| Country: Number of subjects enrolled | United Kingdom: 4 |
| Country: Number of subjects enrolled | Czech Republic: 40 |
| Country: Number of subjects enrolled | Finland: 2 |
| Country: Number of subjects enrolled | Germany: 36 |
| Country: Number of subjects enrolled | Lithuania: 24 |
| Country: Number of subjects enrolled | Panama: 1 |
| Country: Number of subjects enrolled | Peru: 39 |
| Country: Number of subjects enrolled | Romania: 127 |
| Country: Number of subjects enrolled | Russian Federation: 35 |
| Country: Number of subjects enrolled | South Africa: 69 |
| Country: Number of subjects enrolled | Taiwan: 74 |
| Country: Number of subjects enrolled | United States: 309 |
| Country: Number of subjects enrolled | Argentina: 154 |
| Country: Number of subjects enrolled | Canada: 28 |
| Country: Number of subjects enrolled | Colombia: 49 |

| | |
|--------------------------------------|---------------|
| Country: Number of subjects enrolled | Guatemala: 51 |
| Country: Number of subjects enrolled | India: 83 |
| Country: Number of subjects enrolled | Mexico: 57 |
| Worldwide total number of subjects | 1404 |
| EEA total number of subjects | 455 |

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) | 1148 |
| From 65 to 84 years | 256 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

A total of 164 sites enrolled participants in this study.

Pre-assignment

Screening details:

A total of 1765 patients were screened for inclusion in the study and 1404 of these patients were randomized. Of the 361 patients who were not randomized; 295 of these patients were excluded due to screen failures and 66 of these patients were not randomized due to other reasons.

Period 1

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

Arms

| | |
|------------------------------|-----------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Part 1: Placebo |

Arm description:

The placebo treatment group will receive placebo to etoricoxib tablets administered orally once daily for 6 weeks in Part 1 of the study.

| | |
|--|----------|
| Arm type | Placebo |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

The placebo treatment group will receive placebo to etoricoxib tablets administered orally once daily for 6 weeks in Part 1 of the study.

| | |
|------------------|--------------------------|
| Arm title | Part 1: Etoricoxib 60 mg |
|------------------|--------------------------|

Arm description:

The etoricoxib 60 mg treatment group will receive etoricoxib 60 mg tablets administered orally once daily for 6 weeks in Part 1 of the study.

| | |
|--|------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Etoricoxib 60 mg |
| Investigational medicinal product code | |
| Other name | MK-0663 |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

The etoricoxib 60 mg treatment group will receive etoricoxib 60 mg tablets administered orally once daily for 6 weeks in Part 1 of the study.

| | |
|------------------|--------------------------|
| Arm title | Part 1: Etoricoxib 90 mg |
|------------------|--------------------------|

Arm description:

The etoricoxib 90 mg treatment sequence will receive etoricoxib 90 mg tablets administered orally once daily for 6 weeks in Part 1 of the study.

| | |
|----------|--------------|
| Arm type | Experimental |
|----------|--------------|

| | |
|--|------------------|
| Investigational medicinal product name | Etoricoxib 90 mg |
| Investigational medicinal product code | |
| Other name | MK-0663 |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

The etoricoxib 90 mg treatment sequence will receive etoricoxib 90 mg tablets administered orally once daily for 6 weeks in Part 1 of the study.

| Number of subjects in period 1 | Part 1: Placebo | Part 1: Etoricoxib 60 mg | Part 1: Etoricoxib 90 mg |
|---------------------------------------|-----------------|--------------------------|--------------------------|
| Started | 118 | 818 | 468 |
| Completed | 96 | 719 | 413 |
| Not completed | 22 | 99 | 55 |
| Consent withdrawn by subject | - | 11 | 10 |
| Physician decision | - | 4 | - |
| Technical problem | - | 5 | - |
| Adverse event, non-fatal | 4 | 26 | 24 |
| Non-compliance with study drug | - | 1 | 1 |
| Lost to follow-up | 1 | 5 | 3 |
| Lack of efficacy | 17 | 37 | 12 |
| Protocol deviation | - | 10 | 5 |

Period 2

| | |
|------------------------------|-------------------------|
| Period 2 title | Treatment Period 2 |
| Is this the baseline period? | No |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator |

Arms

| | |
|------------------------------|---|
| Are arms mutually exclusive? | Yes |
| Arm title | Part 1/2: Etoricoxib 60 mg/etoricoxib 60 mg |

Arm description:

The Etoricoxib 60 mg/etoricoxib 60 mg treatment sequence will receive etoricoxib 60 mg tablets administered orally once daily for 6 weeks in Part 1 and Part 2 of the study

| | |
|--|-----------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Etoricoxib 60 mg/etoricoxib 60 mg |
| Investigational medicinal product code | |
| Other name | MK-0663 |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

The Etoricoxib 60 mg/etoricoxib 60 mg treatment sequence will receive etoricoxib 60 mg tablets administered orally once daily for 6 weeks in Part 1 and Part 2 of the study.

| | |
|--|---|
| Arm title | Part 1/2: Etoricoxib 60 mg/etoricoxib 90 mg |
| Arm description: The etoricoxib 60 mg/etoricoxib 90 mg treatment sequence will receive etoricoxib 60 mg tablets administered orally once daily for 6 weeks in Part 1 of the study and etoricoxib 90 mg tablets administered orally once daily for 6 weeks in Part 2 of the study. | |
| Arm type | Experimental |
| Investigational medicinal product name | Etoricoxib 60 mg/etoricoxib 90 mg |
| Investigational medicinal product code | |
| Other name | MK-0663 |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

The etoricoxib 60 mg/etoricoxib 90 mg treatment sequence will receive etoricoxib 60 mg tablets administered orally once daily for 6 weeks in Part 1 of the study and etoricoxib 90 mg tablets administered orally once daily for 6 weeks in Part 2 of the study.

| Number of subjects in period 2^[1] | Part 1/2: Etoricoxib 60 mg/etoricoxib 60 mg | Part 1/2: Etoricoxib 60 mg/etoricoxib 90 mg |
|---|---|---|
| Started | 350 | 363 |
| Completed | 334 | 343 |
| Not completed | 16 | 20 |
| Physician decision | 1 | 2 |
| Consent withdrawn by subject | 1 | 1 |
| Adverse event, non-fatal | 6 | 7 |
| Non-compliance with study drug | 1 | 1 |
| Lost to follow-up | 1 | 2 |
| Lack of efficacy | 5 | 7 |
| Protocol deviation | 1 | - |

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: Participants who received etoricoxib 60 mg and completed Part I of the trial continued into Part II and received either etoricoxib 60 mg or etoricoxib 90 mg. Therefore, the number of participants completing Part I for each study arm is not consistent with the number of participants starting Part II for each study arm.

Baseline characteristics

Reporting groups

| | |
|--|--------------------------|
| Reporting group title | Part 1: Placebo |
| Reporting group description: The placebo treatment group will receive placebo to etoricoxib tablets administered orally once daily for 6 weeks in Part 1 of the study. | |
| Reporting group title | Part 1: Etoricoxib 60 mg |
| Reporting group description: The etoricoxib 60 mg treatment group will receive etoricoxib 60 mg tablets administered orally once daily for 6 weeks in Part 1 of the study. | |
| Reporting group title | Part 1: Etoricoxib 90 mg |
| Reporting group description: The etoricoxib 90 mg treatment sequence will receive etoricoxib 90 mg tablets administered orally once daily for 6 weeks in Part 1 of the study. | |

| Reporting group values | Part 1: Placebo | Part 1: Etoricoxib 60 mg | Part 1: Etoricoxib 90 mg |
|---|-----------------|--------------------------|--------------------------|
| Number of subjects | 118 | 818 | 468 |
| Age categorical Units: Subjects | | | |
| In utero | 0 | 0 | 0 |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | 0 |
| Newborns (0-27 days) | 0 | 0 | 0 |
| Infants and toddlers (28 days-23 months) | 0 | 0 | 0 |
| Children (2-11 years) | 0 | 0 | 0 |
| Adolescents (12-17 years) | 0 | 0 | 0 |
| Adults (18-64 years) | 102 | 671 | 375 |
| From 65-84 years | 16 | 147 | 93 |
| 85 years and over | 0 | 0 | 0 |
| Age continuous Units: years | | | |
| arithmetic mean | 53.6 | 53.8 | 54 |
| standard deviation | ± 11 | ± 11.9 | ± 12.3 |
| Gender categorical Units: Subjects | | | |
| Female | 100 | 677 | 395 |
| Male | 18 | 141 | 73 |
| Disease Activity Score using C reactive protein (DAS28-CRP) | | | |
| The DAS28-CRP index (0 - 10 Range) is a composite score of weighted components including tender joint counts of 28, swollen joint counts of 28, patient global assessment of disease activity, and C-reactive protein (CRP). For each observation (Baseline, Week 2, 4, 6, 10, 12), components were combined into a single DAS28-CRP score using the following algorithm: $0.56 \times \sqrt{\text{tender joint count [28]}} + 0.28 \times \sqrt{\text{swollen joint count [28]}} + 0.36 \times \ln(\text{crp} + 1) + 0.014 \times \text{Patient Global Assessment of Disease Activity} + 0.96$. (N = 732, 426, 103 for Etoricoxib 60 mg and 90 mg, and Placebo) | | | |
| Units: Scores on a scale | | | |
| arithmetic mean | 5.65 | 5.64 | 5.62 |
| standard deviation | ± 1.12 | ± 0.99 | ± 1 |
| Patient Global Assessment of Pain | | | |

| | | | |
|---|---------|--------|---------|
| A participant overall assessment of pain on a visual analog scale (VAS) were assessed with a question concerning the amount of pain due to arthritis during the past 48 hours. Pain was assessed on an 100 mm VAS scale with a left-hand marker "no pain" (0 mm) or right-hand marker "extreme pain" (100 mm). (N = 751, 430, 108 for Etoricoxib 60 mg, Etoricoxib 90 mg, and Placebo) | | | |
| Units: Scores on a scale | | | |
| arithmetic mean | 74.08 | 70.84 | 70.58 |
| standard deviation | ± 14.23 | ± 15.5 | ± 15.02 |
| Reporting group values | | | |
| Number of subjects | 1404 | | |
| Age categorical | | | |
| Units: Subjects | | | |
| In utero | 0 | | |
| Preterm newborn infants (gestational age < 37 wks) | 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) | 1148 | | |
| From 65-84 years | 256 | | |
| 85 years and over | 0 | | |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | | | |
| standard deviation | - | | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 1172 | | |
| Male | 232 | | |
| Disease Activity Score using C reactive protein (DAS28-CRP) | | | |
| The DAS28-CRP index (0 - 10 Range) is a composite score of weighted components including tender joint counts of 28, swollen joint counts of 28, patient global assessment of disease activity, and C-reactive protein (CRP). For each observation (Baseline, Week 2, 4, 6, 10, 12), components were combined into a single DAS28-CRP score using the following algorithm: $0.56 \times \sqrt{\text{tender joint count [28]}} + 0.28 \times \sqrt{\text{swollen joint count [28]}} + 0.36 \times \ln(\text{crp} + 1) + 0.014 \times \text{Patient Global Assessment of Disease Activity} + 0.96$. (N = 732, 426, 103 for Etoricoxib 60 mg and 90 mg, and Placebo) | | | |
| Units: Scores on a scale | | | |
| arithmetic mean | | | |
| standard deviation | - | | |
| Patient Global Assessment of Pain | | | |
| A participant overall assessment of pain on a visual analog scale (VAS) were assessed with a question concerning the amount of pain due to arthritis during the past 48 hours. Pain was assessed on an 100 mm VAS scale with a left-hand marker "no pain" (0 mm) or right-hand marker "extreme pain" (100 mm). (N = 751, 430, 108 for Etoricoxib 60 mg, Etoricoxib 90 mg, and Placebo) | | | |
| Units: Scores on a scale | | | |
| arithmetic mean | | | |
| standard deviation | - | | |

End points

End points reporting groups

| | |
|--|---|
| Reporting group title | Part 1: Placebo |
| Reporting group description: The placebo treatment group will receive placebo to etoricoxib tablets administered orally once daily for 6 weeks in Part 1 of the study. | |
| Reporting group title | Part 1: Etoricoxib 60 mg |
| Reporting group description: The etoricoxib 60 mg treatment group will receive etoricoxib 60 mg tablets administered orally once daily for 6 weeks in Part 1 of the study. | |
| Reporting group title | Part 1: Etoricoxib 90 mg |
| Reporting group description: The etoricoxib 90 mg treatment sequence will receive etoricoxib 90 mg tablets administered orally once daily for 6 weeks in Part 1 of the study. | |
| Reporting group title | Part 1/2: Etoricoxib 60 mg/etoricoxib 60 mg |
| Reporting group description: The Etoricoxib 60 mg/etoricoxib 60 mg treatment sequence will receive etoricoxib 60 mg tablets administered orally once daily for 6 weeks in Part 1 and Part 2 of the study | |
| Reporting group title | Part 1/2: Etoricoxib 60 mg/etoricoxib 90 mg |
| Reporting group description: The etoricoxib 60 mg/etoricoxib 90 mg treatment sequence will receive etoricoxib 60 mg tablets administered orally once daily for 6 weeks in Part 1 of the study and etoricoxib 90 mg tablets administered orally once daily for 6 weeks in Part 2 of the study. | |
| Subject analysis set title | Part 1: Etoricoxib 60 mg |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: The etoricoxib 60 mg treatment group will receive etoricoxib 60 mg tablets administered orally once daily for 6 weeks in Part 1 of the study. | |

Primary: Time-Weighted Average Change From Baseline in Disease Activity Score Using C-Reactive Protein [DAS28-CRP] in Part 1 (Etoricoxib vs. Placebo)

| | |
|---|--|
| End point title | Time-Weighted Average Change From Baseline in Disease Activity Score Using C-Reactive Protein [DAS28-CRP] in Part 1 (Etoricoxib vs. Placebo) |
| End point description: The DAS28-CRP index (0-10 Range) is a composite score of weighted components including tender joint counts of 28, swollen joint counts of 28, patient global assessment of disease activity, and C-reactive protein (CRP). For each observation (Baseline, Week 2, 4, 6, 10, 12), components were combined into a single DAS28-CRP score using the following algorithm: $0.56 \times \sqrt{\text{tender joint count [28]}} + 0.28 \times \sqrt{\text{swollen joint count [28]}} + 0.36 \times \ln(\text{crp} + 1) + 0.014 \times \text{Patient Global Assessment of Disease Activity} + 0.96$. The primary objectives of the study compared the efficacy of etoricoxib (90 mg, 60 mg) to placebo in Part 1 of this study so data for only these 3 arms are displayed. The modified intention-to-treat (mITT) population in Part 1 consisted of all randomized participants receiving at least 1 dose of study medication, had baseline data for the analysis endpoint, and least one post-randomization measurement for that endpoint. | |
| End point type | Primary |
| End point timeframe: Baseline and Week 6 | |

| End point values | Part 1: Placebo | Part 1: Etoricoxib 60 mg | Part 1: Etoricoxib 90 mg | |
|--|----------------------|--------------------------|--------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 103 | 732 | 426 | |
| Units: Scores on a scale | | | | |
| least squares mean (confidence interval 95%) | -1.1 (-1.29 to -0.9) | -1.39 (-1.48 to -1.3) | -1.37 (-1.48 to -1.26) | |

Statistical analyses

| Statistical analysis title | Treatment Difference (Etoricoxib 60 mg v. Placebo) |
|---|--|
| Statistical analysis description: | |
| Difference in the least squares means between change from baseline in DAS28-CRP for participants taking Etoricoxib 60 mg at Week 6 vs. change from baseline in DAS28-CRP for participants taking Placebo at Week 6. | |
| Comparison groups | Part 1: Etoricoxib 60 mg v Part 1: Placebo |
| Number of subjects included in analysis | 835 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.004 |
| Method | Tukey-Ciminera-Heysetrend test |
| Parameter estimate | Difference in least squares mean |
| Point estimate | -0.29 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.49 |
| upper limit | -0.09 |

| Statistical analysis title | Treatment Difference (Etoricoxib 90 mg v. Placebo) |
|--|--|
| Statistical analysis description: | |
| Difference in the least squares means between change from baseline in DAS28-CRP for participants taking Etoricoxib 90 mg at Week 6 vs. change from baseline in DAS28-CRP for participants taking Placebo at Week 6 | |
| Comparison groups | Part 1: Placebo v Part 1: Etoricoxib 90 mg |
| Number of subjects included in analysis | 529 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.034 |
| Method | Tukey-Ciminera-Heysetrend test |
| Parameter estimate | Difference in least squares mean |
| Point estimate | -0.27 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.48 |
| upper limit | -0.06 |

Primary: Time-Weighted Average Change From Baseline in Patient Global Assessment of Pain in Part 1 (Etoricoxib vs. Placebo)

| | |
|-----------------|--|
| End point title | Time-Weighted Average Change From Baseline in Patient Global Assessment of Pain in Part 1 (Etoricoxib vs. Placebo) |
|-----------------|--|

End point description:

A participant overall assessment of pain on a visual analog scale (VAS) was assessed with a question concerning the amount of pain due to arthritis during the past 48 hours. Pain was assessed on an 100 mm VAS scale with a left-hand marker "no pain" (0 mm) or right-hand marker "extreme pain" (100 mm). The primary objectives of the study compared the efficacy of etoricoxib (90 mg, 60 mg) to placebo in Part 1 of this study so data for only these 3 arms are displayed. The mITT population in Part 1 consisted of all randomized participants receiving at least 1 dose of study medication, had baseline data for the analysis endpoint, and least one post-randomization measurement for that endpoint.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Baseline and Week 6

| End point values | Part 1: Placebo | Part 1: Etoricoxib 60 mg | Part 1: Etoricoxib 90 mg | |
|--|---------------------------|---------------------------|---------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 108 | 751 | 430 | |
| Units: Scores on a scale | | | | |
| least squares mean (confidence interval 95%) | -20.26 (-24.04 to -16.48) | -28.25 (-30.05 to -26.44) | -30.96 (-33.13 to -28.79) | |

Statistical analyses

| | |
|----------------------------|--|
| Statistical analysis title | Treatment Difference (Etoricoxib 60 mg v. Placebo) |
|----------------------------|--|

Statistical analysis description:

Change from baseline in Patient Global Assessment of Disease Activity at Week 6 for participants treated with Etoricoxib 60 mg minus change from baseline in Patient Global Assessment of Disease Activity at Week 6 for participants treated with Placebo.

| | |
|---|--|
| Comparison groups | Part 1: Etoricoxib 60 mg v Part 1: Placebo |
| Number of subjects included in analysis | 859 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Tukey-Ciminera-Heyse trend test |
| Parameter estimate | Difference in the least squares mean |
| Point estimate | -7.99 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -11.85 |
| upper limit | -4.13 |

| | |
|--|--|
| Statistical analysis title | Treatment Difference (Etoricoxib 90 mg v. Placebo) |
| Statistical analysis description: Change from baseline in Patient Global Assessment of Disease Activity at Week 6 for participants treated with Etoricoxib 90 mg minus change from baseline in Patient Global Assessment of Disease Activity at Week 6 for participants treated with Placebo. | |
| Comparison groups | Part 1: Placebo v Part 1: Etoricoxib 90 mg |
| Number of subjects included in analysis | 538 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Tukey-Ciminera-Heyse trend test |
| Parameter estimate | Difference in least squares mean |
| Point estimate | -10.7 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -14.74 |
| upper limit | -6.66 |

Primary: Percentage of Participants Who Experienced at Least One Adverse Event (AE) in Part 1 and Part 2

| | |
|--|---|
| End point title | Percentage of Participants Who Experienced at Least One Adverse Event (AE) in Part 1 and Part 2 ^{[1][2]} |
| End point description: An AE is defined as any unfavorable and unintended sign including an abnormal laboratory finding, symptom or disease associated with the use of a medical treatment or procedure, regardless of whether it is considered related to the medical treatment or procedure. All Subjects as Treated (ASaT) population, defined as all randomized participants who received at least one study drug. Participants were included in the treatment group corresponding to the study treatment they actually received for the analysis of safety data using the ASaT population. | |
| End point type | Primary |
| End point timeframe: Up to Week 16 | |

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: No statistical analysis of this end point was specified in the protocol or the statistical analysis plan.

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: No statistical analysis of this end point was specified in the protocol or the statistical analysis plan.

| End point values | Part 1: Placebo | Part 1/2: Etoricoxib 60 mg/etoricoxib 60 mg | Part 1/2: Etoricoxib 60 mg/etoricoxib 90 mg | Part 1: Etoricoxib 90 mg |
|-----------------------------------|-----------------|---|---|--------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 118 | 350 | 363 | 467 |
| Units: Percentage of Participants | | | | |

| | | | | |
|-------------------------|------|------|------|----|
| number (not applicable) | 25.4 | 19.1 | 24.5 | 36 |
|-------------------------|------|------|------|----|

| | | | | |
|-----------------------------------|-----------------------------|--|--|--|
| End point values | Part 1: Etoricoxib 60 mg | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 819 | | | |
| Units: Percentage of Participants | | | | |
| number (not applicable) | 30.3 | | | |

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants Who Discontinued Study Drug Due to an AE in Part 1 and Part 2

| | |
|-----------------|--|
| End point title | Percentage of Participants Who Discontinued Study Drug Due to an AE in Part 1 and Part 2 ^[3] ^[4] |
|-----------------|--|

End point description:

An AE is defined as any unfavorable and unintended sign including an abnormal laboratory finding, symptom or disease associated with the use of a medical treatment or procedure, regardless of whether it is considered related to the medical treatment or procedure. ASaT population defined as all randomized participants who received at least one study drug. Participants were included in the treatment group corresponding to the study treatment they actually received for the analysis of safety data using the ASaT population.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Up to Week 12

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: No statistical analysis of this end point was specified in the protocol or the statistical analysis plan.

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: No statistical analysis of this end point was specified in the protocol or the statistical analysis plan.

| | | | | |
|-----------------------------------|-----------------|--|--|-----------------------------|
| End point values | Part 1: Placebo | Part 1/2: Etoricoxib 60 mg/etoricoxib 60 mg | Part 1/2: Etoricoxib 60 mg/etoricoxib 90 mg | Part 1: Etoricoxib 90 mg |
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 118 | 350 | 363 | 467 |
| Units: Percentage of Participants | | | | |
| number (not applicable) | 3.4 | 1.4 | 1.9 | 5.1 |

| | | | | |
|-------------------------|-----------------------------|--|--|--|
| End point values | Part 1: Etoricoxib 60 mg | | | |
|-------------------------|-----------------------------|--|--|--|

| | | | | |
|-----------------------------------|----------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 819 | | | |
| Units: Percentage of Participants | | | | |
| number (not applicable) | 3.3 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Time-Weighted Average Change From Baseline in DAS28-CRP in Part 1 (Etoricoxib 90 mg vs. Etoricoxib 60 mg)

| | |
|-----------------|---|
| End point title | Time-Weighted Average Change From Baseline in DAS28-CRP in Part 1 (Etoricoxib 90 mg vs. Etoricoxib 60 mg) |
|-----------------|---|

End point description:

The DAS28-CRP index (0 - 10 range) is a composite score of weighted components including tender joint counts of 28, swollen joint counts of 28, patient global assessment of disease activity, and C-reactive protein (CRP). For each observation (Baseline, Week 2, 4, 6, 10, 12), components were combined into a single DAS28-CRP score using the following algorithm: $0.56 \times \sqrt{\text{tender joint count [28]}} + 0.28 \times \sqrt{\text{swollen joint count [28]}} + 0.36 \times \ln(\text{crp} + 1) + 0.014 \times \text{Patient Global Assessment of Disease Activity} + 0.96$. A key secondary objective was to compare the relative efficacy between etoricoxib 90 mg and 60 mg in Part 1 of this study. The mITT population in Part 1 consisted of all randomized participants receiving at least 1 dose of study medication, had baseline data for the analysis endpoint, and least one post-randomization measurement for that endpoint.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline and Week 6

| End point values | Part 1: Placebo | Part 1: Etoricoxib 60 mg | Part 1: Etoricoxib 90 mg | |
|--|----------------------|--------------------------|--------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 103 | 732 | 426 | |
| Units: Scores on a scale | | | | |
| least squares mean (confidence interval 95%) | -1.1 (-1.29 to -0.9) | -1.39 (-1.48 to -1.3) | -1.37 (-1.48 to -1.26) | |

Statistical analyses

| | |
|----------------------------|---|
| Statistical analysis title | Treatment Difference (Etoricoxib 60 mg vs. 90 mg) |
|----------------------------|---|

Statistical analysis description:

Difference in the least squares means between change from baseline in DAS28-CRP for participants taking Etoricoxib 60 mg at Week 6 vs. change from baseline in DAS28-CRP for participants taking Etoricoxib 90 mg at Week 6.

| | |
|-------------------|---|
| Comparison groups | Part 1: Etoricoxib 60 mg v Part 1: Etoricoxib 90 mg |
|-------------------|---|

| | |
|---|----------------------------------|
| Number of subjects included in analysis | 1158 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.73 |
| Method | Tukey-Ciminera-Heysetrend test |
| Parameter estimate | Difference in least squares mean |
| Point estimate | 0.02 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.1 |
| upper limit | 0.14 |

Secondary: Time-Weighted Mean Change From Baseline in Patient Global Assessment of Pain in Part 1 (Etoricoxib 90 mg vs. Etoricoxib 60 mg)

| | |
|-----------------|--|
| End point title | Time-Weighted Mean Change From Baseline in Patient Global Assessment of Pain in Part 1 (Etoricoxib 90 mg vs. Etoricoxib 60 mg) |
|-----------------|--|

End point description:

A participant overall assessment of pain on a visual analog scale (VAS) was assessed with a question concerning the amount of pain due to arthritis during the past 48 hours. Pain was assessed on an 100 mm VAS scale with a left-hand marker "no pain" (0 mm) or right-hand marker "extreme pain" (100 mm). A key secondary objective was to compare the relative efficacy between etoricoxib 90 mg and 60 mg in Part 1 of this study. The mITT population in Part 1 consisted of all randomized participants receiving at least 1 dose of study medication, had baseline data for the analysis endpoint, and least one post-randomization measurement for that endpoint.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline and Week 6

| End point values | Part 1: Placebo | Part 1: Etoricoxib 60 mg | Part 1: Etoricoxib 90 mg | |
|--|---------------------------|---------------------------|---------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 108 | 751 | 430 | |
| Units: Scores on a scale | | | | |
| least squares mean (confidence interval 95%) | -20.26 (-24.04 to -16.48) | -28.25 (-30.05 to -26.44) | -30.96 (-33.13 to -28.79) | |

Statistical analyses

| | |
|----------------------------|---|
| Statistical analysis title | Treatment Difference (Etoricoxib 60 mg vs. 90 mg) |
|----------------------------|---|

Statistical analysis description:

Change from baseline in Patient Global Assessment of Disease Activity at Week 6 for participants treated with Etoricoxib 60 mg minus change from baseline in Patient Global Assessment of Disease Activity at Week 6 for participants treated with Etoricoxib 90 mg.

| | |
|-------------------|---|
| Comparison groups | Part 1: Etoricoxib 60 mg v Part 1: Etoricoxib 90 mg |
|-------------------|---|

| | |
|---|----------------------------------|
| Number of subjects included in analysis | 1181 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.019 |
| Method | Tukey-Ciminera-Heyse trend test |
| Parameter estimate | Difference in least squares mean |
| Point estimate | -2.71 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -4.98 |
| upper limit | -0.45 |

Secondary: Average change from Week 6 in Patient Global Assessment of Pain Over Weeks 10 and 12 in Part 2 Among Pain Inadequate Responders from Part 1

| | |
|-----------------|---|
| End point title | Average change from Week 6 in Patient Global Assessment of Pain Over Weeks 10 and 12 in Part 2 Among Pain Inadequate Responders from Part 1 |
|-----------------|---|

End point description:

A participant overall assessment of pain on a visual analog scale (VAS) was assessed with a question concerning the amount of pain due to arthritis during the past 48 hours assessed on an 100 mm VAS scale; left-hand "no pain" (0 mm) or right-hand "extreme pain" (100 mm). Inadequate responders to etoricoxib 60 mg in Part 1 (<50% improvement from baseline in PGAP [VAS] at Week 6) were evaluated for an incremental benefit of increasing the etoricoxib dose to 90 mg in Part 2 compared to remaining on 60 mg in Part 2 for average change from Week 6 over Weeks 10 and 12 in Patient Global Assessment of Pain score. Therefore, data for only these 2 arms are displayed. This population (a subpopulation of the mITT population) was composed of pain inadequate responder (PIRs) in Part 1. PIRs were defined as participants with <50% improvement from baseline in Patient Global Assessment of Pain (VAS) at Week 6 and received at least one dose of study medication in Part 2.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Week 6 and Week 10 to Week 12

| End point values | Part 1/2: Etoricoxib 60 mg/etoricoxib 60 mg | Part 1/2: Etoricoxib 60 mg/etoricoxib 90 mg | | |
|--|--|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 188 | 187 | | |
| Units: Scores on a scale | | | | |
| least squares mean (confidence interval 95%) | -11.96 (-14.96 to -8.97) | -10.35 (-13.32 to -7.39) | | |

Statistical analyses

| | |
|----------------------------|---|
| Statistical analysis title | Treatment Difference (Etoricoxib 60 mg vs. 90 mg) |
|----------------------------|---|

Statistical analysis description:

Change from Week 6 in Patient Global Assessment of Disease Activity over Weeks 10 to 12 for participants treated with Etoricoxib 60 mg/Etoricoxib 60 mg minus change from Week 6 in Patient Global

Assessment of Disease Activity over Weeks 10 to 12 for participants treated with Etoricoxib 60 mg/Etoricoxib 90 mg.

| | |
|---|---|
| Comparison groups | Part 1/2: Etoricoxib 60 mg/etoricoxib 60 mg v Part 1/2: Etoricoxib 60 mg/etoricoxib 90 mg |
| Number of subjects included in analysis | 375 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.327 |
| Method | Covariance model |
| Parameter estimate | Difference in the least squares mean |
| Point estimate | 1.61 |
| Confidence interval | |
| level | Other: 80 % |
| sides | 2-sided |
| lower limit | -0.49 |
| upper limit | 3.71 |

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to Week 16

Adverse event reporting additional description:

The All Participants as Treated (APaT) population was used for the analysis of safety data in this study and consisted of all randomized participants who received at least one dose of study treatment. Participants were included in the treatment group corresponding to the study treatment they actually received for the analysis of safety data.

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 17.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|-----------------|
| Reporting group title | Part 1: Placebo |
|-----------------------|-----------------|

Reporting group description:

The placebo treatment group will receive placebo to etoricoxib tablets administered orally once daily in Part 1 of the study.

| | |
|-----------------------|--------------------------|
| Reporting group title | Part 1: Etoricoxib 60 mg |
|-----------------------|--------------------------|

Reporting group description:

The Etoricoxib 60 mg treatment group will receive etoricoxib tablets 60 mg administered orally once daily in Part 1 of the study.

| | |
|-----------------------|--------------------------|
| Reporting group title | Part 1: Etoricoxib 90 mg |
|-----------------------|--------------------------|

Reporting group description:

The Etoricoxib 90 mg treatment group will receive etoricoxib tablets 90 mg administered orally once daily in Part 1 of the study.

| | |
|-----------------------|----------------------------------|
| Reporting group title | Part 1/2: Etoricoxib 60 mg/60 mg |
|-----------------------|----------------------------------|

Reporting group description:

The Etoricoxib 60 mg/Etoricoxib 60 mg treatment sequence will receive etoricoxib tablets 60 mg administered orally once daily in Part 1 and Part 2 of the study.

| | |
|-----------------------|----------------------------------|
| Reporting group title | Part 1/2: Etoricoxib 60 mg/90 mg |
|-----------------------|----------------------------------|

Reporting group description:

The Etoricoxib 60 mg/Etoricoxib 90 mg treatment sequence will receive etoricoxib tablets 60 mg administered orally once daily in Part 1 of the study and etoricoxib tablets 90 mg administered orally once daily in Part 2 of the study.

| Serious adverse events | Part 1: Placebo | Part 1: Etoricoxib 60 mg | Part 1: Etoricoxib 90 mg |
|---|-----------------|--------------------------|--------------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 118 (0.00%) | 7 / 819 (0.85%) | 2 / 467 (0.43%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Injury, poisoning and procedural complications | | | |
| Head injury | | | |

| | | | |
|--|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 118 (0.00%) | 0 / 819 (0.00%) | 1 / 467 (0.21%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hip fracture | | | |
| subjects affected / exposed | 0 / 118 (0.00%) | 0 / 819 (0.00%) | 0 / 467 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac disorders | | | |
| Acute myocardial infarction | | | |
| subjects affected / exposed | 0 / 118 (0.00%) | 0 / 819 (0.00%) | 0 / 467 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Atrial fibrillation | | | |
| subjects affected / exposed | 0 / 118 (0.00%) | 0 / 819 (0.00%) | 0 / 467 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Coronary artery disease | | | |
| subjects affected / exposed | 0 / 118 (0.00%) | 0 / 819 (0.00%) | 0 / 467 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| Cerebrovascular accident | | | |
| subjects affected / exposed | 0 / 118 (0.00%) | 0 / 819 (0.00%) | 0 / 467 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General disorders and administration site conditions | | | |
| Chest discomfort | | | |
| subjects affected / exposed | 0 / 118 (0.00%) | 1 / 819 (0.12%) | 0 / 467 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 0 / 118 (0.00%) | 2 / 819 (0.24%) | 0 / 467 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|-----------------|-----------------|-----------------|
| Gastrointestinal disorders | | | |
| Gastric ulcer haemorrhage | | | |
| subjects affected / exposed | 0 / 118 (0.00%) | 1 / 819 (0.12%) | 0 / 467 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastroduodenitis | | | |
| subjects affected / exposed | 0 / 118 (0.00%) | 1 / 819 (0.12%) | 0 / 467 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haemorrhoidal haemorrhage | | | |
| subjects affected / exposed | 0 / 118 (0.00%) | 0 / 819 (0.00%) | 0 / 467 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Haemoptysis | | | |
| subjects affected / exposed | 0 / 118 (0.00%) | 1 / 819 (0.12%) | 0 / 467 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skin and subcutaneous tissue disorders | | | |
| Urticaria | | | |
| subjects affected / exposed | 0 / 118 (0.00%) | 1 / 819 (0.12%) | 0 / 467 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthritis | | | |
| subjects affected / exposed | 0 / 118 (0.00%) | 0 / 819 (0.00%) | 0 / 467 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Cellulitis | | | |
| subjects affected / exposed | 0 / 118 (0.00%) | 1 / 819 (0.12%) | 0 / 467 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastroenteritis viral | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 118 (0.00%) | 0 / 819 (0.00%) | 0 / 467 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pyomyositis | | | |
| subjects affected / exposed | 0 / 118 (0.00%) | 0 / 819 (0.00%) | 0 / 467 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 118 (0.00%) | 0 / 819 (0.00%) | 1 / 467 (0.21%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| Serious adverse events | Part 1/2: Etoricoxib 60 mg/60 mg | Part 1/2: Etoricoxib 60 mg/90 mg | |
|---|-------------------------------------|-------------------------------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 4 / 350 (1.14%) | 5 / 363 (1.38%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Injury, poisoning and procedural complications | | | |
| Head injury | | | |
| subjects affected / exposed | 0 / 350 (0.00%) | 0 / 363 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hip fracture | | | |
| subjects affected / exposed | 0 / 350 (0.00%) | 1 / 363 (0.28%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac disorders | | | |
| Acute myocardial infarction | | | |
| subjects affected / exposed | 0 / 350 (0.00%) | 1 / 363 (0.28%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Atrial fibrillation | | | |

| | | | |
|--|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 350 (0.29%) | 0 / 363 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Coronary artery disease | | | |
| subjects affected / exposed | 0 / 350 (0.00%) | 1 / 363 (0.28%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorders | | | |
| Cerebrovascular accident | | | |
| subjects affected / exposed | 0 / 350 (0.00%) | 1 / 363 (0.28%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General disorders and administration site conditions | | | |
| Chest discomfort | | | |
| subjects affected / exposed | 0 / 350 (0.00%) | 0 / 363 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 1 / 350 (0.29%) | 0 / 363 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Gastric ulcer haemorrhage | | | |
| subjects affected / exposed | 0 / 350 (0.00%) | 0 / 363 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastroduodenitis | | | |
| subjects affected / exposed | 0 / 350 (0.00%) | 0 / 363 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haemorrhoidal haemorrhage | | | |
| subjects affected / exposed | 1 / 350 (0.29%) | 0 / 363 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|-----------------|-----------------|--|
| Respiratory, thoracic and mediastinal disorders | | | |
| Haemoptysis | | | |
| subjects affected / exposed | 0 / 350 (0.00%) | 0 / 363 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Skin and subcutaneous tissue disorders | | | |
| Urticaria | | | |
| subjects affected / exposed | 0 / 350 (0.00%) | 0 / 363 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal and connective tissue disorders | | | |
| Arthritis | | | |
| subjects affected / exposed | 1 / 350 (0.29%) | 0 / 363 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Cellulitis | | | |
| subjects affected / exposed | 0 / 350 (0.00%) | 0 / 363 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastroenteritis viral | | | |
| subjects affected / exposed | 0 / 350 (0.00%) | 1 / 363 (0.28%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pyomyositis | | | |
| subjects affected / exposed | 0 / 350 (0.00%) | 1 / 363 (0.28%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 350 (0.00%) | 0 / 363 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

Frequency threshold for reporting non-serious adverse events: 5 %

| Non-serious adverse events | Part 1: Placebo | Part 1: Etoricoxib 60 mg | Part 1: Etoricoxib 90 mg |
|---|-----------------|--------------------------|--------------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 6 / 118 (5.08%) | 25 / 819 (3.05%) | 17 / 467 (3.64%) |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 6 / 118 (5.08%) | 25 / 819 (3.05%) | 17 / 467 (3.64%) |
| occurrences (all) | 8 | 27 | 27 |

| Non-serious adverse events | Part 1/2: Etoricoxib 60 mg/60 mg | Part 1/2: Etoricoxib 60 mg/90 mg | |
|---|----------------------------------|----------------------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 6 / 350 (1.71%) | 6 / 363 (1.65%) | |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 6 / 350 (1.71%) | 6 / 363 (1.65%) | |
| occurrences (all) | 6 | 7 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported