



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 | v1 |
| This version publication date | 08 March 2016 |
| First version publication date | 03 June 2015 |

Trial information

Trial identification

| | |
|-----------------------|-------------|
| Sponsor protocol code | MK-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 | Subject, Investigator |

Arms

| | |
|------------------------------|---------|
| Are arms mutually exclusive? | Yes |
| Arm title | 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 | 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 | 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 | Placebo | Etoricoxib 60 mg | 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 | 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 | 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] | Etoricoxib 60 mg/etoricoxib 60 mg | 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: Per protocol, participants receiving Etoricoxib 60 mg in Part 1 of the study received etoricoxib 60 mg or etoricoxib 90 mg in Part 2 of the study.

Baseline characteristics

Reporting groups

| | |
|--|------------------|
| Reporting group title | 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 | 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 | 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 | Placebo | Etoricoxib 60 mg | 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 | Total | | |
| 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 | 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 | 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 | 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 | 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 | 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. | |

Primary: Time-Weighted Average Change From Baseline in DAS28-CRP in Part 1 (Etoricoxib vs. Placebo)

| | |
|---|--|
| End point title | Time-Weighted Average Change From Baseline in DAS28-CRP in Part 1 (Etoricoxib vs. Placebo) |
| End point description: Disease Activity Score Using C-Reactive Protein [DAS28-CRP] (0 - 10 Range). The DAS28-CRP index 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. | |
| End point type | Primary |
| End point timeframe: Baseline and Week 6 | |

| End point values | Placebo | Etoricoxib 60 mg | Etoricoxib 90 mg | |
|--|----------------------|-----------------------|------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 103 ^[1] | 732 ^[2] | 426 ^[3] | |
| 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) | |

Notes:

[1] - Participants with ≥ 1 dose of study drug, and both baseline and post-baseline data

[2] - Participants with ≥ 1 dose of study drug, and both baseline and post-baseline data

[3] - Participants with ≥ 1 dose of study drug, and both baseline and post-baseline data

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 | Etoricoxib 60 mg v 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 | Placebo v 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. | |
| End point type | Primary |
| End point timeframe: Baseline and Week 6 | |

| End point values | Placebo | Etoricoxib 60 mg | Etoricoxib 90 mg | |
|--|---------------------------|---------------------------|---------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 108 ^[4] | 751 ^[5] | 430 ^[6] | |
| 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) | |

Notes:

[4] - Participants with ≥ 1 dose of study drug, and both baseline and post-baseline data

[5] - Participants with ≥ 1 dose of study drug, and both baseline and post-baseline data

[6] - Participants with ≥ 1 dose of study drug, and both baseline and post-baseline data

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 | Etoricoxib 60 mg v 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 | Placebo v 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 |

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: | Disease Activity Score Using C-Reactive Protein [DAS28-CRP] (0 - 10 Range). The DAS28-CRP index 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. |
| End point type | Secondary |
| End point timeframe: | |
| Baseline and Week 6 | |

| End point values | Placebo | Etoricoxib 60 mg | Etoricoxib 90 mg | |
|--|----------------------|-----------------------|------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 103 ^[7] | 732 ^[8] | 426 ^[9] | |
| 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) | |

Notes:

[7] - Participants with ≥ 1 dose of study drug, and both baseline and post-baseline data

[8] - Participants with ≥ 1 dose of study drug, and both baseline and post-baseline data

[9] - Participants with ≥ 1 dose of study drug, and both baseline and post-baseline data

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 | Etoricoxib 60 mg v 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. |
| End point type | Secondary |
| End point timeframe: | |
| Baseline and Week 6 | |

| End point values | Placebo | Etoricoxib 60 mg | Etoricoxib 90 mg | |
|--|---------------------------|---------------------------|---------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 108 ^[10] | 751 ^[11] | 430 ^[12] | |
| 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) | |

Notes:

[10] - Participants with ≥ 1 dose of study drug, and both baseline and post-baseline data

[11] - Participants with ≥ 1 dose of study drug, and both baseline and post-baseline data

[12] - Participants with ≥ 1 dose of study drug, and both baseline and post-baseline data

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 | Etoricoxib 60 mg v 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. 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). In those participants who were considered inadequate responders to etoricoxib 60 mg in Part 1 (defined as a participant with <50% improvement from baseline in PGAP [VAS] at Week 6), the incremental benefit of increasing the etoricoxib dose from 60 mg (in Part 1) to 90 mg (in Part 2) compared to remaining on 60 mg in Part 2 was evaluated via 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.

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

End point timeframe:

Week 6 and Week 10 to Week 12

| End point values | Etoricoxib 60 mg/etoricoxib 60 mg | Etoricoxib 60 mg/etoricoxib 90 mg | | |
|--|-----------------------------------|-----------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 188 ^[13] | 187 ^[14] | | |
| 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) | | |

Notes:

[13] - Participants with <50% improvement from baseline in PGAP at Week 6 and received at least 1 drug dose

[14] - Participants with <50% improvement from baseline in PGAP at Week 6 and received at least 1 drug dose

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 | Etoricoxib 60 mg/etoricoxib 60 mg v 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 112 days

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