# Clinical trial results:
# A Worldwide, Open Label, Clinical Trial to Examine the Long Term Safety and Tolerability of Rizatriptan in Pediatric Migraineurs for the Treatment of Migraine With or Without Aura

## Summary

| | |
|---|---|
| EudraCT number | 2009-016375-30 |
| Trial protocol | NL FI DE BE ES EE LV SE FR PL DK NO GB Outside EU/EEA |
| Global end of trial date | 18 April 2011 |

### Results information

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 05 April 2016 |
| First version publication date | 07 March 2015 |

## Trial information

### Trial identification

| | |
|---|---|
| Sponsor protocol code | MK-0462-086 |

### Additional study identifiers

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01004263 |
| WHO universal trial number (UTN) | - |

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? | Yes |

Notes:

## Results analysis stage

| | |
|---|---|
| Analysis stage | Final |
| Date of interim/final analysis | 18 April 2011 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 18 April 2011 |
| Global end of trial reached? | Yes |
| Global end of trial date | 18 April 2011 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

To provide long term safety data for rizatriptan in children and adolescents. The primary hypothesis of the study is that rizatriptan is well tolerated in the long term treatment of acute migraine in pediatric patients age 12-17 years.

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. The following additional measure defined for this individual study was in place for the protection of trial subjects: Participants who do not obtain satisfactory relief of their migraine pain at 2 hours after taking study medication may treat their migraine pain with usual care at that time and any time thereafter. However, use of 5-hydroxytryptamine 1 (5-HT1) agonists (triptans) and ergot derivatives is prohibited for 24 hours following administration of study medication. Use of rescue medication must comply with the local product label.

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 25 November 2009 |
| 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 | Finland: 11 |
| Country: Number of subjects enrolled | Netherlands: 3 |
| Country: Number of subjects enrolled | Sweden: 5 |
| Country: Number of subjects enrolled | United States: 587 |
| Worldwide total number of subjects | 606 |
| EEA total number of subjects | 19 |

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) | 606 |
| Adults (18-64 years) | 0 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

A total of 674 patients met inclusion/exclusion criteria and were allocated study drug. Of these, 606 were treated with study drug.

### Period 1

| | |
|---|---|
| Period 1 title | Overall Study (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Not applicable |
| Blinding used | Not blinded |

### Arms

| | |
|---|---|
| **Arm title** | Rizatriptan |

Arm description:

Participants self-administered rizatriptan to treat up to 8 qualifying migraine headaches (mild, moderate, or severe pain intensity) per month, for up to 12 months. Rizatriptan dose, administered as a single oral tablet, was either 5 or 10 mg, based on participant weight (5 mg if <40 kg, 10 mg if ≥40 kg).

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Rizatriptan benzoate |
| Investigational medicinal product code | |
| Other name | MK-0462, Maxalt |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Single dose of rizatriptan as 5 mg or 10 mg orally disintegrating tablet at onset of migraine attack

| **Number of subjects in period 1** | Rizatriptan |
|---|---|
| Started | 606 |
| Completed | 427 |
| Not completed | 179 |
| Lack of qualifying event | 2 |
| Adverse event, serious fatal | 1 |
| Physician decision | 15 |
| Consent withdrawn by subject | 58 |
| Adverse event, non-fatal | 14 |
| Pregnancy | 2 |
| Lost to follow-up | 64 |
| Protocol deviation | 10 |
| Lack of efficacy | 13 |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | Rizatriptan |

Reporting group description:

Participants self-administered rizatriptan to treat up to 8 qualifying migraine headaches (mild, moderate, or severe pain intensity) per month, for up to 12 months. Rizatriptan dose, administered as a single oral tablet, was either 5 or 10 mg, based on participant weight (5 mg if <40 kg, 10 mg if ≥40 kg).

| Reporting group values | Rizatriptan | Total | |
|---|---|---|---|
| Number of subjects | 606 | 606 | |
| Age categorical<br>Units: Subjects | | | |
| Age continuous<br>Units: years<br>arithmetic mean<br>standard deviation | <br><br>14.7<br>± 1.7 | <br><br><br>- | |
| Gender categorical<br>Units: Subjects | | | |
| Female | 372 | 372 | |
| Male | 234 | 234 | |

## End points

### End points reporting groups

| Reporting group title | Rizatriptan |
|---|---|

Reporting group description:

Participants self-administered rizatriptan to treat up to 8 qualifying migraine headaches (mild, moderate, or severe pain intensity) per month, for up to 12 months. Rizatriptan dose, administered as a single oral tablet, was either 5 or 10 mg, based on participant weight (5 mg if <40 kg, 10 mg if ≥40 kg).

### Primary: Number of Participants With Adverse Events (AEs) Within 24 Hours Post Any Dose

| End point title | Number of Participants With Adverse Events (AEs) Within 24 Hours Post Any Dose[1] |
|---|---|

End point description:

An AE is any unfavorable and unintended change in the structure, function or chemistry of the body temporally associated with study drug administration. Participants reported AEs in a diary and these were collected by the study site at visits at 1, 2, 3, 4, 6, 9, and 12 months after Screening visit. Participants with an AE occurring within 24 hours after any dose administered during the study are counted once in this summary.

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

End point timeframe:

Up to 24 hours post dose

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 hypothesis testing was planned for this endpoint.

| End point values | Rizatriptan | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 606[2] | | | |
| Units: Participants | 322 | | | |

Notes:

[2] - Includes participants who administered ≥1 dose of study drug

### Statistical analyses

No statistical analyses for this end point

### Primary: Number of Participants With AEs Within 14 Days Post Any Dose

| End point title | Number of Participants With AEs Within 14 Days Post Any |
|---|---|

End point description:

An AE is any unfavorable and unintended change in the structure, function or chemistry of the body temporally associated with study drug administration. Participants reported AEs in a diary and these were collected by the study site at visits at 1, 2, 3, 4, 6, 9, and 12 months after Screening visit. AEs were assessed in a phone contact 14 days after the last dose of study medication. Participants with an AE occurring within 14 days after any dose administered during the study are counted once in this summary.

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

End point timeframe:

Up to 14 days post dose

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 hypothesis testing was planned for this endpoint.

| **End point values** | Rizatriptan | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 606[4] | | | |
| Units: Participants | 400 | | | |

Notes:

[4] - Includes participants who administered ≥1 dose of study drug

### Statistical analyses

No statistical analyses for this end point

## Primary: Number of Participants Discontinued From Study Due to AEs Occurring Within 24 Hours Post Dose

| End point title | Number of Participants Discontinued From Study Due to AEs Occurring Within 24 Hours Post Dose[5] |
|---|---|

End point description:

An AE is any unfavorable and unintended change in the structure, function or chemistry of the body temporally associated with study drug administration. Participants who discontinued due to an AE occurring within 24 hours post dose are counted in this summary.

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

End point timeframe:

Up to 24 hours post dose

Notes:

[5] - 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 hypothesis testing was planned for this endpoint.

| **End point values** | Rizatriptan | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 606[6] | | | |
| Units: Participants | 4 | | | |

Notes:

[6] - Includes participants who administered ≥1 dose of study drug

### Statistical analyses

No statistical analyses for this end point

## Primary: Number of Participants Discontinued From Study Due to AEs Occurring Within 14 Days Post Dose

| End point title | Number of Participants Discontinued From Study Due to AEs Occurring Within 14 Days Post Dose[7] |
|---|---|

End point description:

An AE is any unfavorable and unintended change in the structure, function or chemistry of the body temporally associated with study drug administration. Participants who discontinued due to an AE occurring within 14 days post dose are counted in this summary.

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

End point timeframe:

Up to 14 days post dose

Notes:

[7] - 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 hypothesis testing was planned for this endpoint.

| **End point values** | Rizatriptan | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 606[8] | | | |
| Units: Participants | 14 | | | |

Notes:

[8] - Includes participants who administered ≥1 dose of study drug

### Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Participant's Migraine Attacks With Pain Freedom at 2 Hours Post Dose

| End point title | Percentage of Participant's Migraine Attacks With Pain Freedom at 2 Hours Post Dose |
|---|---|

End point description:

Pain intensity was assessed using a 5-Face Pain Scale ranging from 1=no pain to 5=very bad pain. Pain freedom (PF) was defined as a reduction in severity from a rating of 5, 4, 3 or 2 (mild, moderate or severe pain) before the dose to a rating of 1 (no pain) at 2 hours after dosing. Pain intensity ratings were reported in diaries returned at visits at 1, 2, 3, 4, 6, 9, and 12 months after Screening visit. PF at 2 hours was summarized as follows: the percentage of treated attacks with PF at 2 hours was calculated for each patient first, then the mean across all patients was calculated.

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

End point timeframe:

2 hours post dose

| **End point values** | Rizatriptan | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 603[9] | | | |
| Units: Percentage of participant's attacks | | | | |
| arithmetic mean (standard deviation) | 46.3 (± 31.9) | | | |

Notes:

[9] - Includes participants with ≥1 treated migraine attack with ≥1 post treatment efficacy evaluation

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Up to 12 months after start of study drug administration

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

### Dictionary used

| | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 13.1 |

### Reporting groups

| | |
|---|---|
| Reporting group title | Rizatriptan |

Reporting group description:

Participants self-administered rizatriptan to treat up to 8 qualifying migraine headaches (mild, moderate, or severe pain intensity) per month, for up to 12 months. Rizatriptan dose, administered as a single oral tablet, was either 5 or 10 mg, based on participant weight (5 mg if <40 kg, 10 mg if ≥40 kg).

| Serious adverse events | Rizatriptan | | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 22 / 606 (3.63%) | | |
| number of deaths (all causes) | 1 | | |
| number of deaths resulting from adverse events | | | |
| Injury, poisoning and procedural complications | | | |
| Fibula fracture | | | |
| subjects affected / exposed | 1 / 606 (0.17%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Road traffic accident | | | |
| subjects affected / exposed | 1 / 606 (0.17%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Tibia fracture | | | |
| subjects affected / exposed | 1 / 606 (0.17%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Upper limb fracture | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 606 (0.17%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Vascular disorders | | | |
| Peripheral ischemia | | | |
| subjects affected / exposed | 1 / 606 (0.17%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cardiac disorders | | | |
| Sinus bradycardia | | | |
| subjects affected / exposed | 1 / 606 (0.17%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Nervous system disorders | | | |
| Migraine | | | |
| subjects affected / exposed | 2 / 606 (0.33%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Syncope | | | |
| subjects affected / exposed | 1 / 606 (0.17%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| General disorders and administration site conditions | | | |
| Fatigue | | | |
| subjects affected / exposed | 1 / 606 (0.17%) | | |
| occurrences causally related to treatment / all | 2 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal disorders | | | |
| Abdominal discomfort | | | |
| subjects affected / exposed | 2 / 606 (0.33%) | | |
| occurrences causally related to treatment / all | 2 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Dyspnea | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 606 (0.17%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Psychiatric disorders | | | |
| Conversion disorder | | | |
| subjects affected / exposed | 1 / 606 (0.17%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Major depression | | | |
| subjects affected / exposed | 1 / 606 (0.17%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Suicidal ideation | | | |
| subjects affected / exposed | 2 / 606 (0.33%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Suicide attempt | | | |
| subjects affected / exposed | 3 / 606 (0.50%) | | |
| occurrences causally related to treatment / all | 0 / 3 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infections and infestations | | | |
| Appendicitis | | | |
| subjects affected / exposed | 2 / 606 (0.33%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastroenteritis | | | |
| subjects affected / exposed | 1 / 606 (0.17%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Viral infection | | | |
| subjects affected / exposed | 1 / 606 (0.17%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

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

| **Non-serious adverse events** | Rizatriptan | | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 284 / 606 (46.86%) | | |
| Injury, poisoning and procedural complications | | | |
| Accidental overdose | | | |
| subjects affected / exposed | 148 / 606 (24.42%) | | |
| occurrences (all) | 216 | | |
| Nervous system disorders | | | |
| Dizziness | | | |
| subjects affected / exposed | 52 / 606 (8.58%) | | |
| occurrences (all) | 94 | | |
| Somnolence | | | |
| subjects affected / exposed | 44 / 606 (7.26%) | | |
| occurrences (all) | 123 | | |
| General disorders and administration site conditions | | | |
| Fatigue | | | |
| subjects affected / exposed | 33 / 606 (5.45%) | | |
| occurrences (all) | 111 | | |
| Gastrointestinal disorders | | | |
| Nausea | | | |
| subjects affected / exposed | 40 / 606 (6.60%) | | |
| occurrences (all) | 77 | | |
| Infections and infestations | | | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 47 / 606 (7.76%) | | |
| occurrences (all) | 56 | | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 31 / 606 (5.12%) | | |
| occurrences (all) | 33 | | |

## 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