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 Units: Subjects			
Age continuous Units: years arithmetic mean standard deviation	 14.7 ± 1.7	 -	
Gender categorical 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