

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

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The objective of this study is to test the safety of the research study drug, MK-0462 (rizatriptan) and to test the ability of study drug to relieve or reduce migraine for the study population.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Headaches
Study type	Interventional

Summary

ID

NL-OMON34736

Source

ToetsingOnline

Brief title

086-01 MAXALT

Condition

- Headaches

Synonym

migraine head ache

Research involving

Human

Sponsors and support

Primary sponsor: Merck & Co., Inc.

Source(s) of monetary or material Support: Merck & Co. Inc.

Intervention

Keyword: MAXALT, pediatric migraine

Outcome measures

Primary outcome

To evaluate the safety and tolerability of rizatriptan in the long term treatment of acute migraine in pediatric patients age 12-17 years.

Secondary outcome

To estimate the efficacy of rizatriptan as measured by pain freedom at 2 hours post dose in the long term treatment of acute migraine in pediatric patients age 12-17 years.

Study description

Background summary

Migraine is a common neurological disorder afflicting children, adolescents and adults. It contributes significantly to school absence, work loss, medication use, impaired quality of life, and health care visits. Rizatriptan (manufactured and marketed as MAXALT by Merck & Co, Inc., Whitehouse Station, NJ) is a 5-HT_{1B/1D} agonist approved at a therapeutic dose of 10 or 5 mg (up to 2 - 3 doses/24 hours depending on local product label; interdose interval of 2 hours or more) for the acute treatment of migraine in adults. Triptans are prescribed for and used by pediatric migraineurs with very limited systematically collected data supporting their safety and efficacy in this population. Two well-controlled trials performed with rizatriptan 5 mg in adolescents aged 12 to 17 failed to demonstrate a statistically significant difference between treatments on the primary endpoint (pain freedom at hour 2 post dose). However, a response trend was observed in the rizatriptan group in the lower age stratum (12-14 years) compared to the higher age stratum (15-17 years), as well as by weight, in that heavier children trended toward

poorer outcomes. These findings suggest that the older and heavier children may have had insufficient exposures based on weight. A third controlled trial conducted by Ahonen et al. applied a weight-based dosing strategy for pediatric migraineurs age 6 to 17, wherein patients weighing < 40 kg received rizatriptan 5 mg or placebo and patients weighing ≥ 40 kg received rizatriptan 10 mg or placebo. This study demonstrated a significant treatment effect for both doses of rizatriptan compared to placebo [1]. Data from a recently completed pharmacokinetic study (P083) demonstrated that exposures following single dose administration of 5 mg rizatriptan ODT to pediatric migraineurs weighing 20-39 kg or 10 mg rizatriptan orally disintegrating tablet (ODT) to pediatric migraineurs weighing ≥ 40 kg were similar to those observed following single dose administration of 10 mg rizatriptan ODT to adults. This study plans to use a similar weight-based dosing strategy to further assess the long term safety and tolerability of rizatriptan in pediatric migraineurs. Two oral formulations of rizatriptan are currently available: solid tablet and ODT. The ODT formulation accounts for slightly more than half of the prescriptions in pediatric patients.

Study objective

The objective of this study is to test the safety of the research study drug, MK-0462 (rizatriptan) and to test the ability of study drug to relieve or reduce migraine for the study population.

Study design

This is an open label study. All patients will receive rizatriptan for up to 12 months. Study medication will be dosed based on the patient's body weight at screening (Visit 1). Patients weighing < 40 kg will receive 5 mg, whereas patients weighing 40 kg or more will receive 10 mg. Patients will be provided with sufficient medication to treat up to 8 migraine attacks per month during the study.

Intervention

Rizatriptan ODT (5 mg and 10 mg) will be provided by the SPONSOR and dosed according to screening body weight as follows: patients weighing < 40 kg will receive rizatriptan 5 mg; and patients weighing ≥ 40 kg will receive rizatriptan 10 mg. Patients will be provided with sufficient medication to treatment up to 8 migraine attacks per month.

Study burden and risks

Reported side effects for MK-0462 (rizatriptan) are:
Numbness, pain and/or pressure (chest, neck, throat and/or jaw region and general), dry, mouth, nausea, dizziness, headache, sleepiness,

weakness/tiredness, seizures, anaphylactic reaction (a potentially life-threatening allergic reaction that requires immediate medical attention)

In addition, an uncommon but potentially life-threatening condition called serotonin syndrome can occur with rizatriptan or other medications in the triptan class particularly when taken together with certain types of antidepressant and mood disorder medications called selective serotonin reuptake inhibitors (SSRIs), such as fluoxetine, paroxetine, sertraline, olanzapine/fluoxetine, citalopram hydrobromide, escitalopram oxalate, and selective serotonin/norepinephrine reuptake inhibitors (SNRIs), such as venlafaxine, and duloxetine.

Contacts

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Scientific

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age

Adolescents (12-15 years)

Adolescents (16-17 years)

Inclusion criteria

1. Patient is between 12 and 17 years of age at screening visit 1, inclusive.
2. Patient weighs ≥ 20 kg.
3. Patient is either:
 - a. of reproductive potential and agrees to maintain true abstinence* or use (or have their partner use) one of the listed highly effective methods of birth control within the projected duration of the study: hormonal contraceptives, intrauterine device (IUD), condoms, diaphragm, and/or vasectomy. The use of barrier contraceptive (condom or diaphragm) should always be supplemented with the use of a spermicide. Complete details regarding contraceptive requirements are specified in protocol Section 3.2.3.2.
 - b. not of reproductive potential. For the purposes of this protocol, the following definitions apply:

A female patient who is not of reproductive potential is defined as: one who 1) has not reached menarche, or 2) is 6 weeks post surgical bilateral oophorectomy, hysterectomy, or bilateral tubal ligation.

A male patient who is not of reproductive potential is defined as: one who has undergone a successful vasectomy. A successful vasectomy is defined as: 1) microscopic documentation of azoospermia, or 2) a vasectomy more than 2 years ago with no resultant pregnancy despite sexual activity post vasectomy.

* If abstinence is not a locally acceptable method of contraception, then another highly effective birth control method must be used.
4. Patient has a history of migraine defined by International Headache Society [IHS] migraine definitions, and meets the following criteria:
 - a. Unilateral or bilateral migraine headache, with or without aura;
 - b. History of migraine attacks for > 6 months; and
 - c. Reports ≥ 1 to ≤ 8 mild, moderate or severe migraine attacks per month in the 2 months prior to screening Visit 1.
5. Patient is able to complete the migraine diary and is cooperative with completing the prestudy assessments. Patients who require help to read should be assisted by an adult; however, the patient will provide the actual responses to the pain scale questions in the migraine diary.
6. The parent or guardian and patient agree to the patient's participation in the study as indicated by parental/guardian signature on the consent form and patient assent.
7. For patients taking migraine prophylactic medication, treatment regimen has been stable for at least 3 months prior to Visit 1.

Exclusion criteria

1. Patient is pregnant (positive serum β -hCG test at screening) or breast-feeding, or is a female expecting to conceive within the projected duration of study participation.
2. Patient has a history of predominantly mild migraine attacks or migraines usually

resolved spontaneously in less than 2 hours.

3. Patient has basilar or hemiplegic migraine headaches (see Appendix 6.2 for diagnostic guidance for basilar type migraines).

4. Patient has >15 headache-days per month OR has taken medication for acute headache on more than 10 days per month in any of the 3 months prior to screening.

5. Patient has clinical, laboratory, or ECG evidence of uncontrolled hypertension, uncontrolled diabetes, HIV disease, any neoplastic disease, or other significant pulmonary, renal, hepatic, endocrine, neurological, or other systemic disease in the opinion of the investigator (e.g., epilepsy; systemic lupus erythematosus; Kawasaki disease; homozygous sickle cell anemia; recurrent syncope).

6. Patient has a history or clinical evidence of any of the following: congenital heart disease suspected or confirmed; atherosclerotic disease; history of cerebrovascular pathology including stroke; Prinzmetal's angina; cardiac arrhythmias requiring medication; and hypertension for age.

7. Patient has a history or current evidence of any clinically significant disease that, according to the investigator, might confound the results of the study [e.g., chronic pain syndromes (i.e., condition requiring daily use of opiates), major psychiatric diagnoses such as schizophrenia, bipolar disorder, or major depression], that complicate the interpretation of the study results, that might interfere with the patient's participation for the full duration of the study, or pose an additional undue risk to the patient.

8. Patient has either demonstrated hypersensitivity to or experienced a serious adverse event in response to rizatriptan.

9. Patient has demonstrated hypersensitivity to or experienced a serious adverse event in response to 3 or more pharmacologic classes of drugs (prescription and over-the-counter).

10. Patient did not experience satisfactory relief from migraine pain with treatment of 2 or more adequate courses of 5HT₁ agonists, in the opinion of the investigator.

11. Patient has a recent history (within the past year) or current evidence of drug or alcohol abuse or is a "recreational user" of illicit drugs

12. Patient is currently taking monoamine oxidase inhibitors, methysergide, or propranolol, and is unable to tolerate withdrawal of these medications for the intervals required.

13. Patient is currently participating or has participated in a study with an investigational compound or device within 30 days of screening. (This includes studies using commercially available compounds or devices for investigational purposes, e.g., new indications). Note: Patients who participated in the acute efficacy study (rizatriptan) may enter into this study within 30 days of completion of the acute study.

14. Patient has abnormal screening laboratory values as per the guidelines listed below or other clinically significant, unexplained laboratory abnormality, according to the investigator:

a. AST > 1.5 x upper limit of normal

b. ALT > 1.5 x upper limit of normal

c. Total bilirubin > 1.5 x upper limit of normal

d. Serum creatinine > 1.5 x upper limit of normal

15. Patient is legally or mentally incapacitated.

16. Patient has undergone major surgery (in the opinion of the investigator) within 30

days of screening or has donated blood products or has had phlebotomy of > 300 ml within 8 weeks of signing informed consent, or intends to donate blood products or receive blood products within 30 days of screening and throughout the study.

17. Patient is unlikely to adhere to study procedures, keep appointments, or is planning to relocate during the study.

Study design

Design

Study phase:	3
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL	
Recruitment status:	Recruitment stopped
Start date (anticipated):	30-03-2010
Enrollment:	27
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Rizatriptan
Generic name:	MAXALT
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO	
Date:	09-12-2009
Application type:	First submission
Review commission:	METC Isala Klinieken (Zwolle)

Approved WMO
Date: 16-02-2010
Application type: First submission
Review commission: METC Isala Klinieken (Zwolle)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2009-016375-30-NL
ClinicalTrials.gov	NCT01004263
CCMO	NL30631.075.09