# Clinical trial results:
# A Randomized, Open-Label Study to Evaluate the Pharmacokinetics of Multiple Doses of Esomeprazole Magnesium in a Pediatric Population of 1 to 11 Year olds with Gastroesophageal Reflux Disease (GERD) or Symptoms of GERD

## Summary

| | |
|---|---|
| EudraCT number | 2012-001157-97 |
| Trial protocol | Outside EU/EEA |
| Global end of trial date | 10 March 2005 |

**Results information**

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 01 February 2017 |
| First version publication date | 08 August 2015 |

## Trial information

**Trial identification**

| | |
|---|---|
| Sponsor protocol code | D9614C00099 |

**Additional study identifiers**

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

Notes:

**Sponsors**

| | |
|---|---|
| Sponsor organisation name | AstraZeneca LP |
| Sponsor organisation address | 1800 Concord Pike, Wilmington, Delaware, United States, 19850 |
| Public contact | AZ Clinical Trial Transparency group, AstraZeneca R&D, ClinicalTrialTransparency@astrazeneca.com |
| Scientific contact | Marta Illueca, MD, FAAP, AstraZeneca LP, 1 302-885-1487, |

Notes:

**Paediatric regulatory details**

| | |
|---|---|
| Is trial part of an agreed paediatric investigation plan (PIP) | Yes |
| EMA paediatric investigation plan number(s) | EMEA-000331-PIP01-08 |
| 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 | 10 March 2005 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 10 March 2005 |
| Global end of trial reached? | Yes |
| Global end of trial date | 10 March 2005 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

To determine the area under the curve (AUC) of esomeprazole after multiple oral doses of 5 mg, 10 mg, and 20 mg esomeprazole magnesium in 1 to 11 year olds, inclusive with GERD or symptoms of GERD.

Protection of trial subjects:

The study was performed in accordance with ethical principles that have their origin in the Declaration of Helsinki and that are consistent with ICH/Good Clinical Practice and applicable regulatory requirements and the AstraZeneca policy on Bioethics. The study was approved by the independent Institutional Review Board/Research Ethics Committee, Coast IRB, 901 Calle Amanecer, Suite 260, San Clemente, CA 92673.
Informed consent was obtained from all subjects prior to initiation of the study.
Subjects could be discontinued from study treatment and assessments at any time, voluntary by subject or as judged by the investigator or AstraZeneca.

Background therapy:

The target subject population was male and female children, aged 1 to 11 years inclusive, who suffered from GERD or symptoms of GERD and were candidates for acid suppression therapy.
Eligible subjects had to be able to tolerate discontinuation of their PPI therapy for 7 days and/or H2RA therapy for 3 days prior to the first dose of study drug.

Evidence for comparator:

No comparator group.

| | |
|---|---|
| Actual start date of recruitment | 22 March 2004 |
| 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 | United States: 31 |
| Worldwide total number of subjects | 31 |
| EEA total number of subjects | 0 |

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 | 2 |

| | |
|---|---|
| months) | |
| Children (2-11 years) | 29 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 0 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details:

First subject enrolled: 22 March 2004
Last subject completed: 31 July 2004

### Pre-assignment

Screening details:

34 subjects were screened. Thirty-one (31) of these subjects were randomized and 3 failed screening. Of the 3 screen failures, 1 could not participate due to scheduling conflicts and 2 had abnormal lab values.

### Period 1

| | |
|---|---|
| Period 1 title | Treatment (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Not blinded |

Blinding implementation details:

Open-Label

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | Esomeprazole 5 mg (Age 1-5 yr) |

Arm description:

Esomeprazole 5 mg (Age 1-5 yr)

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Esomeprazole magnesium |
| Investigational medicinal product code | |
| Other name | NEXIUM |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

5 mg od orally

| | |
|---|---|
| **Arm title** | Esomeprazole 10 mg (Age 1-5 yr) |

Arm description:

Esomeprazole 10 mg (Age 1-5 yr)

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Esomeprazole magnesium |
| Investigational medicinal product code | |
| Other name | NEXIUM |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

10 mg od orally

| | |
|---|---|
| **Arm title** | Esomeprazole 10 mg (6-11 years) |

Arm description:

Esomeprazole 10 mg (6-11 years)

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

| | |
|---|---|
| Investigational medicinal product name | Esomeprazole magnesium |
| Investigational medicinal product code | |
| Other name | NEXIUM |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

10 mg od orally

| | |
|---|---|
| **Arm title** | Esomeprazole 20 mg (6-11 yr) |

Arm description:

Esomeprazole 20 mg (6-11 yr)

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Esomeprazole magnesium |
| Investigational medicinal product code | |
| Other name | NEXIUM |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

20 mg od orally

| **Number of subjects in period 1** | Esomeprazole 5 mg (Age 1-5 yr) | Esomeprazole 10 mg (Age 1-5 yr) | Esomeprazole 10 mg (6-11 years) |
|---|---|---|---|
| Started | 9 | 9 | 7 |
| Completed | 6 | 8 | 7 |
| Not completed | 3 | 1 | 0 |
| Consent withdrawn by subject | 2 | 1 | - |
| Refused to take study medication on Day 1 | 1 | - | - |

| **Number of subjects in period 1** | Esomeprazole 20 mg (6-11 yr) |
|---|---|
| Started | 6 |
| Completed | 6 |
| Not completed | 0 |
| Consent withdrawn by subject | - |
| Refused to take study medication on Day 1 | - |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | Esomeprazole 5 mg (Age 1-5 yr) |
| Reporting group description: Esomeprazole 5 mg (Age 1-5 yr) | |
| Reporting group title | Esomeprazole 10 mg (Age 1-5 yr) |
| Reporting group description: Esomeprazole 10 mg (Age 1-5 yr) | |
| Reporting group title | Esomeprazole 10 mg (6-11 years) |
| Reporting group description: Esomeprazole 10 mg (6-11 years) | |
| Reporting group title | Esomeprazole 20 mg (6-11 yr) |
| Reporting group description: Esomeprazole 20 mg (6-11 yr) | |

| Reporting group values | Esomeprazole 5 mg (Age 1-5 yr) | Esomeprazole 10 mg (Age 1-5 yr) | Esomeprazole 10 mg (6-11 years) |
|---|---|---|---|
| Number of subjects | 9 | 9 | 7 |
| Age Categorical<br>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 | 2 | 0 |
| Children (2-11 years) | 9 | 7 | 7 |
| Adolescents (12-17 years) | 0 | 0 | 0 |
| Adults (18-64 years) | 0 | 0 | 0 |
| From 65-84 years | 0 | 0 | 0 |
| 85 years and over | 0 | 0 | 0 |
| Age Continuous | | | |
| Age (years) | | | |
| Units: years | | | |
| arithmetic mean | 3.8 | 2.3 | 8.4 |
| full range (min-max) | 2 to 5 | 1 to 4 | 6 to 11 |
| Gender Categorical<br>Units: Subjects | | | |
| Female | 6 | 3 | 2 |
| Male | 3 | 6 | 5 |

| Reporting group values | Esomeprazole 20 mg (6-11 yr) | Total | |
|---|---|---|---|
| Number of subjects | 6 | 31 | |
| Age Categorical<br>Units: Subjects | | | |
| In utero | 0 | 0 | |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | |
| Newborns (0-27 days) | 0 | 0 | |

| | | | |
|---|---|---|---|
| Infants and toddlers (28 days-23 months) | 0 | 2 | |
| Children (2-11 years) | 6 | 29 | |
| Adolescents (12-17 years) | 0 | 0 | |
| Adults (18-64 years) | 0 | 0 | |
| From 65-84 years | 0 | 0 | |
| 85 years and over | 0 | 0 | |
| Age Continuous | | | |
| Age (years) | | | |
| Units: years | | | |
| arithmetic mean | 7.8 | | |
| full range (min-max) | 6 to 11 | - | |
| Gender Categorical | | | |
| Units: Subjects | | | |
| Female | 3 | 14 | |
| Male | 3 | 17 | |

**Subject analysis sets**

| | |
|---|---|
| Subject analysis set title | Full data set |
| Subject analysis set type | Intention-to-treat |

Subject analysis set description:

Full data set

| **Reporting group values** | Full data set | | |
|---|---|---|---|
| Number of subjects | 31 | | |
| 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) | 2 | | |
| Children (2-11 years) | 29 | | |
| Adolescents (12-17 years) | 0 | | |
| Adults (18-64 years) | 0 | | |
| From 65-84 years | 0 | | |
| 85 years and over | 0 | | |
| Age Continuous | | | |
| Age (years) | | | |
| Units: years | | | |
| arithmetic mean | 5.2 | | |
| full range (min-max) | 1 to 11 | | |
| Gender Categorical | | | |
| Units: Subjects | | | |
| Female | 14 | | |
| Male | 17 | | |

## End points

### End points reporting groups

| | |
|---|---|
| Reporting group title | Esomeprazole 5 mg (Age 1-5 yr) |
| Reporting group description: Esomeprazole 5 mg (Age 1-5 yr) | |
| Reporting group title | Esomeprazole 10 mg (Age 1-5 yr) |
| Reporting group description: Esomeprazole 10 mg (Age 1-5 yr) | |
| Reporting group title | Esomeprazole 10 mg (6-11 years) |
| Reporting group description: Esomeprazole 10 mg (6-11 years) | |
| Reporting group title | Esomeprazole 20 mg (6-11 yr) |
| Reporting group description: Esomeprazole 20 mg (6-11 yr) | |
| Subject analysis set title | Full data set |
| Subject analysis set type | Intention-to-treat |
| Subject analysis set description: Full data set | |

### Primary: Primary PK parameter AUC

| | |
|---|---|
| End point title | Primary PK parameter AUC[1] |
| End point description: AUC after repeated doses | |
| End point type | Primary |
| End point timeframe: after repetaed doses (5 days) | |

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: Descriptive - No statistical analyses were specified for this primary end point

| End point values | Esomeprazole 5 mg (Age 1-5 yr) | Esomeprazole 10 mg (Age 1-5 yr) | Esomeprazole 10 mg (6-11 years) | Esomeprazole 20 mg (6-11 yr) |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 5[2] | 8[3] | 7[4] | 6[5] |
| Units: micromol*h/L | | | | |
| geometric mean (standard deviation) | 0.74 (± 0.36) | 4.83 (± 2.56) | 3.7 (± 2.05) | 6.28 (± 2.71) |

Notes:

[2] - number of subjects evaluated for AUC

[3] - number of subjects evaluated for AUC

[4] - number of subjects evaluated for AUC

[5] - number of subjects evaluated for AUC

### Statistical analyses

No statistical analyses for this end point

## Adverse events

| Adverse events information | |
|---|---|
| Timeframe for reporting adverse events: Treatment (5 days) | |
| Assessment type | Systematic |

| Dictionary used | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 6.0 |

| Reporting groups | |
|---|---|
| Reporting group title | Esomeprazole 5 mg (Age 1-5 yr) |
| Reporting group description: Esomeprazole 5 mg (Age 1-5 yr) | |
| Reporting group title | Esomeprazole 10 mg (Age 1-5 yr) |
| Reporting group description: Esomeprazole 10 mg (Age 1-5 yr) | |
| Reporting group title | Esomeprazole 10 mg (6-11 years) |
| Reporting group description: Esomeprazole 10 mg (6-11 years) | |
| Reporting group title | Esomeprazole 20 mg (6-11 yr) |
| Reporting group description: Esomeprazole 20 mg (6-11 yr) | |

| Serious adverse events | Esomeprazole 5 mg (Age 1-5 yr) | Esomeprazole 10 mg (Age 1-5 yr) | Esomeprazole 10 mg (6-11 years) |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 9 (0.00%) | 0 / 7 (0.00%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Injury, poisoning and procedural complications | | | |
| Skin laceration | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 9 (0.00%) | 0 / 7 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| Serious adverse events | Esomeprazole 20 mg (6-11 yr) | | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | 0 | | |

| | | | |
|---|---|---|---|
| Injury, poisoning and procedural complications | | | |
| Skin laceration | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

Frequency threshold for reporting non-serious adverse events: 3 %

| **Non-serious adverse events** | Esomeprazole 5 mg (Age 1-5 yr) | Esomeprazole 10 mg (Age 1-5 yr) | Esomeprazole 10 mg (6-11 years) |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 2 / 9 (22.22%) | 0 / 7 (0.00%) |
| Injury, poisoning and procedural complications | | | |
| Excoriation | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 9 (11.11%) | 0 / 7 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Gastrointestinal disorders | | | |
| Faeces discoloured | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 9 (11.11%) | 0 / 7 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |

| **Non-serious adverse events** | Esomeprazole 20 mg (6-11 yr) | | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | | |
| Injury, poisoning and procedural complications | | | |
| Excoriation | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | | |
| occurrences (all) | 0 | | |
| Gastrointestinal disorders | | | |
| Faeces discoloured | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | | |
| occurrences (all) | 0 | | |

## 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