Clinical trial results:
A Randomized, Open-Label Study to Evaluate the Pharmacokinetics of Single Oral Doses of Esomeprazole Magnesium in Pediatric Patients 1 to 11 Years-Old Inclusive with Endoscopically-Proven Gastroesophageal Reflux Disease (GERD)

Summary

EudraCT number	2012-001156-19
Trial protocol	Outside EU/EEA
Global end of trial date	19 September 2008

Results information

Result version number	v1 (current)
This version publication date	01 February 2017
First version publication date	06 August 2015

Trial information

Trial identification

Sponsor protocol code	D9614C00007

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	19 September 2008
Is this the analysis of the primary completion data?	Yes
Primary completion date	19 September 2008
Global end of trial reached?	Yes
Global end of trial date	19 September 2008
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study was to determine the area under the plasma concentration time curve (AUC) of esomeprazole after single oral doses of 5 mg, 10 mg, or 20 mg esomeprazole in pediatric patients 1 to 11 years old, inclusive, with endoscopically proven GERD.

Protection of trial subjects:

This study was performed in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with International Conference on Harmonisation (ICH)/Good Clinical Practice (GCP) and applicable regulatory requirements and the AstraZeneca policy on Bioethics. The study was approved by the independent Institutional Review Board (IRB)/Independent Ethics Committee (IEC). Signed, written informed consent from patient’s parent/guardian with assent from the patient, if appropriate were obtained before any study procedures.

Background therapy:

Other medication considered necessary for the patient's safety and well being could be given at the discretion of the investigator(s). Patients were not allowed to take any prescription or OTC PPIs beginning from 7 days before and H2RAs beginning from 3 days before randomization through completion of study procedures on Day 1. PPIs and H2RAs were resumed after discharge from the CRC at the discretion of the investigator.
Patients were not allowed to take OTC antacids from 24 hours before randomization through completion of study procedures on Day 1. Resumption of treatment with antacids was at the discretion of the investigator.

Evidence for comparator:

No comparator group

Actual start date of recruitment	14 August 2006
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: 28
Worldwide total number of subjects	28
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 months)	5
Children (2-11 years)	23
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: 14 August 2006
Last subject completed: 08 May 2008

Pre-assignment

Screening details:

35 patients were screened and 28 subjects were eligible for study

Pre-assignment period milestones

Number of subjects started	28
Number of subjects completed	28

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	Group A

Arm description:

Subjects 8 to<20 kg, esomeprazole 5 mg

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

Dosage and administration details:

5 mg single oral dose

Arm title	Group B

Arm description:

BW 8 to <20 kg, esomeprazole 10 mg

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

Dosage and administration details:

10 mg single dose orally

Arm title	Group C

Arm description: BW > 20 kg, esomeprazole 10 mg	
Arm type	Experimental
Investigational medicinal product name	Esomeprazole
Investigational medicinal product code	
Other name	NEXIUM
Pharmaceutical forms	Capsule
Routes of administration	Oral use
Dosage and administration details: 10 mg single dose orally	
Arm title	Group D
Arm description: BW > 20kg, esomeprazole 20 mg	
Arm type	Experimental
Investigational medicinal product name	Esomeprazole
Investigational medicinal product code	
Other name	NEXIUM
Pharmaceutical forms	Capsule
Routes of administration	Oral use
Dosage and administration details: 20 mg single dose orally	

Number of subjects in period 1	Group A	Group B	Group C
Started	7	7	6
Completed	7	7	6

Number of subjects in period 1	Group D
Started	8
Completed	8

Baseline characteristics

Reporting groups	
Reporting group title	Group A
Reporting group description:	
Subjects 8 to<20 kg, esomeprazole 5 mg	
Reporting group title	Group B
Reporting group description:	
BW 8 to <20 kg, esomeprazole 10 mg	
Reporting group title	Group C
Reporting group description:	
BW > 20 kg, esomeprazole 10 mg	
Reporting group title	Group D
Reporting group description:	
BW > 20kg, esomeprazole 20 mg	

Reporting group values	Group A	Group B	Group C
Number of subjects	7	7	6
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)	2	3	0
Children (2-11 years)	5	4	6
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			
Full data set, total n=28			
Units: years			
arithmetic mean	3.14	3	8
full range (min-max)	1 to 5	1 to 6	6 to 10
Gender Categorical Units: Subjects			
Female	2	2	2
Male	5	5	4

Reporting group values	Group D	Total	
Number of subjects	8	28	
Age Categorical 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	5	
Children (2-11 years)	8	23	
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			
Full data set, total n=28			
Units: years			
arithmetic mean	8.5		
full range (min-max)	5 to 11	-	
Gender Categorical			
Units: Subjects			
Female	6	12	
Male	2	16	

Subject analysis sets

Subject analysis set title	Full data set
Subject analysis set type	Full analysis

Subject analysis set description:

Full data set total (n=28)

Reporting group values	Full data set		
Number of subjects	28		
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)	5		
Children (2-11 years)	23		
Adolescents (12-17 years)	0		
Adults (18-64 years)	0		
From 65-84 years	0		
85 years and over	0		
Age Continuous			
Full data set, total n=28			
Units: years			
arithmetic mean	5.68		
full range (min-max)	1 to 11		
Gender Categorical			
Units: Subjects			
Female	12		
Male	16		

End points

End points reporting groups

Reporting group title	Group A
Reporting group description: Subjects 8 to<20 kg, esomeprazole 5 mg	
Reporting group title	Group B
Reporting group description: BW 8 to <20 kg, esomeprazole 10 mg	
Reporting group title	Group C
Reporting group description: BW > 20 kg, esomeprazole 10 mg	
Reporting group title	Group D
Reporting group description: BW > 20kg, esomeprazole 20 mg	
Subject analysis set title	Full data set
Subject analysis set type	Full analysis
Subject analysis set description: Full data set total (n=28)	

Primary: AUC

End point title	AUC[1]
End point description: Area under the esomeprazole plasma concentration-time curve	
End point type	Primary
End point timeframe: 1 day	

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 anlysis

End point values	Group A	Group B	Group C	Group D
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6[2]	7	5[3]	7[4]
Units: µmolh/L				
geometric mean (full range (min-max))	0.73 (0.35 to 3.16)	1.32 (0.67 to 3.12)	0.69 (0.35 to 1.37)	3.06 (1.04 to 9.96)

Notes:

[2] - Insufficient no. measurable plasma concentrations in 1 patient to determine AUC

[3] - Insufficient no. measurable plasma concentrations in 1 patient to determine AUC

[4] - Insufficient no. measurable plasma concentrations in 1 patient to determine AUC

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
During single dose treatment through 7-14 days postdose	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	Not known

Reporting groups	
Reporting group title	Group A
Reporting group description:	
Subjects 8 to<20 kg, esomeprazole 5 mg	
Reporting group title	Group B
Reporting group description:	
BW 8 to <20 kg, esomeprazole 10 mg	
Reporting group title	Group C
Reporting group description:	
BW > 20 kg, esomeprazole 10 mg	
Reporting group title	Group D
Reporting group description:	
BW > 20kg, esomeprazole 20 mg	

Serious adverse events	Group A	Group B	Group C
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Serious adverse events	Group D		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 8 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	Group A	Group B	Group C
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 7 (28.57%)	5 / 7 (71.43%)	3 / 6 (50.00%)
Infections and infestations			
Ear infection			
subjects affected / exposed	0 / 7 (0.00%)	2 / 7 (28.57%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
Upper respiratory tract infection			
subjects affected / exposed	1 / 7 (14.29%)	1 / 7 (14.29%)	0 / 6 (0.00%)
occurrences (all)	1	1	0
sinusitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	2 / 6 (33.33%)
occurrences (all)	0	0	2

Non-serious adverse events	Group D		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 8 (37.50%)		
Infections and infestations			
Ear infection			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Upper respiratory tract infection			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
sinusitis			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
05 March 2007	Patients who had an endoscopy within 42 days of enrollment were not required to have an endoscopy at the screening visit.
18 September 2007	Interim analysis added, change in requirement for endoscopy in smaller children, BW criteria extended

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported