Clinical trial results:
A Randomized, Open-Label Study to Evaluate the Pharmacokinetics of Single and Multiple Doses of Esomeprazole Magnesium 20 mg and 40 mg in a Pediatric Population of 12 to 17 Year-Olds with Gastroesophageal Reflux Disease (GERD) or Symptoms of GERD

Summary

EudraCT number	2012-001158-25
Trial protocol	Outside EU/EEA
Global end of trial date	15 July 2004

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	D9614C00094

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	AstraZeneca Pharmaceuticals
Sponsor organisation address	One MedImmune Way, Gaithersburg, MD, United States, 20878
Public contact	AZ Clinical Trial Transparency group, AstraZeneca R&D, ClinicalTrialTransparency@astrazeneca.com
Scientific contact	June Zhao, MD, AstraZeneca Pharmaceuticals, www.June.Zhao@astrazeneca.com

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	15 July 2004
Is this the analysis of the primary completion data?	Yes
Primary completion date	15 July 2004
Global end of trial reached?	Yes
Global end of trial date	15 July 2004
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine AUC after single and repeated (multiple) oral doses of 20 mg and 40 mg esomeprazole magnesium in 12- to 17-year-olds inclusive with GERD or symptoms of GERD.

Protection of trial subjects:

The 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)/Research Ethics Committee, the Arkansas Research Human Volunteers Research Committee.
Informed consent was obtained from all subjects' parent/guardian with assent from all subjects prior to Screening. Subjects were at any time free to discontinue his/her participation in the study without prejudice to further treatment

Background therapy:

Concurrent therapy with PPIs and H2RAs was not permitted within 7 days prior to Day 1 until discharge from the CRC on Day 8.
Any medication, which was considered necessary for the subject's safety and well-being, was allowed at the discretion of the investigator

Evidence for comparator:

No comparator group

Actual start date of recruitment	08 September 2003
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	0

months)	
Children (2-11 years)	0
Adolescents (12-17 years)	28
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

First subject enrolled: 08 September 2003
Last subject completed: 13 October 2003

Pre-assignment

Screening details:

38 subjects were screened and 28 subjects were enrolled and randomised

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 magnesium 20 mg

Arm description:

esomeprazole magnesium 20 mg

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

Arm title	esomeprazole magnesium 40 mg

Arm description:

esomeprazole magnesium 40 mg

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:

40 mg od

Number of subjects in period 1	esomeprazole magnesium 20 mg	esomeprazole magnesium 40 mg
Started	14	14
Completed	14	14

Baseline characteristics

Reporting groups	
Reporting group title	esomeprazole magnesium 20 mg
Reporting group description: esomeprazole magnesium 20 mg	
Reporting group title	esomeprazole magnesium 40 mg
Reporting group description: esomeprazole magnesium 40 mg	

Reporting group values	esomeprazole magnesium 20 mg	esomeprazole magnesium 40 mg	Total
Number of subjects	14	14	28
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)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	14	14	28
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	13.9	14.7	
standard deviation	± 1.98	± 1.68	-
Gender Categorical Units: Subjects			
Female	6	7	13
Male	8	7	15

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	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)	0		
Children (2-11 years)	0		
Adolescents (12-17 years)	28		
Adults (18-64 years)	0		

End points

End points reporting groups

Reporting group title	esomeprazole magnesium 20 mg
Reporting group description: esomeprazole magnesium 20 mg	
Reporting group title	esomeprazole magnesium 40 mg
Reporting group description: esomeprazole magnesium 40 mg	
Subject analysis set title	Full data set
Subject analysis set type	Intention-to-treat
Subject analysis set description: Full data set	

Primary: AUC single dose

End point title	AUC single dose[1]
End point description: AUC (umol*h/L)	
End point type	Primary
End point timeframe: After single 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: There is no statistical analyses specified for the pharmacokinetic results because there was no hypothesis being tested. Discriptive statistis are only presented

End point values	esomeprazole magnesium 20 mg	esomeprazole magnesium 40 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	13		
Units: umol*h/L				
geometric mean (confidence interval 95%)	1.58 (1.07 to 2.32)	5.88 (3.94 to 7.88)		

Statistical analyses

No statistical analyses for this end point

Primary: AUC after repeated dosing

End point title	AUC after repeated dosing[2]
End point description: AUC after repeated dosin	
End point type	Primary
End point timeframe: After repeated dosing	

Notes:

[2] - 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: There is no statistical analyses specified for the pharmacokinetic results because there was no hypothesis being tested. Discriptive statistis are only presented

End point values	esomeprazole magnesium 20 mg	esomeprazole magnesium 40 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	12		
Units: umol*h/L				
geometric mean (confidence interval 95%)	3.65 (2.63 to 5.05)	13.86 (10.85 to 17.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: AUC(0-t) after single dose

End point title	AUC(0-t) after single dose
End point description: AUC(0-t) (umol*h/L) after single dosing	
End point type	Secondary
End point timeframe: After single dose	

End point values	esomeprazole magnesium 20 mg	esomeprazole magnesium 40 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	14		
Units: umol*h/L				
geometric mean (confidence interval 95%)	0.83 (0.37 to 1.84)	4.89 (3.43 to 6.97)		

Statistical analyses

No statistical analyses for this end point

Secondary: AUC(0-t) after repeated dosing

End point title	AUC(0-t) after repeated dosing
End point description: AUC(0-t) (umol*h/L) after repeated dosing	
End point type	Secondary

End point timeframe:
After repeated dosing

End point values	esomeprazole magnesium 20 mg	esomeprazole magnesium 40 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	14		
Units: umol*h/L				
geometric mean (confidence interval 95%)	2.47 (1.37 to 4.46)	11.51 (8.87 to 14.94)		

Statistical analyses

No statistical analyses for this end point

Secondary: Cmax after single dosing

End point title	Cmax after single dosing
End point description: Cmax (umol/L) after single dosing	
End point type	Secondary
End point timeframe: After single dosing	

End point values	esomeprazole magnesium 20 mg	esomeprazole magnesium 40 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	14		
Units: umol/L				
geometric mean (confidence interval 95%)	0.67 (0.34 to 1.84)	2.78 (1.97 to 3.91)		

Statistical analyses

No statistical analyses for this end point

Secondary: Cmax after repeated dosing

End point title	Cmax after repeated dosing
End point description: Cmax (umol/L) after repeated dosing	
End point type	Secondary

End point timeframe:

After repeated dosing

End point values	esomeprazole magnesium 20 mg	esomeprazole magnesium 40 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	14		
Units: umol/L				
geometric mean (confidence interval 95%)	1.45 (0.83 to 2.53)	5.13 (4 to 6.57)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: During enrollement/randomised treatment (8 days)	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	6.0
Reporting groups	
Reporting group title	esomeprazole magnesium 40 mg
Reporting group description: esomeprazole magnesium 40 mg	
Reporting group title	esomeprazole magnesium 20 mg
Reporting group description: esomeprazole magnesium 20 mg	

Serious adverse events	esomeprazole magnesium 40 mg	esomeprazole magnesium 20 mg	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

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

Non-serious adverse events	esomeprazole magnesium 40 mg	esomeprazole magnesium 20 mg	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 14 (7.14%)	3 / 14 (21.43%)	
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 14 (7.14%)	1 / 14 (7.14%)	
occurrences (all)	1	1	
Gastrointestinal disorders			
tooth ache			
subjects affected / exposed	0 / 14 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
vomiting			

subjects affected / exposed	0 / 14 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
Joint swelling			
subjects affected / exposed	0 / 14 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 July 2003	Multiple items

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported