Clinical trial results:
A Phase III, Multicenter, Randomized, Double-blind, Parallel-group Study to Evaluate the Safety of Once Daily Esomeprazole for the Treatment of Clinically Diagnosed Gastroesophageal Reflux Disease (GERD) in Pediatric and Adolescent Patients 12 to 17 Years, Inclusive

Summary

EudraCT number	2012-001136-61
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	16 August 2015

Trial information

Trial identification

Sponsor protocol code	D9614C00098

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, 1 302-885-5514,

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 this study was to evaluate the safety and tolerability of once daily treatment with esomeprazole in pediatric and adolescent patients 12 to 17 years of age, inclusive, with clinically diagnosed 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 ICH/Good Clinical Practice and applicable regulatory requirements and the AstraZeneca policy on Bioethics. The final Clinical Study Protocol (CSP), including the final version of the Informed Consent Form and all advertising used to recruit patients, had to be approved by an Institutional Review Board (IRB) before enrollment of any patient into the study.All patients (and their parents/guardians) were provided with all the information necessary to make an informed decision about their participation in the study, including the nature and intended purpose of the study, possible benefits and possible risks. All information in the informed consent form was provided in language understandable to the patients and their parents/guardians. The patient's parent/guardian's signed and dated informed consent as well as the patient's signed and dated assent were obtained before conducting any procedure specifically for the study. If the patient or patient's parents/guardians could not read, the informed consent form (or assent) was signed and dated by an impartial witness. The person who discussed the informed consent information with the patient also signed and dated the form.Patients could be discontinued from study treatment and assessments at any time, voluntary by the patient who was free to discontinue at anay time, or at the discretion of the investigator(s)

Background therapy:

PPI use within 14 days prior to randomization (Visit 2), including over-the-counter (OTC) PRILOSEC® (AstraZeneca LP) was exclusion criteria, as was any prescription or OTC treatment use for symptoms of GERD, such as H2RA or prokinetics, within 3 days (72 hours) prior to randomization (Visit 2). Antacids were allowed, except for those containing bismuth.

Evidence for comparator:

No comparator group

Actual start date of recruitment	20 February 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	France: 5
Country: Number of subjects enrolled	Italy: 1
Country: Number of subjects enrolled	Canada: 21
Country: Number of subjects enrolled	United States: 122

Worldwide total number of subjects	149
EEA total number of subjects	6

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)	149
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

First patient enrolled: 20 February 2004
Last patient completed: 04 May 2005

Pre-assignment

Screening details:

Out of 157 patients screened for this study, 8 patients failed to be eligible and never received study medication.

Pre-assignment period milestones

Number of subjects started	149
Number of subjects completed	149

Period 1

Period 1 title	Treatment (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Monitor, Carer, Data analyst, Assessor, Subject

Blinding implementation details:

Double-blind

Arms

Are arms mutually exclusive?	Yes
Arm title	Esomeprazole 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 orally

Arm title	Esomeprazole 40 mg

Arm description:

Esomeprazole magnesium 40 mg

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

Dosage and administration details:

40 mg od orally

Number of subjects in period 1	Esomeprazole 20 mg	Esomeprazole 40 mg
Started	76	73
Completed	60	67
Not completed	16	6
Consent withdrawn by subject	4	1
Adverse event, non-fatal	5	1
Lost to follow-up	1	3
Lack of efficacy	2	-
Not eligible, developed discont. crit, 2 not spec.	4	1

Baseline characteristics

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

Reporting group values	Esomeprazole 20 mg	Esomeprazole 40 mg	Total
Number of subjects	76	73	149
Age Categorical			
Age years			
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)	76	73	149
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			
median	14	14	
full range (min-max)	12 to 17	12 to 17	-
Gender Categorical			
Units: Subjects			
Female	47	42	89
Male	29	31	60

Subject analysis sets	
Subject analysis set title	ITT
Subject analysis set type	Intention-to-treat
Subject analysis set description: ITT	

Reporting group values	ITT		
Number of subjects	149		
Age Categorical			
Age years			
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)	149		
Adults (18-64 years)	0		
From 65-84 years	0		
85 years and over	0		
Age Continuous			
Age (years)			
Units: years			
median	14		
full range (min-max)	12 to 17		
Gender Categorical			
Units: Subjects			
Female	89		
Male	60		

End points

End points reporting groups

Reporting group title	Esomeprazole 20 mg
Reporting group description: Esomeprazole magnesium 20 mg	
Reporting group title	Esomeprazole 40 mg
Reporting group description: Esomeprazole magnesium 40 mg	
Subject analysis set title	ITT
Subject analysis set type	Intention-to-treat
Subject analysis set description: ITT	

Primary: Number of patients whose Physician Global Assessment score improved from baseline at their final visit (ITT population)

End point title	Number of patients whose Physician Global Assessment score improved from baseline at their final visit (ITT population)[1]
End point description: Number of patients whose Physician's Globle Assessment score improved from baseline	
End point type	Primary
End point timeframe: From baseline to final Visit	

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: Only Discriptive statistics are provided for the endpoints.

End point values	Esomeprazole 20 mg	Esomeprazole 40 mg	ITT	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	76	73	149	
Units: Number of subjects	55	55	110	

Statistical analyses

No statistical analyses for this end point

Secondary: Heartburn Symptom - average change from baseline at final week

End point title	Heartburn Symptom - average change from baseline at final week
End point description: symptoms were rated on a 4-point scale as follows: 0=none; 1=mild; 2=moderate; 3=severe.	
End point type	Secondary
End point timeframe: Baseline to final week	

End point values	Esomeprazole 20 mg	Esomeprazole 40 mg	ITT	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	73[2]	72[3]	145[4]	
Units: Change in average score				
arithmetic mean (standard deviation)	-0.72 (± 0.97)	-0.71 (± 0.92)	-0.72 (± 0.95)	

Notes:

[2] - All patients who had heartburn symptoms at baseline

[3] - All patients who had heartburn symptoms at baseline

[4] - All patients who had heartburn symptoms at baseline

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: During treatment (8weeks)	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	8.0
Reporting groups	
Reporting group title	Esomeprazole 40 mg
Reporting group description: Esomeprazole magnesium 40 mg	
Reporting group title	Esomeprazole 20 mg
Reporting group description: Esomeprazole magnesium 20 mg	

Serious adverse events	Esomeprazole 40 mg	Esomeprazole 20 mg	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 73 (0.00%)	0 / 75 (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 40 mg	Esomeprazole 20 mg	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	57 / 73 (78.08%)	56 / 75 (74.67%)	
Nervous system disorders			
Headache			
subjects affected / exposed	15 / 73 (20.55%)	12 / 75 (16.00%)	
occurrences (all)	57	56	
General disorders and administration site conditions			
pyrexia			
subjects affected / exposed	2 / 73 (2.74%)	5 / 75 (6.67%)	
occurrences (all)	57	56	
Gastrointestinal disorders			

Abdominal pain			
subjects affected / exposed	9 / 73 (12.33%)	9 / 75 (12.00%)	
occurrences (all)	57	56	
Diarrhoea			
subjects affected / exposed	8 / 73 (10.96%)	6 / 75 (8.00%)	
occurrences (all)	57	56	
Vomiting			
subjects affected / exposed	7 / 73 (9.59%)	5 / 75 (6.67%)	
occurrences (all)	57	56	
Nausea			
subjects affected / exposed	4 / 73 (5.48%)	6 / 75 (8.00%)	
occurrences (all)	57	56	
constipation			
subjects affected / exposed	4 / 73 (5.48%)	2 / 75 (2.67%)	
occurrences (all)	57	56	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	5 / 73 (6.85%)	6 / 75 (8.00%)	
occurrences (all)	57	56	
pharyngolaryngeal pain			
subjects affected / exposed	9 / 73 (12.33%)	1 / 75 (1.33%)	
occurrences (all)	57	56	
Nasal congestion			
subjects affected / exposed	1 / 73 (1.37%)	4 / 75 (5.33%)	
occurrences (all)	57	56	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	9 / 73 (12.33%)	9 / 75 (12.00%)	
occurrences (all)	57	56	
Upper respiratory tract infection			
subjects affected / exposed	4 / 73 (5.48%)	9 / 75 (12.00%)	
occurrences (all)	57	56	
sinusitis			
subjects affected / exposed	4 / 73 (5.48%)	3 / 75 (4.00%)	
occurrences (all)	57	56	

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