Clinical trial results:
A Phase III, Multicentre, Randomized, Double-blind Parallel-group Study to Evaluate the Safety and Clinical Outcome of Once Daily Esomeprazole for the Treatment of Gastroesophageal Reflux Disease (GERD) in Pediatric Patients 1 to 11 Years of Age, Inclusive

Summary

EudraCT number	2004-002370-39
Trial protocol	IT Outside EU/EEA
Global end of trial date	09 November 2005

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	D9614C00097

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, DE, United States, 19850-5437
Public contact	Clinical Trial Transparency, Astrazeneca LP, ClinicalTrialTransparency@astrazeneca.com
Scientific contact	Marta Illueca, MD FAAP, Astrazeneca LP, 01 302 885 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	09 November 2005
Is this the analysis of the primary completion data?	Yes
Primary completion date	09 November 2005
Global end of trial reached?	Yes
Global end of trial date	09 November 2005
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the safety of once daily treatment with esomeprazole in relieving GERD-associated symptoms in pediatric patients 1 to 11 years of age, inclusive.

Protection of trial subjects:

Before first patient into the study, a representative of AstraZeneca visited the investigational study site to:

- determine the adequacy of the facilities
- discuss with the investigator(s) (and other personnel involved with the study) their responsibilities with regard to protocol adherence, and the responsibilities of AstraZeneca or its representatives. This was documented in a Clinical Study Agreement between AstraZeneca and the investigator.

During the study, a monitor from AstraZeneca or company representing AstraZeneca had regular contacts with the investigational site, including visits to:

- provide information and support to the investigator(s)
- confirm that facilities remained acceptable
- confirm that the investigational team was adhering to the protocol, that data were being accurately recorded in the CRFs, and that investigational product accountability checks were being performed
- perform source data verification (a comparison of the data in the CRFs with the patient's medical records at the hospital or practice, and other records relevant to the study). This required direct access to all original records for each patient (eg, clinic charts).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	13 October 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	Belgium: 9
Country: Number of subjects enrolled	United States: 83
Country: Number of subjects enrolled	Italy: 10
Country: Number of subjects enrolled	France: 7
Worldwide total number of subjects	109
EEA total number of subjects	26

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)	20
Children (2-11 years)	89
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 patient enrolled: 13 October 2004
Last patient completed: 09 November 2005

Pre-assignment

Screening details:

Patients underwent screening procedures within 21 days prior to Day 0. . Information on those patients who failed screening was recorded on a Screening Log. 109 patientents were elgible for enrollemtn/randomisation.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Esomeprazole 5 mg
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	esomeprazole
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use
Dosage and administration details: 5 mg Oral	
Arm title	Esomeprazole 10 mg Wt<20 kg
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	esomeprazole
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use
Dosage and administration details: 10 mg oral	
Arm title	Esomeprazole 10 mg Wt >= 20 kg
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	esomeprazole
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:
10 mg oral

Arm title	Esomeprazole 20 mg Wt >= 20kg
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	esomeprazole
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:
20 oral

Number of subjects in period 1	Esomeprazole 5 mg	Esomeprazole 10 mg Wt<20 kg	Esomeprazole 10 mg Wt >= 20 kg
Started	26	23	31
Completed	24	22	26
Not completed	2	1	5
Consent withdrawn by subject	-	-	1
Incorrect Rand & Started Exclusion. Med.	2	-	1
Adverse event, non-fatal	-	1	2
Lack of efficacy	-	-	1

Number of subjects in period 1	Esomeprazole 20 mg Wt >= 20kg
Started	29
Completed	29
Not completed	0
Consent withdrawn by subject	-
Incorrect Rand & Started Exclusion. Med.	-
Adverse event, non-fatal	-
Lack of efficacy	-

Baseline characteristics

Reporting groups	
Reporting group title	Esomeprazole 5 mg
Reporting group description: -	
Reporting group title	Esomeprazole 10 mg Wt<20 kg
Reporting group description: -	
Reporting group title	Esomeprazole 10 mg Wt >= 20 kg
Reporting group description: -	
Reporting group title	Esomeprazole 20 mg Wt >= 20kg
Reporting group description: -	

Reporting group values	Esomeprazole 5 mg	Esomeprazole 10 mg Wt<20 kg	Esomeprazole 10 mg Wt >= 20 kg
Number of subjects	26	23	31
Age categorical			
Number of subjects in each age category			
Units: Subjects			
Infants and toddlers (28 days-23 months)	12	8	0
Children (2-11 years)	14	15	31
Age continuous			
Units: years			
median	2	2	9
full range (min-max)	1 to 6	1 to 6	4 to 11
Gender categorical			
Units: Subjects			
Female	14	14	14
Male	12	9	17

Reporting group values	Esomeprazole 20 mg Wt >= 20kg	Total	
Number of subjects	29	109	
Age categorical			
Number of subjects in each age category			
Units: Subjects			
Infants and toddlers (28 days-23 months)	0	20	
Children (2-11 years)	29	89	
Age continuous			
Units: years			
median	8		
full range (min-max)	4 to 11	-	
Gender categorical			
Units: Subjects			
Female	11	53	
Male	18	56	

Subject analysis sets

Subject analysis set title	ITT
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Intention to treat

Reporting group values	ITT		
Number of subjects	109		
Age categorical			
Number of subjects in each age category			
Units: Subjects			
Infants and toddlers (28 days-23 months)	20		
Children (2-11 years)	89		
Age continuous			
Units: years			
median	6		
full range (min-max)	1 to 11		
Gender categorical			
Units: Subjects			
Female	53		
Male	56		

End points

End points reporting groups

Reporting group title	Esomeprazole 5 mg
Reporting group description: -	
Reporting group title	Esomeprazole 10 mg Wt<20 kg
Reporting group description: -	
Reporting group title	Esomeprazole 10 mg Wt >= 20 kg
Reporting group description: -	
Reporting group title	Esomeprazole 20 mg Wt >= 20kg
Reporting group description: -	
Subject analysis set title	ITT
Subject analysis set type	Intention-to-treat
Subject analysis set description: Intention to treat	

Primary: Number and percentage of subjects whose Physician Global Assesment score improved from baseline at their fianl visit

End point title	Number and percentage of subjects whose Physician Global Assesment score improved from baseline at their fianl visit[1]
End point description:	
End point type	Primary
End point timeframe: End of 8 week treatment period (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: No statistical analyses were specified. Only discriptive statistics are provided

End point values	Esomeprazole 5 mg	Esomeprazole 10 mg Wt<20 kg	Esomeprazole 10 mg Wt >= 20 kg	Esomeprazole 20 mg Wt >= 20kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	26	23	31	29
Units: Number (perecentage) of patients	18	15	25	23

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline at final visit in mean Heartburn Score

End point title	Change from baseline at final visit in mean Heartburn Score
End point description: Change from baseline at final visit in mean Heartburn Score	
End point type	Secondary
End point timeframe: From baseline to final visit	

End point values	Esomeprazole 5 mg	Esomeprazole 10 mg Wt<20 kg	Esomeprazole 10 mg Wt >= 20 kg	Esomeprazole 20 mg Wt >= 20kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	14[2]	10[3]	19[4]	13[5]
Units: Change in average score				
arithmetic mean (standard deviation)	-1.15 (± 0.93)	-1.09 (± 0.86)	-1.32 (± 0.67)	-1.22 (± 0.85)

Notes:

[2] - Only patients with Heartburn at baseline were analysed

[3] - Only patients with Heartburn at baseline were analysed

[4] - Only patients with Heartburn at baseline were analysed

[5] - Only patients with Heartburn at baseline were analysed

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline at final visit in mean Acid Regurtation Score

End point title	Change from baseline at final visit in mean Acid Regurtation Score

End point description:

Change from baseline at final visit in mean Acid Regurtation Score

End point type	Secondary

End point timeframe:

Baseline to final visit

End point values	Esomeprazole 5 mg	Esomeprazole 10 mg Wt<20 kg	Esomeprazole 10 mg Wt >= 20 kg	Esomeprazole 20 mg Wt >= 20kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	17[6]	11[7]	20[8]	11[9]
Units: Change in mean score				
arithmetic mean (standard deviation)	-1.18 (± 0.81)	-1.32 (± 0.93)	-1.24 (± 0.56)	-1.38 (± 0.81)

Notes:

[6] - Only patients with Acid Regurgitation at baseline were analysed

[7] - Only patients with Acid Regurgitation at baseline were analysed

[8] - Only patients with Acid Regurgitation at baseline were analysed

[9] - Only patients with Acid Regurgitation at baseline were analysed

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline at final visit in mean Epigastric Pain Score

End point title	Change from baseline at final visit in mean Epigastric Pain Score

End point description:

Change from baseline at final visit in mean Epigastric Pain Score

End point type	Secondary

End point timeframe:

From baseline to final visit

End point values	Esomeprazole 5 mg	Esomeprazole 10 mg Wt<20 kg	Esomeprazole 10 mg Wt >= 20 kg	Esomeprazole 20 mg Wt >= 20kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	16[10]	13[11]	15[12]	15[13]
Units: Change in mean score				
arithmetic mean (standard deviation)	-1.42 (± 0.61)	-1.02 (± 0.69)	-1.3 (± 0.65)	-1.37 (± 0.67)

Notes:

[10] - Only patients with Epigastric Pain at baseline were analysed

[11] - Only patients with Epigastric Pain at baseline were analysed

[12] - Only patients with Epigastric Pain at baseline were analysed

[13] - Only patients with Epigastric Pain at baseline were analysed

Statistical analyses

No statistical analyses for this end point

Secondary: Number of patients with erosive esophagitis resolution

End point title	Number of patients with erosive esophagitis resolution

End point description:

Number of patients whose EE was resolved at end of study. only patients who had EE at baseline and had an end of studyt endoscope are included in the analysis.

End point type	Secondary

End point timeframe:

Final visit

End point values	Esomeprazole 5 mg	Esomeprazole 10 mg Wt<20 kg	Esomeprazole 10 mg Wt >= 20 kg	Esomeprazole 20 mg Wt >= 20kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11[14]	11[15]	10[16]	13[17]
Units: Patients	11	9	9	11

Notes:

[14] - Only patients with baseline EE & end of study endoscope were analyzed

[15] - Only patients with baseline EE & end of study endoscope were analyzed

[16] - Only patients with baseline EE & end of study endoscope were analyzed

[17] - Only patients with baseline EE & end of study endoscope were analyzed

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Serious adverse events were reported from time of enrollment
Non-serious adverse events were reported after taking randomized treatment until end of eight week treatment period

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	9.1

Reporting groups

Reporting group title	Esomeprazole 5 mg
Reporting group description:	
Esomeprazole 5 mg	
Reporting group title	Esomeprazole 10 mg Wt >= 20 kg
Reporting group description:	
Esomeprazole 10 mg Wt >= 20 kg	
Reporting group title	Esomeprazole 20 mg Wt >= 20kg
Reporting group description:	
Esomeprazole 20 mg Wt >= 20kg	
Reporting group title	Esomeprazole 10 mg Wt<20 kg
Reporting group description:	
Esomeprazole 10 mg Wt<20 kg	

Serious adverse events	Esomeprazole 5 mg	Esomeprazole 10 mg Wt >= 20 kg	Esomeprazole 20 mg Wt >= 20kg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 25 (0.00%)	1 / 31 (3.23%)	1 / 29 (3.45%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Gastrointestinal disorders			
Vomiting aggravated	Additional description: Intractable/bilious vomiting		
subjects affected / exposed	0 / 25 (0.00%)	1 / 31 (3.23%)	0 / 29 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Airway obstruction on anesthetic induction			
subjects affected / exposed	0 / 25 (0.00%)	0 / 31 (0.00%)	1 / 29 (3.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Esomeprazole 10 mg Wt<20 kg		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 23 (4.35%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Gastrointestinal disorders			
Vomiting aggravated	Additional description: Intractable/bilious vomiting		
subjects affected / exposed	1 / 23 (4.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Airway obstruction on anesthetic induction			
subjects affected / exposed	0 / 23 (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: 5 %

Non-serious adverse events	Esomeprazole 5 mg	Esomeprazole 10 mg Wt >= 20 kg	Esomeprazole 20 mg Wt >= 20kg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	17 / 25 (68.00%)	26 / 31 (83.87%)	24 / 29 (82.76%)
Nervous system disorders			
headache			
subjects affected / exposed	1 / 25 (4.00%)	7 / 31 (22.58%)	4 / 29 (13.79%)
occurrences (all)	1	8	4
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	3 / 25 (12.00%)	5 / 31 (16.13%)	3 / 29 (10.34%)
occurrences (all)	5	7	3
Blood and lymphatic system disorders			
Lymphadenopathy			
subjects affected / exposed	2 / 25 (8.00%)	2 / 31 (6.45%)	2 / 29 (6.90%)
occurrences (all)	5	2	2
Gastrointestinal disorders			

Vomiting alone			
subjects affected / exposed	5 / 25 (20.00%)	6 / 31 (19.35%)	7 / 29 (24.14%)
occurrences (all)	6	8	16
Diarrhoea NOS			
subjects affected / exposed	4 / 25 (16.00%)	6 / 31 (19.35%)	3 / 29 (10.34%)
occurrences (all)	4	6	3
Constipation			
subjects affected / exposed	1 / 25 (4.00%)	2 / 31 (6.45%)	1 / 29 (3.45%)
occurrences (all)	1	2	1
Respiratory, thoracic and mediastinal disorders			
cough			
subjects affected / exposed	4 / 25 (16.00%)	5 / 31 (16.13%)	3 / 29 (10.34%)
occurrences (all)	4	6	3
Nasal congestion			
subjects affected / exposed	2 / 25 (8.00%)	3 / 31 (9.68%)	2 / 29 (6.90%)
occurrences (all)	2	5	2
Pharyngolaryngeal pain			
subjects affected / exposed	1 / 25 (4.00%)	4 / 31 (12.90%)	1 / 29 (3.45%)
occurrences (all)	1	4	1
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	2 / 25 (8.00%)	1 / 31 (3.23%)	2 / 29 (6.90%)
occurrences (all)	2	1	2
Viral infection			
subjects affected / exposed	0 / 25 (0.00%)	4 / 31 (12.90%)	2 / 29 (6.90%)
occurrences (all)	0	4	2
Nasopharyngitis			
subjects affected / exposed	3 / 25 (12.00%)	2 / 31 (6.45%)	1 / 29 (3.45%)
occurrences (all)	3	3	1

Non-serious adverse events	Esomeprazole 10 mg Wt<20 kg		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	15 / 23 (65.22%)		
Nervous system disorders			
headache			

subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	4 / 23 (17.39%)		
occurrences (all)	4		
Blood and lymphatic system disorders			
Lymphadenopathy			
subjects affected / exposed	2 / 23 (8.70%)		
occurrences (all)	2		
Gastrointestinal disorders			
Vomiting alone			
subjects affected / exposed	2 / 23 (8.70%)		
occurrences (all)	4		
Diarrhoea NOS			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Constipation			
subjects affected / exposed	3 / 23 (13.04%)		
occurrences (all)	3		
Respiratory, thoracic and mediastinal disorders			
cough			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	2		
Nasal congestion			
subjects affected / exposed	3 / 23 (13.04%)		
occurrences (all)	4		
Pharyngolaryngeal pain			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	3 / 23 (13.04%)		
occurrences (all)	4		
Viral infection			

subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Nasopharyngitis			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
07 July 2004	To update the procedures and entry requirements before the study was started.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported