Clinical trial results:
An Open Single-centre Study on the Pharmacokinetics and Pharmacodynamics of Esomeprazole After Once Daily Oral Administration for 7 Days in Preterm Infants and Neonates

Summary

EudraCT number	2012-001160-29
Trial protocol	Outside EU/EEA
Global end of trial date	10 January 2007

Results information

Result version number	v1 (current)
This version publication date	01 February 2017
First version publication date	13 August 2015

Trial information

Trial identification

Sponsor protocol code	SH-NEC-0002

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	AstraZeneca R&D
Sponsor organisation address	Pepparedsled 1, Mölndal, Sweden,
Public contact	AZ Clinical Trial Transparency group, AstraZeneca R&D, ClinicalTrialTransparency@astrazeneca.com
Scientific contact	Per Lundborg, MD, PhD , AstraZeneca R&D Mölndal, 46 317761000,

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 January 2007
Is this the analysis of the primary completion data?	Yes
Primary completion date	10 January 2007
Global end of trial reached?	Yes
Global end of trial date	10 January 2007
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective was to assess the pharmacokinetics of esomeprazole and its effect on intragastric pH in preterm infants and neonates.

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. Consideration has been given to the International Conference on Harmonisation (ICH) guideline CPMP/ICH/2711/99 (Note for clinical investigation of medicinal products in the pediatric population) when developing the study.The study was approved by the Independent Research Ethics Committee (IEC) of the Women's and Children's Hospital, 72 King William Road, North Adelaide, South Australia 5006
Since all subjects in this study were preterm infants or neonates, informed consent could not be obtained from the subjects themselves. Therefore, the principal investigator ensured that the parent(s) or guardian(s) was given full and adequate oral and written information about the nature, purpose, possible risks and benefits of the study. Parents/guardians were also notified that they were free to withdraw their child from participation in the study at any time. The parent(s)/guardian(s) was given the opportunity to ask questions, and was given time for consideration. The parent's/guardian's signed informed consent was obtained before any study specific procedure was conducted.
Subjects could be withdrawn from study treatment and assessments at any time at the discretion of the investigator.

Background therapy:

The subject population comprised in- and outpatient preterm infants or neonates up to 1 month of age with symptoms of GERD and diagnosis confirmed by pH-monitoring. Medication considered necessary for the subject's safety and well-being was to be given at the discretion of the investigator. Use of any pharmacological antireflux therapy within 72 hours prior to the diagnostic baseline pH impedance monitoring was exclusion criteria. Antacids (egMylanta) or food thickeners could be used +/- 1 hour of the administration of investigational product .

Evidence for comparator:

No comparator group

Actual start date of recruitment	02 June 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	Australia: 26
Worldwide total number of subjects	26
EEA total number of subjects	0

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	19
Newborns (0-27 days)	7
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
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: 2 June 2004
Last patient completed: 8 March 2006

Pre-assignment

Screening details:

38 subjects were screened and 26 were eligible for the study.

Pre-assignment period milestones

Number of subjects started	26
Number of subjects completed	26

Period 1

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

Blinding implementation details:

Open label

Arms

Arm title	Esomeprazole treatment

Arm description:

Esomeprazole 0.5 mg/kg

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:

0.5 mg/kg od orally for 1 week

Number of subjects in period 1	Esomeprazole treatment
Started	26
Completed	25
Not completed	1
Consent withdrawn by subject	1

Baseline characteristics

Reporting groups	
Reporting group title	Treatment period
Reporting group description:	
Esomeprazole	

Reporting group values	Treatment period	Total	
Number of subjects	26	26	
Age Categorical Units: Subjects			
Age Continuous			
Gestational age at birth			
Units: weeks arithmetic mean full range (min-max)	 32.1 23 to 41	 -	
Gender Categorical Units: Subjects			
Female	15	15	
Male	11	11	

Subject analysis sets	
Subject analysis set title	All patients
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
All patients entering treatment period	

Reporting group values	All patients		
Number of subjects	26		
Age Categorical Units: Subjects			
Age Continuous			
Gestational age at birth			
Units: weeks arithmetic mean full range (min-max)	 32.1 23 to 41		
Gender Categorical Units: Subjects			
Female	15		
Male	11		

End points

End points reporting groups

Reporting group title	Esomeprazole treatment
Reporting group description: Esomeprazole 0.5 mg/kg	
Subject analysis set title	All patients
Subject analysis set type	Intention-to-treat
Subject analysis set description: All patients entering treatment period	

Primary: AUCτ

End point title	AUCτ[1]
End point description: Geometric mean of AUCτ (µmol*h/L) after 7 days of oral administration	
End point type	Primary
End point timeframe: After 7 days of oral administration	

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 analysis skpecifed, because it is a single arm study. Only discriptive statistics are presented.

End point values	Esomeprazole treatment			
Subject group type	Reporting group			
Number of subjects analysed	24			
Units: µmol*h/L				
geometric mean (confidence interval 95%)	2.45 (1.63 to 3.68)			

Statistical analyses

No statistical analyses for this end point

Secondary: Css,max

End point title	Css,max
End point description: Geometric mean Css,max (µmol/L) after 7 days oral administration	
End point type	Secondary
End point timeframe: After 7 days oral administration	

End point values	Esomeprazole treatment			
Subject group type	Reporting group			
Number of subjects analysed	24			
Units: µmol/L				
geometric mean (confidence interval 95%)	0.74 (0.54 to 1)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in percentage of time with intragastric pH>4

End point title	Change from baseline in percentage of time with intragastric pH>4

End point description:

Change from baseline in percentage of time (over 24 hours) with intragastric pH>4

End point type	Secondary

End point timeframe:

from baseline to after 7 days oral administration

End point values	Esomeprazole treatment			
Subject group type	Reporting group			
Number of subjects analysed	17			
Units: Percent				
arithmetic mean (confidence interval 95%)	39.6 (28.9 to 50.3)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: During 1 week treatment period and follow-up	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	9

Reporting groups	
Reporting group title	Esomeprazole
Reporting group description: esomeprazole 0.5 mg/kg	
Reporting group title	Follow-up
Reporting group description: The period between time of administration of the investigational product Day 7 plus 24 hours, and the follow-up visit.	

Serious adverse events	Esomeprazole	Follow-up	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 26 (0.00%)	1 / 25 (4.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Infections and infestations			
Pertussis	Additional description: During follow-up period hospitalised due to pertussis		
subjects affected / exposed	0 / 26 (0.00%)	1 / 25 (4.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Esomeprazole	Follow-up	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	8 / 26 (30.77%)	4 / 25 (16.00%)	
Investigations			
Blood urine present			
subjects affected / exposed	1 / 26 (3.85%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Cardiac disorders			

Bradycardia			
subjects affected / exposed	1 / 26 (3.85%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Tachycardia			
subjects affected / exposed	1 / 26 (3.85%)	0 / 25 (0.00%)	
occurrences (all)	2	0	
General disorders and administration site conditions			
Oedema			
subjects affected / exposed	1 / 26 (3.85%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Eye disorders			
Eye discharge			
subjects affected / exposed	0 / 26 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	0	
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	2 / 26 (7.69%)	0 / 25 (0.00%)	
occurrences (all)	2	0	
Diarrhoea			
subjects affected / exposed	1 / 26 (3.85%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Vomiting			
subjects affected / exposed	1 / 26 (3.85%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			
apnoea			
subjects affected / exposed	2 / 26 (7.69%)	0 / 25 (0.00%)	
occurrences (all)	2	0	
Choking			
subjects affected / exposed	1 / 26 (3.85%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Cyanosis neonatal			
subjects affected / exposed	1 / 26 (3.85%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Skin and subcutaneous tissue disorders			

Dermatitis contact			
subjects affected / exposed	1 / 26 (3.85%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			
Pertussis			
subjects affected / exposed	0 / 26 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Respiratory tract infection			
subjects affected / exposed	0 / 26 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Skin candida			
subjects affected / exposed	0 / 26 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
20 January 2004	The mode of administration was changed from per oral by tube or syringe to per oral via a specially designed funnel pan
01 July 2004	An X-ray procedure was added at the pre-entry visit in order to confirm that the pH probe had been correctly positioned
09 September 2004	Due to slower recruitment than expected the recruitment period was prolonged

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported