



## Clinical trial results: Efficacy of Gaviscon in the treatment of gastroesophageal reflux in preterm newborns

### Summary

EudraCT number	2008-001526-13
Trial protocol	IT
Global end of trial date	31 December 2010

### Results information

Result version number	v1 (current)
This version publication date	28 April 2022
First version publication date	28 April 2022

### Trial information

#### Trial identification

Sponsor protocol code	23/2008/O/Sper
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#### Additional study identifiers

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

Notes:

### Sponsors

Sponsor organisation name	IRCCS AOU Bologna
Sponsor organisation address	Via Albertoni, 15, Bologna, Italy, 40138
Public contact	Dr. Luigi Corvaglia, IRCCS AOU Bologna, +39 2143691, luigi.corvaglia@unibo.it
Scientific contact	Dr. Luigi Corvaglia, IRCCS AOU Bologna, +39 2143691, luigi.corvaglia@unibo.it

Notes:

### Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
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	31 May 2010
Is this the analysis of the primary completion data?	Yes
Primary completion date	30 November 2009
Global end of trial reached?	Yes
Global end of trial date	31 December 2010
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

To evaluate the efficacy of sodium alginate in reducing of gastroesophageal reflux (GER) episodes and of apnoeas related to GER in preterm infants.

Protection of trial subjects:

Written informed parental/guardian consent

Background therapy:

For preterm infants with symptomatic GER, a stepwise therapeutical approach, mainly based on conservative interventions (i.e. body positioning 3) is the first line therapeutic choice.

Evidence for comparator:

Antireflux medications, such as histamine-2 receptor (H2) blockers, are commonly used in preterm infants during hospital stay and also after discharge. However, clinical studies demonstrate that these drugs increase the risk of necrotizing enterocolitis in very-low birth-weight infants and may increase the risk of sepsis. Furthermore, prokinetic drugs such as metoclopramide, have shown to cause serious side effects such as irritability, dystonic reactions, drowsiness, oculogyric crisis, emesis and apnoea in infants.

Actual start date of recruitment	01 September 2007
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	Italy: 32
Worldwide total number of subjects	32
EEA total number of subjects	32

Notes:

### Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	32
Newborns (0-27 days)	0
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:

September 2007-November 2009, Neonatal Intensive Care Unit.

### Pre-assignment

Screening details: -

### Pre-assignment period milestones

Number of subjects started	32
Intermediate milestone: Number of subjects	Evaluation of GER: 32
Number of subjects completed	32

### Period 1

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

### Arms

Arm title	Full study population
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Arm description:

Cross-over trial. Each patient underwent a 24 h, continuous and simultaneous measurement of intra-oesophageal pH and multichannel intraluminal electrical impedance (pH-MII – Sandhill Scientific Inc., Highland Ranch, CO, USA), during which the baby was fed eight times, every 3 hours. Sodium alginate (Gaviscon Reckitt Benckiser Healthcare, Hull, UK) was given four times at alternate meals; these meals were defined as 'drug-given' (DG) meals, whereas the remaining four were defined as 'drug-free' (DF) meals. The order of meals was predetermined: specifically, the 2nd, 4th, 6th and 8th meals were DG, whereas the remaining were DF.

Arm type	Experimental
Investigational medicinal product name	Sodium alginate (Gaviscon Reckitt Benckiser Healthcare, Hull, UK)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral suspension
Routes of administration	Oral use

Dosage and administration details:

0.25 mL/Kg per dose at alternate meal (the 2nd, 4th, 6th and 8th in 24 hours), every 6 hours.

<b>Number of subjects in period 1</b>	Full study population
Started	32
Completed	32



## Baseline characteristics

### Reporting groups

Reporting group title	Overall trial
Reporting group description: -	

Reporting group values	Overall trial	Total	
Number of subjects	32	32	
Age categorical			
Units: Subjects			
Preterm newborn-gestational age < 37 wk	32	32	
Age continuous			
Units: weeks			
median	35		
inter-quartile range (Q1-Q3)	34 to 36	-	
Gender categorical			
Units: Subjects			
Female	20	20	
Male	12	12	
Gestational age at birth			
Units: weeks			
median	30		
inter-quartile range (Q1-Q3)	27 to 31	-	
Birthweight			
Units: grams			
median	1098		
inter-quartile range (Q1-Q3)	902 to 1450	-	
Postnatal age			
Units: weeks			
median	35		
inter-quartile range (Q1-Q3)	34 to 36	-	
Wight			
Units: grams			
median	1680		
inter-quartile range (Q1-Q3)	1485 to 1930	-	

### Subject analysis sets

Subject analysis set title	Drug-given meals
Subject analysis set type	Full analysis

Subject analysis set description:

Thirty-two (twelve male) preterm infants with a median gestational age of 30 weeks [interquartile range (IQR), 27–31 weeks] and a median birth weight of 1098 g (IQR, 902–1450 g), studied at a median postnatal age of 35 weeks (IQR, 34–36 weeks) and a median weight of 1680 g (IQR, 1485–1930 g) as they had GER symptoms (frequent regurgitations and postprandial desaturations).

Subject analysis set title	Drug-free meals
Subject analysis set type	Full analysis

Subject analysis set description:

Thirty-two (twelve male) preterm infants with a median gestational age of 30 weeks [interquartile range

(IQR, 27–31 weeks] and a median birth weight of 1098 g (IQR, 902–1450 g), studied at a median postnatal age of 35 weeks (IQR, 34–36 weeks) and a median weight of 1680 g (IQR, 1485–1930 g) as they had GER symptoms (frequent regurgitations and postprandial desaturations).

Reporting group values	Drug-given meals	Drug-free meals	
Number of subjects	32	32	
Age categorical Units: Subjects			
Preterm newborn-gestational age < 37 wk	32	32	
Age continuous Units: weeks median inter-quartile range (Q1-Q3)	35 34 to 36	35 34 to 36	
Gender categorical Units: Subjects			
Female	20	20	
Male	12	12	
Gestational age at birth Units: weeks median inter-quartile range (Q1-Q3)	30 27 to 31	30 27 to 31	
Birthweight Units: grams median inter-quartile range (Q1-Q3)	1098 902 to 1450	1098 902 to 1450	
Postnatal age Units: weeks median inter-quartile range (Q1-Q3)	35 34 to 36	35 34 to 36	
Wight Units: grams median inter-quartile range (Q1-Q3)	1680 1485 to 1930	1680 1485 to 1930	

## End points

### End points reporting groups

Reporting group title	Full study population
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Reporting group description:

Cross-over trial. Each patient underwent a 24 h, continuous and simultaneous measurement of intra-oesophageal pH and multichannel intraluminal electrical impedance (pH-MII – Sandhill Scientific Inc., Highland Ranch, CO, USA), during which the baby was fed eight times, every 3 hours. Sodium alginate (Gaviscon Reckitt Benckiser Healthcare, Hull, UK) was given four times at alternate meals; these meals were defined as 'drug-given' (DG) meals, whereas the remaining four were defined as 'drug-free' (DF) meals. The order of meals was predetermined: specifically, the 2nd, 4th, 6th and 8th meals were DG, whereas the remaining were DF.

Subject analysis set title	Drug-given meals
Subject analysis set type	Full analysis

Subject analysis set description:

Thirty-two (twelve male) preterm infants with a median gestational age of 30 weeks [interquartile range (IQR), 27–31 weeks] and a median birth weight of 1098 g (IQR, 902–1450 g), studied at a median postnatal age of 35 weeks (IQR, 34–36 weeks) and a median weight of 1680 g (IQR, 1485–1930 g) as they had GER symptoms (frequent regurgitations and postprandial desaturations).

Subject analysis set title	Drug-free meals
Subject analysis set type	Full analysis

Subject analysis set description:

Thirty-two (twelve male) preterm infants with a median gestational age of 30 weeks [interquartile range (IQR), 27–31 weeks] and a median birth weight of 1098 g (IQR, 902–1450 g), studied at a median postnatal age of 35 weeks (IQR, 34–36 weeks) and a median weight of 1680 g (IQR, 1485–1930 g) as they had GER symptoms (frequent regurgitations and postprandial desaturations).

### Primary: GER features

End point title	GER features
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End point description:

End point type	Primary
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End point timeframe:

24 hours

End point values	Drug-given meals	Drug-free meals		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	32	32		
Units: Number				
median (inter-quartile range (Q1-Q3))				
total GER episodes	49 (28.50 to 67.00)	58.8 (33.50 to 75.75)		
NaMII- GER	19 (10.00 to 32.75)	18.50 (8.50 to 33.75)		
GER reaching proximal oesophagus	5.50 (4.00 to 9.00)	7.50 (3.00 to 12.00)		
pH-GER	17 (6.00 to 29.75)	29 (13.50 to 44.50)		
aMII-GER	4 (2.00 to 8.25)	6 (2.25 to 11.75)		



### Statistical analyses

<b>Statistical analysis title</b>	GER features
Comparison groups	Drug-given meals v Drug-free meals
Number of subjects included in analysis	64
Analysis specification	Pre-specified
Analysis type	superiority
P-value	≤ 0.05
Method	Wilcoxon (Mann-Whitney)

### Secondary: Total apnoea episodes

End point title	Total apnoea episodes
End point description:	
End point type	Secondary
End point timeframe:	
24 hours	

<b>End point values</b>	Drug-given meals	Drug-free meals		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	32	32		
Units: Number				
median (full range (min-max))	9.5 (0 to 35)	9.5 (0 to 44)		

### Statistical analyses

<b>Statistical analysis title</b>	Total apnoea episodes
Comparison groups	Drug-given meals v Drug-free meals
Number of subjects included in analysis	64
Analysis specification	Pre-specified
Analysis type	superiority
P-value	≤ 0.05
Method	Wilcoxon (Mann-Whitney)

**Secondary: Apnoea related to GER**

End point title	Apnoea related to GER
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End point description:

End point type	Secondary
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End point timeframe:

24 hours

End point values	Drug-given meals	Drug-free meals		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	32	32		
Units: number/min				
median (full range (min-max))	0 (0 to 0.67)	0 (0 to 0.47)		

**Statistical analyses**

<b>Statistical analysis title</b>	Apnoea related to GER
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Comparison groups	Drug-given meals v Drug-free meals
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Number of subjects included in analysis	64
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Analysis specification	Pre-specified
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Analysis type	superiority
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P-value	≤ 0.05
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Method	Wilcoxon (Mann-Whitney)
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## Adverse events

### Adverse events information<sup>[1]</sup>

Timeframe for reporting adverse events:

September 2007-December 2010

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	11.0
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### Reporting groups

Reporting group title	Overall study population
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Reporting group description:

Adverse events related to Gaviscon 1 mL/Kg

Serious adverse events	Overall study population		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 32 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

Frequency threshold for reporting non-serious adverse events: 0.3 %

Non-serious adverse events	Overall study population		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 32 (0.00%)		

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.

Justification: Gaviscon is widely used among pediatric populations and adverse reactions caused by Gaviscon are very rare. For these reasons, non-serious adverse events were not observed in a small group of 32 experimental subjects.

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported