



## Clinical trial results:

### The effect of on demand versus continuous use of proton pump inhibitors on reflux symptoms, quality of life and self-rated health in patients with gastro-oesophageal reflux disease

#### Summary

EudraCT number	2014-001314-25
Trial protocol	NL
Global end of trial date	09 February 2016

#### Results information

Result version number	v1 (current)
This version publication date	10 February 2023
First version publication date	10 February 2023

#### Trial information

##### Trial identification

Sponsor protocol code	KIANANDR140701
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##### Additional study identifiers

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

Notes:

##### Sponsors

Sponsor organisation name	Karolinska Institutet
Sponsor organisation address	Alfred Nobels allé 12, Huddinge, Sweden,
Public contact	Centre for Family Medicine, Karolinska Institutet, 46 0852488000, villvetamer@cefam.se
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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	Interim
Date of interim/final analysis	09 March 2016
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	09 February 2016
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

1. To evaluate whether there is a difference in symptom relief in patients prescribed PPI on demand and patients prescribed continuous use of PPI.
2. To evaluate whether the use of electronic tools developed to facilitate clinical trials in primary care result in a higher recruitment rates than paper-based data collection.

Protection of trial subjects:

Trial subjects were primary care patients that received one of two approved treatments for gastroesophageal reflux disease. The trial subjects were asked to fill out a questionnaire about drug consumption and health related quality of life (QoL), that took approximately 20 minutes each, total 40 minutes. No specific measures were put in place to protect the trial subjects, as they received standard care and the questionnaire was brief and the content should not cause pain or distress.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	13 May 2015
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	Netherlands: 17
Country: Number of subjects enrolled	Greece: 248
Country: Number of subjects enrolled	United Kingdom: 14
Country: Number of subjects enrolled	Poland: 336
Worldwide total number of subjects	615
EEA total number of subjects	615

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)	0
Adults (18-64 years)	615
From 65 to 84 years	0
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details:

The study was conducted between May and December 2015. 36 primary care centres participated in the study: 8 in Greece, 10 in Poland, 8 in the Netherlands and 10 in the UK.

### Pre-assignment

Screening details:

Eligible patients were adults 18 to 65 years of age diagnosed with GERD and requiring PPI treatment i.e. symptoms at least 2 times a week negatively influencing quality of life that had previously been prescribed and obtained symptom relief from PPI use (PPI treatment responders).

### Period 1

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

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	On demand

Arm description:

This patient group was given on demand use of PPI (20 mg Omeprazole on demand, maximum daily intake two pills i.e. 40 mg).

Arm type	Active comparator
Investigational medicinal product name	Omeprazole
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Coated tablet
Routes of administration	Oral use

Dosage and administration details:

20 mg Omeprazole on demand, maximum daily intake two pills i.e. 40 mg

<b>Arm title</b>	Continuous use
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Arm description:

This patient group was given continuous prescription of PPI (20 mg Omeprazole daily).

Arm type	Active comparator
Investigational medicinal product name	Omeprazole
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Coated tablet
Routes of administration	Oral use

Dosage and administration details:

20 mg Omeprazole daily

<b>Number of subjects in period 1</b>	On demand	Continuous use
Started	310	305
Completed	228	231
Not completed	82	74
Lost to follow-up	82	74

## Baseline characteristics

### Reporting groups

Reporting group title	On demand
Reporting group description: This patient group was given on demand use of PPI (20 mg Omeprazole on demand, maximum daily intake two pills i.e. 40 mg).	
Reporting group title	Continuous use
Reporting group description: This patient group was given continuous prescription of PPI (20 mg Omeprazole daily).	

Reporting group values	On demand	Continuous use	Total
Number of subjects	310	305	615
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)			0
Adults (18-64 years)			0
From 65-84 years			0
85 years and over			0
Age continuous Units: years			
median	50	51	
inter-quartile range (Q1-Q3)	41 to 59	41 to 59	-
Gender categorical Units: Subjects			
Female	177	181	358
Male	133	124	257
PPI current user Units: Subjects			
Yes	177	179	356
No	133	126	259

## End points

### End points reporting groups

Reporting group title	On demand
Reporting group description: This patient group was given on demand use of PPI (20 mg Omeprazole on demand, maximum daily intake two pills i.e. 40 mg).	
Reporting group title	Continuous use
Reporting group description: This patient group was given continuous prescription of PPI (20 mg Omeprazole daily).	

### Primary: GERD symptom burden

End point title	GERD symptom burden
End point description:	
End point type	Primary
End point timeframe: From baseline to follow up 8 weeks later	

End point values	On demand	Continuous use		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	228	231		
Units: score				
arithmetic mean (standard deviation)	0.70 ( $\pm$ 0.75)	0.71 ( $\pm$ 0.76)		

### Statistical analyses

Statistical analysis title	Difference in GERD symptom burden
Statistical analysis description: Difference in GERD symptom burden between on demand PPI users and continuous PPI users at follow-up visit	
Comparison groups	Continuous use v On demand
Number of subjects included in analysis	459
Analysis specification	Pre-specified
Analysis type	non-inferiority <sup>[1]</sup>
P-value	= 0.84
Method	Regression, Linear

Notes:

[1] - Mixed effect regression model with interaction time treatment to test for treatment effect

### Primary: SF-12 physical health score

End point title	SF-12 physical health score
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End point description:

End point type	Primary
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End point timeframe:

From baseline to follow up 8 weeks later

End point values	On demand	Continuous use		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	228	231		
Units: score				
arithmetic mean (standard deviation)	51.92 (± 7.75)	51.17 (± 8.73)		

## Statistical analyses

Statistical analysis title	Difference in physical health QoL score
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Statistical analysis description:

Difference in physical health QoL score between on demand PPI users and continuous PPI users at follow-up visit

Comparison groups	On demand v Continuous use
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Number of subjects included in analysis	459
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Analysis specification	Pre-specified
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Analysis type	non-inferiority <sup>[2]</sup>
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P-value	= 0.46
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Method	Regression, Linear
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Notes:

[2] - Mixed effect regression model with interaction time treatment to test for treatment effect

## Primary: SF-12 mental health score

End point title	SF-12 mental health score
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End point description:

End point type	Primary
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End point timeframe:

From baseline to follow up 8 weeks later

End point values	On demand	Continuous use		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	228	231		
Units: score				
arithmetic mean (standard deviation)	46.98 (± 8.15)	48.31 (± 7.20)		



## Statistical analyses

<b>Statistical analysis title</b>	Difference in mental health QoL score
Statistical analysis description: Difference in mental health QoL score between on demand PPI users and continuous PPI users at follow-up visit	
Comparison groups	On demand v Continuous use
Number of subjects included in analysis	459
Analysis specification	Pre-specified
Analysis type	non-inferiority <sup>[3]</sup>
P-value	= 0.17
Method	Regression, Linear

Notes:

[3] - Mixed effect regression model with interaction time treatment to test for treatment effect

## Primary: Self-rated health

End point title	Self-rated health
End point description:	
End point type	Primary
End point timeframe:	
From baseline to follow up 8 weeks later	

<b>End point values</b>	On demand	Continuous use		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	228	231		
Units: score				
arithmetic mean (standard deviation)	2.13 ( $\pm$ 0.80)	2.17 ( $\pm$ 0.88)		

## Statistical analyses

<b>Statistical analysis title</b>	Difference in self-rated health
Statistical analysis description: Difference in self-rated health between on demand PPI users and continuous PPI users at follow-up visit	
Comparison groups	On demand v Continuous use

Number of subjects included in analysis	459
Analysis specification	Pre-specified
Analysis type	non-inferiority <sup>[4]</sup>
P-value	= 0.61
Method	Regression, Linear

Notes:

[4] - Mixed effect regression model with interaction time treatment to test for treatment effect

## Secondary: PPI use last week

End point title	PPI use last week
End point description:	
End point type	Secondary
End point timeframe:	
At follow up (8 weeks)	

End point values	On demand	Continuous use		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	228	231		
Units: dose				
arithmetic mean (standard deviation)	12.10 (± 49.07)	16.45 (± 45.63)		

## Statistical analyses

Statistical analysis title	Difference in PPI intake
Statistical analysis description:	
Difference in PPI intake at follow-up visit	
Comparison groups	On demand v Continuous use
Number of subjects included in analysis	459
Analysis specification	Post-hoc
Analysis type	non-inferiority <sup>[5]</sup>
P-value	= 0.33
Method	Regression, Linear

Notes:

[5] - Mixed effect regression model with interaction time treatment to test for treatment effect

## Adverse events

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

Timeframe for reporting adverse events:

13/05/2015 – 31/12/2015

Assessment type	Non-systematic
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### Dictionary used

Dictionary name	Free text
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Dictionary version	n/a
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### Reporting groups

Reporting group title	On demand
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Reporting group description:

This patient group was given on demand use of PPI (20 mg Omeprazole on demand, maximum daily intake two pills i.e. 40 mg).

Reporting group title	Continuous use
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Reporting group description:

This patient group was given continuous prescription of PPI (20 mg Omeprazole daily).

Serious adverse events	On demand	Continuous use	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 310 (0.00%)	0 / 305 (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: 0 %

Non-serious adverse events	On demand	Continuous use	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 310 (0.00%)	0 / 305 (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: There were no non-serious adverse events recorded for these results.

## 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

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Limitations include missing data on symptoms and health related quality of life of the participants who used the TRANSFoRM tool to complete questionnaires, however, this was largely due to a technical issue and data loss can be assumed to be random.
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Notes: