Clinical trial results:
The effect of naloxone and methylnaltrexone on oesophageal sensitivity in healthy volunteers: a randomized, double-blind placebo controlled study.

Summary

EudraCT number	2012-003409-86
Trial protocol	BE
Global end of trial date	18 December 2014

Results information

Result version number	v1 (current)
This version publication date	04 February 2021
First version publication date	04 February 2021
Summary attachment (see zip file)	Thesis manuscript (Thesis Manuscript_Charlotte Broers (15).pdf)

Trial information

Trial identification

Sponsor protocol code	Methnalox2012

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03014843
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	KULeuven UZLeuven
Sponsor organisation address	Herestraat 49, Leuven, Belgium, 3000
Public contact	KU Leuven, TARGID, 32 16344225, jan.tack@kuleuven.be
Scientific contact	KU Leuven, TARGID, 32 16344225, jan.tack@kuleuven.be

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	20 September 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	18 December 2014
Global end of trial reached?	Yes
Global end of trial date	18 December 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To investigate the acute effect of naloxon and methylnaltrexone administered IV/SC on oesophageal sensitivity in healthy volunteers

Protection of trial subjects:

The identification of trial subjects was protected by using an identification code.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 October 2014
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: 12
Worldwide total number of subjects	12
EEA total number of subjects	12

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)	12
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Healthy volunteers were recruited

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Single blind
Roles blinded	Subject

Arms

Are arms mutually exclusive?	No
Arm title	Methylnaltrexone subcutaneous + placebo infusion

Arm description:

Methylnaltrexone (12mg/0.6mL subcutaneous injection) + infusion of placebo (NaCl 0.9%)

Arm type	Experimental
Investigational medicinal product name	Methylnaltrexone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

12mg/0.6mL methylnaltrexone

Investigational medicinal product name	Saline solution
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

0.9% NaCL via infusion

Arm title	Placebo subcutaneous + naloxone infusion

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Saline solution
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

0.9% NaCL subcutaneous

Investigational medicinal product name	Naloxone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

0.4mg IV bolus injection followed by 20µg/kg/h IV infusion

Arm title	Placebo subcutaneous + placebo infusion
Arm description: -	
Arm type	Placebo
Investigational medicinal product name	Saline solution
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravascular use , Subcutaneous use

Dosage and administration details:

0.9% NaCl injected subcutaneous and infused intravascular

Number of subjects in period 1	Methylnaltrexone subcutaneous + placebo infusion	Placebo subcutaneous + naloxone infusion	Placebo subcutaneous + placebo infusion
Started	12	12	12
Completed	12	12	12

Baseline characteristics

Reporting groups

Reporting group title	Overall trial (overall period)

Reporting group description: -

Reporting group values	Overall trial (overall period)	Total	
Number of subjects	12	12	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	12	12	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous Units: years			
arithmetic mean	31		
full range (min-max)	22 to 51	-	
Gender categorical Units: Subjects			
Female	5	5	
Male	7	7	

End points

End points reporting groups

Reporting group title	Methylnaltrexone subcutaneous + placebo infusion
Reporting group description: Methylnaltrexone (12mg/0.6mL subcutaneous injection) + infusion of placebo (NaCl 0.9%)	
Reporting group title	Placebo subcutaneous + naloxone infusion
Reporting group description: -	
Reporting group title	Placebo subcutaneous + placebo infusion
Reporting group description: -	

Primary: Change in mechanical stimulation between methylnaloxone, naloxone and placebo

End point title	Change in mechanical stimulation between methylnaloxone, naloxone and placebo
End point description:	
End point type	Primary
End point timeframe: Comparison between 3 conditions	

End point values	Methylnaltrexone subcutaneous + placebo infusion	Placebo subcutaneous + naloxone infusion	Placebo subcutaneous + placebo infusion	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	12	12	12	
Units: mL at pain perception threhold				
median (inter-quartile range (Q1-Q3))	19.4 (17.51 to 25.79)	22.78 (15.61 to 40.03)	23.4 (20.81 to 41.94)	

Statistical analyses

Statistical analysis title	Mechanical stimulation ANOVA
Comparison groups	Placebo subcutaneous + placebo infusion v Methylnaltrexone subcutaneous + placebo infusion v Placebo subcutaneous + naloxone infusion
Number of subjects included in analysis	36
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.33
Method	ANOVA

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

For each individual, corresponds to timeframe of study participation (from signing of informed consent untill last visit)

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23

Frequency threshold for reporting non-serious adverse events: 0 %

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: Headache and hunger was recorded during the experiment in some subjects. These non-serious adverse events are to be expected since the subjects needed to be fasted for this study. These symptoms were not regareded as adverse events.

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

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

Small number of subjects included in this study.
Technical problems leading to unreliable data for some measurable variables for some subjects.

Notes: