Clinical trial results:
Placebo-controlled crossover study of the ability of Naloxegol to reverse opioid effect on colonic motor patterns in healthy volunteers

Summary

EudraCT number	2018-000013-20
Trial protocol	BE
Global end of trial date	04 June 2019

Results information

Result version number	v1 (current)
This version publication date	26 October 2023
First version publication date	26 October 2023

Trial information

Trial identification

Sponsor protocol code	2018-000013-20

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	KULeuven UZLeuven Targid
Sponsor organisation address	Herestraat 49, Leuven, Belgium, 3000
Public contact	Jan Tack, KU Leuven - Targid, 0032 16344225, jan.tack@kuleuven.be
Scientific contact	jan Tack, KU Leuven - Targid, 0032 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	10 January 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	04 June 2019
Global end of trial reached?	Yes
Global end of trial date	04 June 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study is to compare the effects of Naloxegol compared to placebo on colonic motility, in combination with the presence or absence of a mu-opioid agonist, codeine. This will be investigated in HVs using high-resolution colonic manometry. Our objective is to correlate colonic motor patterns or a decrease in overall colonic motility to the symptoms in opioid induced constipation.

Protection of trial subjects:

healthy volunteers
sedation
catheter placement performed by experienced gastroenterologist

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	08 May 2018
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: 15
Worldwide total number of subjects	15
EEA total number of subjects	15

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)	15
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

15 healthy volunteers

Pre-assignment

Screening details:

Normal bowel habit
No organic or functional disease affecting the gastrointestinal system.
No previous abdominal surgery other than appendectomy
No intake of laxatives or other medications.

Period 1

Period 1 title	overall period
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Subject

Arms

Are arms mutually exclusive?	No
Arm title	naloxegol

Arm description:

Upon awakening, participants received naloxegol or matching placebo

Arm type	Active comparator
Investigational medicinal product name	naloxegol
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants underwent a colonoscopy after a half dose of standard PEG preparation for colonic manometry catheter placement. Upon awakening, participants received naloxegol 25mg or matching placebo.
In addition, placebo or 60 mg codeine was administered orally, followed by another intake of half this dose one-hour post-prandial.

Arm title	placebo

Arm description:

Upon awakening, participants received naloxegol or matching placebo

Arm type	Placebo
Investigational medicinal product name	placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

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Number of subjects in period 1	naloxegol	placebo
Started	15	15
Completed	15	15

Baseline characteristics

Reporting groups	
Reporting group title	overall period

Reporting group description: -

Reporting group values	overall period	Total	
Number of subjects	15	15	
Age categorical Units: Subjects			
Adults (18-64 years)	15	15	
Age continuous Units: years			
median	31.9		
standard deviation	± 3.6	-	
Gender categorical Units: Subjects			
Female	9	9	
Male	6	6	

End points

End points reporting groups

Reporting group title	naloxegol
Reporting group description:	
Upon awakening, participants received naloxegol or matching placebo	
Reporting group title	placebo
Reporting group description:	
Upon awakening, participants received naloxegol or matching placebo	

Primary: reversal effects of a peripheral-acting mu-opioid receptor antagonist (PAMORA) on colonic motor patterns

End point title	reversal effects of a peripheral-acting mu-opioid receptor antagonist (PAMORA) on colonic motor patterns
End point description:	
End point type	Primary
End point timeframe:	
3 study conditions naloxegol/placebo, placebo/codeine, or naloxegol/codeine	

End point values	naloxegol	placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14[1]	14[2]		
Units: Colonic pressure waves	14	14		

Notes:

[1] - one participant was omitted from the analysis because of a missing trace

[2] - one participant was omitted from the analysis because of a missing trace

Statistical analyses

Statistical analysis title	Colonic pressure waves

Statistical analysis description:

Colonic pressure waves (PWs) were evaluated during sleep, in the fasted state, after a standardized bread meal (645 kcal), and after intraluminal administration of 10 mg bisacodyl.
We analyzed the number and direction of propagation of short PWs (over 3-4 sensors), long PWs (>4 sensors), and high-amplitude propagating contractions (HAPCs; long PWs with an amplitude of ≥100 mmHg for at least 1 sensor and 2 sensors of ≥90 mmHg).

Comparison groups	naloxegol v placebo
Number of subjects included in analysis	28
Analysis specification	Pre-specified
Analysis type	other[3]
P-value	< 0.05
Method	Friedman test

Notes:

[3] - Both short and long synchronous PWs did not occur statistically significantly more or less in one of the 3 conditions, for all time periods. The same result was found for the antegrade PWs in all time periods. Postprandially, long retrograde PWs occurred statistically significantly less often with

naloxegol/placebo compared to placebo/codeine (p=0.04). Additionally, short retrograde PWs occurred less often with naloxegol/placebo than with placebo/codeine (p=0.03).

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 until last visit).

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23

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

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 adverse events in this study

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

None reported