Clinical trial results:
A RANDOMISED, PLACEBO-CONTROLLED, CROSSOVER STUDY TO EVALUATE THE EFFECT OF LINACLOTIDE ON COLONIC MOTILITY ASSESSED WITH INTRALUMINAL COLONIC MANOMETRY IN HEALTHY SUBJECTS

Summary

EudraCT number	2013-004939-73
Trial protocol	BE
Global end of trial date	28 January 2015

Results information

Result version number	v1 (current)
This version publication date	28 December 2024
First version publication date	28 December 2024

Trial information

Trial identification

Sponsor protocol code	LINACLOTIDEPLACEBO

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	TARGID UZLEUVEN KULEUVEN
Sponsor organisation address	Herestraat 49, Leuven, Belgium, 3000
Public contact	Jan Tack, KULEUVEN, 0032 16344225, jan.tack@kuleuven.be
Scientific contact	Jan Tack, KULEUVEN, 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	07 October 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	28 January 2015
Global end of trial reached?	Yes
Global end of trial date	28 January 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

to evaluate the effects of linaclotideas compared to placebo on motility index and on the number of colonic high amplitude propagated contractions (HAPCs) during a 8-hour intraluminal manometry in healthy subjects.

Protection of trial subjects:

healthy volunteers. sedation during colonoscopy

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 January 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: 10
Worldwide total number of subjects	10
EEA total number of subjects	10

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)	10
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

healthy subjects

Pre-assignment

Screening details:

healthy subjects with a normal bowel habit
No diagnosis of organic or functional gastrointestinal disease.
no 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	Subject, Investigator

Arms

Are arms mutually exclusive?	No
Arm title	linaclotide

Arm description:

After 90 min of basal recording, linaclotide 290 µg was administered orally in double-blind, randomized, cross-over fashion, and the recording continued for 180 min before and after a standardized meal

oral intake of 290 µg linaclotide in a single administration, together with 125mL of water;

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

Dosage and administration details:

oral intake of 290 µg linaclotide in a single administration, together with 125mL of water;

Arm title	placebo

Arm description:

After 90 min of basal recording, placebo was administered orally in double-blind, randomized, cross-over fashion, and the recording continued for 180 min before and after a standardized meal
oral intake of placebo, consisting in an empty capsule in a single oral administration, together with 125mL of water

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

Dosage and administration details:

On the first day of each treatment period, after a 12-h fasting period, all subjects were admitted to the Motility Unit. Bowel preparation was performed through a tap water enema. Oral intake of placebo, consisting in an empty capsule in a single oral administration, together with 125mL of water.

Number of subjects in period 1	linaclotide	placebo
Started	10	10
Completed	10	10

Baseline characteristics

Reporting groups	
Reporting group title	overall period

Reporting group description: -

Reporting group values	overall period	Total	
Number of subjects	10	10	
Age categorical Units: Subjects			
Adults (18-64 years)	10	10	
Age continuous Units: years			
arithmetic mean	30.3		
standard deviation	± 10.6	-	
Gender categorical Units: Subjects			
Female	5	5	
Male	5	5	

End points

End points reporting groups

Reporting group title	linaclotide

Reporting group description:

After 90 min of basal recording, linaclotide 290 µg was administered orally in double-blind, randomized, cross-over fashion, and the recording continued for 180 min before and after a standardized meal

oral intake of 290 µg linaclotide in a single administration, together with 125mL of water;

Reporting group title	placebo

Reporting group description:

After 90 min of basal recording, placebo was administered orally in double-blind, randomized, cross-over fashion, and the recording continued for 180 min before and after a standardized meal
oral intake of placebo, consisting in an empty capsule in a single oral administration, together with 125mL of water

Primary: Colonic motility index

End point title	Colonic motility index

End point description:

After 90 min of basal recording, linaclotide 290 µg or placebo were administered orally in double-blind, randomized, cross-over fashion, and the recording continued for 180 min before and after a standardized meal. Colonic motility index of the right, left colon and rectum, expressed as ratio of the baseline value was compared between treatments by means of a mixed models analysis.

End point type	Primary

End point timeframe:

After 90 min of basal recording, linaclotide 290 µg or placebo were administered orally in double-blind, randomized, cross-over fashion, and the recording continued for 180 min before and after a standardized meal.

End point values	linaclotide	placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9[1]	10		
Units: Motility index				
median (inter-quartile range (Q1-Q3))				
preprandial right colon	2.65972 (1.80597 to 4.23004)	1.47693 (1.25567 to 1.76870)		
1h post right colon	3.12884 (2.56553 to 4.66207)	1.53131 (1.26702 to 2.11822)		
preprandial left colon	1.66279 (1.62261 to 3.39836)	1.23797 (1.13288 to 1.81045)		
1h post left colon	2.79077 (2.35410 to 4.34425)	1.46099 (1.31564 to 2.05882)		
preprandial rectum	1.60144 (1.09675 to 2.51950)	1.23251 (1.02711 to 1.57230)		
1h post rectum	1.87186 (1.82752 to 3.21536)	1.25801 (1.01017 to 2.04550)		

Notes:

[1] - the tracing displayed too many artifacts to be properly evaluated and therefore be reliable

Statistical analyses

Statistical analysis title	Colonic motility index

Statistical analysis description:

Colonic motility index (MI; averaged every 15 min in the right and left colon and in the rectum, and expressed as ratio of the baseline value) of four periods (pre-prandial, first, second, and third hour after the meal) was compared between treatments by means of a mixed models analysis with post hoc t tests and Bonferroni correction.

Comparison groups	placebo v linaclotide
Number of subjects included in analysis	19
Analysis specification	Pre-specified
Analysis type	superiority
P-value	≤ 0.05 [2]
Method	Mixed models analysis

Notes:

[2] - Baseline MI did not differ between treatments in the right, left colon and rectum. At mixed models analysis, no treatment effect was found on the ratio of the baseline value of colonic MI in any of the region of the colon

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: No adverse events happened during this study protocol

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