Clinical trial results:
A Phase 3, Open-label, Long-term Safety Study of Oral Linaclotide Administered to Pediatric Participants With Functional Constipation (FC) or Irritable Bowel Syndrome With Constipation (IBS-C)

Summary

EudraCT number	2019-001955-38
Trial protocol	HU BG
Global end of trial date	05 June 2025

Results information

Result version number	v1 (current)
This version publication date	06 December 2025
First version publication date	06 December 2025

Trial information

Trial identification

Sponsor protocol code	LIN-MD-66

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04166058
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	AbbVie
Sponsor organisation address	1 North Waukegan Road , North Chicago, IL , United States, 60064
Public contact	Global Medical Services, AbbVie, 001 8006339110, abbvieclinicaltrials@abbvie.com
Scientific contact	Global Medical Services, AbbVie, 001 8006339110, abbvieclinicaltrials@abbvie.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-000927-PIP01-10
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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	05 June 2025
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	05 June 2025
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

LIN-MD-66 is a Phase 3 open-label study with 24 weeks (Functional Constipation participants) or 52 weeks (Irritable bowel syndrome with constipation participants) of linaclotide exposure that will enroll pediatric participants (6-17 years of age) with FC or IBS-C who completed study intervention in studies LIN-MD-62, LIN-MD-63, or LIN-MD-64 based on the individual study criteria.

Protection of trial subjects:

Parent/guardian/LAR and/or the caregiver of each subject read and understood the information provided about the study and gave written permission.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	19 November 2019
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Canada: 4
Country: Number of subjects enrolled	Israel: 3
Country: Number of subjects enrolled	Netherlands: 4
Country: Number of subjects enrolled	United States: 370
Worldwide total number of subjects	381
EEA total number of subjects	4

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)	170
Adolescents (12-17 years)	209
Adults (18-64 years)	2

From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

The study included a 14 day screening period before Study Day 1.

Period 1

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

Blinding implementation details:

Subjects who completed study LIN-MD-64 at their time of enrollment will be assigned a dose of 290 µg if they choose to receive open-label or continue to receive blinded dose of 145 or 290 µg if they choose to remain on the same blinded dose.

Arms

Are arms mutually exclusive?	Yes
Arm title	FC 72 ug Linaclotide

Arm description:

Functional Constipation (FC) subjects who completed studies LIN-MD-62 and LIN-MD-64 were dosed as follows:

Subjects aged 6 to 11 years received an open-label dose of linaclotide 72 ug, oral capsule, once daily for 24 weeks.

Subjects aged 12 to 17 years were randomized to receive an open-label dose of linaclotide either 72 or 145 ug, oral capsule, once daily for 24 weeks.

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

Dosage and administration details:

An oral capsule that is taken once daily. It may be taken whole or sprinkled into 1 teaspoonful of applesauce or 30mL of bottled water.
FC subjects (LIN-MD-62 and LIN-MD-64 completers): Subjects whom are between the ages of 6-11 years old at their time of enrollment will be assigned a dose of 72 µg. Subjects whom are between the ages of 12-17 years old at their time of enrollment will be randomized at 1:1 ratio to 72 or 145 µg linaclotide.
IBS-C subjects (LINMD-63 and LIN-MD-64 completers): Subjects who completed study LIN-MD-63 at their time of enrollment will be assigned a dose of 290 µg. Subjects who received ≤ 145 µg linaclotide or placebo in study LIN-MD-63 at the time of completion will continue to receive 145 µg. Subjects who completed study LIN-MD-64 at their time of enrollment will be assigned a dose of 290 µg if they choose to receive open-label or continue to receive blinded dose of 145 or 290 µg if they choose to remain on the same blinded dose.

Arm title	FC 145 ug Linaclotide

Arm description:

Functional Constipation (FC) subjects who completed studies LIN-MD-62 and LIN-MD-64 were dosed as follows:

Subjects aged 12 to 17 years were randomized to receive an open-label dose of linaclotide either 72 or 145 ug, oral capsule, once daily for 24 weeks.

Arm type	Experimental

Investigational medicinal product name	linaclotide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

An oral capsule that is taken once daily. It may be taken whole or sprinkled into 1 teaspoonful of applesauce or 30mL of bottled water.
FC subjects (LIN-MD-62 and LIN-MD-64 completers): Subjects whom are between the ages of 6-11 years old at their time of enrollment will be assigned a dose of 72 µg. Subjects whom are between the ages of 12-17 years old at their time of enrollment will be randomized at 1:1 ratio to 72 or 145 µg linaclotide.
IBS-C subjects (LINMD-63 and LIN-MD-64 completers): Subjects who completed study LIN-MD-63 at their time of enrollment will be assigned a dose of 290 µg. Subjects who received ≤ 145 µg linaclotide or placebo in study LIN-MD-63 at the time of completion will continue to receive 145 µg. Subjects who completed study LIN-MD-64 at their time of enrollment will be assigned a dose of 290 µg if they choose to receive open-label or continue to receive blinded dose of 145 or 290 µg if they choose to remain on the same blinded dose.

Arm title	IBS-C 145 ug Linaclotide

Arm description:

Irritable Bowel Syndrome with Constipation (IBS-C) subjects were dosed as follows:

Subjects who received ≤ 145 ug linaclotide or placebo in study LIN-MD-63 received an open-label dose of linaclotide 145 ug, oral capsule, once daily for 52 weeks.

Subjects who completed study LIN-MD-64 had the option to either remain on the same blinded linaclotide dose they were receiving in lead-in study LIN-MD-64 (145 or 290 ug) or received an open-label dose of linaclotide 290 ug, oral capsule, once daily for 52 weeks.

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

Dosage and administration details:

An oral capsule that is taken once daily. It may be taken whole or sprinkled into 1 teaspoonful of applesauce or 30mL of bottled water.
FC subjects (LIN-MD-62 and LIN-MD-64 completers): Subjects whom are between the ages of 6-11 years old at their time of enrollment will be assigned a dose of 72 µg. Subjects whom are between the ages of 12-17 years old at their time of enrollment will be randomized at 1:1 ratio to 72 or 145 µg linaclotide.
IBS-C subjects (LINMD-63 and LIN-MD-64 completers): Subjects who completed study LIN-MD-63 at their time of enrollment will be assigned a dose of 290 µg. Subjects who received ≤ 145 µg linaclotide or placebo in study LIN-MD-63 at the time of completion will continue to receive 145 µg. Subjects who completed study LIN-MD-64 at their time of enrollment will be assigned a dose of 290 µg if they choose to receive open-label or continue to receive blinded dose of 145 or 290 µg if they choose to remain on the same blinded dose.

Arm title	IBS-C 290 ug Linaclotide

Arm description:

Irritable Bowel Syndrome with Constipation (IBS-C) subjects were dosed as follows:

Subjects who completed study LIN-MD-63 received an open-label dose of linaclotide 290 ug, oral capsule, once daily for 52 weeks.

Subjects who completed study LIN-MD-64 had the option to either remain on the same blinded linaclotide dose they were receiving in lead-in study LIN-MD-64 (145 or 290 ug) or received an open-label dose of linaclotide 290 ug, oral capsule, once daily for 52 weeks.

Arm type	Experimental

Investigational medicinal product name	linaclotide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

An oral capsule that is taken once daily. It may be taken whole or sprinkled into 1 teaspoonful of applesauce or 30mL of bottled water.
FC subjects (LIN-MD-62 and LIN-MD-64 completers): Subjects whom are between the ages of 6-11 years old at their time of enrollment will be assigned a dose of 72 µg. Subjects whom are between the ages of 12-17 years old at their time of enrollment will be randomized at 1:1 ratio to 72 or 145 µg linaclotide.
IBS-C subjects (LINMD-63 and LIN-MD-64 completers): Subjects who completed study LIN-MD-63 at their time of enrollment will be assigned a dose of 290 µg. Subjects who received ≤ 145 µg linaclotide or placebo in study LIN-MD-63 at the time of completion will continue to receive 145 µg. Subjects who completed study LIN-MD-64 at their time of enrollment will be assigned a dose of 290 µg if they choose to receive open-label or continue to receive blinded dose of 145 or 290 µg if they choose to remain on the same blinded dose.

Number of subjects in period 1	FC 72 ug Linaclotide	FC 145 ug Linaclotide	IBS-C 145 ug Linaclotide
Started	210	73	22
Completed	189	66	20
Not completed	21	7	2
Consent withdrawn by subject	4	4	1
Physician decision	2	-	-
Adverse event, non-fatal	1	1	-
Other	1	-	-
Pregnancy	1	-	-
Noncompliance with study drug	-	-	-
Lost to follow-up	9	2	1
Protocol deviation	1	-	-
Lack of efficacy	2	-	-

Number of subjects in period 1	IBS-C 290 ug Linaclotide
Started	76
Completed	60
Not completed	16
Consent withdrawn by subject	10
Physician decision	2
Adverse event, non-fatal	-
Other	1
Pregnancy	-
Noncompliance with study drug	2
Lost to follow-up	1
Protocol deviation	-

Lack of efficacy	-

Baseline characteristics

Reporting groups	
Reporting group title	FC 72 ug Linaclotide
Reporting group description:	
Functional Constipation (FC) subjects who completed studies LIN-MD-62 and LIN-MD-64 were dosed as follows: Subjects aged 6 to 11 years received an open-label dose of linaclotide 72 ug, oral capsule, once daily for 24 weeks. Subjects aged 12 to 17 years were randomized to receive an open-label dose of linaclotide either 72 or 145 ug, oral capsule, once daily for 24 weeks.	
Reporting group title	FC 145 ug Linaclotide
Reporting group description:	
Functional Constipation (FC) subjects who completed studies LIN-MD-62 and LIN-MD-64 were dosed as follows: Subjects aged 12 to 17 years were randomized to receive an open-label dose of linaclotide either 72 or 145 ug, oral capsule, once daily for 24 weeks.	
Reporting group title	IBS-C 145 ug Linaclotide
Reporting group description:	
Irritable Bowel Syndrome with Constipation (IBS-C) subjects were dosed as follows: Subjects who received ≤ 145 ug linaclotide or placebo in study LIN-MD-63 received an open-label dose of linaclotide 145 ug, oral capsule, once daily for 52 weeks. Subjects who completed study LIN-MD-64 had the option to either remain on the same blinded linaclotide dose they were receiving in lead-in study LIN-MD-64 (145 or 290 ug) or received an open-label dose of linaclotide 290 ug, oral capsule, once daily for 52 weeks.	
Reporting group title	IBS-C 290 ug Linaclotide
Reporting group description:	
Irritable Bowel Syndrome with Constipation (IBS-C) subjects were dosed as follows: Subjects who completed study LIN-MD-63 received an open-label dose of linaclotide 290 ug, oral capsule, once daily for 52 weeks. Subjects who completed study LIN-MD-64 had the option to either remain on the same blinded linaclotide dose they were receiving in lead-in study LIN-MD-64 (145 or 290 ug) or received an open-label dose of linaclotide 290 ug, oral capsule, once daily for 52 weeks.	

Reporting group values	FC 72 ug Linaclotide	FC 145 ug Linaclotide	IBS-C 145 ug Linaclotide
Number of subjects	210	73	22
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	10.6	14.2	13.7
standard deviation	± 2.96	± 1.78	± 2.68
Gender categorical Units: Subjects			
Female	115	40	15
Male	95	33	7

Ethnicity (NIH/ OMB) Units: Subjects			
Hispanic or Latino	92	37	8
Not Hispanic or Latino	118	36	14
Unknown or Not Reported	0	0	0
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	2	0	0
Asian	2	3	0
Native Hawaiian or Other Pacific Islander	2	0	0
Black or African American	59	17	3
White	142	52	18
More than one race	3	1	1
Unknown or Not Reported	0	0	0

Reporting group values	IBS-C 290 ug Linaclotide	Total	
Number of subjects	76	381	
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	12.9		
standard deviation	± 2.98	-	
Gender categorical Units: Subjects			
Female	45	215	
Male	31	166	
Ethnicity (NIH/ OMB) Units: Subjects			
Hispanic or Latino	29	166	
Not Hispanic or Latino	47	215	
Unknown or Not Reported	0	0	
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	2	
Asian	3	8	
Native Hawaiian or Other Pacific Islander	0	2	
Black or African American	19	98	
White	52	264	
More than one race	1	6	
Unknown or Not Reported	1	1	

End points

End points reporting groups

Reporting group title	FC 72 ug Linaclotide

Reporting group description:

Functional Constipation (FC) subjects who completed studies LIN-MD-62 and LIN-MD-64 were dosed as follows:

Subjects aged 6 to 11 years received an open-label dose of linaclotide 72 ug, oral capsule, once daily for 24 weeks.

Subjects aged 12 to 17 years were randomized to receive an open-label dose of linaclotide either 72 or 145 ug, oral capsule, once daily for 24 weeks.

Reporting group title	FC 145 ug Linaclotide

Reporting group description:

Functional Constipation (FC) subjects who completed studies LIN-MD-62 and LIN-MD-64 were dosed as follows:

Subjects aged 12 to 17 years were randomized to receive an open-label dose of linaclotide either 72 or 145 ug, oral capsule, once daily for 24 weeks.

Reporting group title	IBS-C 145 ug Linaclotide

Reporting group description:

Irritable Bowel Syndrome with Constipation (IBS-C) subjects were dosed as follows:

Subjects who received ≤ 145 ug linaclotide or placebo in study LIN-MD-63 received an open-label dose of linaclotide 145 ug, oral capsule, once daily for 52 weeks.

Subjects who completed study LIN-MD-64 had the option to either remain on the same blinded linaclotide dose they were receiving in lead-in study LIN-MD-64 (145 or 290 ug) or received an open-label dose of linaclotide 290 ug, oral capsule, once daily for 52 weeks.

Reporting group title	IBS-C 290 ug Linaclotide

Reporting group description:

Irritable Bowel Syndrome with Constipation (IBS-C) subjects were dosed as follows:

Subjects who completed study LIN-MD-63 received an open-label dose of linaclotide 290 ug, oral capsule, once daily for 52 weeks.

Subjects who completed study LIN-MD-64 had the option to either remain on the same blinded linaclotide dose they were receiving in lead-in study LIN-MD-64 (145 or 290 ug) or received an open-label dose of linaclotide 290 ug, oral capsule, once daily for 52 weeks.

Primary: Number of Subjects With Treatment-Emergent Adverse Events (TEAEs).

End point title	Number of Subjects With Treatment-Emergent Adverse Events (TEAEs).[1]

End point description:

An adverse event (AE) is defined as any untoward medical occurrence in a patient or clinical investigation subject administered a pharmaceutical product which does not necessarily have a causal relationship with this treatment. The investigator assesses the relationship of each event to the use of study drug. A serious adverse event (SAE) is an event that results in death, is life-threatening, requires or prolongs hospitalization, results in a congenital anomaly, persistent or significant disability/incapacity or is an important medical event that, based on medical judgment, may jeopardize the subject and may require medical or surgical intervention to prevent any of the outcomes listed above. Treatment emergent adverse events/treatment-emergent serious adverse events (TEAEs/TESAEs) are defined as any event that began or worsened in severity on or after the first dose of study drug. Analysis Population Description: Safety Population

End point type	Primary

End point timeframe:

From first dose of study drug until 30 days following last dose of study drug [up to 24 weeks (FC

subjects) or 52 weeks (IBS-C subjects)].

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analyses were performed.

End point values	FC 72 ug Linaclotide	FC 145 ug Linaclotide	IBS-C 145 ug Linaclotide	IBS-C 290 ug Linaclotide
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	210	73	22	76
Units: Subjects				
TEAE	37	15	4	31
TESAE	2	0	0	2

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All-cause mortality and adverse event tables include events reported from the time of informed consent to the end of the study. The median time in follow-up (or mean time participants were followed) was 176.0, 177.0, 373.5, and 369.0 days for

Adverse event reporting additional description:

FC 72 ug linaclotide, FC 145 ug linaclotide, IBS-C 145 ug linaclotide, and IBS-C 290 ug linaclotide, respectively. All AEs were coded using MedDRA version 27.1 and 28.0 for FC and IBS-C participants, respectively.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	27.1, 28.0

Reporting groups

Reporting group title	FC 72 ug Linaclotide

Reporting group description:

Functional Constipation (FC) participants who completed studies LIN-MD-62 and LIN-MD-64 were dosed as follows:

Participants aged 6 to 11 years received an open-label dose of linaclotide 72 ug, oral capsule, once daily for 24 weeks.

Participants aged 12 to 17 years were randomized to receive an open-label dose of linaclotide either 72 or 145 ug, oral capsule, once daily for 24 weeks.

Reporting group title	FC 145 ug Linaclotide

Reporting group description:

Functional Constipation (FC) participants who completed studies LIN-MD-62 and LIN-MD-64 were dosed as follows:

Participants aged 12 to 17 years were randomized to receive an open-label dose of linaclotide either 72 or 145 ug, oral capsule, once daily for 24 weeks.

Reporting group title	IBS-C 145 ug Linaclotide

Reporting group description:

Irritable Bowel Syndrome with Constipation (IBS-C) participants were dosed as follows:

Participants who received ≤ 145 ug linaclotide or placebo in study LIN-MD-63 received an open-label dose of linaclotide 145 ug, oral capsule, once daily for 52 weeks.

Participants who completed study LIN-MD-64 had the option to either remain on the same blinded linaclotide dose they were receiving in lead-in study LIN-MD-64 (145 or 290 ug) or received an open-label dose of linaclotide 290 ug, oral capsule, once daily for 52 weeks.

Reporting group title	IBS-C 290 ug Linaclotide

Reporting group description:

Irritable Bowel Syndrome with Constipation (IBS-C) participants were dosed as follows:

Participants who completed study LIN-MD-63 received an open-label dose of linaclotide 290 ug, oral capsule, once daily for 52 weeks.

Participants who completed study LIN-MD-64 had the option to either remain on the same blinded linaclotide dose they were receiving in lead-in study LIN-MD-64 (145 or 290 ug) or received an open-label dose of linaclotide 290 ug, oral capsule, once daily for 52 weeks.

Serious adverse events	FC 72 ug Linaclotide	FC 145 ug Linaclotide	IBS-C 145 ug Linaclotide
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 210 (0.95%)	0 / 73 (0.00%)	0 / 22 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
POST PROCEDURAL HAEMORRHAGE			
subjects affected / exposed	0 / 210 (0.00%)	0 / 73 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
MIGRAINE			
subjects affected / exposed	0 / 210 (0.00%)	0 / 73 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
CONSTIPATION			
subjects affected / exposed	1 / 210 (0.48%)	0 / 73 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
ADENOIDAL HYPERTROPHY			
subjects affected / exposed	0 / 210 (0.00%)	0 / 73 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NASAL TURBINATE HYPERTROPHY			
subjects affected / exposed	0 / 210 (0.00%)	0 / 73 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
TONSILLAR HYPERTROPHY			
subjects affected / exposed	0 / 210 (0.00%)	0 / 73 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			

MENTAL STATUS CHANGES			
subjects affected / exposed	0 / 210 (0.00%)	0 / 73 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DISRUPTIVE MOOD DYSREGULATION DISORDER			
subjects affected / exposed	1 / 210 (0.48%)	0 / 73 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
PYELONEPHRITIS			
subjects affected / exposed	1 / 210 (0.48%)	0 / 73 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	IBS-C 290 ug Linaclotide		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 76 (2.63%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Injury, poisoning and procedural complications			
POST PROCEDURAL HAEMORRHAGE			
subjects affected / exposed	1 / 76 (1.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
MIGRAINE			
subjects affected / exposed	1 / 76 (1.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
CONSTIPATION			
subjects affected / exposed	0 / 76 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal			

disorders			
ADENOIDAL HYPERTROPHY			
subjects affected / exposed	1 / 76 (1.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
NASAL TURBINATE HYPERTROPHY			
subjects affected / exposed	1 / 76 (1.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
TONSILLAR HYPERTROPHY			
subjects affected / exposed	1 / 76 (1.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
MENTAL STATUS CHANGES			
subjects affected / exposed	1 / 76 (1.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
DISRUPTIVE MOOD DYSREGULATION DISORDER			
subjects affected / exposed	0 / 76 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
PYELONEPHRITIS			
subjects affected / exposed	0 / 76 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	FC 72 ug Linaclotide	FC 145 ug Linaclotide	IBS-C 145 ug Linaclotide
Total subjects affected by non-serious adverse events			
subjects affected / exposed	14 / 210 (6.67%)	5 / 73 (6.85%)	0 / 22 (0.00%)
Gastrointestinal disorders			

DIARRHOEA subjects affected / exposed occurrences (all)	12 / 210 (5.71%) 14	5 / 73 (6.85%) 5	0 / 22 (0.00%) 0
Infections and infestations INFLUENZA subjects affected / exposed occurrences (all)	2 / 210 (0.95%) 2	0 / 73 (0.00%) 0	0 / 22 (0.00%) 0

Non-serious adverse events	IBS-C 290 ug Linaclotide		
Total subjects affected by non-serious adverse events subjects affected / exposed	11 / 76 (14.47%)		
Gastrointestinal disorders DIARRHOEA subjects affected / exposed occurrences (all)	7 / 76 (9.21%) 9		
Infections and infestations INFLUENZA subjects affected / exposed occurrences (all)	4 / 76 (5.26%) 4		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
10 June 2020	Amendment 1 - include enrollment of pediatric subjects ages 7 – 17 years with IBS-C from lead-in study LIN-MD-64. Revise the dosing for all IBS-C subjects, and provide additional clarification and updates.
30 April 2021	Amendment 2 - provide LIN-MD-64 completers with IBS-C the option to continue on the same blinded dose they received in the LIN-MD-64 lead-in study, and to provide additional clarification and updates.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported