Clinical trial results:
A 46-week, Double-blind, Placebo-controlled, Phase 3 Study with a 6-week Randomized-withdrawal Period to Evaluate the Safety and Efficacy of Relamorelin in Patients with Diabetic Gastroparesis

Summary

EudraCT number	2017-002143-15
Trial protocol	GB DE LV HU FR BE DK BG AT ES IT
Global end of trial date	30 October 2020

Results information

Result version number	v1 (current)
This version publication date	20 October 2021
First version publication date	20 October 2021

Trial information

Trial identification

Sponsor protocol code	RLM-MD-03

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03420781
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Allergan
Sponsor organisation address	1st Floor, Marlow International, The Parkway, Marlow Buckinghamshire, United Kingdom, SL7 1YL
Public contact	Therapeutic Area, Head, Allergan, 001 714-246-4500, IR-CTRegistration@Allergan.com
Scientific contact	Therapeutic Area, Head, Allergan, 001 714-246-4500, IR-CTRegistration@Allergan.com

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	30 October 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	30 October 2020
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The main purpose of the study was to compare the efficacy of relamorelin with that of placebo in participants with diabetic gastroparesis (DG). Participants either continued on relamorelin or placebo for 6 additional weeks at the end of the 40-week Treatment Period.

Protection of trial subjects:

All study participants were required to read and sign an Informed Consent Form.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	24 January 2018
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	Bulgaria: 3
Country: Number of subjects enrolled	Hungary: 3
Country: Number of subjects enrolled	Latvia: 6
Country: Number of subjects enrolled	Poland: 6
Country: Number of subjects enrolled	United Kingdom: 1
Country: Number of subjects enrolled	Argentina: 7
Country: Number of subjects enrolled	Brazil: 5
Country: Number of subjects enrolled	Canada: 4
Country: Number of subjects enrolled	Colombia: 5
Country: Number of subjects enrolled	India: 33
Country: Number of subjects enrolled	Israel: 2
Country: Number of subjects enrolled	Malaysia: 2
Country: Number of subjects enrolled	Mexico: 29
Country: Number of subjects enrolled	Russian Federation: 11
Country: Number of subjects enrolled	South Africa: 3
Country: Number of subjects enrolled	Korea, Republic of: 1
Country: Number of subjects enrolled	Ukraine: 30
Country: Number of subjects enrolled	United States: 316
Worldwide total number of subjects	467
EEA total number of subjects	18

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)	355
From 65 to 84 years	111
85 years and over	1

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Participants who completed RLM-MD-01 [NCT03285308] or RLM-MD-02 [NCT03426345] were eligible for enrollment.

Period 1

Period 1 title	Treatment Period (40 weeks)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Carer

Arms

Are arms mutually exclusive?	Yes
Arm title	Treatment Period: Placebo

Arm description:

Placebo-matching relamorelin injected subcutaneously twice daily for up to 40 weeks.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Placebo injected twice daily

Arm title	Treatment Period: Relamorelin 10 µg

Arm description:

Relamorelin 10 micrograms (µg) injected subcutaneously twice daily for up to 40 weeks.

Arm type	Experimental
Investigational medicinal product name	Relamorelin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Relamorelin 10 µg injected twice daily

Number of subjects in period 1	Treatment Period: Placebo	Treatment Period: Relamorelin 10 µg
Started	236	231
Safety Population	235	231
Completed	92	105
Not completed	144	126

Physician decision	3	4
Site Terminated by the Sponsor	1	-
Adverse Event	1	6
Protocol Deviation	-	2
Death	2	2
Reason Not Specified	3	-
Withdrawal by Subject	22	16
Study Terminated by the Sponsor	101	89
Lost to follow-up	10	6
Lack of efficacy	1	1

Period 2

Period 2 title	RW Period: 6 weeks (Week 41 to Week 46)
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Carer

Arms

Are arms mutually exclusive?	Yes
Arm title	RW Period: Placebo then Relamorelin 10 µg

Arm description:

Participants who received placebo-matching relamorelin injected subcutaneously twice daily for 40 weeks, followed by relamorelin 10 µg injected twice daily for up to 6 weeks in the Randomized Withdrawal (RW) Period.

Arm type	Experimental
Investigational medicinal product name	Relamorelin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Relamorelin 10 µg injected twice daily

Arm title	RW Period: Relamorelin 10 µg then Relamorelin 10 µg

Arm description:

Participants who received relamorelin 10 µg injected subcutaneously twice daily for 40 weeks, followed by relamorelin injected twice daily for up to 6 weeks in the RW Period.

Arm type	Experimental
Investigational medicinal product name	Relamorelin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Relamorelin 10 µg injected twice daily

Arm title	RW Period: Relamorelin 10 µg then Placebo

Arm description:

Participants who received relamorelin 10 µg injected subcutaneously twice daily for 40 weeks, followed by placebo-matching relamorelin injected twice daily for up to 6 weeks in the RW Period.

Arm type	Experimental
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Placebo injected twice daily

Number of subjects in period 2[1]	RW Period: Placebo then Relamorelin 10 µg	RW Period: Relamorelin 10 µg then Relamorelin 10 µg	RW Period: Relamorelin 10 µg then Placebo
Started	91	59	43
Completed	85	54	38
Not completed	6	5	5
Adverse Event	-	2	-
Withdrawal by Subject	-	-	2
Study Terminated by the Sponsor	6	3	3

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: 4 participants who completed the Treatment Period did not participate in the RW Period.

Baseline characteristics

Reporting groups	
Reporting group title	Treatment Period: Placebo
Reporting group description:	
Placebo-matching relamorelin injected subcutaneously twice daily for up to 40 weeks.	
Reporting group title	Treatment Period: Relamorelin 10 µg
Reporting group description:	
Relamorelin 10 micrograms (µg) injected subcutaneously twice daily for up to 40 weeks.	

Reporting group values	Treatment Period: Placebo	Treatment Period: Relamorelin 10 µg	Total
Number of subjects	236	231	467
Age categorical Units: Subjects			
Adults (18-64 years)	180	175	355
From 65-84 years	56	55	111
>= 85 years	0	1	1
Age Continuous Units: years			
arithmetic mean	55.5	56.2	
standard deviation	± 11.11	± 11.51	-
Sex: Female, Male Units: participants			
Female	162	166	328
Male	74	65	139
Race Units: Subjects			
American Indian or Alaska Native	3	8	11
Asian	21	18	39
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	37	21	58
White	175	183	358
More than one race	0	1	1
Unknown or Not Reported	0	0	0
Ethnicity Units: Subjects			
Hispanic or Latino	83	82	165
Not Hispanic or Latino	153	149	302
Unknown or Not Reported	0	0	0

End points

End points reporting groups

Reporting group title	Treatment Period: Placebo
Reporting group description:	
Placebo-matching relamorelin injected subcutaneously twice daily for up to 40 weeks.	
Reporting group title	Treatment Period: Relamorelin 10 µg
Reporting group description:	
Relamorelin 10 micrograms (µg) injected subcutaneously twice daily for up to 40 weeks.	
Reporting group title	RW Period: Placebo then Relamorelin 10 µg
Reporting group description:	
Participants who received placebo-matching relamorelin injected subcutaneously twice daily for 40 weeks, followed by relamorelin 10 µg injected twice daily for up to 6 weeks in the Randomized Withdrawal (RW) Period.	
Reporting group title	RW Period: Relamorelin 10 µg then Relamorelin 10 µg
Reporting group description:	
Participants who received relamorelin 10 µg injected subcutaneously twice daily for 40 weeks, followed by relamorelin injected twice daily for up to 6 weeks in the RW Period.	
Reporting group title	RW Period: Relamorelin 10 µg then Placebo
Reporting group description:	
Participants who received relamorelin 10 µg injected subcutaneously twice daily for 40 weeks, followed by placebo-matching relamorelin injected twice daily for up to 6 weeks in the RW Period.	

Primary: Change from Baseline to Week 12 in the Weekly Diabetic Gastroparesis Symptom Severity Score (DGSSS) of the Treatment Period

End point title	Change from Baseline to Week 12 in the Weekly Diabetic Gastroparesis Symptom Severity Score (DGSSS) of the Treatment Period[1]

End point description:

Participants assessed the severity of diabetic gastroparesis symptoms daily using the Diabetic Gastroparesis Symptom Severity Diary (DGSSD), recorded in an electronic diary (e-diary). The DGSSS was derived as the sum of the weekly averages of the 4 DGSSD items: nausea, abdominal pain, postprandial fullness and bloating. Each symptom was scored using an 11-point ordinal scale where: 0=no or not at all uncomfortable to 10=worst possible or most uncomfortable for a total possible DGSSS of 0 (best) to 40 (worst). A negative change from Baseline indicates improvement. Baseline was defined as the average of the 2 weekly DGSSS from the run-in period in the previous studies. Modified-intent-to-treat (mITT) Population included all participants in the ITT population with ≥1 postbaseline assessment of DGSSD. 'n' indicates number analysed is the number of participants with data available at the given time-point.

End point type	Primary

End point timeframe:

Baseline (14-day Run-in Period of the previous relamorelin study RLM-MD-01 or RLM-MD-02) to Week 12 of this study

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 are reported for this endpoint.

End point values	Treatment Period: Placebo	Treatment Period: Relamorelin 10 µg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	235	229		
Units: score on a scale				
arithmetic mean (standard deviation)				
Baseline (n=235, 229)	24.9 (± 5.65)	24.8 (± 6.28)		
Change from Baseline to Week 12 (n=205, 202)	-11.9 (± 9.43)	-11.2 (± 9.00)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants Meeting the Vomiting Responder Criterion During Each of the Last 6 Weeks of the First 12-weeks of the Treatment Period

End point title	Percentage of Participants Meeting the Vomiting Responder Criterion During Each of the Last 6 Weeks of the First 12-weeks of the Treatment Period[2]

End point description:

The number of vomiting episodes in the previous 24 hours were assessed daily by the participant using the DGSSD and were recorded in the e-diary. A Vomiting Responder was defined as a participant with zero weekly vomiting episodes during each of the last 6 weeks of the first 12-weeks of the 40-week Treatment Period. mITT Population included all participants in the ITT population with ≥1 postbaseline assessment of DGSSD.

End point type	Primary

End point timeframe:

Week 6 to Week 12

Notes:

[2] - 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 are reported for this endpoint.

End point values	Treatment Period: Placebo	Treatment Period: Relamorelin 10 µg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	235	229		
Units: percentage of participants				
number (not applicable)	29.4	21.4		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Meeting the Nausea Responder Criterion During Each of the Last 6 Weeks of the First 12-weeks of the Treatment Period

End point title	Percentage of Participants Meeting the Nausea Responder

	Criterion During Each of the Last 6 Weeks of the First 12-weeks of the Treatment Period

End point description:

A Nausea Responder was defined as a participant with improvement (decrease) of at least 2-points in the weekly symptom scores for nausea at each of the last 6 weeks of the first 12-weeks of the 40-week Treatment Period. Nausea was one of the items of the DGSSD assessed daily and recorded in the e-diary by the participant using an 11-point ordinal scale where: 0=no nausea to 10=worst possible nausea. Baseline was defined as the average of the 2 weekly DGSSS from the run-in period in the previous studies. mITT Population included all participants in the ITT population with ≥1 postbaseline assessment of DGSSD.

End point type	Secondary

End point timeframe:

Baseline (14-day Run-in Period of the previous relamorelin study RLM-MD-01 or RLM-MD-02) to (Week 6 to Week 12)

End point values	Treatment Period: Placebo	Treatment Period: Relamorelin 10 µg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	235	229		
Units: percentage of participants				
number (not applicable)	46.0	43.2		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Meeting the Abdominal Pain Responder Criterion During Each of the Last 6 Weeks of the First 12-weeks of the Treatment Period

End point title	Percentage of Participants Meeting the Abdominal Pain Responder Criterion During Each of the Last 6 Weeks of the First 12-weeks of the Treatment Period

End point description:

An Abdominal Pain Responder was defined as a participant with an improvement (decrease) of at least 2-points in the weekly symptom scores for abdominal pain at each of the last 6 weeks of the first 12-weeks of the 40-week Treatment Period. Abdominal pain was one of the items of the DGSSD assessed daily and recorded in the e-diary by the participant using an 11-point ordinal scale where: 0=no abdominal pain to 10=the worst possible abdominal pain and was recorded in an e-diary. Baseline was defined as the average of the 2 weekly DGSSS from the run-in period in the previous studies. mITT Population included all participants in the ITT population with ≥1 postbaseline assessment of DGSSD.

End point type	Secondary

End point timeframe:

Baseline (14-day Run-in Period of the previous relamorelin study RLM-MD-01 or RLM-MD-02) to (Week 6 to Week 12)

End point values	Treatment Period: Placebo	Treatment Period: Relamorelin 10 µg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	235	229		
Units: percentage of participants				
number (not applicable)	40.4	39.7		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Meeting the Bloating Responder Criterion During Each of the Last 6 Weeks of the First 12-weeks of the Treatment Period

End point title	Percentage of Participants Meeting the Bloating Responder Criterion During Each of the Last 6 Weeks of the First 12-weeks of the Treatment Period

End point description:

A Bloating Responder was defined as a participant with an improvement (decrease) of at least 2-points in the weekly symptom scores for bloating at each of the last 6 weeks of the first 12-weeks of the 40-week Treatment Period. Bloating was one of the items of the DGSSD assessed daily and recorded by the participant in the e-diary using an 11-point ordinal scale where: 0=no bloating and 10=the worst possible bloating and was recorded in the e-diary. Baseline was defined as the average of the 2 weekly DGSSS from the run-in period in the previous studies. mITT Population included all participants in the ITT population with ≥1 postbaseline assessment of DGSSD.

End point type	Secondary

End point timeframe:

Baseline (14-day Run-in Period of the previous relamorelin study RLM-MD-01 or RLM-MD-02) to (Week 6 to Week 12)

End point values	Treatment Period: Placebo	Treatment Period: Relamorelin 10 µg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	235	229		
Units: percentage of participants				
number (not applicable)	38.3	38.4		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Meeting the Postprandial Fullness Responder Criterion During Each of the Last 6 Weeks of the First 12-weeks of the Treatment Period

End point title	Percentage of Participants Meeting the Postprandial Fullness Responder Criterion During Each of the Last 6 Weeks of the

	First 12-weeks of the Treatment Period

End point description:

A Postprandial Fullness Responder was defined as a participant with an improvement (decrease) of at least 2-points in the weekly symptom scores for Postprandial Fullness at each of the last 6 weeks of the first 12-weeks of the 40-week Treatment Period. Postprandial Fullness was one of the items of the DGSSD assessed daily and recorded by the participant in the e-diary using an 11-point ordinal scale where: 0=no feeling of fullness until finishing a meal (best) to 10=feeling full after only a few bites (worst). Baseline was defined as the average of the 2 weekly DGSSS from the run-in period in the previous studies. mITT Population included all participants in the ITT population with ≥1 postbaseline assessment of DGSSD.

End point type	Secondary

End point timeframe:

Baseline (14-day Run-in Period of the previous relamorelin study RLM-MD-01 or RLM-MD-02) to (Week 6 to Week 12)

End point values	Treatment Period: Placebo	Treatment Period: Relamorelin 10 µg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	235	229		
Units: percentage of participants				
number (not applicable)	36.6	36.2		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Week 40 in the Average Weekly DGSSS of the Treatment Period

End point title	Change from Baseline to Week 40 in the Average Weekly DGSSS of the Treatment Period

End point description:

Participants assessed the severity of diabetic gastroparesis symptoms daily using the DGSSD, recorded in an e-diary. The DGSSS was derived as the sum of the weekly averages (Week 37 to Week 40) of the 4 DGSSD items: nausea, abdominal pain, postprandial fullness and bloating. Each symptom was scored using an 11-point ordinal scale where: 0=no or not at all uncomfortable to 10=worst possible or most uncomfortable for a total possible DGSSS of 0 (best) to 40 (worst). A negative change from Baseline indicates improvement. Baseline was defined as the average of the 2 weekly DGSSS from the run-in period of the previous studies. mITT Population included all participants in the ITT population with ≥1 postbaseline assessment of DGSSD. 'n' indicates number analysed is the number of participants with data available at the given time-point.

End point type	Secondary

End point timeframe:

Baseline (14-day Run-in Period of the previous relamorelin study RLM-MD-01 or RLM-MD-02) to (Week 37 to Week 40)

End point values	Treatment Period: Placebo	Treatment Period: Relamorelin 10 µg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	235	229		
Units: score on a scale				
arithmetic mean (standard deviation)				
Baseline (n=235, 229)	24.9 (± 5.65)	24.8 (± 6.28)		
Change from Baseline to Week 40 (n=112, 123)	-13.3 (± 10.22)	-12.3 (± 9.20)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Meeting the Vomiting Responder Criterion at Week 40 of the Treatment Period

End point title	Percentage of Participants Meeting the Vomiting Responder Criterion at Week 40 of the Treatment Period

End point description:

The number of vomiting episodes in the previous 24 hours were assessed daily by the participant using the DGSSD and were recorded in the e-diary. A Vomiting Responder was defined as a participant with zero weekly vomiting episodes during the last 4 weeks of the 40-week Treatment Period. mITT Population included all participants in the ITT population with ≥1 postbaseline assessment of DGSSD.

End point type	Secondary

End point timeframe:

Week 37 to Week 40

End point values	Treatment Period: Placebo	Treatment Period: Relamorelin 10 µg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	235	229		
Units: percentage of participants				
number (not applicable)	19.1	18.8		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Week 40 in the Average Weekly Number of Vomiting Episodes of the Treatment Period

End point title	Change from Baseline to Week 40 in the Average Weekly Number of Vomiting Episodes of the Treatment Period

End point description:

The number of vomiting episodes in the previous 24 hours were assessed daily by the participant using

the DGSSD and were recorded in the e-diary. The average weekly number of vomiting episodes were derived as the average of the weekly number of vomiting episodes in the last 4 weeks of the 40-week Treatment Period. A negative change from Baseline indicates improvement. Baseline was defined as the average of the 2 weekly DGSSS from the run-in period in the previous studies. mITT Population included all participants in the ITT population with ≥1 postbaseline assessment of DGSSD. 'n' indicates number analysed is the number of participants with data available at the given time-point.

End point type	Secondary

End point timeframe:

Baseline (14-day Run-in Period of the previous relamorelin study RLM-MD-01 or RLM-MD-02) to (Week 37 to Week 40)

End point values	Treatment Period: Placebo	Treatment Period: Relamorelin 10 µg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	235	229		
Units: vomiting episodes per week				
arithmetic mean (standard deviation)				
Baseline (n=235, 229)	6.8 (± 11.09)	7.3 (± 11.52)		
Change from Baseline to Week 40 (n=112, 123)	-1.8 (± 17.51)	-5.4 (± 11.87)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Week 46 in the Average Weekly DGSSS of the RW Period

End point title	Change from Baseline to Week 46 in the Average Weekly DGSSS of the RW Period

End point description:

Participants assessed the severity of diabetic gastroparesis symptoms daily using the DGSSD, recorded in an e-diary. The DGSSS was derived as the sum of the weekly averages of the 4 DGSSD items: nausea, abdominal pain, postprandial fullness and bloating. Each symptom was scored using an 11-point ordinal scale where: 0=no or not at all uncomfortable to 10=worst possible or most uncomfortable for a total possible DGSSS of 0 (best) to 40 (worst). Average weekly scores are derived as the average of the weekly scores from the 6 weeks of the RW Period. A negative change from Baseline indicates improvement. Baseline was defined as the average of the 2 weekly DGSSS from the run-in period in the previous studies. RW Population included all participants who were re-randomised or assigned to a treatment of RW Period and received ≥1 administration of study treatment during the RW Period. 'n' indicates number analysed is the number of participants with data available at the given time-point.

End point type	Secondary

End point timeframe:

Baseline (14-day Run-in Period of the previous relamorelin study RLM-MD-01 or RLM-MD-02) to (Week 41 to Week 46)

End point values	RW Period: Placebo then Relamorelin 10 µg	RW Period: Relamorelin 10 µg then Relamorelin 10 µg	RW Period: Relamorelin 10 µg then Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	91	58	43	
Units: score on a scale				
arithmetic mean (standard deviation)				
Baseline (n=91, 58, 43)	25.7 (± 5.65)	25.7 (± 6.25)	24.4 (± 5.47)	
Change from Baseline to Week 46 (n=86, 56, 39)	-13.4 (± 10.45)	-12.5 (± 9.71)	-12.5 (± 9.35)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Week 46 in the Average Weekly Number of Vomiting Episodes of the RW Period

End point title	Change from Baseline to Week 46 in the Average Weekly Number of Vomiting Episodes of the RW Period

End point description:

The number of vomiting episodes in the previous 24 hours were assessed daily by the participant using the DGSSD and were recorded in the e-diary. Average weekly number of vomiting episodes are derived as the average of the weekly number of vomiting episodes from the six weeks of the RW Period. A negative change from Baseline indicates improvement. Baseline was defined as the average of the 2 weekly DGSSS from the run-in period in the previous studies. RW Population included all participants who were re-randomised or assigned to a treatment of RW Period and received ≥1 administration of study treatment during the RW Period. 'n' indicates number analysed is the number of participants with data available at the given time-point.

End point type	Secondary

End point timeframe:

Baseline (14-day Run-in Period of the previous relamorelin study RLM-MD-01 or RLM-MD-02) to (Week 41 to Week 46)

End point values	RW Period: Placebo then Relamorelin 10 µg	RW Period: Relamorelin 10 µg then Relamorelin 10 µg	RW Period: Relamorelin 10 µg then Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	91	58	43	
Units: vomiting episodes per week				
arithmetic mean (standard deviation)				
Baseline (n=91, 58, 43)	6.1 (± 7.01)	9.9 (± 11.92)	4.2 (± 4.73)	
Change from Baseline to Week 46 (n=86, 56, 39)	-1.8 (± 18.40)	-7.3 (± 10.23)	-1.8 (± 6.12)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants who Experienced One or More Treatment-Emergent Adverse Events (TEAE)

End point title	Number of Participants who Experienced One or More Treatment-Emergent Adverse Events (TEAE)

End point description:

An adverse event (AE) is any untoward medical occurrence in a patient or clinical study participant, temporally associated with the use of study treatment, whether or not considered related to the study treatment. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with the use of study treatment. A TEAE is an AE that begins or worsens after receiving study drug. Safety Population included all participants in the ITT population who received ≥1 administration of study treatment in Treatment Period. RW Population included all participants who were re-randomised or assigned to a treatment of RW population and received ≥1 administration of study treatment during the RW Period.

End point type	Secondary

End point timeframe:

First dose of study drug to within 30 days of the last dose of study drug (Up to approximately 50 weeks)

End point values	Treatment Period: Placebo	RW Period: Placebo then Relamorelin 10 µg	Treatment Period: Relamorelin 10 µg	RW Period: Relamorelin 10 µg then Relamorelin 10 µg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	235	91	231	59
Units: participants	129	18	131	12

End point values	RW Period: Relamorelin 10 µg then Placebo			
Subject group type	Reporting group			
Number of subjects analysed	43			
Units: participants	8			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Potential Clinically Significant (PCS) Clinical Laboratory Results

End point title	Number of Participants with Potential Clinically Significant (PCS) Clinical Laboratory Results

End point description:

Clinical Laboratory values:Hematology,Chemistry,Urinalysis tests. The investigator determined if results were clinically significant. Only those categories where at least 1 person had a non-PCS value at Baseline and met PCS criterion at least once during postbaseline are reported. Safety Population:all participants in ITT population who received ≥1 administration of study treatment in Treatment Period.

RW Population:all participants who were re-randomised or assigned to a treatment of RW population and received ≥1 administration of study treatment during RW Period. 'n'=number analysed is the number of participants with non-PCS Baseline values and at least one post-baseline assessment.
ACC=AbsoluteCellCount,ULN=upper limit of normal value,LLN=lower limit of normal value,L=liter,MCV=MeanCorpuscularVolume,fL=femtoliter,PC=PlateletCount,RBC=RedBloodCell,WBC=WhiteBloodCell,BUN=BloodUreaNitrogen,TF=TotalFasting,Hb=Glycohemoglobin,AT=aminotransferase,U=unit,mmol=millimoles,µmol=micromoles.

End point type	Secondary

End point timeframe:

Up to 46 weeks

End point values	Treatment Period: Placebo	RW Period: Placebo then Relamorelin 10 µg	Treatment Period: Relamorelin 10 µg	RW Period: Relamorelin 10 µg then Relamorelin 10 µg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	235	91	231	59
Units: participants				
Eosinophils ACC[10^9/L]:>3×ULN(n=227,225,91,5	2	0	1	1
Hematocrit (RATIO): >1.1×ULN (n=214,224,86,59,42)	1	2	2	1
Hematocrit (RATIO): <0.9×LLN (n=214,224,86,59,42)	7	4	7	0
Hemoglobin [g/L]: <0.9×LLN (n=214,220,86,58,42)	13	5	14	1
LymphocytesACC(10^9/L):<0.8×LLN;n=226,221,90,57,42	1	0	4	0
MCV [fL]: >1.1×ULN (n=222,224,89,59,43)	2	1	3	0
MCV [fL]: <0.9×LLN (n=222,224,89,59,43)	4	1	0	0
NeutrophilsACC(10^9/L):>1.5×ULN;n=224,221,90,57,41	0	2	2	0
NeutrophilsACC(10^9/L):<0.8×LLN;n=224,221,90,57,41	6	2	4	0
PC,Thrombocytes;10^9/L:>1.5×ULN;n=227,224,91,59,42	0	0	1	0
PC,Thrombocytes;10^9/L:<0.5×LLN;n=227,224,91,59,42	1	0	0	0
RBC Count (10^12/L): >1.1×ULN (n=223,224,90,58,42)	1	0	0	0
RBC Count (10^12/L): <0.9×LLN (n=223,224,90,58,42)	4	4	8	1
WBC Count (10^9/L): <0.7×LLN (n=227,225,91,59,42)	2	0	0	0
Alanine AT [U/L]: >=3×ULN (n=227,225,91,59,43)	2	0	2	2
Albumin (g/L): <0.9×LLN (n=225,226,90,59,43)	1	1	1	0
AlkalinePhosphatase;U/L:>=3×ULN;n=227,226,91,59,43	0	0	3	0
Aspartate AT (U/L): >=3×ULN (n=227,225,91,59,42)	3	0	2	0
Bicarbonate [mmol/L]:>1.1×ULN (n=223,218,91,58,41)	3	1	2	1

Bicarbonate (mmol)/L:>0.9×LLN (n=223,218,91,58,41)	6	2	9	4
Bilirubin,Total;µmol/L:>1.5×ULN;n=227,226,91,59,43	1	0	0	0
BUN (mmol/L): >1.2×ULN (n=207,207,84,52,39)	29	8	20	4
Calcium (mmol/L): >1.1×ULN (n=225,221,90,57,42)	1	1	0	0
Calcium (mmol/L): <0.9×LLN (n=225,221,90,57,42)	1	0	0	0
Chloride (mmol/L): <0.9×LLN (n=227,226,91,59,43)	2	1	1	0
CholesterolTF(mmol/L):>1.6×ULN(n=221,222,90,59,43)	4	0	1	1
Creatinine (µmol/L): >1.3×ULN (n=211,213,84,51,41)	22	5	16	2
Glucose Fasting,mmol/L:>2.5×ULN;n=206,201,	41	9	33	9
Glucose Fasting,mmol/L:<0.9×LLN;n=206,201,8	14	4	9	2
HbA1C: Increase of >=0.5% (n=224,223,91,59,43)	134	62	138	26
HbA1C: Increase of >=1% (n=224,223,91,59,43)	134	62	138	26
Phosphorus (mmol/L):>1.1×ULN (n=221,219,88,56,43)	10	4	12	4
Phosphorus (mmol/L):<0.9×LLN (n=221,219,88,56,43)	4	0	3	0
Potassium (mmol/L): <0.9×LLN (n=227,226,91,59,43)	0	2	0	0
Protein, Total (g/L):>1.1×ULN (n=225,226,90,59,43)	0	0	1	0
Protein, Total (g/L):<0.9×LLN (n=225,226,90,59,43)	0	0	1	0
Triglycerides,mmol/L: >=3×ULN(n=217,216,87,58,42)	9	4	11	4
Uric Acid,Urate;µmol/L:>1.1×ULN;n=192,18	31	5	31	3
Uric Acid,Urate;µmol/L:<0.9×LLN;n=192,18	3	1	4	0

End point values	RW Period: Relamorelin 10 µg then Placebo			
Subject group type	Reporting group			
Number of subjects analysed	43			
Units: participants				
Eosinophils ACC[10^9/L]:>3×ULN(n=227,225,91,5	1			
Hematocrit (RATIO): >1.1×ULN (n=214,224,86,59,42)	0			
Hematocrit (RATIO): <0.9×LLN (n=214,224,86,59,42)	2			
Hemoglobin [g/L]: <0.9×LLN (n=214,220,86,58,42)	4			
LymphocytesACC(10^9/L):<0.8×LLN;n=226,221,90,57,42	0			

MCV [fL]: >1.1×ULN (n=222,224,89,59,43)	0			
MCV [fL]: <0.9×LLN (n=222,224,89,59,43)	0			
NeutrophilsACC(10^9/L):>1.5×ULN;n=224,221,90,57,41	0			
NeutrophilsACC(10^9/L):<0.8×LLN;n=224,221,90,57,41	0			
PC,Thrombocytes;10^9/L:>1.5×ULN;n=227,224,91,59,42	0			
PC,Thrombocytes;10^9/L:<0.5×LLN;n=227,224,91,59,42	0			
RBC Count (10^12/L): >1.1×ULN (n=223,224,90,58,42)	0			
RBC Count (10^12/L): <0.9×LLN (n=223,224,90,58,42)	0			
WBC Count (10^9/L): <0.7×LLN (n=227,225,91,59,42)	0			
Alanine AT [U/L]: >=3×ULN (n=227,225,91,59,43)	1			
Albumin (g/L): <0.9×LLN (n=225,226,90,59,43)	1			
AlkalinePhosphatase;U/L:>=3×ULN;n=227,226,91,59,43	0			
Aspartate AT (U/L): >=3×ULN (n=227,225,91,59,42)	0			
Bicarbonate [mmol/L]:>1.1×ULN (n=223,218,91,58,41)	0			
Bicarbonate (mmol)/L:>0.9×LLN (n=223,218,91,58,41)	1			
Bilirubin,Total;µmol/L:>1.5×ULN;n=227,226,91,59,43	0			
BUN (mmol/L): >1.2×ULN (n=207,207,84,52,39)	4			
Calcium (mmol/L): >1.1×ULN (n=225,221,90,57,42)	0			
Calcium (mmol/L): <0.9×LLN (n=225,221,90,57,42)	1			
Chloride (mmol/L): <0.9×LLN (n=227,226,91,59,43)	1			
CholesterolTF(mmol/L):>1.6×ULN(n=221,222,90,59,43)	0			
Creatinine (µmol/L): >1.3×ULN (n=211,213,84,51,41)	3			
Glucose Fasting,mmol/L:>2.5×ULN;n=206,201,	4			
Glucose Fasting,mmol/L:<0.9×LLN;n=206,201,8	2			
HbA1C: Increase of >=0.5% (n=224,223,91,59,43)	28			
HbA1C: Increase of >=1% (n=224,223,91,59,43)	28			
Phosphorus (mmol/L):>1.1×ULN (n=221,219,88,56,43)	4			
Phosphorus (mmol/L):<0.9×LLN (n=221,219,88,56,43)	0			
Potassium (mmol/L): <0.9×LLN (n=227,226,91,59,43)	0			
Protein, Total (g/L):>1.1×ULN (n=225,226,90,59,43)	0			
Protein, Total (g/L):<0.9×LLN (n=225,226,90,59,43)	1			

Triglycerides,mmol/L: >=3×ULN(n=217,216,87,58,42)	2			
Uric Acid,Urate;µmol/L:>1.1×ULN;n=192,18	1			
Uric Acid,Urate;µmol/L:<0.9×LLN;n=192,18	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Clinically Meaningful Trends for Vital Signs

End point title	Number of Participants with Clinically Meaningful Trends for Vital Signs

End point description:

Vital Signs included assessments of heart rate, respiratory rate, systolic and diastolic blood pressure, and body temperature. The investigator determined if the results were clinically significant. Safety Population included all participants in the ITT population who received ≥1 administration of study treatment in Treatment Period. RW Population included all participants who were re-randomised or assigned to a treatment of RW population and received ≥1 administration of study treatment during the RW Period.

End point type	Secondary

End point timeframe:

Up to 46 weeks

End point values	Treatment Period: Placebo	RW Period: Placebo then Relamorelin 10 µg	Treatment Period: Relamorelin 10 µg	RW Period: Relamorelin 10 µg then Relamorelin 10 µg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	235	91	231	59
Units: participants	0	0	0	0

End point values	RW Period: Relamorelin 10 µg then Placebo			
Subject group type	Reporting group			
Number of subjects analysed	43			
Units: participants	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Clinically Significant Abnormal Electrocardiogram (ECG) Results

End point title	Number of Participants with Clinically Significant Abnormal Electrocardiogram (ECG) Results

End point description:

A standard 12-lead ECG was performed. The investigator determined if the abnormal results were clinically significant. Safety Population included all participants in the ITT population who received ≥1 administration of study treatment in Treatment Period. RW Population included all participants who were re-randomised or assigned to a treatment of RW population and received ≥1 administration of study treatment during the RW Period.

End point type	Secondary

End point timeframe:

Up to 46 weeks

End point values	Treatment Period: Placebo	RW Period: Placebo then Relamorelin 10 µg	Treatment Period: Relamorelin 10 µg	RW Period: Relamorelin 10 µg then Relamorelin 10 µg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	235	91	231	59
Units: participants	3	0	2	0

End point values	RW Period: Relamorelin 10 µg then Placebo			
Subject group type	Reporting group			
Number of subjects analysed	43			
Units: participants	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with a ≥1% Increase in Glycosylated Hemoglobin A1c (HBA1c)

End point title	Number of Participants with a ≥1% Increase in Glycosylated Hemoglobin A1c (HBA1c)

End point description:

Safety Population included all participants in the ITT population who received ≥1 administration of study treatment in Treatment Period. RW Population included all participants who were re-randomised or assigned to a treatment of RW population and received ≥1 administration of study treatment during the RW Period. Overall number analysed is the number of participants with non-PCS Baseline values and at least one postbaseline assessment.

End point type	Secondary

End point timeframe:

Up to 46 weeks

End point values	Treatment Period: Placebo	RW Period: Placebo then Relamorelin 10 µg	Treatment Period: Relamorelin 10 µg	RW Period: Relamorelin 10 µg then Relamorelin 10 µg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	224	91	223	59
Units: participants	134	62	138	26

End point values	RW Period: Relamorelin 10 µg then Placebo			
Subject group type	Reporting group			
Number of subjects analysed	43			
Units: participants	28			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Anti-relamorelin Antibody Testing Results

End point title	Number of Participants with Anti-relamorelin Antibody Testing Results[3]

End point description:

A blood sample was collected that was sent to a laboratory for an anti-relamorelin antibody screening test. A positive screening test was confirmed by an immunodepletion assay. Safety Population included all participants who received ≥ 1 administration of double-blind study treatment (N=231 in the Relamorelin 10 µg arm). Anti-relamorelin antibody testing was only done for those participants who received treatment with relamorelin. No data was transferred to the sponsor. The one batch that was analysed, failed and was not repeated.

End point type	Secondary

End point timeframe:

Up to 46 weeks

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Not all Baseline arms are applicable to this endpoint.

End point values	Treatment Period: Relamorelin 10 µg			
Subject group type	Reporting group			
Number of subjects analysed	0[4]			
Units: participants				

Notes:
[4] - No data was transferred to the sponsor. One batch that was analysed, failed and was not repeated.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

First dose of study drug to within 30 days of the last dose of study drug (Up to approximately 50 weeks)

Adverse event reporting additional description:

All-Cause Mortality:all randomised participants. Adverse Events:Safety Population-all participants in ITT who received ≥1 administration of study treatment in Treatment Period; RW Population:all participants who were re-randomised or assigned to a treatment of RW population and received ≥1 administration of study treatment during the RW Period.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.1

Reporting groups

Reporting group title	Treatment Period: Relamorelin 10 µg

Reporting group description:

Relamorelin 10 µg injected subcutaneously twice daily for up to 40 weeks.

Reporting group title	Treatment Period: Placebo

Reporting group description:

Placebo-matching relamorelin injected subcutaneously twice daily for up to 40 weeks.

Reporting group title	RW Period: Relamorelin 10 µg then Relamorelin 10 µg

Reporting group description:

Participants who received relamorelin 10 µg injected subcutaneously twice daily for 40 weeks, followed by relamorelin injected twice daily for up to 6 weeks in the RW Period.

Reporting group title	RW Period: Relamorelin 10 µg then Placebo

Reporting group description:

Participants who received relamorelin 10 µg injected subcutaneously twice daily for 40 weeks, followed by placebo-matching relamorelin injected twice daily for up to 6 weeks in the RW Period.

Reporting group title	RW Period: Placebo then Relamorelin 10 µg

Reporting group description:

Participants who received placebo-matching relamorelin injected subcutaneously twice daily for 40 weeks, followed by relamorelin 10 µg injected twice daily for up to 6 weeks in the RW Period.

Serious adverse events	Treatment Period: Relamorelin 10 µg	Treatment Period: Placebo	RW Period: Relamorelin 10 µg then Relamorelin 10 µg
Total subjects affected by serious adverse events			
subjects affected / exposed	20 / 231 (8.66%)	24 / 235 (10.21%)	2 / 59 (3.39%)
number of deaths (all causes)	2	3	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Bladder transitional cell carcinoma metastatic			

subjects affected / exposed	0 / 231 (0.00%)	1 / 235 (0.43%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 231 (0.00%)	1 / 235 (0.43%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertensive urgency			
subjects affected / exposed	0 / 231 (0.00%)	1 / 235 (0.43%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Orthostatic hypotension			
subjects affected / exposed	0 / 231 (0.00%)	1 / 235 (0.43%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral vascular disorder			
subjects affected / exposed	0 / 231 (0.00%)	1 / 235 (0.43%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Accelerated hypertension			
subjects affected / exposed	0 / 231 (0.00%)	0 / 235 (0.00%)	0 / 59 (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
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	1 / 231 (0.43%)	0 / 235 (0.00%)	0 / 59 (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
Non-cardiac chest pain			
subjects affected / exposed	0 / 231 (0.00%)	1 / 235 (0.43%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	1 / 231 (0.43%)	0 / 235 (0.00%)	0 / 59 (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
Dyspnoea			
subjects affected / exposed	1 / 231 (0.43%)	0 / 235 (0.00%)	0 / 59 (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
Acute respiratory distress syndrome			
subjects affected / exposed	0 / 231 (0.00%)	1 / 235 (0.43%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory distress			
subjects affected / exposed	0 / 231 (0.00%)	0 / 235 (0.00%)	0 / 59 (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			
Suicidal ideation			
subjects affected / exposed	1 / 231 (0.43%)	0 / 235 (0.00%)	0 / 59 (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
Confusional state			
subjects affected / exposed	0 / 231 (0.00%)	1 / 235 (0.43%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychogenic tremor			
subjects affected / exposed	0 / 231 (0.00%)	1 / 235 (0.43%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Blood pressure increased			

subjects affected / exposed	1 / 231 (0.43%)	0 / 235 (0.00%)	0 / 59 (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
Injury, poisoning and procedural complications			
Chemical poisoning			
subjects affected / exposed	0 / 231 (0.00%)	1 / 235 (0.43%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fall			
subjects affected / exposed	0 / 231 (0.00%)	1 / 235 (0.43%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rib fracture			
subjects affected / exposed	0 / 231 (0.00%)	0 / 235 (0.00%)	0 / 59 (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
Cardiac disorders			
Coronary artery disease			
subjects affected / exposed	1 / 231 (0.43%)	3 / 235 (1.28%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Supraventricular extrasystoles			
subjects affected / exposed	1 / 231 (0.43%)	0 / 235 (0.00%)	0 / 59 (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
Cardiac failure congestive			
subjects affected / exposed	0 / 231 (0.00%)	2 / 235 (0.85%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Acute myocardial infarction			
subjects affected / exposed	0 / 231 (0.00%)	1 / 235 (0.43%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Atrial fibrillation			
subjects affected / exposed	0 / 231 (0.00%)	1 / 235 (0.43%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial tachycardia			
subjects affected / exposed	0 / 231 (0.00%)	1 / 235 (0.43%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiomyopathy			
subjects affected / exposed	0 / 231 (0.00%)	1 / 235 (0.43%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	0 / 231 (0.00%)	0 / 235 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Postinfarction angina			
subjects affected / exposed	0 / 231 (0.00%)	0 / 235 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	1 / 231 (0.43%)	1 / 235 (0.43%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			
subjects affected / exposed	1 / 231 (0.43%)	1 / 235 (0.43%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hemiparesis			
subjects affected / exposed	1 / 231 (0.43%)	0 / 235 (0.00%)	0 / 59 (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
Hypoaesthesia			

subjects affected / exposed	1 / 231 (0.43%)	0 / 235 (0.00%)	0 / 59 (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
Syncope			
subjects affected / exposed	0 / 231 (0.00%)	1 / 235 (0.43%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertensive encephalopathy			
subjects affected / exposed	0 / 231 (0.00%)	0 / 235 (0.00%)	0 / 59 (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			
Pancreatitis			
subjects affected / exposed	2 / 231 (0.87%)	0 / 235 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain			
subjects affected / exposed	1 / 231 (0.43%)	1 / 235 (0.43%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hiatus hernia			
subjects affected / exposed	1 / 231 (0.43%)	1 / 235 (0.43%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Duodenitis			
subjects affected / exposed	1 / 231 (0.43%)	0 / 235 (0.00%)	0 / 59 (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
Pancreatitis acute			
subjects affected / exposed	1 / 231 (0.43%)	0 / 235 (0.00%)	0 / 59 (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
Vomiting			

subjects affected / exposed	1 / 231 (0.43%)	0 / 235 (0.00%)	0 / 59 (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
Intestinal ischaemia			
subjects affected / exposed	0 / 231 (0.00%)	1 / 235 (0.43%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Skin and subcutaneous tissue disorders			
Skin ulcer			
subjects affected / exposed	0 / 231 (0.00%)	2 / 235 (0.85%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dermatitis			
subjects affected / exposed	0 / 231 (0.00%)	1 / 235 (0.43%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	3 / 231 (1.30%)	4 / 235 (1.70%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nephrolithiasis			
subjects affected / exposed	1 / 231 (0.43%)	0 / 235 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Musculoskeletal chest pain			
subjects affected / exposed	1 / 231 (0.43%)	1 / 235 (0.43%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoarthritis			
subjects affected / exposed	1 / 231 (0.43%)	0 / 235 (0.00%)	0 / 59 (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

Rotator cuff syndrome			
subjects affected / exposed	1 / 231 (0.43%)	0 / 235 (0.00%)	0 / 59 (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
Pain in extremity			
subjects affected / exposed	0 / 231 (0.00%)	1 / 235 (0.43%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Osteomyelitis			
subjects affected / exposed	1 / 231 (0.43%)	2 / 235 (0.85%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	1 / 231 (0.43%)	1 / 235 (0.43%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			
subjects affected / exposed	1 / 231 (0.43%)	1 / 235 (0.43%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	1 / 231 (0.43%)	1 / 235 (0.43%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abscess limb			
subjects affected / exposed	1 / 231 (0.43%)	0 / 235 (0.00%)	0 / 59 (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
Atypical pneumonia			
subjects affected / exposed	1 / 231 (0.43%)	0 / 235 (0.00%)	0 / 59 (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
COVID-19			

subjects affected / exposed	1 / 231 (0.43%)	0 / 235 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	1 / 231 (0.43%)	0 / 235 (0.00%)	0 / 59 (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
Cellulitis gangrenous			
subjects affected / exposed	1 / 231 (0.43%)	0 / 235 (0.00%)	0 / 59 (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
Diverticulitis			
subjects affected / exposed	1 / 231 (0.43%)	0 / 235 (0.00%)	0 / 59 (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
Localised infection			
subjects affected / exposed	1 / 231 (0.43%)	0 / 235 (0.00%)	0 / 59 (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
Pyelonephritis			
subjects affected / exposed	1 / 231 (0.43%)	0 / 235 (0.00%)	0 / 59 (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
Staphylococcal bacteraemia			
subjects affected / exposed	1 / 231 (0.43%)	0 / 235 (0.00%)	0 / 59 (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
Staphylococcal infection			
subjects affected / exposed	1 / 231 (0.43%)	0 / 235 (0.00%)	0 / 59 (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
Bronchitis			

subjects affected / exposed	0 / 231 (0.00%)	1 / 235 (0.43%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 231 (0.00%)	1 / 235 (0.43%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis viral			
subjects affected / exposed	0 / 231 (0.00%)	1 / 235 (0.43%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infected dermal cyst			
subjects affected / exposed	0 / 231 (0.00%)	1 / 235 (0.43%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis acute			
subjects affected / exposed	0 / 231 (0.00%)	1 / 235 (0.43%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal abscess			
subjects affected / exposed	0 / 231 (0.00%)	1 / 235 (0.43%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 231 (0.00%)	1 / 235 (0.43%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	0 / 231 (0.00%)	1 / 235 (0.43%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urosepsis			

subjects affected / exposed	0 / 231 (0.00%)	1 / 235 (0.43%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Diabetic ketoacidosis			
subjects affected / exposed	3 / 231 (1.30%)	2 / 235 (0.85%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoglycaemia			
subjects affected / exposed	1 / 231 (0.43%)	1 / 235 (0.43%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertriglyceridaemia			
subjects affected / exposed	1 / 231 (0.43%)	0 / 235 (0.00%)	0 / 59 (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
Metabolic acidosis			
subjects affected / exposed	0 / 231 (0.00%)	1 / 235 (0.43%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	RW Period: Relamorelin 10 µg then Placebo	RW Period: Placebo then Relamorelin 10 µg	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 43 (2.33%)	3 / 91 (3.30%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Bladder transitional cell carcinoma metastatic			
subjects affected / exposed	0 / 43 (0.00%)	0 / 91 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Deep vein thrombosis			

subjects affected / exposed	0 / 43 (0.00%)	0 / 91 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertensive urgency			
subjects affected / exposed	0 / 43 (0.00%)	0 / 91 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Orthostatic hypotension			
subjects affected / exposed	0 / 43 (0.00%)	0 / 91 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral vascular disorder			
subjects affected / exposed	0 / 43 (0.00%)	0 / 91 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Accelerated hypertension			
subjects affected / exposed	1 / 43 (2.33%)	0 / 91 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 43 (0.00%)	0 / 91 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-cardiac chest pain			
subjects affected / exposed	0 / 43 (0.00%)	1 / 91 (1.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	0 / 43 (0.00%)	0 / 91 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Dyspnoea			
subjects affected / exposed	0 / 43 (0.00%)	0 / 91 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute respiratory distress syndrome			
subjects affected / exposed	0 / 43 (0.00%)	0 / 91 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory distress			
subjects affected / exposed	0 / 43 (0.00%)	1 / 91 (1.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Suicidal ideation			
subjects affected / exposed	0 / 43 (0.00%)	0 / 91 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Confusional state			
subjects affected / exposed	0 / 43 (0.00%)	0 / 91 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychogenic tremor			
subjects affected / exposed	0 / 43 (0.00%)	0 / 91 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Blood pressure increased			
subjects affected / exposed	0 / 43 (0.00%)	0 / 91 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Chemical poisoning			

subjects affected / exposed	0 / 43 (0.00%)	0 / 91 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fall			
subjects affected / exposed	0 / 43 (0.00%)	0 / 91 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rib fracture			
subjects affected / exposed	1 / 43 (2.33%)	0 / 91 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Coronary artery disease			
subjects affected / exposed	0 / 43 (0.00%)	0 / 91 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Supraventricular extrasystoles			
subjects affected / exposed	0 / 43 (0.00%)	0 / 91 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure congestive			
subjects affected / exposed	0 / 43 (0.00%)	0 / 91 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute myocardial infarction			
subjects affected / exposed	0 / 43 (0.00%)	0 / 91 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	0 / 43 (0.00%)	0 / 91 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial tachycardia			

subjects affected / exposed	0 / 43 (0.00%)	0 / 91 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiomyopathy			
subjects affected / exposed	0 / 43 (0.00%)	0 / 91 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			
subjects affected / exposed	0 / 43 (0.00%)	0 / 91 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postinfarction angina			
subjects affected / exposed	0 / 43 (0.00%)	0 / 91 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	0 / 43 (0.00%)	0 / 91 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischaemic attack			
subjects affected / exposed	0 / 43 (0.00%)	0 / 91 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hemiparesis			
subjects affected / exposed	0 / 43 (0.00%)	0 / 91 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoaesthesia			
subjects affected / exposed	0 / 43 (0.00%)	0 / 91 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			

subjects affected / exposed	1 / 43 (2.33%)	0 / 91 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertensive encephalopathy			
subjects affected / exposed	1 / 43 (2.33%)	0 / 91 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Pancreatitis			
subjects affected / exposed	0 / 43 (0.00%)	0 / 91 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain			
subjects affected / exposed	0 / 43 (0.00%)	0 / 91 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hiatus hernia			
subjects affected / exposed	0 / 43 (0.00%)	0 / 91 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenitis			
subjects affected / exposed	0 / 43 (0.00%)	0 / 91 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis acute			
subjects affected / exposed	0 / 43 (0.00%)	0 / 91 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	0 / 43 (0.00%)	0 / 91 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal ischaemia			

subjects affected / exposed	0 / 43 (0.00%)	0 / 91 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Skin ulcer			
subjects affected / exposed	0 / 43 (0.00%)	0 / 91 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dermatitis			
subjects affected / exposed	0 / 43 (0.00%)	0 / 91 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 43 (2.33%)	0 / 91 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephrolithiasis			
subjects affected / exposed	0 / 43 (0.00%)	0 / 91 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Musculoskeletal chest pain			
subjects affected / exposed	1 / 43 (2.33%)	0 / 91 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoarthritis			
subjects affected / exposed	0 / 43 (0.00%)	0 / 91 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rotator cuff syndrome			
subjects affected / exposed	0 / 43 (0.00%)	0 / 91 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Pain in extremity			
subjects affected / exposed	0 / 43 (0.00%)	0 / 91 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Osteomyelitis			
subjects affected / exposed	0 / 43 (0.00%)	0 / 91 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	0 / 43 (0.00%)	1 / 91 (1.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic shock			
subjects affected / exposed	0 / 43 (0.00%)	0 / 91 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	0 / 43 (0.00%)	0 / 91 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abscess limb			
subjects affected / exposed	0 / 43 (0.00%)	0 / 91 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atypical pneumonia			
subjects affected / exposed	0 / 43 (0.00%)	0 / 91 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19			
subjects affected / exposed	0 / 43 (0.00%)	1 / 91 (1.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			

subjects affected / exposed	0 / 43 (0.00%)	1 / 91 (1.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis gangrenous			
subjects affected / exposed	0 / 43 (0.00%)	0 / 91 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis			
subjects affected / exposed	0 / 43 (0.00%)	0 / 91 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Localised infection			
subjects affected / exposed	0 / 43 (0.00%)	0 / 91 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			
subjects affected / exposed	0 / 43 (0.00%)	0 / 91 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal bacteraemia			
subjects affected / exposed	0 / 43 (0.00%)	0 / 91 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal infection			
subjects affected / exposed	0 / 43 (0.00%)	0 / 91 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	0 / 43 (0.00%)	0 / 91 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			

subjects affected / exposed	0 / 43 (0.00%)	0 / 91 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis viral			
subjects affected / exposed	0 / 43 (0.00%)	0 / 91 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infected dermal cyst			
subjects affected / exposed	0 / 43 (0.00%)	0 / 91 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis acute			
subjects affected / exposed	0 / 43 (0.00%)	0 / 91 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal abscess			
subjects affected / exposed	0 / 43 (0.00%)	0 / 91 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	0 / 43 (0.00%)	0 / 91 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			
subjects affected / exposed	0 / 43 (0.00%)	0 / 91 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urosepsis			
subjects affected / exposed	0 / 43 (0.00%)	0 / 91 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Diabetic ketoacidosis			

subjects affected / exposed	0 / 43 (0.00%)	0 / 91 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoglycaemia			
subjects affected / exposed	0 / 43 (0.00%)	0 / 91 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertriglyceridaemia			
subjects affected / exposed	0 / 43 (0.00%)	0 / 91 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolic acidosis			
subjects affected / exposed	0 / 43 (0.00%)	0 / 91 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Treatment Period: Relamorelin 10 µg	Treatment Period: Placebo	RW Period: Relamorelin 10 µg then Relamorelin 10 µg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	27 / 231 (11.69%)	18 / 235 (7.66%)	0 / 59 (0.00%)
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	16 / 231 (6.93%)	13 / 235 (5.53%)	0 / 59 (0.00%)
occurrences (all)	22	13	0
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	12 / 231 (5.19%)	7 / 235 (2.98%)	0 / 59 (0.00%)
occurrences (all)	21	7	0

Non-serious adverse events	RW Period: Relamorelin 10 µg then Placebo	RW Period: Placebo then Relamorelin 10 µg	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 43 (0.00%)	0 / 91 (0.00%)	

Infections and infestations Urinary tract infection subjects affected / exposed occurrences (all)	 0 / 43 (0.00%) 0	 0 / 91 (0.00%) 0	
Metabolism and nutrition disorders Hyperglycaemia subjects affected / exposed occurrences (all)	 0 / 43 (0.00%) 0	 0 / 91 (0.00%) 0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
29 March 2018	The following changes were implemented with Amendment 1: -Increased the number of study sites from 300 to 400 -Added anti-relamorelin antibodies as a secondary endpoint –Indicated that the Early Termination Visit was performed as soon as possible after the decision has been made -Included inspection of injection sites -Indicated that pregnancy testing was performed if required by local regulations -Indicated that a clinically significant injection site reaction should be reported as an adverse event (AE) -Added exclusion criterion regarding exclusion of participants involved in the conduct of administration of the study, or enrolled at another site -Provided an exception to the opioid prohibition -Indicated that the Early Termination Visit was performed as soon as possible after the decision to discontinue was made -Revised the time Period for AE/serious adverse event (SAE) collection to include "until 30 days after" the final visit -Amended the major adverse cardiovascular events (MACE) text for clarity and to describe the planned adjudication process -Amended physical examinations to add text about injection site inspection and clinically significant injection site reactions -Revised the contraception guidance and added recommendations for acceptable birth control methods.
04 March 2019	The following changes were implemented with Amendment 2: -Modified primary endpoint to specify "change from Baseline (CFB) at Week 12"; defined Vomiting Week 12 Responder for primary endpoint; deleted diabetic gastroparesis symptom severity diary (DGSSS) Week 40 Responder as a secondary endpoint -Increased the number of sites from approximately 400 to approximately 700 -Added electrocardiogram (ECG) assessment at Visit 4 -Modified clinical hypotheses -Added a cross reference to inclusion criterion -Deleted option for investigator to contact sponsor if the participant could not inject study treatment into abdomen -Unblinding procedures modified -Provided more specific guidelines for prohibiting anti-emetics; added 5-Hydroxytryptamine receptor 4 (5HT4) agonists; added tramadol as an opioid example -Removed antihistamines as an example of an anti-emetic drug -Removed "non-compliance with study treatment" -Added requirement for the investigator to contact the sponsor under specific conditions -Added the phrase "Inadequate Control of Diabetes" to section title -Specified 10 micrograms (µg) twice a day (BID) or 20 µg/day as maximum recommended dose and deleted statement referencing a dose of greater than 150 µg BID to be considered an overdose -Added CFB mixed model for repeated measures (MMRM) methodology and description, defined MMRM -Updated DGSSS key endpoint, along with description, timing, and methodology; deleted DGSSS Week 40 Responder as a secondary endpoint -Updated language with regards to the key endpoints -Replaced language about specific analyses and how they were described in statistical analysis plan (SAP).
04 March 2019	-Added a requirement for a Data Safety Monitoring Board (DSMB) to review interim safety data at defined intervals throughout the study -Additional criteria added for informed consent (IC) process for written documentation to be obtained in accordance with relevant country and local privacy requirements -Replaced requirement for records and documents to be retained for 15 years after study completion to requirement for them to be retained as per the clinical trial agreement -Added bullet about relevant country requirements -Revised procedures for reporting AE of special interest (AESIs); specified that specific diabetic gastroparesis (DG) manifestations were captured in the DGSSS -Identified specific AESIs -Added more options to highly effective methods that are user independent; added example of bilateral tubal occlusion; moved list of "Acceptable Methods" to table from text; specified that 2 acceptable methods of contraception should be used during treatment; female participants who become pregnant: deleted text that an elective termination is an AE or SAE; provided examples and details for abnormal pregnancy outcomes, including genetic abnormalities; deleted hormonal contraception's susceptible interaction with study intervention -Corrected trial length from 52 to 46 weeks.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
30 October 2020	The study was prematurely terminated on 30 October 2020 as the sponsor decided not to develop the investigational product further. The study termination was not due to any safety concerns. As a result, only descriptive primary and secondary efficacy analyses and selected key safety analyses were conducted.	-

Notes:

Limitations and caveats

None reported