



Clinical trial results:

A Multicenter, Open-label, Metabolic Balance Study to Evaluate the Effects of Apraglutide on Intestinal Absorption in Adult Subjects with Short Bowel Syndrome, Intestinal Failure (SBS-IF), and Colon-incontinuity (CIC)

Summary

EudraCT number	2020-005129-99
Trial protocol	FR BE DK
Global end of trial date	06 June 2023

Results information

Result version number	v1 (current)
This version publication date	15 August 2024
First version publication date	15 August 2024

Trial information

Trial identification

Sponsor protocol code	TA799-013
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04964986
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	VectivBio AG
Sponsor organisation address	Aeschenvorstadt 36, Basel, Switzerland, 4051
Public contact	Clinical Trial Information Desk, VectivBio AG, clinicaltrial.enquiries@vectivbio.com
Scientific contact	Clinical Trial Information Desk, VectivBio AG, clinicaltrial.enquiries@vectivbio.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	06 June 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	06 June 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objectives of this trial were to evaluate the safety and tolerability of apraglutide and the efficacy of apraglutide in increasing intestinal energy absorption assessed by bomb calorimetry in relation to metabolic balance assessments.

Protection of trial subjects:

This trial was performed in compliance with:

- Declaration of Helsinki (revised version of Fortaleza, Brazil, 2013).
- The ICH-GCP guidelines (ICH E6 (R2), November 2016).
- European Union Clinical Trials Regulation No. 536/2014.
- Any amendments to these regulations.
- Local laws and regulations.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	14 June 2021
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Belgium: 8
Country: Number of subjects enrolled	France: 2
Worldwide total number of subjects	10
EEA total number of subjects	10

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	8

From 65 to 84 years	2
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 10 participants with SBS-IF and CIC were enrolled as planned, eight participants at the Belgium site and two participants at the France site. A total of nine participants were treated and analyzed.

Pre-assignment

Screening details: -

Pre-assignment period milestones

Number of subjects started	10
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Number of subjects completed	9
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Pre-assignment subject non-completion reasons

Reason: Number of subjects	Enrolled but not treated: 1
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Period 1

Period 1 title	Overall Study (overall period)
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Is this the baseline period?	Yes
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Allocation method	Not applicable
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Blinding used	Not blinded
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Arms

Arm title	Apraglutide
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Arm description:

All participants received, based on their body weight, either 2.5 mg (<50 kg) or 5 mg (≥50 kg) apraglutide once weekly, for 52 weeks. The investigational medicinal product (IMP) was administered subcutaneously (SC).

Arm type	Experimental
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Investigational medicinal product name	Apraglutide
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Investigational medicinal product code	TA799
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Other name	
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Pharmaceutical forms	Powder for solution for injection
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Routes of administration	Subcutaneous use
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Dosage and administration details:

The IMP was administered SC.

Number of subjects in period 1 ^[1]	Apraglutide
Started	9
Completed	9

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: One participant was enrolled but not treated.

Baseline characteristics

Reporting groups

Reporting group title	Apraglutide
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Reporting group description:

All participants received, based on their body weight, either 2.5 mg (<50 kg) or 5 mg (≥50 kg) apraglutide once weekly, for 52 weeks. The investigational medicinal product (IMP) was administered subcutaneously (SC).

Reporting group values	Apraglutide	Total	
Number of subjects	9	9	
Age categorical Units: Subjects			
Adults (18-64 years)	8	8	
From 65-84 years	1	1	
Age continuous Units: years arithmetic mean standard deviation	46.8 ± 17.46	-	
Gender categorical Units: Subjects			
Female	7	7	
Male	2	2	
Ethnicity Units: Subjects			
Hispanic or Latino	1	1	
Not Hispanic or Latino	8	8	
Race Units: Subjects			
White	9	9	

End points

End points reporting groups

Reporting group title	Apraglutide
Reporting group description: All participants received, based on their body weight, either 2.5 mg (<50 kg) or 5 mg (≥50 kg) apraglutide once weekly, for 52 weeks. The investigational medicinal product (IMP) was administered subcutaneously (SC).	

Primary: Number of Participants who Experienced a Treatment-Emergent Adverse Event (TEAE)

End point title	Number of Participants who Experienced a Treatment-Emergent Adverse Event (TEAE) ^[1]
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End point description:

Applicable to Protocol V4.0 implemented in Belgium (classed as secondary endpoint in Protocol V3.0 [implemented in France]).

A TEAE was any unfavorable and unintended sign, symptom, or disease temporally associated with apraglutide, whether or not related, that occurred or worsened after the dose of apraglutide. A serious TEAE was defined as any TEAE that resulted in death, was life-threatening, required inpatient hospitalization or prolongation of existing hospitalization, resulted in persistent or significant disability/incapacity, was a congenital anomaly/birth defect or was an important medical event. Clinically significant changes from baseline in clinical chemistry, hematology, hemostasis, anti-drug antibodies (ADAs), and urine analysis were reported as adverse events.

Adverse events of special interest (AESI):

- Injection site reaction
- Gastrointestinal obstruction
- Gallbladder, biliary, and pancreatic disease
- Fluid overload
- Colorectal polyps
- Malignancies

End point type	Primary
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End point timeframe:

Day 1 up to approximately 55 weeks

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 additional statistical analysis was pre-specified for this endpoint.

End point values	Apraglutide			
Subject group type	Reporting group			
Number of subjects analysed	9 ^[2]			
Units: participants				
At least one TEAE	9			
At least one treatment-related TEAE	5			
At least one TESAE	3			
At least one treatment-related TESAE	1			
At least one treatment-emergent AESI	3			
At least one TEAE leading to dose interruption	1			
At least one TEAE leading to dose discontinuation	0			

Notes:

[2] - The safety analysis set included all participants exposed to trial medication.

Statistical analyses

No statistical analyses for this end point

Primary: Absolute Change in Absorption of Energy Over Metabolic Balance (MB) Periods From Baseline at Week 48

End point title	Absolute Change in Absorption of Energy Over Metabolic Balance (MB) Periods From Baseline at Week 48 ^[3]
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End point description:

Applicable to Protocol V3.0 implemented in France (classed as secondary endpoint in Protocol V4.0 [implemented in Belgium]).

The absorption was defined as dietary intake minus output from fecal excretion over a 72-hour MB period at a given analysis time point. Since dietary intake and fecal excretion were measured daily, i.e., up to three measurements may contribute to absorption calculations, the average over all available daily absorption measurements over the 72-hour period were used for analysis.

The full analysis set included all participants who received at least one dose of trial treatment and contributed at least one valid post-baseline efficacy point.

The increase from baseline at Week 48 was statistically significant (p-value=0.041). The p-value was computed based on the paired t-test.

End point type	Primary
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End point timeframe:

Baseline and Week 48

Notes:

[3] - 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: Additional statistical analysis presented as free-text due to inability to add this for single arm trials within EudraCT.

End point values	Apraglutide			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: kJ/day				
arithmetic mean (standard deviation)				
Week 48	1133.963 (± 1399.8793)			

Statistical analyses

No statistical analyses for this end point

Secondary: Relative Change From Baseline in Actual Weekly Parenteral Support (PS) Volume at Weeks 4, 24, and 52

End point title	Relative Change From Baseline in Actual Weekly Parenteral Support (PS) Volume at Weeks 4, 24, and 52
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End point description:

The sum of daily PS volume (including extra fluids) from weekly PS diary data recorded for the corresponding analysis timepoint was used for analysis.

The full analysis set included all participants who received at least one dose of trial treatment and contributed at least one valid post-baseline efficacy point.

End point type	Secondary
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End point timeframe:

Baseline, Week 4, Week 24, and Week 52

End point values	Apraglutide			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: percentage change in PS volume				
arithmetic mean (standard deviation)				
Week 4	-0.73 (± 2.709)			
Week 24	-39.99 (± 22.588)			
Week 52	-52.44 (± 29.192)			

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute Change From Baseline in Actual Weekly PS Volume at Weeks 24 and 52

End point title	Absolute Change From Baseline in Actual Weekly PS Volume at Weeks 24 and 52
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End point description:

The sum of daily PS volume (including extra fluids) from weekly PS diary data recorded for the corresponding analysis timepoint was used for analysis.

The full analysis set included all participants who received at least one dose of trial treatment and contributed at least one valid post-baseline efficacy point.

At Week 24 and Week 52, significant decreases (p-values=<0.001 for both) in mean PS volume were reported. The p-values were computed based on the paired t-test.

End point type	Secondary
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End point timeframe:

Baseline, Week 24 and Week 52

End point values	Apraglutide			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: mL				
arithmetic mean (standard deviation)				
Week 24	-3510.000 (± 1893.7859)			
Week 52	-4701.778 (± 2389.9652)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants Who Achieved a Reduction of at Least 1 Day Per Week of PS From Baseline at Weeks 24 and 52

End point title	Number of Participants Who Achieved a Reduction of at Least 1 Day Per Week of PS From Baseline at Weeks 24 and 52
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End point description:

Participants were considered to have a reduction of at least one day per week of PS from Baseline (incl. extra fluids) if the number of days with PS from weekly PS diary data recorded for the corresponding analysis timepoint was smaller compared to the number of days with PS from weekly PS diary data for Baseline.

The full analysis set included all participants who received at least one dose of trial treatment and contributed at least one valid post-baseline efficacy point.

End point type	Secondary
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End point timeframe:

Baseline, Week 24 and Week 52

End point values	Apraglutide			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: participants				
Week 24	5			
Week 52	7			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants Considered Clinical Responders at Weeks 24 and 52

End point title	Number of Participants Considered Clinical Responders at Weeks 24 and 52
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End point description:

Clinical response was defined as a 20% reduction of PS volume from Baseline. The sum of daily PS volume (including extra fluids) from weekly PS diary data recorded for the corresponding analysis timepoint was used for analysis.

The full analysis set included all participants who received at least one dose of trial treatment and contributed at least one valid post-baseline efficacy point.

End point type	Secondary
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End point timeframe:

Baseline, Week 24 and 52

End point values	Apraglutide			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: participants				
Week 24	7			
Week 52	9			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants Who Achieved Enteral Autonomy at Weeks 24 and 52

End point title	Number of Participants Who Achieved Enteral Autonomy at Weeks 24 and 52
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End point description:

Enteral autonomy was defined as a participant not receiving PS for hydration or parenteral nutrition (PN) for calories. Participants may have still received minimal fluid to maintain patency of the central line or for specific elemental/micro-nutrient needs (e.g., <100 mL fluid for administration of magnesium).

The full analysis set included all participants who received at least one dose of trial treatment and contributed at least one valid post-baseline efficacy point.

End point type	Secondary
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End point timeframe:

Week 24 and Week 52

End point values	Apraglutide			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: participants				
Week 24	0			
Week 52	2			

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute Change in Total Energy in PN From Baseline at Weeks 24 and 52

End point title	Absolute Change in Total Energy in PN From Baseline at Weeks 24 and 52
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End point description:

PN was defined as PS that includes protein, carbohydrate, fat, vitamins, and/or trace elements.

The full analysis set included all participants who received at least one dose of trial treatment and contributed at least one valid post-baseline efficacy point.

At Week 24 and Week 52, there was a significant decrease (p-value=0.002 and p-value=<0.001, respectively) in mean total energy from baseline. The p-values were computed based on the paired t-test.

End point type	Secondary
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End point timeframe:

Baseline, Week 24 and Week 52

End point values	Apraglutide			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: kcal				
arithmetic mean (standard deviation)				
Week 24	-2763.889 ($\pm$ 1830.8065)			
Week 52	-3510.111 ($\pm$ 1927.2066)			

Statistical analyses

No statistical analyses for this end point

Secondary: Relative Change in Absorption of Energy Over MB Periods From Baseline at Week 48

End point title	Relative Change in Absorption of Energy Over MB Periods From Baseline at Week 48
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End point description:

The absorption was defined as dietary intake minus output from fecal excretion over a 72-hour MB period at a given analysis time point. Since dietary intake and fecal excretion were measured daily, i.e., up to three measurements may contribute to absorption calculations, the average over all available daily absorption measurements over the 72-hour period were used for analysis.

The full analysis set included all participants who received at least one dose of trial treatment and contributed at least one valid post-baseline efficacy point.

End point type	Secondary
End point timeframe:	
Baseline and Week 48	

End point values	Apraglutide			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: percentage energy absorption				
arithmetic mean (standard deviation)				
Week 48	29.23 (± 36.898)			

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute Change in Absorption of Macronutrients Over MB Periods From Baseline at Weeks 4 and 48

End point title	Absolute Change in Absorption of Macronutrients Over MB Periods From Baseline at Weeks 4 and 48
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End point description:

The absorption was defined as dietary intake minus output from fecal excretion over a 72-hour MB period at a given analysis time point. Since dietary intake and fecal excretion were measured daily, i.e., up to three measurements may contribute to absorption calculations, the average over all available daily absorption measurements over the 72-hour period were used for analysis.

The full analysis set included all participants who received at least one dose of trial treatment and contributed at least one valid post-baseline efficacy point.

Fat absorption increase at Weeks 4 and 48 was not statistically significant (p-value=0.294 and 0.155, respectively). Carbohydrate absorption at Week 4 was not statistically significant (p-value=0.260); however, the increase at Week 48 was statistically significant (p-value=0.024). Protein absorption increase at Weeks 4 and 48 was not statistically significant (p-value=0.096 and 0.075, respectively). P-values were computed based on paired t-test.

End point type	Secondary
End point timeframe:	
Baseline, Week 4 and Week 48	

End point values	Apraglutide			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: kJ/day				
arithmetic mean (standard deviation)				
Fat - Week 4	247.281 (± 661.1866)			

Fat - Week 48	406.741 ($\pm$ 776.4802)			
Carbohydrate - Week 4	272.881 ($\pm$ 675.1125)			
Carbohydrate - Week 48	877.011 ($\pm$ 945.2279)			
Protein - Week 4	176.178 ($\pm$ 280.0788)			
Protein - Week 48	194.400 ($\pm$ 285.2597)			

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute Change in Urine Volume over MB Periods From Baseline at Week 4 and Week 48

End point title	Absolute Change in Urine Volume over MB Periods From Baseline at Week 4 and Week 48
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End point description:

Based on average daily urine volume data derived as per balance period calculations.

The full analysis set included all participants who received at least one dose of trial treatment and contributed at least one valid post-baseline efficacy point.

At Week 4, there was a non-significant increase from baseline (p-value=0.063). At Week 48, there was a non-significant decrease from baseline (p-value=0.112). The p-values were computed based on the paired t-test.

End point type	Secondary
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End point timeframe:

Baseline, Week 4 and Week 48

End point values	Apraglutide			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: mL/day				
arithmetic mean (standard deviation)				
Week 4	246.889 ($\pm$ 343.3609)			
Week 48	-178.556 ($\pm$ 299.5613)			

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute Change in Absorption of Energy Over MB Periods From Baseline at Week 4

End point title	Absolute Change in Absorption of Energy Over MB Periods From Baseline at Week 4
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End point description:

The absorption was defined as dietary intake minus output from fecal excretion over a 72-hour MB period at a given analysis time point. Since dietary intake and fecal excretion were measured daily, i.e., up to three measurements may contribute to absorption calculations, the average over all available daily absorption measurements over the 72-hour period were used for analysis.

The full analysis set included all participants who received at least one dose of trial treatment and contributed at least one valid post-baseline efficacy point.

The increase from baseline at Week 4 was not statistically significant (p-value= 0.306). The p-value was computed based on the paired t-test.

End point type	Secondary
End point timeframe:	
Baseline and Week 4	

End point values	Apraglutide			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: kJ/day				
arithmetic mean (standard deviation)	494.259 ($\pm$ 1355.5857)			

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute Change in Urinary Electrolytes over MB Periods From Baseline at Week 4 and Week 48

End point title	Absolute Change in Urinary Electrolytes over MB Periods From Baseline at Week 4 and Week 48
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End point description:

Since urinary electrolytes data were measured over the 72-hour MB period, the average of all available results was used for analyses for each MB parameter at a given analysis time point.

The full analysis set included all participants who received at least one dose of trial treatment and contributed at least one valid post-baseline efficacy point.

No significant changes from baseline were reported at Week 4 or Week 48 for calcium, magnesium, potassium, or creatinine. A significant change from baseline was reported for sodium at Week 4 (p-value=0.004) but not Week 48. A significant change from baseline in urea was reported at Week 48 (p-value=0.009) but not Week 4.

End point type	Secondary
End point timeframe:	
Baseline, Week 4 and Week 48	

End point values	Apraglutide			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: cmol/L				
arithmetic mean (standard deviation)				
Calcium - Week 4	0.1444 (± 1.09818)			
Calcium - Week 48	-0.5532 (± 2.28264)			
Magnesium - Week 4	-0.258 (± 0.8370)			
Magnesium - Week 48	-2.306 (± 3.1400)			
Sodium - Week 4	31.668 (± 24.1946)			
Sodium - Week 48	17.097 (± 50.1676)			
Potassium - Week 4	2.047 (± 16.8154)			
Potassium - Week 48	-8.012 (± 13.5798)			
Urea - Week 4	7.693 (± 59.2590)			
Urea - Week 48	-89.649 (± 77.9786)			
Creatinine - Week 4	0.198 (± 1.0071)			
Creatinine - Week 48	-0.011 (± 1.3283)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Pittsburgh Sleep Quality Inventory (PSQI) Total Score at Week 24 and Week 52

End point title	Change from Baseline in Pittsburgh Sleep Quality Inventory (PSQI) Total Score at Week 24 and Week 52
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End point description:

The PSQI is a patient-reported questionnaire used to measure the quality and patterns of sleep, over the past month. The PSQI has seven components: subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleep medication, and daytime dysfunction over the last month. Minimum Score = 0 (better); Maximum Score = 21 (worse). A negative change from baseline represents a reduction in symptoms.

The full analysis set included all participants who received at least one dose of trial treatment and contributed at least one valid post-baseline efficacy point.

The decrease in mean PSQI total score at Week 24 was not statistically significant (p-value=0.066); however, the decrease at Week 52 was statistically significant (p-value=0.015). The p-values were computed based on the paired t-test.

End point type	Secondary
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End point timeframe:

Baseline, Week 24 and Week 52

End point values	Apraglutide			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: score on a scale				
arithmetic mean (standard deviation)				
Week 24	-1.89 (± 2.667)			
Week 52	-1.56 (± 1.509)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Patient Global Impression of Change (PGIC) at Week 24 and Week 52

End point title	Change from Baseline in Patient Global Impression of Change (PGIC) at Week 24 and Week 52
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End point description:

PGIC v2.0 is a single-item questionnaire using a 5-point verbal rating scale, to assess overall change in the participants status after taking the IMP. Response options range from 2= very much better to -2= very much worse.

The full analysis set included all participants who received at least one dose of trial treatment and contributed at least one valid post-baseline efficacy point.

End point type	Secondary
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End point timeframe:

Baseline, Week 24 and Week 52

End point values	Apraglutide			
Subject group type	Reporting group			
Number of subjects analysed	9 ^[4]			
Units: participants				
Week 24: 2 Much Better	6			
Week 24: 1 A Little Better	2			
Week 52: 2 Much Better	8			
Week 52: 1 A Little Better	1			

Notes:

[4] - Week 24 n = 8.

Statistical analyses

No statistical analyses for this end point

Secondary: Patient Global Impression of Treatment Satisfaction (PGI-TS) at Week 24 and Week 52

End point title	Patient Global Impression of Treatment Satisfaction (PGI-TS) at Week 24 and Week 52
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End point description:

This form is a single-item questionnaire assessing the participant's satisfaction with the trial medication over the preceding 7 days. Response options range from -2 to 2, very dissatisfied to very satisfied.

The full analysis set included all participants who received at least one dose of trial treatment and contributed at least one valid post-baseline efficacy point.

End point type	Secondary
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End point timeframe:

Week 24 and Week 52

End point values	Apraglutide			
Subject group type	Reporting group			
Number of subjects analysed	9 ^[5]			
Units: participants				
Week 24: 2 Very Satisfied	5			
Week 24: 1 Satisfied	3			
Week 52: 2 Very Satisfied	3			
Week 52: 1 Satisfied	6			

Notes:

[5] - Week 24 n = 8.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Patient Global Impression of Satisfaction with Parenteral Support (PGI-SPS) at Week 24 and Week 52

End point title	Change from Baseline in Patient Global Impression of Satisfaction with Parenteral Support (PGI-SPS) at Week 24 and Week 52
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End point description:

This is a single-item questionnaire assessing the participant's satisfaction with PS over the preceding 7 days. Response options range from -2 to 2, very dissatisfied to very satisfied. A reduction from baseline represents a decrease in satisfaction.

The full analysis set included all participants who received at least one dose of trial treatment and contributed at least one valid post-baseline efficacy point.

End point type	Secondary
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End point timeframe:

Week 24 and Week 52

End point values	Apraglutide			
Subject group type	Reporting group			
Number of subjects analysed	5			
Units: score on a scale				
arithmetic mean (standard deviation)				
Week 24 (n = 5)	-0.20 (± 0.447)			
Week 52 (n = 4)	0.00 (± 0.000)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Patient Global Impression of Parenteral Support Impact (PGI-PSI) at Week 24 and Week 52

End point title	Change from Baseline in Patient Global Impression of Parenteral Support Impact (PGI-PSI) at Week 24 and Week 52
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End point description:

This is a three-item questionnaire assessing the impact of PS on the participant's sleep, daily activities, and quality of life (QoL) over the past 7 days. All questions have response options ranging from 0 to 4, not at all to extremely. A reduction from baseline represents a decrease in symptoms.

The full analysis set included all participants who received at least one dose of trial treatment and contributed at least one valid post-baseline efficacy point.

End point type	Secondary
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End point timeframe:

Baseline, Week 24 and Week 52

End point values	Apraglutide			
Subject group type	Reporting group			
Number of subjects analysed	5 ^[6]			
Units: score on a scale				
arithmetic mean (standard deviation)				
Sleep Impact: Week 24	-0.40 (± 1.517)			
Sleep Impact: Week 52	-0.50 (± 1.291)			
Daily Activities Impact: Week 24	-0.80 (± 1.643)			
Daily Activities Impact: Week 52	-1.00 (± 1.414)			
QoL Impact: Week 24	-1.40 (± 1.140)			
QoL Impact: Week 52	-1.25 (± 0.957)			

Notes:

[6] - Week 52 n = 4.

Statistical analyses

No statistical analyses for this end point

Secondary: Trough Apraglutide Plasma Concentration (Ctrough)

End point title Trough Apraglutide Plasma Concentration (Ctrough)

End point description:

The safety analysis set included all participants exposed to trial medication.

End point type Secondary

End point timeframe:

Pre-dose on Weeks 2, 4, 12, 24, 32, 40, 48, and 52

End point values	Apraglutide			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: ng/mL				
arithmetic mean (standard deviation)				
Week 2 (n = 4)	1.928 (± 0.7058)			
Week 4 (n = 3)	1.217 (± 0.2902)			
Week 12 (n = 5)	1.934 (± 0.6665)			
Week 24 (n = 4)	2.863 (± 1.0668)			
Week 32 (n = 7)	1.739 (± 0.6805)			
Week 40 (n = 5)	2.386 (± 0.9587)			
Week 48 (n = 3)	3.810 (± 1.1031)			
Week 52 (n = 9)	2.678 (± 1.4039)			

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Plasma Citrulline Level

End point title Mean Plasma Citrulline Level

End point description:

The safety analysis set included all participants exposed to trial medication.

End point type Secondary

End point timeframe:

Baseline and Weeks 2, 4, 12, 24, 32, 40, 48, and 52

End point values	Apraglutide			
Subject group type	Reporting group			
Number of subjects analysed	9 ^[7]			
Units: µmol/L				
arithmetic mean (standard deviation)				
Baseline	11.571 (± 9.7091)			
Week 2	13.516 (± 9.8136)			
Week 4	15.531 (± 12.4055)			
Week 12	14.860 (± 12.2165)			
Week 24	14.810 (± 11.8877)			
Week 32	14.994 (± 12.6880)			
Week 40	17.860 (± 15.8020)			
Week 48	16.638 (± 14.9346)			
Week 52	14.714 (± 11.7896)			

Notes:

[7] - Week 4 n = 8.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Day 1 up to approximately 55 weeks

Adverse event reporting additional description:

The safety analysis set included all participants exposed to trial medication.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	24.0
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Reporting groups

Reporting group title	Apraglutide
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Reporting group description:

All participants received, based on their body weight, either 2.5 mg (<50 kg) or 5 mg (≥50 kg) apraglutide once weekly, for 52 weeks. The IMP was administered SC.

Serious adverse events	Apraglutide		
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 9 (33.33%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pancreatitis acute			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Cholangitis			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Campylobacter gastroenteritis			

subjects affected / exposed	1 / 9 (11.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Septic shock			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Product issues			
Device dislocation			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Apraglutide		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	9 / 9 (100.00%)		
Vascular disorders			
Haematoma			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Complication associated with device			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Catheter site irritation			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Injection site erythema			
subjects affected / exposed	2 / 9 (22.22%)		
occurrences (all)	7		

Injection site pruritus subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 6		
Fatigue subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1		
Injection site haematoma subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1		
Injection site pain subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1		
Respiratory, thoracic and mediastinal disorders Dysphonia subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1		
Investigations Weight decreased subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1		
Injury, poisoning and procedural complications Procedural vomiting subjects affected / exposed occurrences (all)	2 / 9 (22.22%) 3		
Procedural pain subjects affected / exposed occurrences (all)	2 / 9 (22.22%) 2		
Bone contusion subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1		
Post procedural complication subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1		
Post procedural haematoma subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1		

Procedural nausea subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1		
Radius fracture subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1		
Vascular access site pain subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1		
Nervous system disorders Headache subjects affected / exposed occurrences (all)	2 / 9 (22.22%) 2		
Dizziness subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1		
Metabolic encephalopathy subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1		
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1		
Gastrointestinal disorders Stomatitis subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1		
Vomiting subjects affected / exposed occurrences (all)	5 / 9 (55.56%) 42		
Diarrhoea subjects affected / exposed occurrences (all)	3 / 9 (33.33%) 3		
Abdominal pain subjects affected / exposed occurrences (all)	2 / 9 (22.22%) 3		
Anal fissure			

subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Anorectal discomfort			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Regurgitation			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Hepatobiliary disorders			
Portal vein thrombosis			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Nephrolithiasis			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 9 (22.22%)		
occurrences (all)	2		
Musculoskeletal chest pain			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Musculoskeletal stiffness			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Tenosynovitis stenosaurs			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Infections and infestations			
Influenza			
subjects affected / exposed	2 / 9 (22.22%)		
occurrences (all)	2		

Oral herpes			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Sinusitis			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
COVID-19			
subjects affected / exposed	2 / 9 (22.22%)		
occurrences (all)	2		
Vascular device infection			
subjects affected / exposed	2 / 9 (22.22%)		
occurrences (all)	3		
Nasopharyngitis			
subjects affected / exposed	5 / 9 (55.56%)		
occurrences (all)	5		
Viral upper respiratory tract infection			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Asymptomatic COVID-19			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	2		
Iron deficiency			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	2		
Hypocalcaemia			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Hypomagnesaemia			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Magnesium deficiency			

subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
24 February 2020	• Corrected inconsistencies and typos • Corrected the wording of the primary endpoint • Updates to inclusion and exclusion criteria • Updated planned trial dates • Added glutamine to the list of prior medications to be specifically recorded • Added fecal sample testing for H. pylori at baseline and added vital signs assessment at Visit 3 (Day 0); reduced the time window for the final visit of the treatment period (Visit 17, Week 52) to ± 2 days • Specified that body temperature is to be taken in the axilla for all vital signs assessments • Additional clinical chemistry parameters to be tested • Included microbiota questionnaires and measurement of hip and waist circumference • Updated the number of biopsies required for the experimental trials and clarified the distinction between standard and single-cell ribonucleic acid sequencing • Specified the parameters to be analyzed for microbiota, and the duration of sample storage and results archiving • Added details of the considerations on IMP dose reduction and temporary discontinuation of IMP • Specified that in the case that a vulnerable participant enters the trial, the Principal Investigator is encouraged to consult their local independent ethics committee/institutional review board for guidance
03 September 2021	• Corrected inconsistencies and typos • Minor wording changes and clarifications • Sponsor representative changed • Abbreviations list updated • Synopsis: clarified definition of short bowel syndrome and deleted PS definition • Secondary endpoints and Section 5.1.9 PROs updated • Updated inclusion and exclusion criteria • Updates to Tables 1 and 2 • Section 2.2: wording added to include definitions of PS, fluids, and other parameters during the trial • Section 2.2.1: inclusion of wording regarding history of vomiting • Section 4.5: Added further details on the PS reduction procedure • Section 4.7 and exclusion criteria: use of somatostatin analogs removed • Section 4.7.1 & 4.7.2: Definition of use of antibiotics updated. Added routine vaccinations allowed • Section 5.1.11: ADA follow up procedures post EOT clarified • Section 5.2.9: Total HCO₃⁻ added to blood lab tests at safety evaluation post PS reduction • Section 6.6.2: Updated the stopping rules • Section 8: Added section regarding DMC • Section 10.2.1: Updated that biomarker samples will be stored for 15 years • Section 16.5: Electrolytes all now analyzed by Atomic absorptiometry

07 February 2022	• General changes to improve clarity and minor formatting issues • International Coordinating Investigator changed • Primary objective changed to evaluate the safety and tolerability of apraglutide • Evaluation of calories added to secondary objectives • Primary endpoints updated to reflect the change in primary objective by including AEs, AESIs, clinical laboratory assessment and ADA • Addition of the Week 4 assessment in relative change from baseline in actual weekly PS volume • Changes to secondary endpoints • Section 1.5.2.4: Definition of enteral autonomy added • Inclusion criterion 2 clarified • Table 1: Addition of definition of MB period • Table 2: Addition of Bristol Stool Form Scale on Days 2 and 3 • Section 2.1: Additional background added • Section 2.2: Confirmation that infusion of a small amount of fluid to maintain catheter patency is not considered PS • Section 2.2.1: Added that investigator can use clinical judgment to demonstrate that the small intestine is <200 cm • Section 2.2.2: Additional instructions relating to drinking menu and enteral nutrition • Section 4.5: Clarifications on PS volume reduction criteria and process and clarification on method of calculation baseline urine average
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Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported