Clinical trial results:
A Randomized, Open-label, 24-Week Safety, Efficacy, and Pharmacokinetic Study of Teduglutide in Infants 4 to 12 Months of Age with Short Bowel Syndrome Who are Dependent on Parenteral Support

Summary

EudraCT number	2017-003606-40
Trial protocol	GB FI IT FR
Global end of trial date	24 September 2020

Results information

Result version number	v1 (current)
This version publication date	28 March 2021
First version publication date	28 March 2021

Trial information

Trial identification

Sponsor protocol code	SHP633-301

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03571516
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Shire
Sponsor organisation address	300 ShireWay, Lexington, United States, MA 02421
Public contact	Study Director, Shire, +1 866 842 5335, ClinicalTransparency@shire.com
Scientific contact	Study Director, Shire, +1 866 842 5335, ClinicalTransparency@shire.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-000482-PIP01-08
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	24 September 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	24 September 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study was to evaluate the safety, efficacy/pharmacodynamics(PD) and pharmacokinetics (PK) of teduglutide treatment in infants with short bowel syndrome (SBS) dependent on parenteral support.

Protection of trial subjects:

The study was conducted in accordance with the ethical principles that have their origins in the Declaration of Helsinki and in compliance with all applicable industry regulations, International Conference on Harmonisation (ICH) Good Clinical Practice (GCP) Guideline E6 (1996), European Union (EU) Directive 2001/20/EC, as well as all applicable national and local laws and regulations.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	31 August 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	Finland: 2
Country: Number of subjects enrolled	United Kingdom: 8
Worldwide total number of subjects	10
EEA total number of subjects	2

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)	10
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	0
From 65 to 84 years	0

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at Finland and United Kingdom between 31 August 2018 (first subject first visit) and 24 September 2020 (last subject last visit).

Pre-assignment

Screening details:

A total of 10 subjects were enrolled into the study, of which 8 subjects completed the study.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Teduglutide (TED)

Arm description:

Subjects (infants) 4 to 12 months of corrected gestational aged received 0.05 milligram per kilogram (mg/kg) of teduglutide subcutaneous (SC) injection once daily (QD) in addition to standard medical therapy for 24 weeks.

Arm type	Experimental
Investigational medicinal product name	Revestive
Investigational medicinal product code	A16AX08
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects (infants) received 0.05 mg/kg of teduglutide SC injection into abdomen or into either the thigh or arm.

Arm title	Standard of Care (SOC)

Arm description:

Subjects (infants) 4 to 12 months of corrected gestational aged received standard medical therapy for 24 weeks.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Number of subjects in period 1	Teduglutide (TED)	Standard of Care (SOC)
Started	5	5
Completed	4	4
Not completed	1	1
Consent withdrawn by subject	-	1
Severe diarrhea	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Teduglutide (TED)
Reporting group description:	
Subjects (infants) 4 to 12 months of corrected gestational aged received 0.05 milligram per kilogram (mg/kg) of teduglutide subcutaneous (SC) injection once daily (QD) in addition to standard medical therapy for 24 weeks.	
Reporting group title	Standard of Care (SOC)
Reporting group description:	
Subjects (infants) 4 to 12 months of corrected gestational aged received standard medical therapy for 24 weeks.	

Reporting group values	Teduglutide (TED)	Standard of Care (SOC)	Total
Number of subjects	5	5	10
Age Categorical Units: Subjects			
Age Continuous Units: months			
arithmetic mean	8.5	8.3	
standard deviation	± 3.09	± 2.65	-
Gender Categorical Units: Subjects			
Female	1	2	3
Male	4	3	7
Ethnicity Units: Subjects			
Hispanic or Latino	0	0	0
Not Hispanic or Latino	5	5	10
Race Units: Subjects			
White	4	4	8
Asian	1	1	2

End points

End points reporting groups

Reporting group title	Teduglutide (TED)
Reporting group description:	
Subjects (infants) 4 to 12 months of corrected gestational aged received 0.05 milligram per kilogram (mg/kg) of teduglutide subcutaneous (SC) injection once daily (QD) in addition to standard medical therapy for 24 weeks.	
Reporting group title	Standard of Care (SOC)
Reporting group description:	
Subjects (infants) 4 to 12 months of corrected gestational aged received standard medical therapy for 24 weeks.	

Primary: Number of Subjects Who Achieved At least 20 Percent (%) Reduction From Baseline in Weight-normalized Parenteral Support (PS) Volume at End of Treatment/Early Termination (EOT/ET)

End point title	Number of Subjects Who Achieved At least 20 Percent (%) Reduction From Baseline in Weight-normalized Parenteral Support (PS) Volume at End of Treatment/Early Termination (EOT/ET)[1]
End point description:	
Number of subjects who achieved at least 20% reduction from baseline in weight-normalized PS volume at EOT/ET (up to Week 24) were reported. EOT/ET was defined as the last available visit after the date of first dose (or randomization in standard of care treatment group) during the 24-week treatment period. Intent-to-Treat (ITT) set consisted of all subjects randomized in the study.	
End point type	Primary
End point timeframe:	
Baseline, EOT/ET (up to Week 24)	
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 and comparision analysis were performed for this endpoint.	

End point values	Teduglutide (TED)	Standard of Care (SOC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	5		
Units: Subjects				
Dairy Data: EOT/ET	3	1		
Prescribed Data: EOT/ET	3	3		

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma Concentration of Teduglutide at Nominal Time Points (Baseline at Pre-dose, and 1 Hour and 4 Hours Post-dose; 2 Hours Post-dose at Week 7)

End point title	Plasma Concentration of Teduglutide at Nominal Time Points (Baseline at Pre-dose, and 1 Hour and 4 Hours Post-dose; 2 Hours Post-dose at Week 7)[2]

End point description:

Mean plasma concentration of teduglutide at nominal time points was reported. Pharmacokinetic (PK) set included all subjects who received at least one dose of teduglutide and have at least one evaluable and interpretable post-dose PK concentration value. Here, the number of subjects analysed refer to the subjects evaluable for this endpoint and n=number of subjects analysed refer to the subjects evaluable for this specific time points. Data was not planned to be collected and analysed for SOC arm.

End point type	Secondary

End point timeframe:

Baseline: Pre-dose, 1, 4 hours post-dose, and 2 hours post-dose on Week 7

Notes:

[2] - 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: This endpoint was only planned to be analysed for the reporting group of "Teduglutide" arm.

End point values	Teduglutide (TED)			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: Nanogram per milliliter (ng/mL)				
median (full range (min-max))				
Baseline: At Pre-dose (n=4)	0.00 (0.000 to 0.00)			
Baseline: At 1 hour (n=3)	16.300 (7.25 to 25.70)			
Baseline: At 4 hour (n=4)	8.385 (3.86 to 22.5)			
Week 7: At 2 hours (n=2)	16.950 (14.80 to 19.10)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Treatment-emergent Adverse Events (TEAEs)

End point title	Number of Subjects With Treatment-emergent Adverse Events (TEAEs)

End point description:

An adverse event (AE) was any untoward medical occurrence in a clinical investigation subject administered a pharmaceutical product and that does not necessarily have a causal relationship with this treatment. TEAEs are defined as AEs that start or deteriorate on or after the date of the first dose of investigational product. Safety set consisted of all subjects who met the following criteria: Teduglutide treatment arm: subjects who received at least 1 dose of teduglutide and had undergone at least 1 post baseline safety assessment; Standard of care treatment arm: subjects who had undergone at least 1 post baseline safety assessment.

End point type	Secondary

End point timeframe:

From start of study treatment up to end of study (EOS) (up to Week 28)

End point values	Teduglutide (TED)	Standard of Care (SOC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	5		
Units: Subjects	5	5		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Body Weight Z-score at Week 24

End point title	Change From Baseline in Body Weight Z-score at Week 24

End point description:

Body weight was measured using Z-score. Z-score was calculated as (observed value - median value of the reference population)/standard deviation value of reference population. A negative Z-score indicates values lower than the mean while a positive Z-score indicates values higher than the mean. Change from baseline in body weight Z-score at Week 24 was reported. Safety set consisted of all subjects who met the following criteria: Teduglutide treatment arm: subjects who received at least 1 dose of teduglutide and had undergone at least 1 post baseline safety assessment; Standard of care treatment arm: subjects who had undergone at least 1 post baseline safety assessment. Here, the number of subjects analysed refer to the subjects evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 24

End point values	Teduglutide (TED)	Standard of Care (SOC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	3		
Units: Z-score				
arithmetic mean (standard deviation)	-0.408 (± 0.377)	-0.289 (± 0.278)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Length Z-Score at Week 24

End point title	Change From Baseline in Length Z-Score at Week 24

End point description:

Length was measured using Z-score. Z-score was calculated as (observed value - median value of the reference population)/standard deviation value of reference population. A negative Z-score indicates values lower than the mean while a positive Z-score indicates values higher than the mean. Change from baseline in length Z-score at Week 24 was reported. Safety set consisted of all subjects who met the following criteria: Teduglutide treatment arm: subjects who received at least 1 dose of teduglutide and had undergone at least 1 post baseline safety assessment; Standard of care treatment arm: subjects who had undergone at least 1 post baseline safety assessment. Here, the number of subjects analysed refer to the subjects evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 24

End point values	Teduglutide (TED)	Standard of Care (SOC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	2		
Units: Z-Score				
arithmetic mean (standard deviation)	-0.274 (± 1.258)	-0.422 (± 0.384)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Head Circumference Z-Score at Week 24

End point title	Change From Baseline in Head Circumference Z-Score at Week 24

End point description:

Head circumference was measured using Z-score. Z-score was calculated as (observed value - median value of the reference population)/standard deviation value of reference population. A negative Z-score indicates values lower than the mean while a positive Z-score indicates values higher than the mean. Change from baseline in head circumference Z-score at Week 24 was reported. Safety set consisted of all subjects who met the following criteria: Teduglutide treatment arm: subjects who received at least 1 dose of teduglutide and had undergone at least 1 post baseline safety assessment; Standard of care treatment arm: subjects who had undergone at least 1 post baseline safety assessment. Here, the number of subjects analysed refer to the subjects evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 24

End point values	Teduglutide (TED)	Standard of Care (SOC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	2		
Units: Z-Score				
arithmetic mean (standard deviation)	-0.544 (± 0.446)	-0.167 (± 0.690)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Weight-for-Length Z-Score at Week 24

End point title	Change From Baseline in Weight-for-Length Z-Score at Week

	24

End point description:

Weight-for-length was measured using Z-score. Z-score was calculated as (observed value - median value of the reference population)/standard deviation value of reference population. A negative Z-score indicates values lower than the mean while a positive Z-score indicates values higher than the mean. Change from baseline in weight-for-length Z-score at Week 24 was reported. Safety set consisted of all subjects who met the following criteria: Teduglutide treatment arm: subjects who received at least 1 dose of teduglutide and had undergone at least 1 post baseline safety assessment; Standard of care treatment arm: subjects who had undergone at least 1 post baseline safety assessment. Here, the number of subjects analysed refer to the subjects evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 24

End point values	Teduglutide (TED)	Standard of Care (SOC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	3		
Units: Z-Score				
arithmetic mean (standard deviation)	-0.447 (± 1.042)	-0.058 (± 0.992)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Average Total Urine Output at Week 24

End point title	Change From Baseline in Average Total Urine Output at Week 24

End point description:

Average total urine output was recorded over a 48-hour period of nutritional stability at Week 24 was reported. Safety set consisted of all subjects who met the following criteria: Teduglutide treatment arm: subjects who received at least 1 dose of teduglutide and had undergone at least 1 post baseline safety assessment; Standard of care treatment arm: subjects who had undergone at least 1 post baseline safety assessment. Here, the number of subjects analysed refer to the subjects evaluable for this endpoint. Here, milliliter per kilogram per day is abbreviated as mL/kg/day.

End point type	Secondary

End point timeframe:

Baseline, Week 24

End point values	Teduglutide (TED)	Standard of Care (SOC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	3		
Units: mL/kg/day				
arithmetic mean (standard deviation)	-0.61 (± 14.548)	10.25 (± 17.383)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Fecal Output at Week 24

End point title	Change From Baseline in Fecal Output at Week 24

End point description:

Change from baseline in the fecal output (Average number of stools per day) at Week 24 was reported. Safety set consisted of all subjects who met the following criteria: Teduglutide treatment arm: subjects who received at least 1 dose of teduglutide and had undergone at least 1 post baseline safety assessment; Standard of care treatment arm: subjects who had undergone at least 1 post baseline safety assessment. Here, the number of subjects analysed refer to the subjects evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 24

End point values	Teduglutide (TED)	Standard of Care (SOC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	3		
Units: Average number of stools per day				
arithmetic mean (standard deviation)	-3.33 (± 3.547)	1.67 (± 1.756)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Positive Specific Antibodies to Teduglutide

End point title	Number of Subjects With Positive Specific Antibodies to Teduglutide[3]

End point description:

Number of subjects with positive specific antibodies to teduglutide were used to summarize the presence of antibodies. Safety set consisted of all subjects who met the following criteria: Teduglutide treatment arm: subjects who received at least 1 dose of teduglutide and had undergone at least 1 post baseline safety assessment; Standard of care treatment arm: subjects who had undergone at least 1 post baseline safety assessment. Here, the number of subjects analysed signifies subjects who were evaluable for this endpoint. Data for this endpoint was not planned to be collected and analyzed for SOC group.

End point type	Secondary

End point timeframe:

Baseline, EOS (up to week 28)

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: This endpoint was only planned to be analysed for the reporting group of "Teduglutide" arm.

End point values	Teduglutide (TED)			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: Subjects	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects Who Achieved At least 20 Percent (%) Reduction From Baseline in Weight-normalized Parenteral Support (PS) Caloric Intake at End of Treatment/Early Termination (EOT/ET)

End point title	Number of Subjects Who Achieved At least 20 Percent (%) Reduction From Baseline in Weight-normalized Parenteral Support (PS) Caloric Intake at End of Treatment/Early Termination (EOT/ET)

End point description:

Number of subjects who achieved at least 20% reduction from baseline in weight-normalized PS caloric intake at EOT/ET (up to Week 24) were reported. EOT/ET was defined as the last available visit after the date of first dose (or randomization in standard of care treatment group) during the 24-week treatment period. ITT set consisted of all subjects randomized in the study.

End point type	Secondary

End point timeframe:

Baseline, EOT/ET (up to Week 24)

End point values	Teduglutide (TED)	Standard of Care (SOC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	5		
Units: Subjects				
Dairy Data: EOT/ET	3	1		
Prescribed Data: EOT/ET	3	3		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects Who Achieved 100 Percent (%) Reduction in Complete Weaning Off (Enteral Autonomy) Parenteral Support (PS) Volume at Week 24

End point title	Number of Subjects Who Achieved 100 Percent (%) Reduction

	in Complete Weaning Off (Enteral Autonomy) Parenteral Support (PS) Volume at Week 24

End point description:

Number of subjects who achieved 100% reduction in complete weaning off (enteral autonomy) PS volume at Week 24 were reported. ITT set consisted of all subjects randomized in the study. Here, the number of subjects analysed signifies subjects who were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Week 24

End point values	Teduglutide (TED)	Standard of Care (SOC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	4		
Units: Subjects	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects Who Achieved 100 Percent (%) Reduction in Complete Weaning Off (Enteral Autonomy) Parenteral Support (PS) Volume at End of Study (EOS)

End point title	Number of Subjects Who Achieved 100 Percent (%) Reduction in Complete Weaning Off (Enteral Autonomy) Parenteral Support (PS) Volume at End of Study (EOS)

End point description:

Number of subjects who achieved 100% reduction in complete weaning off (enteral autonomy) PS volume at EOS (up to Week 28) were reported. ITT set consisted of all subjects randomized in the study. Here, the number of subjects analysed signifies subjects who were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

EOS (up to Week 28)

End point values	Teduglutide (TED)	Standard of Care (SOC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	5		
Units: Subjects	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Weight-normalized Parenteral Support (PS) Volume at End of Treatment/Early Termination (EOT/ET)

End point title	Change From Baseline in Weight-normalized Parenteral Support (PS) Volume at End of Treatment/Early Termination (EOT/ET)

End point description:

Change from baseline in weight-normalized PS volume at EOT/ET (up to Week 24) was reported. EOT/ET was defined as the last available visit after the date of first dose (or randomization in standard of care treatment group) during the 24-week treatment period. ITT set consisted of all subjects randomized in the study. Here, n=number of subjects analysed refer to the subjects evaluable for this specific time points.

End point type	Secondary

End point timeframe:

Baseline, EOT/ET (up to Week 24)

End point values	Teduglutide (TED)	Standard of Care (SOC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	5		
Units: mL/kg/day				
arithmetic mean (standard deviation)				
Dairy Data: EOT/ET (n=5, 3)	-21.54 (± 28.909)	-9.51 (± 7.497)		
Prescribed Data: EOT/ET (n=5, 5)	-22.90 (± 26.940)	-14.90 (± 12.323)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in Weight-normalized Parenteral Support (PS) Volume at End of Treatment/Early Termination (EOT/ET)

End point title	Percent Change From Baseline in Weight-normalized Parenteral Support (PS) Volume at End of Treatment/Early Termination (EOT/ET)

End point description:

Percent change from baseline in weight-normalized PS volume at EOT/ET (up to Week 24) was reported. EOT/ET was defined as the last available visit after the date of first dose (or randomization in standard of care treatment group) during the 24-week treatment period. ITT set consisted of all subjects randomized in the study. Here, n=number of subjects analysed refer to the subjects evaluable for this specific time points.

End point type	Secondary

End point timeframe:

Baseline, EOT/ET (up to Week 24)

End point values	Teduglutide (TED)	Standard of Care (SOC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	5		
Units: Percent change				
arithmetic mean (standard deviation)				
Dairy Data: EOT/ET (n=5, 3)	-24.77 (± 34.723)	-16.75 (± 16.392)		
Prescribed Data: EOT/ET (n=5, 5)	-27.28 (± 33.518)	-22.39 (± 17.198)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Weight-normalized Parenteral Support (PS) Caloric Intake at End of Treatment/Early Termination (EOT/ET)

End point title	Change From Baseline in Weight-normalized Parenteral Support (PS) Caloric Intake at End of Treatment/Early Termination (EOT/ET)

End point description:

Change from baseline in weight-normalized PS caloric intake at EOT/ET (up to Week 24) were reported. EOT/ET was defined as the last available visit after the date of first dose (or randomization in standard of care treatment group) during the 24-week treatment period. Here, kilo-calories per kilogram per day was abbreviated as (kcal/kg/day). ITT set consisted of all subjects randomized in the study. Here, n=number of subjects analysed refer to the subjects evaluable for this specific time points.

End point type	Secondary

End point timeframe:

Baseline, EOT/ET (up to Week 24)

End point values	Teduglutide (TED)	Standard of Care (SOC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	5		
Units: kcal/kg/day				
arithmetic mean (standard deviation)				
Dairy Data: EOT/ET (n=5, 3)	-16.14 (± 17.547)	-6.10 (± 10.386)		
Prescribed Data: EOT/ET (n=5, 5)	-15.31 (± 17.839)	-20.40 (± 21.024)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in Weight-normalized Parenteral Support (PS) Caloric Intake at End of Treatment/Early Termination (EOT/ET)

End point title	Percent Change From Baseline in Weight-normalized Parenteral

	Support (PS) Caloric Intake at End of Treatment/Early Termination (EOT/ET)

End point description:

Percent change from baseline in weight-normalized PS caloric intake at EOT/ET (up to Week 24) were reported. EOT/ET was defined as the last available visit after the date of first dose (or randomization in standard of care treatment group) during the 24-week treatment period. ITT set consisted of all subjects randomized in the study. Here, n=number of subjects analysed refer to the subjects evaluable for this specific time points.

End point type	Secondary

End point timeframe:

Baseline, EOT/ET (up to Week 24)

End point values	Teduglutide (TED)	Standard of Care (SOC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	5		
Units: Percent change				
arithmetic mean (standard deviation)				
Dairy Data: EOT/ET (n=5, 3)	-27.00 (± 29.473)	-13.68 (± 21.873)		
Prescribed Data: EOT/ET (n=5, 5)	-27.81 (± 30.777)	-38.86 (± 39.893)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Weight-normalized Enteral Nutrition (EN) Volume at End of Treatment/Early Termination (EOT/ET)

End point title	Change From Baseline in Weight-normalized Enteral Nutrition (EN) Volume at End of Treatment/Early Termination (EOT/ET)

End point description:

Change from baseline in weight-normalized EN volume at EOT/ET (up to Week 24) was reported. EOT/ET was defined as the last available visit after the date of first dose (or randomization in standard of care treatment group) during the 24-week treatment period. ITT set consisted of all subjects randomized in the study. Here, n=number of subjects analysed refer to the subjects evaluable for this specific time points.

End point type	Secondary

End point timeframe:

Baseline, EOT/ET (up to Week 24)

End point values	Teduglutide (TED)	Standard of Care (SOC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	5		
Units: mL/kg/day				
arithmetic mean (standard deviation)				

Dairy Data: EOT/ET (n=4, 3)	16.14 (± 18.683)	-15.25 (± 31.496)		
Prescribed Data: EOT/ET (n=4, 5)	-1.28 (± 2.563)	2.27 (± 22.232)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in Weight-normalized Enteral Nutrition (EN) volume at End of Treatment/Early Termination (EOT/ET)

End point title	Percent Change From Baseline in Weight-normalized Enteral Nutrition (EN) volume at End of Treatment/Early Termination (EOT/ET)

End point description:

Percent change from baseline in weight-normalized EN volume at EOT/ET (up to Week 24) was reported. EOT/ET was defined as the last available visit after the date of first dose (or randomization in standard of care treatment group) during the 24-week treatment period. ITT set consisted of all subjects randomized in the study. Here, '99999' indicates that standard deviation was not analysed for this category as there were only one subjects available at specified time points. Here, n=number of subjects analysed refer to the subjects evaluable for this specific time points.

End point type	Secondary

End point timeframe:

Baseline, EOT/ET (up to Week 24)

End point values	Teduglutide (TED)	Standard of Care (SOC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	5		
Units: Percent change				
arithmetic mean (standard deviation)				
Dairy Data: EOT/ET (n=2, 2)	273.20 (± 246.784)	-44.25 (± 78.847)		
Prescribed Data: EOT/ET (n=1, 4)	-16.40 (± 99999)	14.80 (± 69.834)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Weight-normalized Enteral Nutrition (EN) Caloric Intake at End of Treatment/Early Termination (EOT/ET)

End point title	Change From Baseline in Weight-normalized Enteral Nutrition (EN) Caloric Intake at End of Treatment/Early Termination (EOT/ET)

End point description:

Change from baseline in weight-normalized EN caloric intake at EOT/ET (up to Week 24) were reported. EOT/ET was defined as the last available visit after the date of first dose (or randomization in standard of care treatment group) during the 24-week treatment period. ITT set consisted of all subjects

randomized in the study. Here, n=number of subjects analysed refer to the subjects evaluable for this specific time points.

End point type	Secondary

End point timeframe:

Baseline, EOT/ET (up to Week 24)

End point values	Teduglutide (TED)	Standard of Care (SOC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	5		
Units: kcal/kg/day				
arithmetic mean (standard deviation)				
Dairy Data: EOT/ET (n=4, 3)	9.08 (± 10.662)	-9.38 (± 21.402)		
Prescribed Data: EOT/ET (n=4, 5)	-1.15 (± 2.306)	3.11 (± 16.285)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in Weight-normalized Enteral Nutrition (EN) Caloric Intake at End of Treatment/Early Termination (EOT/ET)

End point title	Percent Change From Baseline in Weight-normalized Enteral Nutrition (EN) Caloric Intake at End of Treatment/Early Termination (EOT/ET)

End point description:

Percent change from baseline in weight-normalized EN caloric intake at EOT/ET (up to Week 24) were reported. EOT/ET was defined as the last available visit after the date of first dose (or randomization in standard of care treatment group) during the 24-week treatment period. ITT set consisted of all subjects randomized in the study. Here, '99999' indicates that standard deviation was not analysed for this category as there were only one subjects available at specified time points. Here, n=number of subjects analysed refer to the subjects evaluable for this specific time points.

End point type	Secondary

End point timeframe:

Baseline, EOT/ET (up to Week 24)

End point values	Teduglutide (TED)	Standard of Care (SOC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	5		
Units: Percent change				
arithmetic mean (standard deviation)				
Dairy Data: EOT/ET (n=2, 2)	207.06 (± 153.159)	-44.25 (± 78.847)		
Prescribed Data: EOT/ET (n=1, 4)	-16.40 (± 99999)	24.18 (± 78.115)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects Who Achieved At least 20 Percent (%) Increase From Baseline in Weight-normalized Enteral Nutrition (EN) Volume at End of Treatment/Early Termination (EOT/ET)

End point title	Number of Subjects Who Achieved At least 20 Percent (%) Increase From Baseline in Weight-normalized Enteral Nutrition (EN) Volume at End of Treatment/Early Termination (EOT/ET)

End point description:

Number of subjects who achieved at least 20% increase from baseline in weight-normalized EN volume at EOT/ET was reported. EOT/ET was defined as the last available visit after the date of first dose (or randomization in standard of care treatment group) during the 24-week treatment period. ITT set consisted of all subjects randomized in the study.

End point type	Secondary

End point timeframe:

Baseline, EOT/ET (up to Week 24)

End point values	Teduglutide (TED)	Standard of Care (SOC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	5		
Units: Subjects				
Dairy Data: EOT/ET	2	0		
Prescribed Data: EOT/ET	0	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects Who Achieved At least 20 Percent (%) Increase From Baseline in Weight-normalized Enteral Nutrition (EN) Caloric Intake at End of Treatment/Early Termination (EOT/ET)

End point title	Number of Subjects Who Achieved At least 20 Percent (%) Increase From Baseline in Weight-normalized Enteral Nutrition (EN) Caloric Intake at End of Treatment/Early Termination (EOT/ET)

End point description:

Number of subjects who achieved at least 20% increase from baseline in weight-normalized EN caloric intake at EOT/ET was reported. EOT/ET was defined as the last available visit after the date of first dose (or randomization in standard of care treatment group) during the 24-week treatment period. ITT set consisted of all subjects randomized in the study.

End point type	Secondary

End point timeframe:
Baseline, EOT/ET (up to Week 24)

End point values	Teduglutide (TED)	Standard of Care (SOC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	5		
Units: Subjects				
Dairy Data: EOT/ET	2	0		
Prescribed Data: EOT/ET	0	2		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From start of study treatment up to end of study (EOS) (up to Week 28)	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	21.0

Reporting groups	
Reporting group title	Teduglutide
Reporting group description:	
Subjects (infants) 4 to 12 months of corrected gestational aged received 0.05 mg/kg of teduglutide SC injection once daily for 24 weeks.	
Reporting group title	Standard of Care (SOC)
Reporting group description:	
Subjects (infants) 4 to 12 months of corrected gestational aged received standard medical therapy for 24 weeks.	

Serious adverse events	Teduglutide	Standard of Care (SOC)	
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 5 (80.00%)	3 / 5 (60.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Investigations			
Transaminases increased			
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Ataxia			
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Immune system disorders			
Immunisation reaction			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Device related infection			
subjects affected / exposed	0 / 5 (0.00%)	2 / 5 (40.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Product issues			
Device breakage			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device leakage			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device occlusion			
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Metabolic acidosis			
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Teduglutide	Standard of Care (SOC)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 5 (100.00%)	5 / 5 (100.00%)	

Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	
occurrences (all)	2	0	
Blood iron decreased			
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Faecal volume increased			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Respiratory rate increased			
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Serum ferritin decreased			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Transaminases increased			
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	2	
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Lip injury			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Skin abrasion			
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Blood and lymphatic system disorders			
Anaemia			

subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Iron deficiency anaemia			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 5 (20.00%)	1 / 5 (20.00%)	
occurrences (all)	1	1	
Secretion discharge			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	
occurrences (all)	2	0	
Abdominal distension			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	
occurrences (all)	3	0	
Abnormal faeces			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Constipation			
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Diarrhoea			
subjects affected / exposed	2 / 5 (40.00%)	0 / 5 (0.00%)	
occurrences (all)	3	0	
Faeces discoloured			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Flatulence			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Frequent bowel movements			

subjects affected / exposed	2 / 5 (40.00%)	0 / 5 (0.00%)	
occurrences (all)	2	0	
Gastrointestinal sounds abnormal			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Mucous stools			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Retching			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Teething			
subjects affected / exposed	0 / 5 (0.00%)	2 / 5 (40.00%)	
occurrences (all)	0	3	
Vomiting			
subjects affected / exposed	3 / 5 (60.00%)	1 / 5 (20.00%)	
occurrences (all)	8	2	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 5 (20.00%)	1 / 5 (20.00%)	
occurrences (all)	1	1	
Rhinorrhoea			
subjects affected / exposed	1 / 5 (20.00%)	1 / 5 (20.00%)	
occurrences (all)	1	1	
Skin and subcutaneous tissue disorders			
Dermatitis diaper			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	
occurrences (all)	2	0	
Eczema			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Rash papular			
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Psychiatric disorders			

Irritability			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Sleep disorder			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			
Gastroenteritis norovirus			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Hand-foot-and-mouth disease			
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Medical device site infection			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Nasopharyngitis			
subjects affected / exposed	2 / 5 (40.00%)	0 / 5 (0.00%)	
occurrences (all)	2	0	
Respiratory tract infection viral			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	
occurrences (all)	2	0	
Upper respiratory tract infection			
subjects affected / exposed	1 / 5 (20.00%)	2 / 5 (40.00%)	
occurrences (all)	1	2	
Viral infection			
subjects affected / exposed	1 / 5 (20.00%)	1 / 5 (20.00%)	
occurrences (all)	1	1	
Product issues			
Device breakage			
subjects affected / exposed	1 / 5 (20.00%)	1 / 5 (20.00%)	
occurrences (all)	1	1	
Device occlusion			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Metabolism and nutrition disorders			

Decreased appetite			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	
occurrences (all)	2	0	
Hypoglycaemia			
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Hypophagia			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
18 January 2018	Protocol Amendment 1: - Clarification that subjects must have been 4 to 12 months corrected gestational age at screening. - Pharmacokinetic sampling on Week 6 was moved to Week 7 so that samples could be collected without exceeding the weekly/monthly total blood volume restrictions. Clarification that blood for post-dose PK samples might be taken within ±10 minutes of the time pre-specified. - Teduglutide dose adjustments were changed to Week 12 rather than at every clinic visit to reduce the site burden. - Assessment of the 5-level EuroQol five dimensions questionnaire was removed to reduce the caregiver burden.
04 December 2018	Protocol Amendment 2: - The dose selection rationale was updated with results from a simulation work using the previous population PK model. Based on the totality of clinical data, 0.05 mg/kg once daily was expected to provide comparable Cmax concentrations in infants as compared to pediatric subjects with SBS and was recommended as an evaluation dosing regimen in Study SHP633-301.
24 May 2019	Amendment 3: - The significant change in this amendment included the deletion of inclusion criterion 6: "Lack of terminal ileum and ileocecal valve." due to difficulties in enrollment.
17 December 2019	Protocol Amendment 4: - Specification that the pre-dose PK sample was not to be collected from subjects who weighed lesser than (<) 7 kilograms (kg). The optional PK measurement at Week 12 was removed; postbaseline PK samples were to be performed at Week 7. The information to be collected for PK assessments was clarified. - Clarification that subjects might enroll in an extension study at EOS if that study was open to enrollment at the time of the SHP633-301 EOS.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported