



Clinical trial results:

A Prospective, Open-label, Long-term Safety and Efficacy Study of Teduglutide in Japanese Pediatric Subjects with Short Bowel Syndrome Who Completed SHP633-302

Summary

EudraCT number	2021-005404-36
Trial protocol	Outside EU/EEA
Global end of trial date	02 November 2021

Results information

Result version number	v1 (current)
This version publication date	12 May 2022
First version publication date	12 May 2022

Trial information

Trial identification

Sponsor protocol code	SHP633-305
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03268811
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Shire
Sponsor organisation address	300 Shire Way, 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)	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	02 November 2021
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	02 November 2021
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 long-term safety and tolerability of teduglutide treatment in Japanese pediatric participants with short bowel syndrome (SBS) who completed Study SHP633-302 (2020-005791-35).

Protection of trial subjects:

This clinical study was conducted in accordance with the study protocol and the ethical principles that have their origin in the World Medical Association Declaration of Helsinki. In addition, it was consistent with the standards stipulated in Article 14, Paragraph 3, and Article 80-2 of the Law on Securing Quality, Efficacy and Safety of Products including Pharmaceuticals and Medical Devices in Japan, the "Ministerial Ordinance on the Standards for the Implementation of Clinical Studies on Pharmaceutical Product" in Japan, and International Council For Harmonisation (ICH) Good Clinical Practices (GCP).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	23 August 2017
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	Japan: 9
Worldwide total number of subjects	9
EEA total number of subjects	0

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)	2
Children (2-11 years)	6
Adolescents (12-17 years)	1
Adults (18-64 years)	0
From 65 to 84 years	0

85 years and over	0
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Subject disposition

Recruitment

Recruitment details:

The study was conducted at 6 centers in Japan from 23 August 2017 (first participant first visit) and 02 November 2021 (last participant last visit).

Pre-assignment

Screening details:

A total of 9 Japanese pediatric participants who completed Study SHP633-302 (2020-005791-35) were enrolled into the extension study based on age of participants i.e., 7 children (aged 1 through 15 years of age) and 2 infants (aged 4 months through < 12 months of corrected gestational age).

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Total Children (Aged: 1 to 15 Years)

Arm description:

Participants aged from 1 through 15 years who participated in the core study (SHP633-302 [2020-005791-35]) were enrolled into this extension study and received teduglutide 0.05 milligram per kilogram (mg/kg) subcutaneous (SC) injection once daily for 24 weeks in each treatment cycle (Cycles 1 to 9 [Each cycle=28 weeks]) depending on the disease course.

Arm type	Experimental
Investigational medicinal product name	Teduglutide
Investigational medicinal product code	SHP633
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants received teduglutide 0.05 mg/kg SC injection once daily into 1 of the 4 quadrants of the abdomen or either thigh or arm.

Arm title	Infants (Corrected Gestational Age: 4 to < 12 Months)
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Arm description:

Participants (Infants) from 4 through < 12 months of corrected gestational age who participated in the core study (SHP633-302 [2020-005791-35]) were enrolled into this extension study and received teduglutide 0.05 mg/kg SC injection once daily for 24 weeks in each treatment cycle (Cycles 1 to 9 [Each cycle=28 weeks]) depending on the disease course.

Arm type	Experimental
Investigational medicinal product name	Teduglutide
Investigational medicinal product code	SHP633
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants received teduglutide 0.05 mg/kg SC injection once daily into 1 of the 4 quadrants of the abdomen or either thigh or arm.

Number of subjects in period 1	Total Children (Aged: 1 to 15 Years)	Infants (Corrected Gestational Age: 4 to < 12 Months)
Started	7	2
Completed	7	1
Not completed	0	1
Adverse event, non-fatal	-	1

Baseline characteristics

Reporting groups

Reporting group title	Total Children (Aged: 1 to 15 Years)
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Reporting group description:

Participants aged from 1 through 15 years who participated in the core study (SHP633-302 [2020-005791-35]) were enrolled into this extension study and received teduglutide 0.05 milligram per kilogram (mg/kg) subcutaneous (SC) injection once daily for 24 weeks in each treatment cycle (Cycles 1 to 9 [Each cycle=28 weeks]) depending on the disease course.

Reporting group title	Infants (Corrected Gestational Age: 4 to < 12 Months)
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Reporting group description:

Participants (Infants) from 4 through < 12 months of corrected gestational age who participated in the core study (SHP633-302 [2020-005791-35]) were enrolled into this extension study and received teduglutide 0.05 mg/kg SC injection once daily for 24 weeks in each treatment cycle (Cycles 1 to 9 [Each cycle=28 weeks]) depending on the disease course.

Reporting group values	Total Children (Aged: 1 to 15 Years)	Infants (Corrected Gestational Age: 4 to < 12 Months)	Total
Number of subjects	7	2	9
Age categorical			
Units: Subjects			
Aged: 1 to 15 Years	7	0	7
Corrected Gestation Age: 4 to < 12 months	0	2	2
Gender categorical			
Units: Subjects			
Male	6	1	7
Female	1	1	2
Race			
Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	7	2	9
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	0	0	0
More than one race	0	0	0
Unknown or Not Reported	0	0	0
Ethnicity			
Units: Subjects			
Hispanic or Latino	0	0	0
Not Hispanic or Latino	7	2	9
Unknown or Not Reported	0	0	0

End points

End points reporting groups

Reporting group title	Total Children (Aged: 1 to 15 Years)
Reporting group description: Participants aged from 1 through 15 years who participated in the core study (SHP633-302 [2020-005791-35]) were enrolled into this extension study and received teduglutide 0.05 milligram per kilogram (mg/kg) subcutaneous (SC) injection once daily for 24 weeks in each treatment cycle (Cycles 1 to 9 [Each cycle=28 weeks]) depending on the disease course.	
Reporting group title	Infants (Corrected Gestational Age: 4 to < 12 Months)
Reporting group description: Participants (Infants) from 4 through < 12 months of corrected gestational age who participated in the core study (SHP633-302 [2020-005791-35]) were enrolled into this extension study and received teduglutide 0.05 mg/kg SC injection once daily for 24 weeks in each treatment cycle (Cycles 1 to 9 [Each cycle=28 weeks]) depending on the disease course.	

Primary: Number of Participants With Treatment-emergent Adverse Events (TEAEs)

End point title	Number of Participants With Treatment-emergent Adverse Events (TEAEs) ^[1]
End point description: An Adverse Event (AE) was any untoward medical occurrence in a clinical investigation participant administered a pharmaceutical product and that does not necessarily have a causal relationship with this treatment. TEAEs were defined as any AEs whose onset occurred, severity worsened or intensity increased after receiving the investigational product (IP) in the core study (SHP633-302 [2020-005791-35]) or this extension study. The safety population included all enrolled participants in the study and who received at least one dose of teduglutide (in study SHP633-302 [2020-005791-35] or SHP633-305 [2021-005404-36]). Number of participants with TEAEs were reported. Baseline refers to the baseline value of the core study (SHP633-302 [2020-005791-35]).	
End point type	Primary
End point timeframe: From Baseline up to follow-up (up to 50 months)	
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 comparison analyses were performed for this endpoint.	

End point values	Total Children (Aged: 1 to 15 Years)	Infants (Corrected Gestational Age: 4 to < 12 Months)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	2		
Units: Participants	7	2		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Clinically Significant Abnormalities in Vital Signs

End point title	Number of Participants With Clinically Significant Abnormalities in Vital Signs ^[2]
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End point description:

Vital sign assessments included pulse rate, blood pressure (systolic and diastolic blood pressure) and body temperature. Number of participants with clinically significant abnormalities in vital signs which were deemed clinically significant by the investigator were reported. The safety population included all enrolled participants in the study and who received at least one dose of teduglutide (in study SHP633-302 [2020-005791-35] or SHP633-305 [2021-005404-36]). Baseline refers to the baseline value of the core study (SHP633-302 [2020-005791-35]).

End point type	Primary
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End point timeframe:

From Baseline up to follow-up (up to 50 months)

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 and comparison analyses were performed for this endpoint.

End point values	Total Children (Aged: 1 to 15 Years)	Infants (Corrected Gestational Age: 4 to < 12 Months)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	2		
Units: Participants	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Clinically Significant Abnormalities in Laboratory Parameters

End point title	Number of Participants With Clinically Significant Abnormalities in Laboratory Parameters ^[3]
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End point description:

Clinical laboratory parameters included biochemistry, hematology and urinalysis. Number of participants with clinically significant abnormalities in laboratory parameters which were deemed clinically significant by the investigator were reported. The safety population included all enrolled participants in the study and who received at least one dose of teduglutide (in study SHP633-302 [2020-005791-35] or SHP633-305 [2021-005404-36]). Baseline refers to the baseline value of the core study (SHP633-302 [2020-005791-35]).

End point type	Primary
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End point timeframe:

From Baseline up to follow-up (up to 50 months)

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: No statistical and comparison analyses were performed for this endpoint.

End point values	Total Children (Aged: 1 to 15 Years)	Infants (Corrected Gestational Age: 4 to < 12 Months)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	2		
Units: Participants				
Biochemistry	5	1		
Hematology	1	0		
Urinalysis	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Percent Change From Baseline in Average Total Urine Output at End of Treatment (EOT) of Last Cycle During Teduglutide Treatment

End point title	Percent Change From Baseline in Average Total Urine Output at End of Treatment (EOT) of Last Cycle During Teduglutide Treatment ^[4]
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End point description:

Average total urine output was recorded over a 48-hour period of parental support (PS) stability before every scheduled site visit and within 1 week of implementing any PS adjustment. The Average daily urine output milliliter per kilogram per day (mL/kg/day) was calculated as: (Total urine output over 48 hours / 2) / body weight (kilogram [kg]) where total urine output was calculated as the sum of the urine output in milliliter (mL) and the urine-only diaper weights in gram (g) (1g = 1mL) for the participant collected on the output diary form of electronic case report from (eCRF). Safety Population. Here, "number of participants analysed" refer to the participants evaluable for this endpoint. Baseline refers to the baseline value of the core study (SHP633-302 [2020-005791-35]).

End point type	Primary
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End point timeframe:

Baseline, EOT of last cycle (up to Month 45) (Each Cycle 1 to 8 = 24 weeks, and Cycle 9 = 4 weeks)

Notes:

[4] - 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 comparison analyses were performed for this endpoint.

End point values	Total Children (Aged: 1 to 15 Years)	Infants (Corrected Gestational Age: 4 to < 12 Months)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	2		
Units: Percent Change				
arithmetic mean (standard deviation)	-37.228 (± 42.9396)	146.881 (± 295.8061)		

Statistical analyses

No statistical analyses for this end point

Primary: Percent Change From Baseline in Average Number of Stools Per Day at EOT of Last Cycle During Teduglutide Treatment

End point title	Percent Change From Baseline in Average Number of Stools Per Day at EOT of Last Cycle During Teduglutide Treatment ^[5]
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End point description:

Fecal output was recorded over a 48-hour period of PS stability before every scheduled site visit and within 1 week of implementing any PS adjustment. The average daily fecal output was summarized by the average number of stools per day. The average number of stools per day was calculated as (sum of the daily data in a 48-hour period/2). The safety population included all enrolled participants in the study and who received at least one dose of teduglutide (in study SHP633-302 [2020-005791-35] or SHP633-305 [2021-005404-36]). Here, "number of participants analysed" refer to the participants evaluable for this endpoint. Percent change from baseline in average number of stools per day at EOT of last cycle during teduglutide treatment was reported. Baseline refers to the baseline value of the core study (SHP633-302 [2020-005791-35]).

End point type	Primary
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End point timeframe:

Baseline, EOT of last cycle (up to Month 45) (Each Cycle 1 to 8 = 24 weeks, and Cycle 9 = 4 weeks)

Notes:

[5] - 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 comparison analyses were performed for this endpoint.

End point values	Total Children (Aged: 1 to 15 Years)	Infants (Corrected Gestational Age: 4 to < 12 Months)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	2		
Units: Percent Change				
arithmetic mean (standard deviation)	24.37 (± 63.623)	50.00 (± 0.000)		

Statistical analyses

No statistical analyses for this end point

Primary: Percent Change From Baseline in Average Stool/Mixed Stool Diaper Weight at EOT of Last Cycle During Teduglutide Treatment

End point title	Percent Change From Baseline in Average Stool/Mixed Stool Diaper Weight at EOT of Last Cycle During Teduglutide Treatment ^[6]
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End point description:

Fecal output was recorded over a 48-hour period of PS stability before every scheduled site visit and within 1 week of implementing any PS adjustment. The average daily fecal output was summarized by the average stool/mixed stool diaper weight (gram per kilogram per day [g/kg/day]). The body weight was used to calculate the daily stool/mixed stool diaper weight (g/kg/day). Safety population. Here, "number of participants analysed" refer to the participants evaluable for this endpoint. Percent change from baseline in average stool/mixed stool diaper weight at EOT of last cycle during teduglutide treatment was reported. Baseline refers to the baseline value of the core study (SHP633-302 [2020-005791-35]). Here, '99999' indicates that standard deviation could not be estimated for single subject for the specified arm.

End point type	Primary
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End point timeframe:

Baseline, EOT of last cycle (up to Month 45) (Each Cycle 1 to 8 = 24 weeks, and Cycle 9 = 4 weeks)

Notes:

[6] - 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 comparison analyses were performed for this endpoint.

End point values	Total Children (Aged: 1 to 15 Years)	Infants (Corrected Gestational Age: 4 to < 12 Months)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1	2		
Units: Percent Change				
arithmetic mean (standard deviation)	-12.678 ($\pm$ 99999)	206.017 ($\pm$ 332.4580)		

Statistical analyses

No statistical analyses for this end point

Primary: Percent Change From Baseline in Average Total Ostomy Output at EOT of Last Cycle During Teduglutide Treatment

End point title	Percent Change From Baseline in Average Total Ostomy Output at EOT of Last Cycle During Teduglutide Treatment ^[7]
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End point description:

Fecal output was recorded over a 48-hour period of PS stability before every scheduled site visit and within 1 week of implementing any PS adjustment. The body weight was used to calculate the average total ostomy output per day (mL/kg/day) using a formula analogous to that used to calculate the average daily urine output. The safety population included all enrolled participants in the study and who received at least one dose of teduglutide (in study SHP633-302 [2020-005791-35] or SHP633-305 [2021-005404-36]). Here, "number of participants analysed" refer to the participants evaluable for this endpoint. Percent change from baseline in average total ostomy output at EOT of last cycle during teduglutide treatment was reported. Baseline refers to the baseline value of the core study (SHP633-302 [2020-005791-35]).

End point type	Primary
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End point timeframe:

Baseline, EOT of last cycle (up to Month 45) (Each Cycle 1 to 8 = 24 weeks, and Cycle 9 = 4 weeks)

Notes:

[7] - 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 comparison analyses were performed for this endpoint.

End point values	Total Children (Aged: 1 to 15 Years)	Infants (Corrected Gestational Age: 4 to < 12 Months)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0 ^[8]	2		
Units: Percent Change				
arithmetic mean (standard deviation)	()	3.143 ($\pm$)		

Notes:

[8] - As no participant was analyzed for this arm, therefore data was not reported.

Statistical analyses

No statistical analyses for this end point

Primary: Percent Change From Baseline in Average Bristol Stool Form Score at EOT of Last Cycle During Teduglutide Treatment

End point title	Percent Change From Baseline in Average Bristol Stool Form Score at EOT of Last Cycle During Teduglutide Treatment ^[9]
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End point description:

Fecal output was recorded over a 48-hour period of PS stability before every scheduled site visit and within 1 week of implementing any PS adjustment. The average daily fecal output was summarized the average typical stool form score using Bristol Stool Form Scale. The average typical stool form score was calculated as (sum of the daily data in a 48-hour period / 2). Typical Stool Form based on Bristol Stool Form Scale: 1 - Separate hard lumps, hard to pass, 2 - Sausage-shaped, but lumpy, 3 - Like a sausage but with cracks on the surface, 4- Like a sausage or snake, smooth and soft, 5- Soft blobs with clear-cut edges, 6- Fluffy pieces with ragged edges, a mushy stool, 7- Watery, no solid pieces, Entirely liquid. Safety population. Here, "number of participants analysed" refer to the participants evaluable for this endpoint. Baseline refers to the baseline value of the core study (SHP633-302 [2020-005791-35]). A negative change from baseline indicates improvement.

End point type	Primary
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End point timeframe:

Baseline, EOT of last cycle (up to Month 45) (Each Cycle 1 to 8 = 24 weeks, and Cycle 9 = 4 weeks)

Notes:

[9] - 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 comparison analyses were performed for this endpoint.

End point values	Total Children (Aged: 1 to 15 Years)	Infants (Corrected Gestational Age: 4 to < 12 Months)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	2		
Units: Percent Change				
arithmetic mean (standard deviation)	-7.51 (± 16.758)	0.00 (± 0.000)		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Anti-drug antibodies (ADAs) (Including Neutralizing Antibodies) at EOT of Last Cycle During Teduglutide Treatment

End point title	Number of Participants With Anti-drug antibodies (ADAs) (Including Neutralizing Antibodies) at EOT of Last Cycle During Teduglutide Treatment ^[10]
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End point description:

Number of participants with ADAs (including NABs) to teduglutide were used to summarize the presence of antibodies. The participants who tested positive for ADAs (including NABs) were reported. The safety population included all enrolled participants in the study and who received at least one dose of teduglutide (in study SHP633-302 [2020-005791-35] or SHP633-305 [2021-005404-36]). Here, "number of participants analysed" signifies participants who were evaluable for this endpoint and "n" signifies to participants evaluable at given timepoints. Baseline refers to the baseline value of the core study (SHP633-302 [2020-005791-35]).

End point type	Primary
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End point timeframe:

Baseline, EOT of last cycle (up to Month 45) (Each Cycle 1 to 8 = 24 weeks, and Cycle 9 = 4 weeks)

Notes:

[10] - 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 comparison analyses were performed for this endpoint.

End point values	Total Children (Aged: 1 to 15 Years)	Infants (Corrected Gestational Age: 4 to < 12 Months)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	2		
Units: Participants				
Positive ADA: EOT of Last Cycle (n= 6, 2)	5	0		
Positive NABs: EOT of Last Cycle (n= 5, 0)	4	0		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Clinically Significant Changes in Gastrointestinal (GI) Specific Testing

End point title	Number of Participants With Clinically Significant Changes in Gastrointestinal (GI) Specific Testing ^[11]
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End point description:

GI specific testing included colonoscopy or sigmoidoscopy, abdominal ultrasound, fecal occult blood testing, upper GI series with small bowel follow-through (UGI/SBFT). Number of participants with clinically significant changes findings in gastrointestinal specific testing were reported. The safety population included all enrolled participants in the study and who received at least one dose of teduglutide (in study SHP633-302 [2020-005791-35] or SHP633-305 [2021-005404-36]). Here, "number of participants analysed" refer to the participants evaluable for this endpoint. Baseline refers to the baseline value of the core study (SHP633-302 [2020-005791-35]).

End point type	Primary
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End point timeframe:

Baseline, EOT of last cycle (up to Month 45) (Each Cycle 1 to 8 = 24 weeks, and Cycle 9 = 4 weeks)

Notes:

[11] - 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 comparison analyses were performed for this endpoint.

End point values	Total Children (Aged: 1 to 15 Years)	Infants (Corrected Gestational Age: 4 to < 12 Months)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	2		
Units: Participants	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in Body Weight For Age Z-Score at EOT of Last Cycle During Teduglutide Treatment

End point title	Change From Baseline in Body Weight For Age Z-Score at EOT of Last Cycle During Teduglutide Treatment ^[12]
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End point description:

Body weight was measured using Age Z-score. A Z-score was the deviation of the value for an individual from the mean value of the reference population divided by the standard deviation for the reference population. Centers for Disease Control and Prevention (age ≥ 2 years old) and World Health Organization (age < 2 years old) Z-score calculation charts were used for calculation. A negative Z-score indicates values lower than the mean while a positive Z-score indicates values higher than the mean. Safety population. Here, "number of participants analysed" refer to the participants evaluable for this endpoint. Change from baseline in body weight for age Z-Score at EOT of last cycle during teduglutide treatment was reported. Baseline refers to the baseline value of the core study (SHP633-302 [2020-005791-35]).

End point type	Primary
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End point timeframe:

Baseline, EOT of last cycle (up to Month 45) (Each Cycle 1 to 8 = 24 weeks, and Cycle 9 = 4 weeks)

Notes:

[12] - 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 comparison analyses were performed for this endpoint.

End point values	Total Children (Aged: 1 to 15 Years)	Infants (Corrected Gestational Age: 4 to < 12 Months)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	2		
Units: z-score				
arithmetic mean (standard deviation)	0.229 ($\pm$ 0.5636)	3.982 ($\pm$ 3.6363)		

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in Height For Age Z-Score at EOT of Cycle 1 During Teduglutide Treatment

End point title	Change From Baseline in Height For Age Z-Score at EOT of Cycle 1 During Teduglutide Treatment ^[13]
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End point description:

Height was measured using Age Z-Score. A Z-score was the deviation of the value for an individual from the mean value of the reference population divided by the standard deviation for the reference population. Centers for Disease Control and Prevention (age $\geq$ 2 years old) and World Health Organization (age < 2 years old) Z-score calculation charts were used for calculation. A negative Z-score indicates values lower than the mean while a positive Z-score indicates values higher than the mean. Safety population. Here, "number of participants analysed" refer to the participants evaluable for this endpoint. Change from baseline in height for age Z-Score at EOT of cycle 1 during teduglutide treatment was reported. Baseline refers to the baseline value of the core study (SHP633-302 [2020-005791-35]).

End point type	Primary
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End point timeframe:

Baseline, EOT of Cycle 1 (up to 24 Weeks)

Notes:

[13] - 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 comparison analyses were performed for this endpoint.

End point values	Total Children (Aged: 1 to 15 Years)	Infants (Corrected Gestational Age: 4 to < 12 Months)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	2		
Units: Z-score				
arithmetic mean (standard deviation)	0.002 ($\pm$ 0.6049)	1.376 ($\pm$ 0.3363)		

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in Height For Age Z-Score at EOT of Cycle 2 During Teduglutide Treatment

End point title	Change From Baseline in Height For Age Z-Score at EOT of Cycle 2 During Teduglutide Treatment ^[14]
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End point description:

Height was measured using Age Z-Score. A Z-score was the deviation of the value for an individual from the mean value of the reference population divided by the standard deviation for the reference population. Centers for Disease Control and Prevention (age $\geq$ 2 years old) and World Health Organization (age < 2 years old) Z-score calculation charts were used for calculation. A negative Z-score indicates values lower than the mean while a positive Z-score indicates values higher than the mean. Safety population. Here, "number of participants analysed" refer to the participants evaluable for this endpoint. Baseline refers to the baseline value of the core study (SHP633-302 [2020-005791-35]). Here, '99999' indicates that standard deviation could not be estimated for single subject for the specified arm.

End point type	Primary
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End point timeframe:

Baseline, EOT of Cycle 2 (up to 48 weeks)

Notes:

[14] - 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 comparison analyses were performed for this endpoint.

End point values	Total Children (Aged: 1 to 15 Years)	Infants (Corrected Gestational Age: 4 to < 12 Months)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	1		
Units: Z-score				
arithmetic mean (standard deviation)	0.152 (± 0.5181)	3.114 (± 99999)		

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in Height For Age Z-Score at EOT of Cycle 3 During Teduglutide Treatment

End point title	Change From Baseline in Height For Age Z-Score at EOT of Cycle 3 During Teduglutide Treatment ^[15]
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End point description:

Height was measured using Age Z-Score. A Z-score was the deviation of the value for an individual from the mean value of the reference population divided by the standard deviation for the reference population. Centers for Disease Control and Prevention (age ≥ 2 years old) and World Health Organization (age < 2 years old) Z-score calculation charts were used for calculation. A negative Z-score indicates values lower than the mean while a positive Z-score indicates values higher than the mean. Safety population. Here, "number of participants analysed" refer to the participants evaluable for this endpoint. Baseline refers to the baseline value of the core study (SHP633-302 [2020-005791-35]). Here, '99999' indicates that standard deviation could not be estimated for single subject for the specified arm.

End point type	Primary
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End point timeframe:

Baseline, EOT of Cycle 3 (up to 72 weeks)

Notes:

[15] - 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 comparison analyses were performed for this endpoint.

End point values	Total Children (Aged: 1 to 15 Years)	Infants (Corrected Gestational Age: 4 to < 12 Months)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	1		
Units: Z-score				
arithmetic mean (standard deviation)	0.098 (± 0.3467)	3.554 (± 99999)		

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in Height For Age Z-Score at EOT of Cycle 4 During

Teduglutide Treatment

End point title	Change From Baseline in Height For Age Z-Score at EOT of Cycle 4 During Teduglutide Treatment ^[16]
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End point description:

Height was measured using Age Z-Score. A Z-score was the deviation of the value for an individual from the mean value of the reference population divided by the standard deviation for the reference population. Centers for Disease Control and Prevention (age ≥ 2 years old) and World Health Organization (age < 2 years old) Z-score calculation charts were used for calculation. A negative Z-score indicates values lower than the mean while a positive Z-score indicates values higher than the mean. Safety population. Here, "number of participants analysed" refer to the participants evaluable for this endpoint. Baseline refers to the baseline value of the core study (SHP633-302 [2020-005791-35]). Here, '99999' indicates that standard deviation could not be estimated for single subject for the specified arm.

End point type	Primary
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End point timeframe:

Baseline, EOT of Cycle 4 (up to 96 weeks)

Notes:

[16] - 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 comparison analyses were performed for this endpoint.

End point values	Total Children (Aged: 1 to 15 Years)	Infants (Corrected Gestational Age: 4 to < 12 Months)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	1		
Units: Z-score				
arithmetic mean (standard deviation)	0.126 ($\pm$ 0.2622)	3.542 ($\pm$ 99999)		

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in Height For Age Z-Score at EOT of Cycle 5 During Teduglutide Treatment

End point title	Change From Baseline in Height For Age Z-Score at EOT of Cycle 5 During Teduglutide Treatment ^[17]
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End point description:

Height was measured using Age Z-Score. A Z-score was the deviation of the value for an individual from the mean value of the reference population divided by the standard deviation for the reference population. Centers for Disease Control and Prevention (age ≥ 2 years old) and World Health Organization (age < 2 years old) Z-score calculation charts were used for calculation. A negative Z-score indicates values lower than the mean while a positive Z-score indicates values higher than the mean. Safety population. Here, "number of participants analysed" refer to the participants evaluable for this endpoint. Baseline refers to the baseline value of the core study (SHP633-302 [2020-005791-35]).

End point type	Primary
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End point timeframe:

Baseline, EOT of Cycle 5 (up to 120 weeks)

Notes:

[17] - 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 comparison analyses were performed for this endpoint.

End point values	Total Children (Aged: 1 to 15 Years)	Infants (Corrected Gestational Age: 4 to < 12 Months)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	0 ^[18]		
Units: Z-score				
arithmetic mean (standard deviation)	0.342 (± 0.1012)	()		

Notes:

[18] - As no participant was analyzed for this arm, therefore data was not reported.

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in Height For Age Z-Score at EOT of Cycle 6 During Teduglutide Treatment

End point title	Change From Baseline in Height For Age Z-Score at EOT of Cycle 6 During Teduglutide Treatment ^[19]
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End point description:

Height was measured using Age Z-Score. A Z-score was the deviation of the value for an individual from the mean value of the reference population divided by the standard deviation for the reference population. Centers for Disease Control and Prevention (age ≥ 2 years old) and World Health Organization (age < 2 years old) Z-score calculation charts were used for calculation. A negative Z-score indicates values lower than the mean while a positive Z-score indicates values higher than the mean. Safety population. Here, "number of participants analysed" refer to the participants evaluable for this endpoint. Baseline refers to the baseline value of the core study (SHP633-302 [2020-005791-35]).

End point type	Primary
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End point timeframe:

Baseline, EOT of Cycle 6 (up to 144 weeks)

Notes:

[19] - 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 comparison analyses were performed for this endpoint.

End point values	Total Children (Aged: 1 to 15 Years)	Infants (Corrected Gestational Age: 4 to < 12 Months)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	0 ^[20]		
Units: Z-Score				
arithmetic mean (standard deviation)	0.276 (± 0.2593)	()		

Notes:

[20] - As no participant was analyzed for this arm, therefore data was not reported.

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in Height For Age Z-Score at EOT of Cycle 7 During Teduglutide Treatment

End point title	Change From Baseline in Height For Age Z-Score at EOT of Cycle 7 During Teduglutide Treatment ^[21]
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End point description:

Height was measured using Age Z-Score. A Z-score was the deviation of the value for an individual from the mean value of the reference population divided by the standard deviation for the reference population. Centers for Disease Control and Prevention (age ≥ 2 years old) and World Health Organization (age < 2 years old) Z-score calculation charts were used for calculation. A negative Z-score indicates values lower than the mean while a positive Z-score indicates values higher than the mean. Safety population. Here, "number of participants analysed" refer to the participants evaluable for this endpoint. Baseline refers to the baseline value of the core study (SHP633-302 [2020-005791-35]). Here, '99999' indicates that standard deviation could not be estimated for single subject for the specified arm.

End point type	Primary
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End point timeframe:

Baseline, EOT of Cycle 7 (up to 168 weeks)

Notes:

[21] - 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 comparison analyses were performed for this endpoint.

End point values	Total Children (Aged: 1 to 15 Years)	Infants (Corrected Gestational Age: 4 to < 12 Months)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1	0 ^[22]		
Units: Z-Score				
arithmetic mean (standard deviation)	0.570 (± 99999)	()		

Notes:

[22] - As no participant was analyzed for this arm, therefore data was not reported.

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in Height For Age Z-Score at EOT of Cycle 8 During Teduglutide Treatment

End point title	Change From Baseline in Height For Age Z-Score at EOT of Cycle 8 During Teduglutide Treatment ^[23]
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End point description:

Height was measured using Age Z-Score. A Z-score was the deviation of the value for an individual from the mean value of the reference population divided by the standard deviation for the reference population. Centers for Disease Control and Prevention (age ≥ 2 years old) and World Health Organization (age < 2 years old) Z-score calculation charts were used for calculation. A negative Z-score indicates values lower than the mean while a positive Z-score indicates values higher than the mean. Safety population. Here, "number of participants analysed" refer to the participants evaluable for this endpoint. Baseline refers to the baseline value of the core study (SHP633-302 [2020-005791-35]). Here, '99999' indicates that standard deviation could not be estimated for single subject for the specified arm.

End point type	Primary
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End point timeframe:

Baseline, EOT of Cycle 8 (up to 192 weeks)

Notes:

[23] - 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 comparison analyses were performed for this endpoint.

End point values	Total Children (Aged: 1 to 15 Years)	Infants (Corrected Gestational Age: 4 to < 12 Months)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1	0 ^[24]		
Units: Z-Score				
arithmetic mean (standard deviation)	0.851 (± 99999)	()		

Notes:

[24] - As no participant was analyzed for this arm, therefore data was not reported.

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in Height For Age Z-Score at EOT of Cycle 9 During Teduglutide Treatment

End point title	Change From Baseline in Height For Age Z-Score at EOT of Cycle 9 During Teduglutide Treatment ^[25]
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End point description:

Height was measured using Age Z-Score. A Z-score was the deviation of the value for an individual from the mean value of the reference population divided by the standard deviation for the reference population. Centers for Disease Control and Prevention (age ≥ 2 years old) and World Health Organization (age < 2 years old) Z-score calculation charts were used for calculation. A negative Z-score indicates values lower than the mean while a positive Z-score indicates values higher than the mean. Safety population. Here, "number of participants analysed" refer to the participants evaluable for this endpoint. Baseline refers to the baseline value of the core study (SHP633-302 [2020-005791-35]). Here, '99999' indicates that standard deviation could not be estimated for single subject for the specified arm.

End point type	Primary
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End point timeframe:

Baseline, EOT of Cycle 9 (up to 196 weeks)

Notes:

[25] - 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 comparison analyses were performed for this endpoint.

End point values	Total Children (Aged: 1 to 15 Years)	Infants (Corrected Gestational Age: 4 to < 12 Months)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1	0 ^[26]		
Units: Z-Score				
arithmetic mean (standard deviation)	0.477 (± 99999)	()		

Notes:

[26] - As no participant was analyzed for this arm, therefore data was not reported.

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in Head Circumference for Age Z-score at EOT of

Cycle 1 During Teduglutide Treatment

End point title	Change From Baseline in Head Circumference for Age Z-score at EOT of Cycle 1 During Teduglutide Treatment ^[27]
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End point description:

Head circumference was measured using Age Z-score. A Z-score was the deviation of the value for an individual from the mean value of the reference population divided by the standard deviation for the reference population. Centers for Disease Control and Prevention (age ≥ 2 years old) and World Health Organization (age < 2 years old) Z-score calculation charts were used for calculation. A negative Z-score indicates values lower than the mean while a positive Z-score indicates values higher than the mean. Safety population. Here, "number of participants analysed" refer to the participants evaluable for this endpoint. Baseline refers to the baseline value of the core study (SHP633-302 [2020-005791-35]).

End point type	Primary
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End point timeframe:

Baseline, EOT of Cycle 1 (up to 24 weeks)

Notes:

[27] - 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 comparison analyses were performed for this endpoint.

End point values	Total Children (Aged: 1 to 15 Years)	Infants (Corrected Gestational Age: 4 to < 12 Months)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0 ^[28]	2		
Units: Z-score				
arithmetic mean (standard deviation)	()	2.400 (± 0.6472)		

Notes:

[28] - As no participant was analyzed for this arm, therefore data was not reported.

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in Head Circumference for Age Z-score at EOT of Cycle 2 During Teduglutide Treatment

End point title	Change From Baseline in Head Circumference for Age Z-score at EOT of Cycle 2 During Teduglutide Treatment ^[29]
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End point description:

Head circumference was measured using Age Z-score. A Z-score was the deviation of the value for an individual from the mean value of the reference population divided by the standard deviation for the reference population. Centers for Disease Control and Prevention (age ≥ 2 years old) and World Health Organization (age < 2 years old) Z-score calculation charts were used for calculation. A negative Z-score indicates values lower than the mean while a positive Z-score indicates values higher than the mean. Safety population. Here, "number of participants analysed" refer to the participants evaluable for this endpoint. Baseline refers to the baseline value of the core study (SHP633-302 [2020-005791-35]). Here, '99999' indicates that standard deviation could not be estimated for single subject for the specified arm.

End point type	Primary
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End point timeframe:

Baseline, EOT of Cycle 2 (up to 48 weeks)

Notes:

[29] - 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 comparison analyses were performed for this endpoint.

End point values	Total Children (Aged: 1 to 15 Years)	Infants (Corrected Gestational Age: 4 to < 12 Months)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0 ^[30]	1		
Units: Z-score				
arithmetic mean (standard deviation)	()	1.431 (± 99999)		

Notes:

[30] - As no participant was analyzed for this arm, therefore data was not reported.

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in Head Circumference for Age Z-score at EOT of Cycle 3 During Teduglutide Treatment

End point title	Change From Baseline in Head Circumference for Age Z-score at EOT of Cycle 3 During Teduglutide Treatment ^[31]
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End point description:

Head circumference was measured using Age Z-score. A Z-score was the deviation of the value for an individual from the mean value of the reference population divided by the standard deviation for the reference population. Centers for Disease Control and Prevention (age ≥ 2 years old) and World Health Organization (age < 2 years old) Z-score calculation charts were used for calculation. A negative Z-score indicates values lower than the mean while a positive Z-score indicates values higher than the mean. Safety population. Here, "number of participants analysed" refer to the participants evaluable for this endpoint. Baseline refers to the baseline value of the core study (SHP633-302 [2020-005791-35]). Here, '99999' indicates that standard deviation could not be estimated for single subject for the specified arm.

End point type	Primary
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End point timeframe:

Baseline, EOT of Cycle 3 (up to 72 weeks)

Notes:

[31] - 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 comparison analyses were performed for this endpoint.

End point values	Total Children (Aged: 1 to 15 Years)	Infants (Corrected Gestational Age: 4 to < 12 Months)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0 ^[32]	1		
Units: Z-score				
arithmetic mean (standard deviation)	()	2.080 (± 99999)		

Notes:

[32] - As no participant was analyzed for this arm, therefore data was not reported.

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in Head Circumference for Age Z-score at EOT of

Cycle 4 During Teduglutide Treatment

End point title	Change From Baseline in Head Circumference for Age Z-score at EOT of Cycle 4 During Teduglutide Treatment ^[33]
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End point description:

Head circumference was measured using Age Z-score. A Z-score was the deviation of the value for an individual from the mean value of the reference population divided by the standard deviation for the reference population. Centers for Disease Control and Prevention (age ≥ 2 years old) and World Health Organization (age < 2 years old) Z-score calculation charts were used for calculation. A negative Z-score indicates values lower than the mean while a positive Z-score indicates values higher than the mean. Safety population. Here, "number of participants analysed" refer to the participants evaluable for this endpoint. Baseline refers to the baseline value of the core study (SHP633-302 [2020-005791-35]). Here, '99999' indicates that standard deviation could not be estimated for single subject for the specified arm.

End point type	Primary
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End point timeframe:

Baseline, EOT of Cycle 4 (up to 76 weeks)

Notes:

[33] - 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 comparison analyses were performed for this endpoint.

End point values	Total Children (Aged: 1 to 15 Years)	Infants (Corrected Gestational Age: 4 to < 12 Months)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0 ^[34]	1		
Units: Z-score				
arithmetic mean (standard deviation)	()	2.055 (± 99999)		

Notes:

[34] - As no participant was analyzed for this arm, therefore data was not reported.

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in Body Mass Index (BMI) for Age Z-score at EOT of Cycle 1 During Teduglutide Treatment

End point title	Change From Baseline in Body Mass Index (BMI) for Age Z-score at EOT of Cycle 1 During Teduglutide Treatment ^[35]
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End point description:

BMI Z-score was calculated by using the height and weight Age Z-score. A Z-score was the deviation of the value for an individual from the mean value of the reference population divided by the standard deviation for the reference population. Centers for Disease Control and Prevention (age ≥ 2 years old) and World Health Organization (age < 2 years old) Z-score calculation charts were used for calculation. A negative Z-score indicates values lower than the mean while a positive Z-score indicates values higher than the mean. Safety population. Here, "number of participants analysed" refer to the participants evaluable for this endpoint. Baseline refers to the baseline value of the core study (SHP633-302 [2020-005791-35]).

End point type	Primary
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End point timeframe:

Baseline, EOT of Cycle 1 (up to 24 weeks)

Notes:

[35] - 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 comparison analyses were performed for this endpoint.

End point values	Total Children (Aged: 1 to 15 Years)	Infants (Corrected Gestational Age: 4 to < 12 Months)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	0 ^[36]		
Units: Z-score				
arithmetic mean (standard deviation)	0.090 (± 0.6642)	()		

Notes:

[36] - As no participant was analyzed for this arm, therefore data was not reported.

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in BMI for Age Z-score at EOT of Cycle 2 During Teduglutide Treatment

End point title	Change From Baseline in BMI for Age Z-score at EOT of Cycle 2 During Teduglutide Treatment ^[37]
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End point description:

BMI Z-score was calculated by using the height and weight Age Z-score. A Z-score was the deviation of the value for an individual from the mean value of the reference population divided by the standard deviation for the reference population. Centers for Disease Control and Prevention (age ≥ 2 years old) and World Health Organization (age < 2 years old) Z-score calculation charts were used for calculation. A negative Z-score indicates values lower than the mean while a positive Z-score indicates values higher than the mean. Safety population. Here, "number of participants analysed" refer to the participants evaluable for this endpoint. Baseline refers to the baseline value of the core study (SHP633-302 [2020-005791-35]).

End point type	Primary
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End point timeframe:

Baseline, EOT of Cycle 2 (up to 48 weeks)

Notes:

[37] - 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 comparison analyses were performed for this endpoint.

End point values	Total Children (Aged: 1 to 15 Years)	Infants (Corrected Gestational Age: 4 to < 12 Months)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	0 ^[38]		
Units: Z-score				
arithmetic mean (standard deviation)	0.489 (± 0.8474)	()		

Notes:

[38] - As no participant was analyzed for this arm, therefore data was not reported.

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in BMI for Age Z-score at EOT of Cycle 3 During

Teduglutide Treatment

End point title	Change From Baseline in BMI for Age Z-score at EOT of Cycle 3 During Teduglutide Treatment ^[39]
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End point description:

BMI Z-score was calculated by using the height and weight Age Z-score. A Z-score was the deviation of the value for an individual from the mean value of the reference population divided by the standard deviation for the reference population. Centers for Disease Control and Prevention (age ≥ 2 years old) and World Health Organization (age < 2 years old) Z-score calculation charts were used for calculation. A negative Z-score indicates values lower than the mean while a positive Z-score indicates values higher than the mean. Safety population. Here, "number of participants analysed" refer to the participants evaluable for this endpoint. Baseline refers to the baseline value of the core study (SHP633-302 [2020-005791-35]).

End point type	Primary
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End point timeframe:

Baseline, EOT of Cycle 3 (up to 72 weeks)

Notes:

[39] - 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 comparison analyses were performed for this endpoint.

End point values	Total Children (Aged: 1 to 15 Years)	Infants (Corrected Gestational Age: 4 to < 12 Months)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	0 ^[40]		
Units: Z-score				
arithmetic mean (standard deviation)	0.409 ($\pm$ 1.1688)	()		

Notes:

[40] - As no participant was analyzed for this arm, therefore data was not reported.

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in BMI for Age Z-score at EOT of Cycle 4 During Teduglutide Treatment

End point title	Change From Baseline in BMI for Age Z-score at EOT of Cycle 4 During Teduglutide Treatment ^[41]
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End point description:

BMI Z-score was calculated by using the height and weight Age Z-score. A Z-score was the deviation of the value for an individual from the mean value of the reference population divided by the standard deviation for the reference population. Centers for Disease Control and Prevention (age ≥ 2 years old) and World Health Organization (age < 2 years old) Z-score calculation charts were used for calculation. A negative Z-score indicates values lower than the mean while a positive Z-score indicates values higher than the mean. Safety population. Here, "number of participants analysed" refer to the participants evaluable for this endpoint. Baseline refers to the baseline value of the core study (SHP633-302 [2020-005791-35]).

End point type	Primary
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End point timeframe:

Baseline, EOT of Cycle 4 (up to 96 weeks)

Notes:

[41] - 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 comparison analyses were performed for this endpoint.

End point values	Total Children (Aged: 1 to 15 Years)	Infants (Corrected Gestational Age: 4 to < 12 Months)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	0 ^[42]		
Units: Z-score				
arithmetic mean (standard deviation)	0.118 (± 0.8827)	()		

Notes:

[42] - As no participant was analyzed for this arm, therefore data was not reported.

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in BMI for Age Z-score at EOT of Cycle 5 During Teduglutide Treatment

End point title	Change From Baseline in BMI for Age Z-score at EOT of Cycle 5 During Teduglutide Treatment ^[43]
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End point description:

BMI Z-score was calculated by using the height and weight Age Z-score. A Z-score was the deviation of the value for an individual from the mean value of the reference population divided by the standard deviation for the reference population. Centers for Disease Control and Prevention (age ≥ 2 years old) and World Health Organization (age < 2 years old) Z-score calculation charts were used for calculation. A negative Z-score indicates values lower than the mean while a positive Z-score indicates values higher than the mean. Safety population. Here, "number of participants analysed" refer to the participants evaluable for this endpoint. Baseline refers to the baseline value of the core study (SHP633-302 [2020-005791-35]).

End point type	Primary
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End point timeframe:

Baseline, EOT of Cycle 5 (up to 120 weeks)

Notes:

[43] - 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 comparison analyses were performed for this endpoint.

End point values	Total Children (Aged: 1 to 15 Years)	Infants (Corrected Gestational Age: 4 to < 12 Months)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	0 ^[44]		
Units: Z-score				
arithmetic mean (standard deviation)	0.070 (± 0.9770)	()		

Notes:

[44] - As no participant was analyzed for this arm, therefore data was not reported.

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in BMI for Age Z-score at EOT of Cycle 6 During

Teduglutide Treatment

End point title	Change From Baseline in BMI for Age Z-score at EOT of Cycle 6 During Teduglutide Treatment ^[45]
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End point description:

BMI Z-score was calculated by using the height and weight Age Z-score. A Z-score was the deviation of the value for an individual from the mean value of the reference population divided by the standard deviation for the reference population. Centers for Disease Control and Prevention (age ≥ 2 years old) and World Health Organization (age < 2 years old) Z-score calculation charts were used for calculation. A negative Z-score indicates values lower than the mean while a positive Z-score indicates values higher than the mean. Safety population. Here, "number of participants analysed" refer to the participants evaluable for this endpoint. Baseline refers to the baseline value of the core study (SHP633-302 [2020-005791-35]).

End point type	Primary
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End point timeframe:

Baseline, EOT of Cycle 6 (up to 144 weeks)

Notes:

[45] - 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 comparison analyses were performed for this endpoint.

End point values	Total Children (Aged: 1 to 15 Years)	Infants (Corrected Gestational Age: 4 to < 12 Months)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	0 ^[46]		
Units: Z-score				
arithmetic mean (standard deviation)	0.925 ($\pm$ 0.2556)	()		

Notes:

[46] - As no participant was analyzed for this arm, therefore data was not reported.

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in BMI for Age Z-score at EOT of Cycle 7 During Teduglutide Treatment

End point title	Change From Baseline in BMI for Age Z-score at EOT of Cycle 7 During Teduglutide Treatment ^[47]
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End point description:

BMI Z-score was calculated by using the height and weight Age Z-score. A Z-score was the deviation of the value for an individual from the mean value of the reference population divided by the standard deviation for the reference population. Centers for Disease Control and Prevention (age ≥ 2 years old) and World Health Organization (age < 2 years old) Z-score calculation charts were used for calculation. A negative Z-score indicates values lower than the mean while a positive Z-score indicates values higher than the mean. Safety population. Here, "number of participants analysed" refer to the participants evaluable for this endpoint. Baseline refers to the baseline value of the core study (SHP633-302 [2020-005791-35]). Here, '99999' indicates that standard deviation could not be estimated for single subject for the specified arm.

End point type	Primary
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End point timeframe:

Baseline, EOT of Cycle 7 (up to 168 weeks)

Notes:

[47] - 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 comparison analyses were performed for this endpoint.

End point values	Total Children (Aged: 1 to 15 Years)	Infants (Corrected Gestational Age: 4 to < 12 Months)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1	0 ^[48]		
Units: Z-score				
arithmetic mean (standard deviation)	0.839 (± 99999)	()		

Notes:

[48] - As no participant was analyzed for this arm, therefore data was not reported.

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in BMI for Age Z-score at EOT of Cycle 8 During Teduglutide Treatment

End point title	Change From Baseline in BMI for Age Z-score at EOT of Cycle 8 During Teduglutide Treatment ^[49]
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End point description:

BMI Z-score was calculated by using the height and weight Age Z-score. A Z-score was the deviation of the value for an individual from the mean value of the reference population divided by the standard deviation for the reference population. Centers for Disease Control and Prevention (age ≥ 2 years old) and World Health Organization (age < 2 years old) Z-score calculation charts were used for calculation. A negative Z-score indicates values lower than the mean while a positive Z-score indicates values higher than the mean. Safety population. Here, "number of participants analysed" refer to the participants evaluable for this endpoint. Baseline refers to the baseline value of the core study (SHP633-302 [2020-005791-35]). Here, '99999' indicates that standard deviation could not be estimated for single subject for the specified arm.

End point type	Primary
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End point timeframe:

Baseline, EOT of Cycle 8 (up to 192 weeks)

Notes:

[49] - 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 comparison analyses were performed for this endpoint.

End point values	Total Children (Aged: 1 to 15 Years)	Infants (Corrected Gestational Age: 4 to < 12 Months)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1	0 ^[50]		
Units: Z-score				
arithmetic mean (standard deviation)	0.015 (± 99999)	()		

Notes:

[50] - As no participant was analyzed for this arm, therefore data was not reported.

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in BMI for Age Z-score at EOT of Cycle 9 During

Teduglutide Treatment

End point title	Change From Baseline in BMI for Age Z-score at EOT of Cycle 9 During Teduglutide Treatment ^[51]
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End point description:

BMI Z-score was calculated by using the height and weight Age Z-score. A Z-score was the deviation of the value for an individual from the mean value of the reference population divided by the standard deviation for the reference population. Centers for Disease Control and Prevention (age ≥ 2 years old) and World Health Organization (age < 2 years old) Z-score calculation charts were used for calculation. A negative Z-score indicates values lower than the mean while a positive Z-score indicates values higher than the mean. Safety population. Here, "number of participants analysed" refer to the participants evaluable for this endpoint. Baseline refers to the baseline value of the core study (SHP633-302 [2020-005791-35]). Here, '99999' indicates that standard deviation could not be estimated for single subject for the specified arm.

End point type	Primary
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End point timeframe:

Baseline, EOT of Cycle 9 (up to 196 weeks)

Notes:

[51] - 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 comparison analyses were performed for this endpoint.

End point values	Total Children (Aged: 1 to 15 Years)	Infants (Corrected Gestational Age: 4 to < 12 Months)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1	0 ^[52]		
Units: Z-score				
arithmetic mean (standard deviation)	0.480 (± 99999)	()		

Notes:

[52] - As no participant was analyzed for this arm, therefore data was not reported.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants Who Achieved At Least 20 Percent (%) Reduction From Baseline in Participants Diary Parenteral Support (PS) Volume at EOT of Each Cycle During Teduglutide Treatment

End point title	Number of Participants Who Achieved At Least 20 Percent (%) Reduction From Baseline in Participants Diary Parenteral Support (PS) Volume at EOT of Each Cycle During Teduglutide Treatment
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End point description:

PS (parenteral nutrition or intravenous fluids) was considered for managing nutritional support in terms of volume during the treatment period. Percent reduction in weight-normalized diary PS values from baseline was calculated using the formula: % reduction in PS value at the visit = ([average daily value at the scheduled visit – average daily value at baseline of the core study (SHP633-302 [2020-005791-35]) / average daily value at baseline of the core study (SHP633-302 [2020-005791-35])) * 100. Number of participants who achieved at least 20% reduction from baseline in participants diary PS volume at EOT of each cycle during teduglutide treatment were reported. Baseline refers to the baseline value of the core study (SHP633-302 [2020-005791-35]). Safety population. Here, "number of participants analysed" signifies participants who were evaluable for this endpoint and "n" signifies to participants evaluable at given timepoints.

End point type	Secondary
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End point timeframe:

Baseline, EOT of each cycle 1, 2, 3, 4, 5, 6, 7, 8 and 9 (Each Cycle 1 to 8 = 24 weeks, and Cycle 9 = 4

End point values	Total Children (Aged: 1 to 15 Years)	Infants (Corrected Gestational Age: 4 to < 12 Months)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	2		
Units: Participants				
At EOT of Cycle 1 (n= 6, 2)	4	1		
At EOT of Cycle 2 (n= 6, 1)	4	1		
At EOT of Cycle 3 (n= 6, 1)	6	1		
At EOT of Cycle 4 (n= 5, 1)	5	1		
At EOT of Cycle 5 (n= 3, 0)	3	0		
At EOT of Cycle 6 (n= 2, 0)	2	0		
At EOT of Cycle 7 (n= 1, 0)	1	0		
At EOT of Cycle 8 (n= 1, 0)	1	0		
At EOT of Cycle 9 (n= 1, 0)	1	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants Who Achieved At Least 20 Percent (%) Reduction From Baseline in Investigator Prescribed PS Volume at EOT of Each Cycle During Teduglutide Treatment

End point title	Number of Participants Who Achieved At Least 20 Percent (%) Reduction From Baseline in Investigator Prescribed PS Volume at EOT of Each Cycle During Teduglutide Treatment
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End point description:

PS (parenteral nutrition or intravenous fluids) was considered for managing nutritional support in terms of volume during the treatment period. Percent reduction in weight-normalized prescribed PS values from baseline was calculated using the formula: % reduction in PS value at the visit = ([average daily value at the scheduled visit – average daily value at baseline of the core study (SHP633-302 [2020-005791-35]) / average daily value at baseline of the core study (SHP633-302 [2020-005791-35])) *100. Number of participants who achieved at least 20% reduction from baseline in investigator prescribed PS volume at EOT of each cycle during teduglutide treatment were reported. Baseline refers to the baseline value of the core study (SHP633-302 [2020-005791-35]). Safety population. Here, "number of participants analysed" signifies participants who were evaluable for this endpoint and "n" signifies to participants evaluable at given timepoints.

End point type	Secondary
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End point timeframe:

Baseline, EOT of each cycle 1, 2, 3, 4, 5, 6, 7, 8 and 9 (Each Cycle 1 to 8 = 24 weeks, and Cycle 9 = 4 weeks)

End point values	Total Children (Aged: 1 to 15 Years)	Infants (Corrected Gestational Age: 4 to < 12 Months)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	2		
Units: Participants				
At EOT of Cycle 1 (n= 6, 2)	5	1		
At EOT of Cycle 2 (n= 6, 1)	5	1		
At EOT of Cycle 3 (n= 6, 1)	6	1		
At EOT of Cycle 4 (n= 5, 1)	5	1		
At EOT of Cycle 5 (n= 3, 0)	3	0		
At EOT of Cycle 6 (n= 2, 0)	2	0		
At EOT of Cycle 7 (n= 1, 0)	1	0		
At EOT of Cycle 8 (n= 1, 0)	1	0		
At EOT of Cycle 9 (n= 1, 0)	1	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Participant Diary PS Volume at EOT of Each Cycle During Teduglutide Treatment

End point title	Change From Baseline in Participant Diary PS Volume at EOT of Each Cycle During Teduglutide Treatment
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End point description:

PS (parenteral nutrition or intravenous fluids) was considered for managing nutritional support in terms of volume during the treatment period. Change from baseline in participants diary PS volume at EOT of each cycle during teduglutide treatment was reported. Baseline refers to the baseline value of the core study (SHP633-302 [2020-005791-35]). Safety population. Here, "number of participants analysed" signifies participants who were evaluable for this endpoint and "n" signifies to participants evaluable at given timepoints. Here, '99999' indicates that standard deviation could not be estimated for single subject for the specified arm.

End point type	Secondary
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End point timeframe:

Baseline, EOT of each cycle 1, 2, 3, 4, 5, 6, 7, 8 and 9 (Each Cycle 1 to 8 = 24 weeks, and Cycle 9 = 4 weeks)

End point values	Total Children (Aged: 1 to 15 Years)	Infants (Corrected Gestational Age: 4 to < 12 Months)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	2		
Units: mL/kg/day				
arithmetic mean (standard deviation)				
Change at EOT of Cycle 1 (n= 6, 2)	-21.5 (± 11.83)	-31.9 (± 16.24)		

Change at EOT of Cycle 2 (n= 6, 1)	-25.5 (± 14.38)	-54.2 (± 99999)		
Change at EOT of Cycle 3 (n= 6, 1)	-32.1 (± 18.19)	-62.8 (± 99999)		
Change at EOT of Cycle 4 (n= 5, 1)	-37.2 (± 24.10)	-95.8 (± 99999)		
Change at EOT of Cycle 5 (n= 3, 0)	-54.8 (± 26.58)	9999 (± 9999)		
Change at EOT of Cycle 6 (n= 2, 0)	-63.8 (± 31.57)	9999 (± 9999)		
Change at EOT of Cycle 7 (n= 1, 0)	-93.8 (± 99999)	9999 (± 9999)		
Change at EOT of Cycle 8 (n= 1, 0)	-80.3 (± 99999)	9999 (± 9999)		
Change at EOT of Cycle 9 (n= 1, 0)	-79.1 (± 99999)	9999 (± 9999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in Participant Diary PS Volume at EOT of Each Cycle During Teduglutide Treatment

End point title	Percent Change From Baseline in Participant Diary PS Volume at EOT of Each Cycle During Teduglutide Treatment
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End point description:

PS (parenteral nutrition or intravenous fluids) was considered for managing nutritional support in terms of volume during the treatment period. Percent change from baseline in participants diary PS volume at EOT of each cycle during teduglutide treatment was reported. Baseline refers to the baseline value of the core study (SHP633-302 [2020-005791-35]). Safety population. Here, "number of participants analysed" signifies participants who were evaluable for this endpoint and "n" signifies to participants evaluable at given timepoints. Here, '99999' indicates that standard deviation could not be estimated for single subject for the specified arm.

End point type	Secondary
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End point timeframe:

Baseline, EOT of each cycle 1, 2, 3, 4, 5, 6, 7, 8 and 9 (Each Cycle 1 to 8 = 24 weeks, and Cycle 9 = 4 weeks)

End point values	Total Children (Aged: 1 to 15 Years)	Infants (Corrected Gestational Age: 4 to < 12 Months)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	2		
Units: Percent change				
arithmetic mean (standard deviation)				
Percent change at EOT of Cycle 1 (n=6, 2)	-39.6 (± 34.86)	-32.5 (± 18.10)		
Percent change at EOT of Cycle 2 (n=6, 1)	-44.3 (± 33.11)	-56.6 (± 99999)		
Percent change at EOT of Cycle 3 (n=6, 1)	-52.8 (± 28.54)	-65.6 (± 99999)		

Percent change at EOT of Cycle 4 (n=5, 1)	-62.9 (± 26.18)	-100.0 (± 99999)		
Percent change at EOT of Cycle 5 (n=3, 0)	-73.9 (± 5.30)	9999 (± 9999)		
Percent change at EOT of Cycle 6 (n=2, 0)	-75.7 (± 0.54)	9999 (± 9999)		
Percent change at EOT of Cycle 7 (n=1, 0)	-82.9 (± 99999)	9999 (± 9999)		
Percent change at EOT of Cycle 8 (n=1, 0)	-70.9 (± 99999)	9999 (± 9999)		
Percent change at EOT of Cycle 9 (n=1, 0)	-69.8 (± 99999)	9999 (± 9999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Investigator Prescribed PS Volume at EOT of Each Cycle During Teduglutide Treatment

End point title	Change From Baseline in Investigator Prescribed PS Volume at EOT of Each Cycle During Teduglutide Treatment
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End point description:

PS (parenteral nutrition or intravenous fluids) was considered for managing nutritional support in terms of volume during the treatment period. Change from baseline in investigator prescribed PS volume at EOT of each cycle during teduglutide treatment was reported. Baseline refers to the baseline value of the core study (SHP633-302 [2020-005791-35]). Safety population. Here, "number of participants analysed" signifies participants who were evaluable for this endpoint and "n" signifies to participants evaluable at given timepoints. Here, '99999' indicates that standard deviation could not be estimated for single subject for the specified arm.

End point type	Secondary
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End point timeframe:

Baseline, EOT of each cycle 1, 2, 3, 4, 5, 6, 7, 8 and 9 (Each Cycle 1 to 8 = 24 weeks, and Cycle 9 = 4 weeks)

End point values	Total Children (Aged: 1 to 15 Years)	Infants (Corrected Gestational Age: 4 to < 12 Months)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	2		
Units: mL/kg/day				
arithmetic mean (standard deviation)				
Change at EOT of Cycle 1 (n= 6, 2)	-20.9 (± 11.06)	-31.3 (± 26.77)		
Change at EOT of Cycle 2 (n= 6, 1)	-28.0 (± 13.51)	-60.6 (± 99999)		
Change at EOT of Cycle 3 (n= 6, 1)	-34.8 (± 21.13)	-67.5 (± 99999)		
Change at EOT of Cycle 4 (n= 5, 1)	-36.3 (± 23.52)	-98.7 (± 99999)		
Change at EOT of Cycle 5 (n= 3, 0)	-53.3 (± 26.24)	9999 (± 9999)		

Change at EOT of Cycle 6 (n= 2, 0)	-63.6 (± 32.10)	9999 (± 9999)		
Change at EOT of Cycle 7 (n= 1, 0)	-91.8 (± 99999)	9999 (± 9999)		
Change at EOT of Cycle 8 (n= 1, 0)	-77.3 (± 99999)	9999 (± 9999)		
Change at EOT of Cycle 9 (n= 1, 0)	-77.9 (± 99999)	9999 (± 9999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in Investigator Prescribed PS Volume at EOT of Each Cycle During Teduglutide Treatment

End point title	Percent Change From Baseline in Investigator Prescribed PS Volume at EOT of Each Cycle During Teduglutide Treatment
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End point description:

PS (parenteral nutrition or intravenous fluids) was considered for managing nutritional support in terms of volume during the treatment period. Percent change from baseline in investigator prescribed PS volume at EOT of each cycle during teduglutide treatment was reported. Baseline refers to the baseline value of the core study (SHP633-302 [2020-005791-35]). Safety population. Here, "number of participants analysed" signifies participants who were evaluable for this endpoint and "n" signifies to participants evaluable at given timepoints. Here, '99999' indicates that standard deviation could not be estimated for single subject for the specified arm.

End point type	Secondary
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End point timeframe:

Baseline, EOT of each cycle 1, 2, 3, 4, 5, 6, 7, 8 and 9 (Each Cycle 1 to 8 = 24 weeks, and Cycle 9 = 4 weeks)

End point values	Total Children (Aged: 1 to 15 Years)	Infants (Corrected Gestational Age: 4 to < 12 Months)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	2		
Units: Percent change				
arithmetic mean (standard deviation)				
Percent change at EOT of Cycle 1 (n= 6, 2)	-38.8 (± 35.19)	-32.1 (± 26.51)		
Percent change at EOT of Cycle 2 (n= 6, 1)	-46.9 (± 30.42)	-61.4 (± 99999)		
Percent change at EOT of Cycle 3 (n= 6, 1)	-55.4 (± 27.78)	-68.3 (± 99999)		
Percent change at EOT of Cycle 4 (n= 5, 1)	-62.5 (± 26.45)	-100.0 (± 99999)		
Percent change at EOT of Cycle 5 (n= 3, 0)	-73.3 (± 5.51)	9999 (± 9999)		
Percent change at EOT of Cycle 6 (n= 2, 0)	-76.3 (± 2.41)	9999 (± 9999)		
Percent change at EOT of Cycle 7 (n= 1, 0)	-83.0 (± 99999)	9999 (± 9999)		

Percent change at EOT of Cycle 8 (n= 1, 0)	-69.9 (± 99999)	9999 (± 9999)		
Percent change at EOT of Cycle 9 (n= 1, 0)	-70.5 (± 99999)	9999 (± 9999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants Who Achieved Enteral Autonomy PS Volume at EOT of Each Cycle During Teduglutide Treatment

End point title	Number of Participants Who Achieved Enteral Autonomy PS Volume at EOT of Each Cycle During Teduglutide Treatment
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End point description:

Enteral autonomy (completely weaned off PS) was defined as the first visit where there is no use of PS for the 7 days prior to the visit and there is no prescribed PS at that visit, and the participants remains off PS for the remainder of the treatment period of that cycle. Number of participants who achieved enteral autonomy off PS volume at EOT of each cycle during teduglutide treatment were reported. Safety population. Here, "number of participants analysed" signifies participants who were evaluable for this endpoint and "n" signifies to participants evaluable at given timepoints. Baseline refers to the baseline value of the core study (SHP633-302 [2021-005404-36]). Here, '99999' indicates that standard deviation could not be estimated for single subject for the specified arm.

End point type	Secondary
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End point timeframe:

Baseline, EOT of each cycle 1, 2, 3, 4, 5, 6, 7, 8 and 9 (Each Cycle 1 to 8 = 24 weeks, and Cycle 9 = 4 weeks)

End point values	Total Children (Aged: 1 to 15 Years)	Infants (Corrected Gestational Age: 4 to < 12 Months)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	2		
Units: Participants				
At EOT of Cycle 1 (n= 6, 2)	1	0		
At EOT of Cycle 2 (n= 6, 1)	1	0		
At EOT of Cycle 3 (n= 6, 1)	1	0		
At EOT of Cycle 4 (n= 5, 1)	1	1		
At EOT of Cycle 5 (n= 3, 0)	0	0		
At EOT of Cycle 6 (n= 2, 0)	0	0		
At EOT of Cycle 7 (n= 1, 0)	0	0		
At EOT of Cycle 8 (n= 1, 0)	0	0		
At EOT of Cycle 9 (n= 1, 0)	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Days Per Week of Diary PS Usage at EOT of Each Cycle During Teduglutide Treatment

End point title	Change From Baseline in Days Per Week of Diary PS Usage at EOT of Each Cycle During Teduglutide Treatment
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End point description:

Days per week of diary PS was calculated as: Days per week of actual PS = (number of days with non-zero values for PS volume within the 7 days prior to the visit / number of days for which any PS intake data was recorded within the 7 days prior to the visit) * 7. Change from baseline in days per week of diary PS usage at EOT of each cycle during teduglutide treatment was reported. Safety population. Here, "number of participants analysed" signifies participants who were evaluable for this endpoint and "n" signifies to participants evaluable at given timepoints. Baseline refers to the baseline value of the core study (SHP633-302 [2021-005404-36]). Here, '99999' indicates that standard deviation could not be estimated for single subject for the specified arm and "9999" indicates mean and SD could not estimated as no participant were analysed for specified arm

End point type	Secondary
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End point timeframe:

Baseline, EOT of each cycle 1, 2, 3, 4, 5, 6, 7, 8 and 9 (Each Cycle 1 to 8 = 24 weeks, and Cycle 9 = 4 weeks)

End point values	Total Children (Aged: 1 to 15 Years)	Infants (Corrected Gestational Age: 4 to < 12 Months)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	2		
Units: Days/week				
arithmetic mean (standard deviation)				
Change at EOT of Cycle 1 (n= 6, 2)	-1.2 (± 2.86)	0.0 (± 0.00)		
Change at EOT of Cycle 2 (n= 6, 1)	-1.2 (± 2.86)	0.0 (± 99999)		
Change at EOT of Cycle 3 (n= 6, 1)	-1.2 (± 2.86)	0.0 (± 99999)		
Change at EOT of Cycle 4 (n= 5, 1)	-1.4 (± 3.13)	-7.0 (± 99999)		
Change at EOT of Cycle 5 (n= 3, 0)	0.0 (± 0.00)	9999 (± 9999)		
Change at EOT of Cycle 6 (n= 2, 0)	0.0 (± 0.00)	9999 (± 9999)		
Change at EOT of Cycle 7 (n= 1, 0)	0.0 (± 99999)	9999 (± 9999)		
Change at EOT of Cycle 8 (n= 1, 0)	0.0 (± 99999)	9999 (± 9999)		
Change at EOT of Cycle 9 (n= 1, 0)	0.0 (± 99999)	9999 (± 9999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Days Per Week of Prescribed PS Usage at EOT of Each Cycle During Teduglutide Treatment

End point title	Change From Baseline in Days Per Week of Prescribed PS Usage at EOT of Each Cycle During Teduglutide Treatment
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End point description:

Days per week of Prescribed PS was calculated as: Days per week of actual PS = (number of days with non-zero values for PS volume within the 7 days prior to the visit / number of days for which any PS intake data was recorded within the 7 days prior to the visit) * 7. Change from baseline in days Per week of prescribed PS usage at EOT of each cycle during teduglutide treatment was reported. Safety

population. Here, "number of participants analysed" signifies participants who were evaluable for this endpoint and "n" signifies to participants evaluable at given timepoints. Baseline refers to the baseline value of the core study (SHP633-302 [2021-005404-36]). Here, '99999' indicates that standard deviation could not be estimated for single subject for the specified arm and "9999" indicates mean and SD could not be estimated as no participant were analysed for specified arm.

End point type	Secondary
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End point timeframe:

Baseline, EOT of each cycle 1, 2, 3, 4, 5, 6, 7, 8 and 9 (Each Cycle 1 to 8 = 24 weeks, and Cycle 9 = 4 weeks)

End point values	Total Children (Aged: 1 to 15 Years)	Infants (Corrected Gestational Age: 4 to < 12 Months)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	2		
Units: Days/week				
arithmetic mean (standard deviation)				
Change at EOT of Cycle 1 (n= 6, 2)	-1.2 (± 2.86)	0.0 (± 0.00)		
Change at EOT of Cycle 2 (n= 6, 1)	-1.2 (± 2.86)	0.0 (± 99999)		
Change at EOT of Cycle 3 (n= 6, 1)	-1.2 (± 2.86)	0.0 (± 99999)		
Change at EOT of Cycle 4 (n= 5, 1)	-1.4 (± 3.13)	-7.0 (± 99999)		
Change at EOT of Cycle 5 (n= 3, 0)	0.0 (± 0.00)	9999 (± 9999)		
Change at EOT of Cycle 6 (n= 2, 0)	0.0 (± 0.00)	9999 (± 9999)		
Change at EOT of Cycle 7 (n= 1, 0)	0.0 (± 99999)	9999 (± 9999)		
Change at EOT of Cycle 8 (n= 1, 0)	0.0 (± 99999)	9999 (± 9999)		
Change at EOT of Cycle 9 (n= 1, 0)	0.0 (± 99999)	9999 (± 9999)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From baseline up to follow-up (up to 50 months)

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	20.0
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Reporting groups

Reporting group title	Infants (Corrected Gestational Age: 4 to < 12 Months)
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Reporting group description:

Participants (Infants) from 4 through < 12 months of corrected gestational age who participated in the core study (SHP633-302 [2020-005791-35]) were enrolled into this extension study and received teduglutide 0.05 mg/kg SC injection for 24 weeks in each treatment cycle (Cycles 1 to 9 [Each cycle=28 weeks]) depending on the disease course.

Reporting group title	Total Children (Aged: 1 to 15 Years)
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Reporting group description:

Participants aged from 1 through 15 years who participated in the core study (SHP633-302 [2020-005791-35]) were enrolled into this extension study and received teduglutide 0.05 mg/kg SC injection for 24 weeks in each treatment cycle (Cycles 1 to 9 [Each cycle=28 weeks]) depending on the disease course.

Serious adverse events	Infants (Corrected Gestational Age: 4 to < 12 Months)	Total Children (Aged: 1 to 15 Years)	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 2 (100.00%)	7 / 7 (100.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Surgical and medical procedures			
Central venous catheter removal			
subjects affected / exposed	0 / 2 (0.00%)	1 / 7 (14.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Seizure			
subjects affected / exposed	1 / 2 (50.00%)	0 / 7 (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			
Pyrexia			

subjects affected / exposed	0 / 2 (0.00%)	1 / 7 (14.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Colonic haematoma			
subjects affected / exposed	0 / 2 (0.00%)	1 / 7 (14.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enteritis			
subjects affected / exposed	0 / 2 (0.00%)	1 / 7 (14.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterocolitis			
subjects affected / exposed	0 / 2 (0.00%)	1 / 7 (14.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus			
subjects affected / exposed	0 / 2 (0.00%)	1 / 7 (14.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis acute			
subjects affected / exposed	1 / 2 (50.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	0 / 2 (0.00%)	1 / 7 (14.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Arthritis bacterial			
subjects affected / exposed	0 / 2 (0.00%)	1 / 7 (14.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Beta haemolytic streptococcal			

infection			
subjects affected / exposed	0 / 2 (0.00%)	1 / 7 (14.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device related infection			
subjects affected / exposed	1 / 2 (50.00%)	4 / 7 (57.14%)	
occurrences causally related to treatment / all	0 / 1	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis adenovirus			
subjects affected / exposed	1 / 2 (50.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Medical device site infection			
subjects affected / exposed	0 / 2 (0.00%)	1 / 7 (14.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Otitis media			
subjects affected / exposed	1 / 2 (50.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Streptococcal infection			
subjects affected / exposed	0 / 2 (0.00%)	1 / 7 (14.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			
subjects affected / exposed	1 / 2 (50.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral pharyngitis			
subjects affected / exposed	0 / 2 (0.00%)	1 / 7 (14.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral upper respiratory tract infection			

subjects affected / exposed	1 / 2 (50.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Product issues			
Device breakage			
subjects affected / exposed	1 / 2 (50.00%)	3 / 7 (42.86%)	
occurrences causally related to treatment / all	0 / 2	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device damage			
subjects affected / exposed	0 / 2 (0.00%)	2 / 7 (28.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device occlusion			
subjects affected / exposed	0 / 2 (0.00%)	1 / 7 (14.29%)	
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 / 2 (0.00%)	1 / 7 (14.29%)	
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	Infants (Corrected Gestational Age: 4 to < 12 Months)	Total Children (Aged: 1 to 15 Years)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 2 (100.00%)	7 / 7 (100.00%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Neoplasm			
subjects affected / exposed	0 / 2 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
General disorders and administration site conditions			

Injection site pain subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	1 / 7 (14.29%) 1	
Injection site reaction subjects affected / exposed occurrences (all)	1 / 2 (50.00%) 1	0 / 7 (0.00%) 0	
Pyrexia subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	3 / 7 (42.86%) 4	
Immune system disorders Food allergy subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	1 / 7 (14.29%) 4	
Seasonal allergy subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	1 / 7 (14.29%) 1	
Respiratory, thoracic and mediastinal disorders Asthma subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	1 / 7 (14.29%) 1	
Cough subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	2 / 7 (28.57%) 2	
Epistaxis subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	1 / 7 (14.29%) 1	
Rhinitis allergic subjects affected / exposed occurrences (all)	1 / 2 (50.00%) 1	0 / 7 (0.00%) 0	
Rhinorrhoea subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	1 / 7 (14.29%) 1	
Upper respiratory tract inflammation subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	1 / 7 (14.29%) 1	
Psychiatric disorders			

Head banging subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	1 / 7 (14.29%) 1	
Product issues Device damage subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	1 / 7 (14.29%) 1	
Investigations Alanine aminotransferase increased alternative assessment type: Systematic subjects affected / exposed occurrences (all)	1 / 2 (50.00%) 2	0 / 7 (0.00%) 0	
Amylase increased alternative assessment type: Systematic subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	1 / 7 (14.29%) 1	
Aspartate aminotransferase increased subjects affected / exposed occurrences (all)	1 / 2 (50.00%) 1	0 / 7 (0.00%) 0	
Blood alkaline phosphatase increased subjects affected / exposed occurrences (all)	1 / 2 (50.00%) 1	0 / 7 (0.00%) 0	
Eosinophil count increased subjects affected / exposed occurrences (all)	1 / 2 (50.00%) 1	0 / 7 (0.00%) 0	
Lipase increased subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	1 / 7 (14.29%) 1	
Transaminases increased subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	1 / 7 (14.29%) 1	
Injury, poisoning and procedural complications Auricular haematoma subjects affected / exposed occurrences (all)	1 / 2 (50.00%) 1	0 / 7 (0.00%) 0	
Epiphyseal injury			

subjects affected / exposed	0 / 2 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Contusion			
subjects affected / exposed	1 / 2 (50.00%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Fracture			
subjects affected / exposed	0 / 2 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Fall			
subjects affected / exposed	0 / 2 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Gastrostomy tube site complication			
subjects affected / exposed	0 / 2 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Heat stroke			
subjects affected / exposed	0 / 2 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Injury corneal			
subjects affected / exposed	0 / 2 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Ligament injury			
subjects affected / exposed	0 / 2 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Procedural pain			
subjects affected / exposed	0 / 2 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Wound complication			
subjects affected / exposed	0 / 2 (0.00%)	2 / 7 (28.57%)	
occurrences (all)	0	2	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 2 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Eye disorders			
Conjunctivitis allergic			

subjects affected / exposed	0 / 2 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	2	
Eye discharge			
subjects affected / exposed	0 / 2 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Strabismus			
subjects affected / exposed	0 / 2 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	0 / 2 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	2	
Abdominal pain			
subjects affected / exposed	0 / 2 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Cheilitis			
subjects affected / exposed	0 / 2 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	2	
Constipation			
subjects affected / exposed	0 / 2 (0.00%)	2 / 7 (28.57%)	
occurrences (all)	0	2	
Dental caries			
subjects affected / exposed	0 / 2 (0.00%)	2 / 7 (28.57%)	
occurrences (all)	0	2	
Enteritis			
subjects affected / exposed	0 / 2 (0.00%)	2 / 7 (28.57%)	
occurrences (all)	0	5	
Enterocolitis			
subjects affected / exposed	0 / 2 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Gastric disorder			
subjects affected / exposed	0 / 2 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Lip dry			
subjects affected / exposed	0 / 2 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	

Nausea			
subjects affected / exposed	0 / 2 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Rectal prolapse			
subjects affected / exposed	0 / 2 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Stomatitis			
subjects affected / exposed	0 / 2 (0.00%)	2 / 7 (28.57%)	
occurrences (all)	0	2	
Hepatobiliary disorders			
Drug-induced liver injury			
subjects affected / exposed	0 / 2 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	0 / 2 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Dermatitis allergic			
subjects affected / exposed	0 / 2 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Dermatitis			
subjects affected / exposed	1 / 2 (50.00%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Dermatitis diaper			
subjects affected / exposed	1 / 2 (50.00%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Drug eruption			
subjects affected / exposed	0 / 2 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Dry skin			
subjects affected / exposed	0 / 2 (0.00%)	2 / 7 (28.57%)	
occurrences (all)	0	2	
Eczema			
subjects affected / exposed	0 / 2 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	2	
Haemorrhage subcutaneous			

subjects affected / exposed	0 / 2 (0.00%)	2 / 7 (28.57%)	
occurrences (all)	0	2	
Miliaria			
subjects affected / exposed	0 / 2 (0.00%)	2 / 7 (28.57%)	
occurrences (all)	0	2	
Rash			
subjects affected / exposed	0 / 2 (0.00%)	3 / 7 (42.86%)	
occurrences (all)	0	4	
Skin erosion			
subjects affected / exposed	0 / 2 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Skin induration			
subjects affected / exposed	0 / 2 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Urticaria			
subjects affected / exposed	0 / 2 (0.00%)	2 / 7 (28.57%)	
occurrences (all)	0	3	
Musculoskeletal and connective tissue disorders			
Joint swelling			
subjects affected / exposed	0 / 2 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Myalgia			
subjects affected / exposed	0 / 2 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Infections and infestations			
Adenoviral conjunctivitis			
subjects affected / exposed	0 / 2 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Conjunctivitis			
subjects affected / exposed	1 / 2 (50.00%)	1 / 7 (14.29%)	
occurrences (all)	3	1	
Epididymitis			
subjects affected / exposed	0 / 2 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Hand-foot-and-mouth disease			

subjects affected / exposed	0 / 2 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Gastroenteritis			
subjects affected / exposed	0 / 2 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Influenza			
subjects affected / exposed	0 / 2 (0.00%)	2 / 7 (28.57%)	
occurrences (all)	0	2	
Infected bite			
subjects affected / exposed	0 / 2 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Medical device site infection			
subjects affected / exposed	1 / 2 (50.00%)	1 / 7 (14.29%)	
occurrences (all)	1	1	
Oral candidiasis			
subjects affected / exposed	1 / 2 (50.00%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Periodontitis			
subjects affected / exposed	0 / 2 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	2	
Upper respiratory tract infection			
subjects affected / exposed	1 / 2 (50.00%)	0 / 7 (0.00%)	
occurrences (all)	2	0	
Viral infection			
subjects affected / exposed	1 / 2 (50.00%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Viral upper respiratory tract infection			
subjects affected / exposed	1 / 2 (50.00%)	4 / 7 (57.14%)	
occurrences (all)	5	25	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 2 (50.00%)	2 / 7 (28.57%)	
occurrences (all)	1	6	
Hypomagnesaemia			
subjects affected / exposed	0 / 2 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	

Hypozaemia			
subjects affected / exposed	0 / 2 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Metabolic acidosis			
subjects affected / exposed	0 / 2 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	5	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
26 May 2017	Amendment 1: - Clarification that medical history and SBS history collected at study entry were updates to data collected at the start of the core study. - Clarification that during the no-teduglutide treatment period, visits would take place approximately every 12 weeks. - Clarification that PS prescription was collected at the screening visit. - Sigmoidoscopy was added as the alternate to colonoscopy throughout the protocol. - Clarification that unscheduled laboratory tests were performed at the investigational site laboratory, as needed. - Clarification on visit schedule when a participant prematurely discontinues IP during a teduglutide treatment cycle. - Clarification on handling of an investigational drug, which is for single use only and should be used within 3 hours following reconstitution. - Removal of urine sodium from the list of urinalysis parameters to be tested.
24 January 2018	Amendment 2: - Revised investigational product (IP) administration language to provide oversight on IP administration. - Added direct bilirubin to the list of laboratory tests. - Clarifications that the drug administration diary can be completed by site staff, added "guardian" to replace "legally authorized representative", and updated the emergency contact information and the product quality complaint section.
20 July 2018	Amendment 3: - Update of the number of participants from 5 to 7. - Addition of the study population of 2 cohorts based on age of participants at the time of entry into the core study: the infant cohort 4 to less than 12 months of corrected gestational age and children 1 to 15 years of age. - To minimize risk to participants, a new escape criterion was added allowing those who had escaped during the follow-up period of a previous teduglutide treatment cycle to omit the follow-up period during subsequent teduglutide treatment cycles. - Modified teduglutide treatment exclusion criterion 1 on participants body weight to accommodate younger children (exclude participants if weight less than 5 kg). - Clarified the requirement from the study physician to observe the parent/guardian administering the IP at least twice before permitting the parent/guardian to administer teduglutide to a single observation. - Clarified blood pressure collection to same extremity rather than same arm (arm is not used in small children). - Clarified that IP compliance is calculated from diaries. - Deleted the 4 hour observation period at initial dosing since participants were already exposed to teduglutide in the core study. - Omitted saved serum samples for participants less than 10 kg. - Updates for number of enrolled participants, corporate name change, medical monitor change, deletion of duplicate text, and other minor editorial corrections

06 November 2020	Amendment 4: - Sponsor name changed to include both Shire Human Genetic Therapies, Inc. (USA) and Takeda Pharmaceutical Company Limited. - Transferred back the role of in-country clinical caretaker from IQVIA Services Japan K.K to the sponsor. The sponsor is now responsible for notifying the relevant regulatory authorities of related, unexpected serious adverse events (SAEs). - Updated the end of the planned study period to December 2021. - Expanded the timing to perform a colonoscopy/sigmoidoscopy at the end of a teduglutide treatment cycle (CxW24). Participants who received 2 treatment cycles (48 weeks of teduglutide exposure) will undergo a colonoscopy/sigmoidoscopy before the next cycle of teduglutide treatment. Colonoscopy/sigmoidoscopy performed after the Visit CxW24 (± 4 days) window and before the next cycle of teduglutide treatment will not be considered a protocol deviation. All other visit procedures must adhere to the (± 4 days) visit window. - Added a new section entitled "Changes to Study Procedures Due to a Pandemic". The purpose of these changes is to maintain the participant safety, confidentiality, and study integrity in the context of healthcare delivery challenges presented by the COVID-19 pandemic. - Clarified the definition of an overdose as the administration of the investigational product at a dose or frequency greater than 0.05 mg/kg subcutaneous once daily. An overdose occurs if any of the following criteria are met: * More than 0.05 mg/kg is given at any one time * Consecutive doses are spaced less than 12 hours apart * Any more than 0.05 mg/kg in one day - Changed the data monitoring committee meeting frequency. The DMC members will review the data approximately every 6 months (previously 3 months) during the study treatment periods (date of the first participants first dose to date of the last participants last dose). - Updated contact information and responsible personnel.
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Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported