EU Clinical Trials Register

Clinical trial results:
A 24-week Safety, Efficacy, Pharmacodynamic, and Pharmacokinetic Study of Teduglutide in
Japanese Pediatric Subjects, Aged 4 Months through 15 Years, with Short Bowel Syndrome who are Dependent on Parenteral Support

Summary

EudraCT number	2020-005791-35
Trial protocol	Outside EU/EEA
Global end of trial date	21 January 2020

Results information

Result version number	v1 (current)
This version publication date	04 February 2021
First version publication date	04 February 2021

Trial information

Trial identification

Sponsor protocol code	SHP633-302

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02980666
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	21 January 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	21 January 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to evaluate the safety, tolerability, efficacy, pharmacodynamics (PD), and pharmacokinetics (PK) of teduglutide in Japanese pediatric subjects (4 months through 15 years of age) with short bowel syndrome (SBS) who were dependent on parenteral support (PS).

Protection of trial subjects:

The study was conducted in accordance with current applicable industry regulations, International Council for Harmonisation (ICH) Good Clinical Practice (GCP) Guideline E6 (1996) and any updates, European Union (EU) Directive 2001/20/EC and its updates, the ethical principles in the Declaration of Helsinki, and local ethical and legal requirements.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	13 January 2017
Long term follow-up planned	Yes
Long term follow-up rationale	Efficacy, Safety
Long term follow-up duration	9 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Japan: 10
Worldwide total number of subjects	10
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)	8
Adolescents (12-17 years)	0
Adults (18-64 years)	0

From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 6 centers in Japan between 13 January 2017 (first subject first visit) and 21 January 2020 (last subject last visit).

Pre-assignment

Screening details:

A total of 10 Japanese subjects were enrolled into the study, including 8 children age 1 through 15 years of age and 2 infants aged 4 months through < 12 months of corrected gestational age. All the subjects received treatment and completed the study.

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:

Subjects aged from 1 through 15 years received teduglutide 0.05 milligram per kilogram per day (mg/kg/day) subcutaneous (SC) injection once daily for 24 weeks and completed the study at Week 28.

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:

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

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

Arm description:

Subjects (Infants) from 4 through < 12 months of corrected gestational age received teduglutide 0.05 mg/kg/day SC injection once daily for 24 weeks and completed the study at Week 28.

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:

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

Number of subjects in period 1	Total Children (Aged: 1 to 15 Years)	Infants (Corrected Gestational Age: 4 to < 12 months)
Started	8	2
Completed	8	2

Baseline characteristics

Reporting groups

Reporting group title	Total Children (Aged: 1 to 15 Years)
Reporting group description:	
Subjects aged from 1 through 15 years received teduglutide 0.05 milligram per kilogram per day (mg/kg/day) subcutaneous (SC) injection once daily for 24 weeks and completed the study at Week 28.	
Reporting group title	Infants (Corrected Gestational Age: 4 to < 12 months)
Reporting group description:	
Subjects (Infants) from 4 through < 12 months of corrected gestational age received teduglutide 0.05 mg/kg/day SC injection once daily for 24 weeks and completed the study at Week 28.	

Reporting group values	Total Children (Aged: 1 to 15 Years)	Infants (Corrected Gestational Age: 4 to < 12 months)	Total
Number of subjects	8	2	10
Age Categorical			
Units: Subjects			
1 to 15 Years	8	0	8
4 to < 12 months	0	2	2
Sex: Female, Male			
Units: Subjects			
Female	1	1	2
Male	7	1	8
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	0	0	0
Not Hispanic or Latino	8	2	10
Unknown or Not Reported	0	0	0
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	8	2	10
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

End points

End points reporting groups

Reporting group title	Total Children (Aged: 1 to 15 Years)
Reporting group description:	
Subjects aged from 1 through 15 years received teduglutide 0.05 milligram per kilogram per day (mg/kg/day) subcutaneous (SC) injection once daily for 24 weeks and completed the study at Week 28.	
Reporting group title	Infants (Corrected Gestational Age: 4 to < 12 months)
Reporting group description:	
Subjects (Infants) from 4 through < 12 months of corrected gestational age received teduglutide 0.05 mg/kg/day SC injection once daily for 24 weeks and completed the study at Week 28.	

Primary: Absolute Change From Baseline in Parenteral Support (PS) Volume at End of Treatment (EOT) Based on Dairy Data

End point title	Absolute Change From Baseline in Parenteral Support (PS) Volume at End of Treatment (EOT) Based on Dairy Data[1]
End point description:	
Absolute change from baseline in PS volume at EOT (up to Week 24) based on dairy data was reported. EOT was defined as the last available measurement after the date of first dose during the 24-week treatment period. Here, milliliter per kilogram per day is abbreviated as mL/kg/day. Intention-to-treat (ITT) population consisted of all subjects who were enrolled into the study and met all eligible criteria for the study.	
End point type	Primary
End point timeframe:	
Baseline, EOT (up to Week 24)	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical and 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	8	2		
Units: mL/kg/day				
arithmetic mean (standard deviation)	-11.8 (± 8.47)	-26.2 (± 13.61)		

Statistical analyses

No statistical analyses for this end point

Primary: Percent Change From Baseline in Parenteral Support (PS) Volume at End of Treatment (EOT) Based on Dairy Data

End point title	Percent Change From Baseline in Parenteral Support (PS) Volume at End of Treatment (EOT) Based on Dairy Data[2]

End point description:

Percent change from baseline in PS volume at EOT (up to Week 24) based on dairy data was reported. EOT was defined as the last available measurement after the date of first dose during the 24-week treatment period. ITT population consisted of all subjects who were enrolled into the study and met all eligible criteria for the study.

End point type	Primary

End point timeframe:

Baseline, EOT (up to Week 24)

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	8	2		
Units: Percent Change				
arithmetic mean (standard deviation)	-27.7 (± 31.79)	-26.7 (± 15.14)		

Statistical analyses

No statistical analyses for this end point

Primary: Absolute Change From Baseline in Parenteral Support (PS) Caloric Intake at End of Treatment (EOT) Based on Dairy Data

End point title	Absolute Change From Baseline in Parenteral Support (PS) Caloric Intake at End of Treatment (EOT) Based on Dairy Data[3]

End point description:

Absolute change from baseline in PS caloric intake at EOT (up to Week 24) based on dairy data was reported. EOT was defined as the last available measurement after the date of first dose during the 24-week treatment period. Here, kilo-calories per kilogram per day was abbreviated as (kcal/kg/day). ITT population consisted of all subjects who were enrolled into the study and met all eligible criteria for the study.

End point type	Primary

End point timeframe:

Baseline, EOT (up to Week 24)

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	8	2		
Units: kcal/kg/day				

arithmetic mean (standard deviation)	-7.2 (± 8.70)	-13.8 (± 3.17)

Statistical analyses

No statistical analyses for this end point

Primary: Percent Change From Baseline in Parenteral Support (PS) Caloric Intake at End of Treatment (EOT) Based on Dairy Data

End point title	Percent Change From Baseline in Parenteral Support (PS) Caloric Intake at End of Treatment (EOT) Based on Dairy Data[4]

End point description:

Percent change from baseline in PS caloric intake at EOT (up to Week 24) based on dairy data was reported. EOT was defined as the last available measurement after the date of first dose during the 24-week treatment period. ITT population consisted of all subjects who were enrolled into the study and met all eligible criteria for the study.

End point type	Primary

End point timeframe:

Baseline, EOT (up to Week 24)

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	8	2		
Units: Percent change				
arithmetic mean (standard deviation)	-26.2 (± 33.00)	-25.7 (± 2.73)		

Statistical analyses

No statistical analyses for this end point

Primary: Absolute Change From Baseline in Plasma Citrulline at End of Treatment (EOT)

End point title	Absolute Change From Baseline in Plasma Citrulline at End of Treatment (EOT)[5]

End point description:

Absolute change from baseline in plasma citrulline at EOT (up to Week 24) was reported. EOT was defined as the last available measurement after the date of first dose during the 24-week treatment period. ITT population consisted of all subjects who were enrolled into the study and met all eligible criteria for the study.

End point type	Primary

End point timeframe:

Baseline, EOT (up to Week 24)

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	8	0[6]		
Units: Micromoles per liter (mcmol/L)				
arithmetic mean (standard deviation)	3.2 (± 4.28)	()		

Notes:

[6] - Data for this end point was not planned to be collected and analysed for infants.

Statistical analyses

No statistical analyses for this end point

Primary: Percent Change From Baseline in Plasma Citrulline at End of Treatment (EOT)

End point title	Percent Change From Baseline in Plasma Citrulline at End of Treatment (EOT)[7]

End point description:

Percent change from baseline in plasma citrulline at EOT (up to Week 24) was reported. EOT was defined as the last available measurement after the date of first dose during the 24-week treatment period. ITT population consisted of all subjects who were enrolled into the study and met all eligible criteria for the study.

End point type	Primary

End point timeframe:

Baseline, EOT (up to Week 24)

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	8	0[8]		
Units: Percent change				
arithmetic mean (standard deviation)	39.2 (± 39.46)	()		

Notes:

[8] - Data for this endpoint was not planned to be collected and analysed for infants.

Statistical analyses

No statistical analyses for this end point

Primary: Absolute Change From Baseline in Enteral Nutritional (EN) Volume at End of Treatment (EOT) Based on Dairy Data

End point title	Absolute Change From Baseline in Enteral Nutritional (EN) Volume at End of Treatment (EOT) Based on Dairy Data[9]

End point description:

Absolute change from baseline in EN volume at EOT (up to Week 24) based on dairy data was reported. EOT was defined as the last available measurement after the date of first dose during the 24-week treatment period. ITT population consisted of all subjects who were enrolled into the study and met all eligible criteria for this study.

End point type	Primary

End point timeframe:

Baseline, EOT (up to Week 24)

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	8	2		
Units: mL/kg/day				
arithmetic mean (standard deviation)	1.0 (± 7.14)	0.6 (± 2.15)		

Statistical analyses

No statistical analyses for this end point

Primary: Percent Change From Baseline in Enteral Nutritional (EN) Volume at End of Treatment (EOT) Based on Dairy Data

End point title	Percent Change From Baseline in Enteral Nutritional (EN) Volume at End of Treatment (EOT) Based on Dairy Data[10]

End point description:

Percent change from baseline in EN volume at EOT (up to Week 24) based on dairy data was reported. EOT was defined as the last available measurement after the date of first dose during the 24-week treatment period. ITT population consisted of all subjects who were enrolled into the study and met all eligible criteria for this study. Here, the number of subjects analysed refer to the subjects evaluable for this endpoint.

End point type	Primary

End point timeframe:

Baseline, EOT (up to Week 24)

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	4	2		
Units: Percent change				
arithmetic mean (standard deviation)	53.1 (± 111.01)	-23.2 (± 36.89)		

Statistical analyses

No statistical analyses for this end point

Primary: Absolute Change From Baseline in Enteral Nutritional (EN) Caloric Intake at End of Treatment (EOT) Based on Dairy Data

End point title	Absolute Change From Baseline in Enteral Nutritional (EN) Caloric Intake at End of Treatment (EOT) Based on Dairy Data[11]

End point description:

Absolute change from baseline in EN caloric intake at EOT (up to Week 24) based on dairy data was reported. EOT was defined as the last available measurement after the date of first dose during the 24-week treatment period. ITT population consisted of all subjects who were enrolled into the study and met all eligible criteria for this study.

End point type	Primary

End point timeframe:

Baseline, EOT (up to Week 24)

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	8	2		
Units: kcal/kg/day				
arithmetic mean (standard deviation)	0.8 (± 5.60)	0.3 (± 1.03)		

Statistical analyses

No statistical analyses for this end point

Primary: Percent Change From Baseline in Enteral Nutritional (EN) Caloric Intake at End of Treatment (EOT) Based on Dairy Data

End point title	Percent Change From Baseline in Enteral Nutritional (EN) Caloric Intake at End of Treatment (EOT) Based on Dairy Data[12]

End point description:

Percent change from baseline in EN caloric intake at EOT (up to Week 24) based on dairy data was reported. EOT was defined as the last available measurement after the date of first dose during the 24-week treatment period. ITT population consisted of all subjects who were enrolled into the study and met all eligible criteria for this study. Here, the number of subjects analysed refer to the subjects evaluable for this endpoint.

End point type	Primary

End point timeframe:

Baseline, EOT (up to Week 24)

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	4	2		
Units: Percent change				
arithmetic mean (standard deviation)	56.8 (± 117.88)	-24.2 (± 38.06)		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects Who Achieved At least 20 Percent (%) Reduction in Parenteral Support (PS) Volume at Week 24

End point title	Number of Subjects Who Achieved At least 20 Percent (%) Reduction in Parenteral Support (PS) Volume at Week 24[13]

End point description:

Number of subjects who achieved at least 20% reduction in PS volume at Week 24 was reported. ITT population consisted of all subjects who were enrolled into the study and met all eligible criteria for this study. Here, the number of subjects analysed refer to the subjects evaluable for this endpoint.

End point type	Primary

End point timeframe:

Week 24

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	7	2		
Units: Subjects	4	1		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects Who Achieved At least 20 Percent (%) Reduction in Parenteral Support (PS) Volume at End of Treatment (EOT)

End point title	Number of Subjects Who Achieved At least 20 Percent (%) Reduction in Parenteral Support (PS) Volume at End of Treatment (EOT)[14]

End point description:

Number of subjects who achieved at least 20% reduction in PS volume at EOT (up to Week 24) was reported. EOT was defined as the last available measurement after the date of first dose during the 24-week treatment period. ITT population consisted of all subjects who were enrolled into the study and met all eligible criteria for this study.

End point type	Primary

End point timeframe:

EOT (up to Week 24)

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	8	2		
Units: Subjects	4	1		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects Who Achieved 100 Percent (%) Reduction in Complete Weaning of Parenteral Support (PS) Volume at End of Treatment (EOT)

End point title	Number of Subjects Who Achieved 100 Percent (%) Reduction in Complete Weaning of Parenteral Support (PS) Volume at End of Treatment (EOT)[15]

End point description:

Number of subjects who achieved at least 100% reduction in complete weaning of PS volume at EOT (up to Week 24) was reported. EOT was defined as the last available measurement after the date of first dose during the 24-week treatment period. ITT population consisted of all subjects who were enrolled into the study and met all eligible criteria for this study.

End point type	Primary

End point timeframe:

EOT (up to Week 24)

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	8	2		
Units: Subjects	1	0		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects Who Achieved Greater Than or Equal to (>=) 20 Percent (%) Reduction in Parenteral Support (PS) Volume at Week 28

End point title	Number of Subjects Who Achieved Greater Than or Equal to (>=) 20 Percent (%) Reduction in Parenteral Support (PS) Volume at Week 28[16]

End point description:

Number of subjects who achieved >= 20% reduction in PS volume at Week 28 was reported. ITT population consisted of all subjects who were enrolled into the study and met all eligible criteria for this study.

End point type	Primary

End point timeframe:

Week 28

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	8	2		
Units: Subjects	3	1		

Statistical analyses

No statistical analyses for this end point

Primary: Absolute Change From End of Treatment (EOT) in Parenteral Support (PS)

Volume at End of Study (EOS) Based on Dairy Data

End point title	Absolute Change From End of Treatment (EOT) in Parenteral Support (PS) Volume at End of Study (EOS) Based on Dairy Data[17]

End point description:

Absolute change from EOT (up to Week 24) in PS volume at EOS (up to Week 28) based on dairy data was reported. EOT was defined as the last available measurement after the date of first dose during the 24-week treatment period. ITT population consisted of all subjects who were enrolled into the study and met all eligible criteria for this study.

End point type	Primary

End point timeframe:

EOT (up to Week 24), EOS (up to Week 28)

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	8	2		
Units: mL/kg/day				
arithmetic mean (standard deviation)	3.9 (± 7.06)	-3.8 (± 0.67)		

Statistical analyses

No statistical analyses for this end point

Primary: Percent Change From End of Treatment (EOT) in Parenteral Support (PS) Volume at End of Study (EOS) Based on Dairy Data

End point title	Percent Change From End of Treatment (EOT) in Parenteral Support (PS) Volume at End of Study (EOS) Based on Dairy Data[18]

End point description:

Percent change from EOT (up to Week 24) in PS volume at EOS (up to Week 28) based on dairy data was reported. EOT was defined as the last available measurement after the date of first dose during the 24-week treatment period. ITT population consisted of all subjects who were enrolled into the study and met all eligible criteria for this study. Here, the number of subjects analysed refer to the subjects evaluable for this endpoint.

End point type	Primary

End point timeframe:

EOT (up to Week 24), EOS (up to Week 28)

Notes:

[18] - 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: Percent change				
arithmetic mean (standard deviation)	9.8 (± 19.59)	-5.5 (± 2.35)		

Statistical analyses

No statistical analyses for this end point

Primary: Absolute Change From End of Treatment (EOT) in Parenteral Support (PS) Caloric Intake at End of Study (EOS) Based on Dairy Data

End point title	Absolute Change From End of Treatment (EOT) in Parenteral Support (PS) Caloric Intake at End of Study (EOS) Based on Dairy Data[19]

End point description:

Absolute change from EOT (up to Week 24) in PS caloric intake at EOS (up to Week 28) based on dairy data was reported. EOT was defined as the last available measurement after the date of first dose during the 24-week treatment period. ITT population consisted of all subjects who were enrolled into the study and met all eligible criteria for this study.

End point type	Primary

End point timeframe:

EOT (up to Week 24), EOS (up to Week 28)

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	8	2		
Units: kcal/kg/day				
arithmetic mean (standard deviation)	0.5 (± 6.16)	-4.0 (± 1.38)		

Statistical analyses

No statistical analyses for this end point

Primary: Percent Change From End of Treatment (EOT) in Parenteral Support (PS) Caloric Intake at End of Study (EOS) Based on Dairy Data

End point title	Percent Change From End of Treatment (EOT) in Parenteral Support (PS) Caloric Intake at End of Study (EOS) Based on Dairy Data[20]

End point description:

Percent change from EOT (up to Week 24) in PS caloric intake at EOS (up to Week 28) based on dairy data was reported. EOT was defined as the last available measurement after the date of first dose during the 24-week treatment period. ITT population consisted of all subjects who were enrolled into the study and met all eligible criteria for this study. Here, the number of subjects analysed refer to the subjects evaluable for this endpoint.

End point type	Primary

End point timeframe:

EOT (up to Week 24), EOS (up to Week 28)

Notes:

[20] - 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: Percent change				
arithmetic mean (standard deviation)	3.5 (± 19.17)	-10.3 (± 4.40)		

Statistical analyses

No statistical analyses for this end point

Primary: Absolute Change From End of Treatment (EOT) in Plasma Citrulline at End of Study (EOS)

End point title	Absolute Change From End of Treatment (EOT) in Plasma Citrulline at End of Study (EOS)[21]

End point description:

Absolute change from EOT (up to Week 24) in plasma citrulline at EOS (up to Week 28) was reported. EOT was defined as the last available measurement after the date of first dose during the 24-week treatment period. ITT population consisted of all subjects who were enrolled into the study and met all eligible criteria for this study.

End point type	Primary

End point timeframe:

EOT (up to Week 24), EOS (up to Week 28)

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	8	0[22]		
Units: Micromoles (mcM)				
arithmetic mean (standard deviation)	-2.9 (± 2.87)	( )		

Notes:

[22] - Data for this endpoint was not planned to be collected and analysed for infants.

Statistical analyses

No statistical analyses for this end point

Primary: Percent Change From End of Treatment (EOT) in Plasma Citrulline at End of Study (EOS)

End point title	Percent Change From End of Treatment (EOT) in Plasma Citrulline at End of Study (EOS)[23]

End point description:

Percent change from EOT (up to Week 24) in plasma citrulline at EOS (up to Week 28) was reported. EOT was defined as the last available measurement after the date of first dose during the 24-week treatment period. ITT population consisted of all subjects who were enrolled into the study and met all eligible criteria for this study.

End point type	Primary

End point timeframe:

EOT (up to Week 24), EOS (up to Week 28)

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	8	0[24]		
Units: Percent change				
arithmetic mean (standard deviation)	-20.0 (± 24.16)	()		

Notes:

[24] - Data for this endpoint was not planned to be collected and analysed for infants.

Statistical analyses

No statistical analyses for this end point

Primary: Absolute Change From End of Treatment (EOT) in Enteral Nutritional (EN) Volume at End of Study (EOS) Based on Dairy Data

End point title	Absolute Change From End of Treatment (EOT) in Enteral Nutritional (EN) Volume at End of Study (EOS) Based on Dairy Data[25]

End point description:

Absolute change from EOT (up to Week 24) in EN volume at EOS (up to Week 28) based on dairy data was reported. EOT was defined as the last available measurement after the date of first dose during the 24-week treatment period. ITT population consisted of all subjects who were enrolled into the study and met all eligible criteria for this study.

End point type	Primary

End point timeframe:
EOT (up to Week 24), EOS (up to Week 28)

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	8	2		
Units: mL/kg/day				
arithmetic mean (standard deviation)	-1.5 (± 3.24)	-2.8 (± 3.98)		

Statistical analyses

No statistical analyses for this end point

Primary: Percent Change From End of Treatment (EOT) in Enteral Nutritional (EN) Volume at End of Study (EOS) Based on Dairy Data

End point title	Percent Change From End of Treatment (EOT) in Enteral Nutritional (EN) Volume at End of Study (EOS) Based on Dairy Data[26]

End point description:
Percent change from EOT (up to Week 24) in EN volume at EOS (up to Week 28) based on dairy data was reported. EOT was defined as the last available measurement after the date of first dose during the 24-week treatment period. ITT population consisted of all subjects who were enrolled into the study and met all eligible criteria for this study. Here, the number of subjects analysed refer to the subjects evaluable for this endpoint.

End point type	Primary

End point timeframe:
EOT (up to Week 24), EOS (up to Week 28)

Notes:
[26] - 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	4	2		
Units: Percent change				
arithmetic mean (standard deviation)	-22.1 (± 28.06)	-1.4 (± 8.25)		

Statistical analyses

No statistical analyses for this end point

Primary: Absolute Change From End of Treatment (EOT) in Enteral Nutritional (EN) Caloric Intake at End of Study (EOS) Based on Dairy Data

End point title	Absolute Change From End of Treatment (EOT) in Enteral Nutritional (EN) Caloric Intake at End of Study (EOS) Based on Dairy Data[27]

End point description:

Absolute change from EOT (up to Week 24) in EN caloric intake at EOS (up to Week 28) based on dairy data was reported. EOT was defined as the last available measurement after the date of first dose during the 24-week treatment period. ITT population consisted of all subjects who were enrolled into the study and met all eligible criteria for this study.

End point type	Primary

End point timeframe:

EOT (up to Week 24), EOS (up to Week 28)

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	8	2		
Units: kcal/kg/day				
arithmetic mean (standard deviation)	-1.1 (± 2.64)	-1.4 (± 1.97)		

Statistical analyses

No statistical analyses for this end point

Primary: Percent Change From End of Treatment (EOT) in Enteral Nutritional (EN) Caloric Intake at End of Study (EOS) Based on Dairy Data

End point title	Percent Change From End of Treatment (EOT) in Enteral Nutritional (EN) Caloric Intake at End of Study (EOS) Based on Dairy Data[28]

End point description:

Percent change from EOT (up to Week 24) in EN caloric intake at EOS (up to Week 28) based on dairy data was reported. EOT was defined as the last available measurement after the date of first dose during the 24-week treatment period. ITT population consisted of all subjects who were enrolled into the study and met all eligible criteria for this study. Here, the number of subjects analysed refer to the subjects evaluable for this endpoint.

End point type	Primary

End point timeframe:

EOT (up to Week 24), EOS (up to Week 28)

Notes:

[28] - 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	4	2		
Units: Percent change				
arithmetic mean (standard deviation)	-22.1 (± 28.16)	-3.0 (± 6.03)		

Statistical analyses

No statistical analyses for this end point

Primary: Absolute Change From Baseline in Number of Hours per Day of Parenteral Support (PS) Usage at End of Treatment (EOT) Based on Dairy Data

End point title	Absolute Change From Baseline in Number of Hours per Day of Parenteral Support (PS) Usage at End of Treatment (EOT) Based on Dairy Data[29]

End point description:

Absolute change from baseline in number of hours per day of PS Usage at EOT (up to Week 24) based on dairy data was reported. EOT was defined as the last available measurement after the date of first dose during the 24-week treatment period. ITT population consisted of all subjects who were enrolled into the study and met all eligible criteria for this study.

End point type	Primary

End point timeframe:

Baseline, EOT (up to Week 24)

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	8	2		
Units: Hours per day (hours/day)				
arithmetic mean (standard deviation)	-2.1 (± 4.16)	0.0 (± 0.00)		

Statistical analyses

No statistical analyses for this end point

Primary: Absolute Change From Baseline in Number of Days per Week of Parenteral Support (PS) Usage at End of Treatment (EOT) Based on Dairy Data

End point title	Absolute Change From Baseline in Number of Days per Week of Parenteral Support (PS) Usage at End of Treatment (EOT) Based on Dairy Data[30]

End point description:

Absolute change from baseline in number of days per Week of PS usage at EOT (up to Week 24) based on dairy data was reported. EOT was defined as the last available measurement after the date of first dose during the 24-week treatment period. ITT population consisted of all subjects who were enrolled into the study and met all eligible criteria for this study.

End point type	Primary

End point timeframe:

Baseline, EOT (up to Week 24)

Notes:

[30] - 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	8	2		
Units: Days per week				
arithmetic mean (standard deviation)	-0.9 (± 2.47)	0.0 (± 0.00)		

Statistical analyses

No statistical analyses for this end point

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

End point title	Number of Subjects With Treatment-emergent Adverse Events (TEAEs)[31]

End point description:

An Adverse Event (AE) was any untoward medical occurrence in a clinical investigation subject administered a pharmaceutical product and that does not necessarily have a causal relationship with this treatment. TEAEs were defined as any AEs whose onset occurred, severity worsened, or intensity increased after receiving the investigational product. Safety population consisted of all subjects in the ITT population who received at least 1 administration of investigational product with any safety follow-up.

End point type	Primary

End point timeframe:

From start of study drug administration up to EOS (up to Week 28)

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	8	2		
Units: Subjects	8	2		

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in Body Weight for age Z-score at Week 28

End point title	Change From Baseline in Body Weight for age Z-score at Week 28[32]

End point description:

Body weight was measured using age Z-score. A Z-score was defined as 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. A negative Z-score indicates values lower than the mean while a positive Z-score indicates values higher than the mean. Change from baseline in body weight for age Z-score at Week 28 was reported. Safety population consisted of all subjects in the ITT population who received at least 1 administration of investigational product with any safety follow-up.

End point type	Primary

End point timeframe:

Baseline, Week 28

Notes:

[32] - 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	8	2		
Units: Z-score				
arithmetic mean (standard deviation)	0.177 (± 0.3625)	2.332 (± 1.1503)		

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in Height for Age Z-score at Week 28

End point title	Change From Baseline in Height for Age Z-score at Week 28[33]

End point description:

Height was measured using age Z-score. A Z-score was defined as 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. A negative Z-score indicates values lower than the mean while a positive Z-score indicates values higher than the mean. Change from baseline in height for age Z-score at Week 28 was reported. Safety population consisted of all subjects in the ITT population who received at least 1 administration of investigational product with any safety follow-up.

End point type	Primary

End point timeframe:

Baseline, Week 28

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	8	2		
Units: Z-score				
arithmetic mean (standard deviation)	0.024 (± 0.4841)	1.056 (± 0.6968)		

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in Head Circumference for Age Z-score at Week 28

End point title	Change From Baseline in Head Circumference for Age Z-score at Week 28[34]

End point description:

Head circumference was measured using age Z-score. A Z-score was defined as 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. A negative Z-score indicates values lower than the mean while a positive Z-score indicates values higher than the mean. Change from baseline in head circumference for age Z-score at Week 28 was reported. Safety population consisted of all subjects in the ITT population who received at least 1 administration of investigational product with any safety follow-up.

End point type	Primary

End point timeframe:

Baseline, Week 28

Notes:

[34] - 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[35]	2		
Units: Z-score				
arithmetic mean (standard deviation)	()	1.559 (± 0.6116)		

Notes:

[35] - Data for this endpoint was not planned to be collected and analysed for Total Children.

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Clinically Significant Changes in Vital Signs Reported as Treatment Emergent Adverse Events (TEAEs)

End point title	Number of Subjects With Clinically Significant Changes in Vital Signs Reported as Treatment Emergent Adverse Events (TEAEs)[36]

End point description:

Vital sign assessments included pulse rate, blood pressure, or body temperature. Number of subjects with clinically significant changes in vital signs by the investigator were recorded as TEAEs. Safety population consisted of all subjects in the ITT population who received at least 1 administration of investigational product with any safety follow-up.

End point type	Primary

End point timeframe:

From start of study drug administration up to EOS (up to Week 28)

Notes:

[36] - 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	8	2		
Units: Subjects	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Clinically Significant Changes in Electrocardiogram (ECG) Reported as Treatment Emergent Adverse Events (TEAEs)

End point title	Number of Subjects With Clinically Significant Changes in Electrocardiogram (ECG) Reported as Treatment Emergent Adverse Events (TEAEs)[37]

End point description:

12-lead ECG was performed. Any change in ECG assessments which were deemed to be clinically significant changes were recorded as TEAEs. Safety population consisted of all subjects in the ITT population who received at least 1 administration of investigational product with any safety follow-up.

End point type	Primary

End point timeframe:

From start of study drug administration up to EOS (up to Week 28)

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	8	2		
Units: Subjects	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Clinically Significant Laboratory Abnormalities Reported as Treatment Emergent Adverse Events (TEAEs)

End point title	Number of Subjects With Clinically Significant Laboratory Abnormalities Reported as Treatment Emergent Adverse Events (TEAEs)[38]

End point description:

Clinical laboratory assessments included biochemistry, hematology, coagulation, urinalysis. The number of subjects with clinically significant laboratory abnormalities were reported as TEAEs. Safety population consisted of all subjects in the ITT population who received at least 1 administration of investigational product with any safety follow-up.

End point type	Primary

End point timeframe:

From start of study drug administration up to EOS (up to Week 28)

Notes:

[38] - 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	8	2		
Units: Subjects	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in the Average Urine Output at Week 28

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

End point description:

Average urine output was recorded in measured volume at Week 28 was reported. Safety population consisted of all subjects in the ITT population who received at least 1 administration of investigational product with any safety follow-up. Here, the number of subjects analysed refer to the subjects evaluable for this endpoint. Here, '99999' indicates that standard deviation was not estimated as only single

subject was analysed for the specified arm.

End point type	Primary

End point timeframe:

Baseline, Week 28

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	7	1		
Units: mL/kg/day				
arithmetic mean (standard deviation)	-22.317 (± 34.8252)	-48.879 (± 99999)		

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in the Fecal Output at Week 28

End point title	Change From Baseline in the Fecal Output at Week 28[40]

End point description:

Change from baseline in the fecal output (Average number of stools per day) at Week 28 was recorded. Safety population consisted of all subjects in the ITT population who received at least 1 administration of investigational product with any safety follow-up. Here, the number of subjects analysed refer to the subjects evaluable for this endpoint. Here, '99999' indicates that standard deviation was not estimated as only single subject was analysed for the specified arm.

End point type	Primary

End point timeframe:

Baseline, Week 28

Notes:

[40] - 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	1		
Units: Average number of stools per day				
arithmetic mean (standard deviation)	-0.64 (± 1.547)	2.50 (± 99999)		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Positive Specific Antibodies to Teduglutide

End point title	Number of Subjects With Positive Specific Antibodies to Teduglutide[41]

End point description:

Number of subjects with positive specific antibodies to teduglutide were used to summarize the presence of antibodies. Safety population consisted of all subjects in the ITT population who received at least 1 administration of investigational product with any safety follow-up.

End point type	Primary

End point timeframe:

From start of study drug administration up to EOS (up to Week 28)

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	8	2		
Units: Subjects	1	2		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Clinically Significant Abnormal Findings in Gastrointestinal (GI) Specific Testing

End point title	Number of Subjects With Clinically Significant Abnormal Findings in Gastrointestinal (GI) Specific Testing[42]

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). EOT was defined as the last available measurement after the date of first dose during the 24-week treatment period. Number of subjects with clinically significant abnormal findings in gastrointestinal specific testing were reported. Safety population consisted of all subjects in the ITT population who received at least 1 administration of investigational product with any safety follow-up.

End point type	Primary

End point timeframe:

Baseline, EOT (up to Week 24)

Notes:

[42] - 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	8	0[43]		
Units: Subjects	0			

Notes:

[43] - Data for this endpoint was not planned to be collected and analysed for infants.

Statistical analyses

No statistical analyses for this end point

Primary: Area Under the Concentration-time Curve at Steady State (AUCtau,ss) of Teduglutide in Plasma

End point title	Area Under the Concentration-time Curve at Steady State (AUCtau,ss) of Teduglutide in Plasma[44]

End point description:

Since only 2 sparse PK samples were collected during the study, PK parameters were not estimated and analysed using this study samples. Therefore, no PK parameters were reported in this study.

End point type	Primary

End point timeframe:

Baseline: Pre-dose, 1, 6 hours post-dose; Week 4: Pre-dose, 2, 4 hours post-dose

Notes:

[44] - 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[45]	0[46]		
Units: hour*nanogram per milliliter (hr*ng/mL)				
arithmetic mean (standard deviation)	()	()		

Notes:

[45] - PK was planned to be reported with other clinical studies. Hence,no individual PK data was reported.
[46] - PK was planned to be reported with other clinical studies. Hence,no individual PK data was reported.

Statistical analyses

No statistical analyses for this end point

Primary: Maximum Plasma Concentration at Steady-state (Cmax,ss) of Teduglutide in Plasma

End point title	Maximum Plasma Concentration at Steady-state (Cmax,ss) of Teduglutide in Plasma[47]

End point description:

Since only 2 sparse PK samples were collected during the study, PK parameters were not estimated and analysed using this study samples. Therefore, no PK parameters were reported in this study.

End point type	Primary

End point timeframe:

Baseline: Pre-dose, 1, 6 hours post-dose; Week 4: Pre-dose, 2, 4 hours post-dose

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	0[48]	0[49]		
Units: nanogram per milliliter (ng/mL)				
arithmetic mean (standard deviation)	()	()		

Notes:

[48] - PK was planned to be reported with other clinical studies. Hence,no individual PK data was reported.
[49] - PK was planned to be reported with other clinical studies. Hence,no individual PK data was reported.

Statistical analyses

No statistical analyses for this end point

Primary: Minimum Plasma Concentration at Steady-state (Cmin.ss) of Teduglutide in Plasma

End point title	Minimum Plasma Concentration at Steady-state (Cmin.ss) of Teduglutide in Plasma[50]

End point description:

Since only 2 sparse PK samples were collected during the study, PK parameters were not estimated and analysed using this study samples. Therefore, no PK parameters were reported in this study.

End point type	Primary

End point timeframe:

Baseline: Pre-dose, 1, 6 hours post-dose; Week 4: Pre-dose, 2, 4 hours post-dose

Notes:

[50] - 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[51]	0[52]		
Units: ng/mL				
arithmetic mean (standard deviation)	()	()		

Notes:

[51] - PK was planned to be reported with other clinical studies. Hence,no individual PK data was reported.
[52] - PK was planned to be reported with other clinical studies. Hence,no individual PK data was reported.

Statistical analyses

No statistical analyses for this end point

Primary: Time to Reach Maximum Observed Drug Concentration (Tmax) of Teduglutide in Plasma

End point title	Time to Reach Maximum Observed Drug Concentration (Tmax) of Teduglutide in Plasma[53]

End point description:

Since only 2 sparse PK samples were collected during the study, PK parameters were not estimated and analysed using this study samples. Therefore, no PK parameters were reported in this study.

End point type	Primary

End point timeframe:

Baseline: Pre-dose, 1, 6 hours post-dose; Week 4: Pre-dose, 2, 4 hours post-dose

Notes:

[53] - 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[54]	0[55]		
Units: hour				
median (full range (min-max))	(to)	(to)		

Notes:

[54] - PK was planned to be reported with other clinical studies. Hence, no individual PK data was reported.
[55] - PK was planned to be reported with other clinical studies. Hence, no individual PK data was reported.

Statistical analyses

No statistical analyses for this end point

Primary: Terminal-Phase Half-life (t1/2) of Teduglutide in Plasma

End point title	Terminal-Phase Half-life (t1/2) of Teduglutide in Plasma[56]

End point description:

Since only 2 sparse PK samples were collected during the study, PK parameters were not estimated and analysed using this study samples. Therefore, no PK parameters were reported in this study.

End point type	Primary

End point timeframe:

Baseline: Pre-dose, 1, 6 hours post-dose; Week 4: Pre-dose, 2, 4 hours post-dose

Notes:

[56] - 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[57]	0[58]		
Units: hour				
median (full range (min-max))	(to)	(to)		

Notes:

[57] - PK was planned to be reported with other clinical studies. Hence,no individual PK data was reported.

[58] - PK was planned to be reported with other clinical studies. Hence,no individual PK data was reported.

Statistical analyses

No statistical analyses for this end point

Primary: Apparent Clearance (CL/F) of Teduglutide

End point title	Apparent Clearance (CL/F) of Teduglutide[59]

End point description:

Since only 2 sparse PK samples were collected during the study, PK parameters were not estimated and analysed using this study samples. Therefore, no PK parameters were reported in this study.

End point type	Primary

End point timeframe:

Baseline: Pre-dose, 1, 6 hours post-dose; Week 4: Pre-dose, 2, 4 hours post-dose

Notes:

[59] - 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[60]	0[61]		
Units: Liter per hour (L/hr)				
arithmetic mean (standard deviation)	()	()		

Notes:

[60] - PK was planned to be reported with other clinical studies. Hence,no individual PK data was reported.

[61] - PK was planned to be reported with other clinical studies. Hence,no individual PK data was reported.

Statistical analyses

No statistical analyses for this end point

Primary: Apparent Volume of Distribution (V[lambda z]/F) of Teduglutide

End point title	Apparent Volume of Distribution (V[lambda z]/F) of

End point description:

Since only 2 sparse PK samples were collected during the study, PK parameters were not estimated and analysed using this study samples. Therefore, no PK parameters were reported in this study.

End point type	Primary

End point timeframe:

Baseline: Pre-dose, 1, 6 hours post-dose; Week 4: Pre-dose, 2, 4 hours post-dose

Notes:

[62] - 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[63]	0[64]		
Units: per hour				
arithmetic mean (standard deviation)	()	()		

Notes:

[63] - PK was planned to be reported with other clinical studies. Hence,no individual PK data was reported.
[64] - PK was planned to be reported with other clinical studies. Hence,no individual PK data was reported.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From start of study drug administration up to end of the study (up to Week 28)

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.0

Reporting groups

Reporting group title	Total Children (1 - 15 years)

Reporting group description:

Subjects with aged from 1 through 15 years received teduglutide 0.05 mg/kg/day SC injection once daily for 24 weeks and completed the study at Week 28.

Reporting group title	Infants (4 - 12 months)

Reporting group description:

Subjects with Infants aged from 4 through less than 12 months received teduglutide 0.05 mg/kg/day SC injection once daily for 24 weeks and completed the study at Week 28.

Serious adverse events	Total Children (1 - 15 years)	Infants (4 - 12 months)	
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 8 (75.00%)	2 / 2 (100.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 8 (0.00%)	2 / 2 (100.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	1 / 8 (12.50%)	0 / 2 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 8 (12.50%)	0 / 2 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Enterocolitis			
subjects affected / exposed	2 / 8 (25.00%)	0 / 2 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Upper respiratory tract inflammation			
subjects affected / exposed	0 / 8 (0.00%)	1 / 2 (50.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Adenovirus infection			
subjects affected / exposed	1 / 8 (12.50%)	0 / 2 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device related infection			
subjects affected / exposed	3 / 8 (37.50%)	1 / 2 (50.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	1 / 8 (12.50%)	0 / 2 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hand-foot-and-mouth disease			
subjects affected / exposed	1 / 8 (12.50%)	0 / 2 (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	2 / 8 (25.00%)	0 / 2 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			
subjects affected / exposed	0 / 8 (0.00%)	1 / 2 (50.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

Product issues			
Device damage			
subjects affected / exposed	1 / 8 (12.50%)	0 / 2 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Total Children (1 - 15 years)	Infants (4 - 12 months)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	8 / 8 (100.00%)	1 / 2 (50.00%)	
Investigations			
Amylase increased			
subjects affected / exposed	1 / 8 (12.50%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Injury, poisoning and procedural complications			
Frostbite			
subjects affected / exposed	1 / 8 (12.50%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Gastrostomy tube site complication			
subjects affected / exposed	1 / 8 (12.50%)	0 / 2 (0.00%)	
occurrences (all)	2	0	
Vaccination complication			
subjects affected / exposed	0 / 8 (0.00%)	1 / 2 (50.00%)	
occurrences (all)	0	1	
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 8 (12.50%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Injection site bruising			
subjects affected / exposed	2 / 8 (25.00%)	0 / 2 (0.00%)	
occurrences (all)	9	0	
Catheter site granuloma			
subjects affected / exposed	1 / 8 (12.50%)	0 / 2 (0.00%)	
occurrences (all)	1	0	

Injection site erythema			
subjects affected / exposed	3 / 8 (37.50%)	0 / 2 (0.00%)	
occurrences (all)	12	0	
Injection site haematoma			
subjects affected / exposed	1 / 8 (12.50%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Injection site induration			
subjects affected / exposed	1 / 8 (12.50%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Injection site pain			
subjects affected / exposed	1 / 8 (12.50%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Injection site rash			
subjects affected / exposed	1 / 8 (12.50%)	0 / 2 (0.00%)	
occurrences (all)	4	0	
Injection site reaction			
subjects affected / exposed	1 / 8 (12.50%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Pyrexia			
subjects affected / exposed	2 / 8 (25.00%)	0 / 2 (0.00%)	
occurrences (all)	3	0	
Immune system disorders			
Food allergy			
subjects affected / exposed	1 / 8 (12.50%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	1 / 8 (12.50%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Abdominal pain			
subjects affected / exposed	1 / 8 (12.50%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Constipation			
subjects affected / exposed	2 / 8 (25.00%)	0 / 2 (0.00%)	
occurrences (all)	2	0	
Dental caries			

subjects affected / exposed	1 / 8 (12.50%)	0 / 2 (0.00%)
occurrences (all)	1	0
Enteritis		
subjects affected / exposed	1 / 8 (12.50%)	0 / 2 (0.00%)
occurrences (all)	1	0
Enterocolitis		
subjects affected / exposed	0 / 8 (0.00%)	1 / 2 (50.00%)
occurrences (all)	0	1
Gastritis		
subjects affected / exposed	1 / 8 (12.50%)	0 / 2 (0.00%)
occurrences (all)	1	0
Proctalgia		
subjects affected / exposed	1 / 8 (12.50%)	0 / 2 (0.00%)
occurrences (all)	1	0
Reproductive system and breast disorders		
Balanoposthitis		
subjects affected / exposed	1 / 8 (12.50%)	0 / 2 (0.00%)
occurrences (all)	1	0
Respiratory, thoracic and mediastinal disorders		
Upper respiratory tract inflammation		
subjects affected / exposed	0 / 8 (0.00%)	1 / 2 (50.00%)
occurrences (all)	0	2
Skin and subcutaneous tissue disorders		
Dermatitis contact		
subjects affected / exposed	0 / 8 (0.00%)	1 / 2 (50.00%)
occurrences (all)	0	1
Dermatitis diaper		
subjects affected / exposed	1 / 8 (12.50%)	1 / 2 (50.00%)
occurrences (all)	1	2
Dry skin		
subjects affected / exposed	2 / 8 (25.00%)	1 / 2 (50.00%)
occurrences (all)	2	1
Eczema		
subjects affected / exposed	1 / 8 (12.50%)	0 / 2 (0.00%)
occurrences (all)	1	0
Rash		

subjects affected / exposed	4 / 8 (50.00%)	0 / 2 (0.00%)	
occurrences (all)	5	0	

Infections and infestations			
Device related infection			
subjects affected / exposed	1 / 8 (12.50%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Gingivitis			
subjects affected / exposed	1 / 8 (12.50%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Hand-foot-and-mouth disease			
subjects affected / exposed	1 / 8 (12.50%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Influenza			
subjects affected / exposed	1 / 8 (12.50%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Medical device site infection			
subjects affected / exposed	2 / 8 (25.00%)	0 / 2 (0.00%)	
occurrences (all)	2	0	
Otitis media			
subjects affected / exposed	0 / 8 (0.00%)	1 / 2 (50.00%)	
occurrences (all)	0	1	
Pharyngitis streptococcal			
subjects affected / exposed	1 / 8 (12.50%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Rhinitis			
subjects affected / exposed	1 / 8 (12.50%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Viral upper respiratory tract infection			
subjects affected / exposed	6 / 8 (75.00%)	1 / 2 (50.00%)	
occurrences (all)	6	1	

Product issues			
Device damage			
subjects affected / exposed	2 / 8 (25.00%)	0 / 2 (0.00%)	
occurrences (all)	2	0	

Metabolism and nutrition disorders			

Dehydration			
subjects affected / exposed	1 / 8 (12.50%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Hyperlipasaemia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Hypertriglyceridaemia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Hyperzincaemia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 2 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
27 April 2016	Amendment 1: - Identification of age range (1 through 15 years old). - Update of severity of AEs (Utility of severity criteria of AE from National Cancer Institute-Common Terminology Criteria for Adverse Events (NCI-CTCAE) to evaluate dose interruption). - Addition of continuation of output diary data collection over a 48-hour period of PS and enteral nutrition (EN) stability before every site visit.
06 June 2017	Amendment 2: - Change of examination (removal of urine osmolality and urine sodium from the urinalysis).
24 January 2018	Amendment 3: - Addition of direct bilirubin in laboratory tests.
12 June 2018	Amendment 4: - Addition of infants with 4 months through <12 months corrected gestational age.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

 None reported