Clinical trial results:
A Phase 3, Open-label Safety Study of Teduglutide in Japanese Pediatric Patients With Short Bowel Syndrome Who are Dependent on Parenteral Support, Aged 4 Months of Corrected Gestational Age or Older, and Requiring the Dosing of 1.25 mg Formulation

Summary

EudraCT number	2022-003572-16
Trial protocol	Outside EU/EEA
Global end of trial date	27 September 2023

Results information

Result version number	v1 (current)
This version publication date	05 April 2024
First version publication date	05 April 2024

Trial information

Trial identification

Sponsor protocol code	TAK-633-3008

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05027308
WHO universal trial number (UTN)	U1111-1267-3327

Notes:

Sponsors

Sponsor organisation name	Takeda
Sponsor organisation address	95 Hayden Avenue, Lexington, United States, MA 02421
Public contact	Study Director, Takeda, TrialDisclosures@takeda.com
Scientific contact	Study Director, Takeda, TrialDisclosures@takeda.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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	27 September 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	27 September 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of the trial was to check for side effects from teduglutide in Japanese Children With Short Bowel Syndrome.

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	04 January 2022
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Japan: 3
Worldwide total number of subjects	3
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)	1
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:

Three participants took part in the study at six investigative sites in Japan from 4 January 2022 to 27 September 2023.

Pre-assignment

Screening details:

Pediatric participants with a diagnosis of short bowel syndrome (SBS) dependent on parenteral support (PS) were enrolled in the study based on the eligibility criteria to receive teduglutide.

Period 1

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

Arms

Arm title	Teduglutide

Arm description:

Participants received teduglutide 0.05 milligram per kilogram [mg/kg] (0.025 mg/kg for participants with moderate or greater renal impairment) subcutaneous [SC] injection once daily in a 28-week treatment cycle consisting of a 24-week treatment period followed by a 4-week no treatment follow-up period for a maximum of 3 cycles.

Arm type	Experimental
Investigational medicinal product name	Teduglutide
Investigational medicinal product code	
Other name	TAK-633
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Teduglutide 0.05 mg/kg SC injection

Number of subjects in period 1	Teduglutide
Started	3
Completed	3

Baseline characteristics

Reporting groups	
Reporting group title	Teduglutide
Reporting group description:	
Participants received teduglutide 0.05 milligram per kilogram [mg/kg] (0.025 mg/kg for participants with moderate or greater renal impairment) subcutaneous [SC] injection once daily in a 28-week treatment cycle consisting of a 24-week treatment period followed by a 4-week no treatment follow-up period for a maximum of 3 cycles.	

Reporting group values	Teduglutide	Total	
Number of subjects	3	3	
Age Categorical Units: Subjects			
Gender categorical Units: Subjects			
Female	2	2	
Male	1	1	
Age categorical Units: Subjects			
<= 18 years	3	3	
Between 18 and 65	0	0	
>= 65 years	0	0	
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	3	3	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	0	0	
White	0	0	
More than one race	0	0	
Unknown or Not Reported	0	0	
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	0	0	
Not Hispanic or Latino	3	3	
Unknown or Not Reported	0	0	
Region of Enrollment Units: Subjects			
Japan Japan	3	3	
Weight for Age Z-Score at Baseline			
A z-score is 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.			
Units: Z score			
arithmetic mean	-3.017		
standard deviation	± 1.8048	-	
Height for Age Z-Score at Baseline			

A z-score is 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.			
Units: Z score			
arithmetic mean	-3.060		
standard deviation	± 1.1601	-	

End points

End points reporting groups

Reporting group title	Teduglutide

Reporting group description:

Participants received teduglutide 0.05 milligram per kilogram [mg/kg] (0.025 mg/kg for participants with moderate or greater renal impairment) subcutaneous [SC] injection once daily in a 28-week treatment cycle consisting of a 24-week treatment period followed by a 4-week no treatment follow-up period for a maximum of 3 cycles.

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 AE is defined as any untoward medical occurrence in a clinical investigation participant administered a drug; it does not necessarily have to 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 Analysis Set included all participants who received at least 1 dose of study teduglutide.

End point type	Primary

End point timeframe:

From first dose of study drug until follow-up visit (4 weeks after end of treatment [EOT]/end of termination [ET] {up to 47.3-51.3 weeks})

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive statistics were planned to be analysed for this endpoint.

End point values	Teduglutide			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: participants				
Number of participants analyzed	3			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Adverse Events of Special Interest (AESIs)

End point title	Number of Participants With Adverse Events of Special Interest (AESIs)[2]

End point description:

An AE is defined as any untoward medical occurrence in a clinical investigation participant administered a drug; it does not necessarily have to have a causal relationship with this treatment. An AESI, whether serious or non-serious, is one of scientific and medical concern specific to the compound or program, for which ongoing monitoring and rapid communication by the investigator to the sponsor may be appropriate. Safety Analysis Set included all participants who received at least 1 dose of study teduglutide.

End point type	Primary

End point timeframe:

From first dose of study drug until follow-up visit (4 weeks after EOT/ET [up to 47.3-51.3 weeks])

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: Only descriptive statistics were planned to be analysed for this endpoint.

End point values	Teduglutide			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: participants				
Number of participants analyzed	0			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Serious Adverse Events (SAEs)

End point title	Number of Participants With Serious Adverse Events (SAEs)[3]

End point description:

An AE is defined as any untoward medical occurrence in a clinical investigation participant administered a drug; it does not necessarily have to have a causal relationship with this treatment. An SAE is defined as any untoward medical occurrence that at any dose: results in death, is life threatening, requires inpatient hospitalization or prolongation of existing hospitalization, results in persistent or significant disability/incapacity, leads to a congenital anomaly /birth defect, is the other important medical event. Safety Analysis Set included all participants who received at least 1 dose of study teduglutide.

End point type	Primary

End point timeframe:

From first dose of study drug until follow-up visit (4 weeks after EOT/ET [up to 47.3-51.3 weeks])

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: Only descriptive statistics were planned to be analysed for this endpoint.

End point values	Teduglutide			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: participants				
Number of participants analyzed	3			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Clinically Significant Abnormalities in Vital Signs Reported as an Adverse Event

End point title	Number of Participants With Clinically Significant Abnormalities in Vital Signs Reported as an Adverse Event[4]

End point description:

Vital signs include systolic and diastolic blood pressure, heart rate and body temperature. Safety Analysis Set included all participants who received at least 1 dose of study teduglutide.

End point type	Primary

End point timeframe:

From first dose of study drug until follow-up visit (4 weeks after EOT/ET [up to 47.3-51.3 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: Only descriptive statistics were planned to be analysed for this endpoint.

End point values	Teduglutide			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: participants				
Number of participants analyzed	0			

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in Z-Score of Body Weight at EOT

End point title	Change From Baseline in Z-Score of Body Weight at EOT[5]

End point description:

A z-score is 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. Safety Analysis Set included all participants who received at least 1 dose of study teduglutide.

End point type	Primary

End point timeframe:

Baseline, EOT (up to 47.3-51.3 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: Only descriptive statistics were planned to be analysed for this endpoint.

End point values	Teduglutide			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: Z score				
arithmetic mean (standard deviation)				
Number of participants analyzed	1.637 (± 2.8839)			

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in Z-Score of Height at EOT

End point title	Change From Baseline in Z-Score of Height at EOT[6]

End point description:

A z-score is 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. Safety Analysis Set included all participants who received at least 1 dose of study teduglutide.

End point type	Primary

End point timeframe:

Baseline, EOT (up to 47.3-51.3 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: Only descriptive statistics were planned to be analysed for this endpoint.

End point values	Teduglutide			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: Z score				
arithmetic mean (standard deviation)				
Number of participants analyzed	0.590 (± 1.9949)			

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in Z-Score of Head Circumference at EOT

End point title	Change From Baseline in Z-Score of Head Circumference at EOT[7]

End point description:

A z-score is 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. Safety Analysis Set included all participants who received at least 1 dose of study teduglutide. Number of subjects analysed is the number of participants with data available for analyses.

End point type	Primary

End point timeframe:

Baseline, EOT (up to 47.3-51.3 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: Only descriptive statistics were planned to be analysed for this endpoint.

End point values	Teduglutide			
Subject group type	Reporting group			
Number of subjects analysed	2			
Units: Z score				
arithmetic mean (standard deviation)				
Number of participants analyzed	1.130 (± 0.4101)			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With a Change in Stool Output Reported as an Adverse Event

End point title	Number of Participants With a Change in Stool Output Reported as an Adverse Event[8]

End point description:

Urine and stool output was recorded and calculated in the output diary over a 48-hour period of PS and EN stability before every site visit and within 1 week of implementing a change in the PS prescription. Safety Analysis Set included all participants who received at least 1 dose of study teduglutide.

End point type	Primary

End point timeframe:

From first dose of study drug until follow-up visit (4 weeks after EOT/ET [up to 47.3-51.3 weeks])

Notes:

[8] - 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: Only descriptive statistics were planned to be analysed for this endpoint.

End point values	Teduglutide			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: participants	0			

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in Z-Score of Weight-for-Length at EOT

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

End point description:

A z-score is 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. Safety Analysis Set included all participants who received at least 1 dose of study teduglutide. Overall number analyzed is the number of participants with data available for analyses.

End point type	Primary

End point timeframe:

Baseline, EOT (up to 47.3-51.3 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: Only descriptive statistics were planned to be analysed for this endpoint.

End point values	Teduglutide			
Subject group type	Reporting group			
Number of subjects analysed	1			
Units: Z score				
arithmetic mean (standard deviation)				
Number of participants analyzed	4.240 (± 999)			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With a Change in Urine Output Reported as an Adverse Event

End point title	Number of Participants With a Change in Urine Output Reported as an Adverse Event[10]

End point description:

Urine and stool output was recorded and calculated in the output diary over a 48-hour period of parenteral support (PS) and enteral nutrition (EN) stability before every site visit and within 1 week of implementing a change in the PS prescription. Safety Analysis Set included all participants who received at least 1 dose of study teduglutide.

End point type	Primary

End point timeframe:

From first dose of study drug until follow-up visit (4 weeks after EOT/ET [up to 47.3-51.3 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: Only descriptive statistics were planned to be analysed for this endpoint.

End point values	Teduglutide			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: participants	1			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With any Laboratory Safety Finding Reported as an Adverse Event

End point title	Number of Participants With any Laboratory Safety Finding Reported as an Adverse Event[11]

End point description:

Laboratory safety parameters included biochemistry, hematology, and urinalysis. Safety Analysis Set included all participants who received at least 1 dose of study teduglutide.

End point type	Primary

End point timeframe:

From first dose of study drug until follow-up visit (4 weeks after EOT/ET [up to 47.3-51.3 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: Only descriptive statistics were planned to be analysed for this endpoint.

End point values	Teduglutide			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: participants	1			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in PS Volume

End point title	Change From Baseline in PS Volume

End point description:

PS (parenteral nutrition or intravenous fluids) was considered for managing nutritional support in terms of volume and calories during the treatment period. An end of treatment (EOT) was defined as the last determination of endpoint of the last cycle. Full Analysis Set included all enrolled participants, who were not screen failures, regardless of whether participants took any dose of teduglutide in the study. For Cycle 2, Week 24, n=2; Cycle 3, n=1.

End point type	Secondary

End point timeframe:

Baseline, Cycle 1 = Week 1, 2, 4, 8, 12, 16, 20, 24, and EOT, Cycle 2: Week 0, 1, 2, 4, 8, 12, 16, 20, 24, and EOT, Cycle 3 = Week 0, 1, 2, and EOT and overall EOT (for up to 47.3-51.3 weeks) [cycle length=28 weeks]

End point values	Teduglutide			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: milliliters per kilograms (mL/kg)/day				
arithmetic mean (standard deviation)				
Cycle 1, Week 1	4.82 (± 13.391)			
Cycle 1, Week 2	11.27 (± 26.175)			
Cycle 1, Week 4	-1.51 (± 8.881)			
Cycle 1, Week 8	13.48 (± 19.471)			
Cycle 1, Week 12	6.97 (± 22.006)			
Cycle 1, Week 16	1.61 (± 22.136)			
Cycle 1, Week 20	2.94 (± 8.794)			
Cycle 1, Week 24	1.24 (± 12.938)			
Cycle 1, EOT	1.24 (± 12.938)			
Cycle 2, Week 0	0.07 (± 17.520)			
Cycle 2, Week 1	0.26 (± 20.634)			

Cycle 2, Week 2	-2.81 (± 18.432)			
Cycle 2, Week 4	-0.62 (± 16.671)			
Cycle 2, Week 8	-6.00 (± 18.175)			
Cycle 2, Week 12	-10.21 (± 16.645)			
Cycle 2, Week 16	-13.03 (± 14.937)			
Cycle 2, Week 20	-9.73 (± 3.073)			
Cycle 2, Week 24	-10.50 (± 6.059)			
Cycle 2, EOT	-10.98 (± 4.363)			
Cycle 3, Week 0	-17.69 (± 999)			
Cycle 3, Week 1	-18.79 (± 999)			
Cycle 3, Week 2	-6.93 (± 999)			
Cycle 3, EOT	-6.93 (± 999)			
Overall EOT	-13.13 (± 37.259)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in PS Volume

End point title	Percent Change From Baseline in PS Volume

End point description:

Percent change from baseline in PS volume was calculated as follows; (PS volume at each point [Week 1, 2, 4, 8, 12, 16, 20, 24, and EOT] - PS volume at baseline)/ PS volume at baseline *100 (percent). PS (parenteral nutrition or intravenous fluids) was to be considered for managing nutritional support in terms of volume and calories during the treatment period. An EOT was defined as the last determination of endpoint of the last cycle. Full Analysis Set included all enrolled participants, who were not screen failures, regardless of whether participants took any dose of teduglutide in the study. For Cycle 2, Week 24, n=2; Cycle 3, n=1.

End point type	Secondary

End point timeframe:

Baseline, Cycle 1 = Week 1, 2, 4, 8, 12, 16, 20, 24, and EOT, Cycle 2 = Week 0, 1, 2, 4, 8, 12, 16, 20, 24, and EOT, Cycle 3 = Week 0, 1, 2, and EOT and overall EOT (for up to 47.3-51.3 weeks) [cycle length=28 weeks]

End point values	Teduglutide			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: percent change				
arithmetic mean (standard deviation)				
Cycle 1, Week 1	3.13 (± 10.041)			
Cycle 1, Week 2	7.82 (± 19.334)			

Cycle 1, Week 4	-1.31 (± 6.491)			
Cycle 1, Week 8	10.27 (± 13.788)			
Cycle 1, Week 12	5.83 (± 15.979)			
Cycle 1, Week 16	1.89 (± 16.386)			
Cycle 1, Week 20	1.82 (± 6.673)			
Cycle 1, Week 24	0.66 (± 9.511)			
Cycle 1, EOT	0.66 (± 9.511)			
Cycle 2, Week 0	-0.07 (± 12.808)			
Cycle 2, Week 1	0.11 (± 15.080)			
Cycle 2, Week 2	-2.32 (± 13.465)			
Cycle 2, Week 4	-0.71 (± 12.202)			
Cycle 2, Week 8	-4.81 (± 13.214)			
Cycle 2, Week 12	-8.42 (± 11.909)			
Cycle 2, Week 16	-10.14 (± 10.452)			
Cycle 2, Week 20	-8.20 (± 0.509)			
Cycle 2, Week 24	-9.28 (± 2.092)			
Cycle 2, EOT	-9.11 (± 1.508)			
Cycle 3, Week 0	-12.86 (± 999)			
Cycle 3, Week 1	-13.67 (± 999)			
Cycle 3, Week 2	-5.04 (± 999)			
Cycle 3, EOT	-5.04 (± 999)			
Overall EOT	-10.99 (± 27.093)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants who Demonstrate at least 20 Percent (%) Reduction From Baseline in PS Volume

End point title	Number of Participants who Demonstrate at least 20 Percent (%) Reduction From Baseline in PS Volume

End point description:

PS (parenteral nutrition or intravenous fluids) was considered for managing nutritional support in terms of volume and calories during the treatment period. An EOT was defined as the last determination of endpoint of the last cycle. Full Analysis Set included all enrolled participants, who were not screen failures, regardless of whether participants took any dose of teduglutide in the study. For Cycle 2, Week 24, n=2; Cycle 3, n=1.

End point type	Secondary

End point timeframe:

Baseline, Cycle 1 = Week 1, 2, 4, 8, 12, 16, 20, 24, and EOT, Cycle 2 = Week 0, 1, 2, 4, 8, 12, 16, 20, 24, and EOT, Cycle 3 = Week 0, 1, 2, and EOT and overall EOT (for up to 47.3-51.3 weeks) [cycle

length=28 weeks]

End point values	Teduglutide			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: participants				
Cycle 1, Week 1	0			
Cycle 1, Week 2	0			
Cycle 1, Week 4	0			
Cycle 1, Week 8	0			
Cycle 1, Week 12	0			
Cycle 1, Week 16	1			
Cycle 1, Week 20	0			
Cycle 1, Week 24	0			
Cycle 1, EOT	0			
Cycle 2, Week 0	0			
Cycle 2, Week 1	1			
Cycle 2, Week 2	1			
Cycle 2, Week 4	0			
Cycle 2, Week 8	1			
Cycle 2, Week 12	1			
Cycle 2, Week 16	1			
Cycle 2, Week 20	0			
Cycle 2, Week 24	0			
Cycle 2, EOT	0			
Cycle 3, Week 0	0			
Cycle 3, Week 1	0			
Cycle 3, Week 2	0			
Cycle 3, EOT	0			
Overall EOT	1			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants who Achieved Enteral Autonomy

End point title	Number of Participants who Achieved Enteral Autonomy

End point description:

Achieving enteral autonomy is defined as complete weaning off PS. PS (parenteral nutrition or intravenous fluids) was to be considered for managing nutritional support in terms of volume and calories during the treatment period. Full Analysis Set included all enrolled participants, who were not screen failures, regardless of whether participants took any dose of teduglutide in the study. For Cycle 2, Week 24, n=2; Cycle 3, n=1.

End point type	Secondary

End point timeframe:

Cycle 1 = Week 1, 2, 4, 8, 12, 16, 20, 24, and EOT, Cycle 2 = Week 0, 1, 2, 4, 8, 12, 16, 20, 24, and EOT, Cycle 3 = Week 0, 1, 2, and EOT and overall EOT (for up to 47.3-51.3 weeks) [cycle length=28 weeks]

End point values	Teduglutide			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: participants				
Cycle 1, Week 1	0			
Cycle 1, Week 2	0			
Cycle 1, Week 4	0			
Cycle 1, Week 8	0			
Cycle 1, Week 12	0			
Cycle 1, Week 16	0			
Cycle 1, Week 20	0			
Cycle 1, Week 24	0			
Cycle 1, EOT	0			
Cycle 2, Week 0	0			
Cycle 2, Week 1	0			
Cycle 2, Week 2	0			
Cycle 2, Week 4	0			
Cycle 2, Week 8	0			
Cycle 2, Week 12	0			
Cycle 2, Week 16	0			
Cycle 2, Week 20	0			
Cycle 2, Week 24	0			
Cycle 2, EOT	0			
Cycle 3, Week 0	0			
Cycle 3, Week 1	0			
Cycle 3, Week 2	0			
Cycle 3, EOT	0			
Overall EOT	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Number of Days per Week of PS Usage at EOT

End point title	Change from Baseline in Number of Days per Week of PS Usage at EOT

End point description:

PS (parenteral nutrition or intravenous fluids) was considered for managing nutritional support in terms of volume and calories during the treatment period. Full Analysis Set included all enrolled participants, who were not screen failures, regardless of whether participants took any dose of teduglutide in the study. For Cycle 2, Week 24, n=2; Cycle 3, n=1.

End point type	Secondary

End point timeframe:

Baseline, Cycle 1 = Week 1, 2, 4, 8, 12, 16, 20, 24, and EOT, Cycle 2 = Week 0, 1, 2, 4, 8, 12, 16, 20, 24, and EOT, Cycle 3 = Week 0, 1, 2, and EOT, and overall EOT (for 47.3-51.3 weeks) [cycle length=28 weeks]

End point values	Teduglutide			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: days per week				
arithmetic mean (standard deviation)				
Cycle 1, Week 1	0.0 (± 0.00)			
Cycle 1, Week 2	0.0 (± 0.00)			
Cycle 1, Week 4	0.0 (± 0.00)			
Cycle 1, Week 8	0.0 (± 0.00)			
Cycle 1, Week 12	0.0 (± 0.00)			
Cycle 1, Week 16	0.0 (± 0.00)			
Cycle 1, Week 20	0.0 (± 0.00)			
Cycle 1, Week 24	0.0 (± 0.00)			
Cycle 1, EOT	0.0 (± 0.00)			
Cycle 2, Week 0	0.0 (± 0.00)			
Cycle 2, Week 1	0.0 (± 0.00)			
Cycle 2, Week 2	0.0 (± 0.00)			
Cycle 2, Week 4	0.0 (± 0.00)			
Cycle 2, Week 8	0.0 (± 0.00)			
Cycle 2, Week 12	0.0 (± 0.00)			
Cycle 2, Week 16	0.0 (± 0.00)			
Cycle 2, Week 20	0.0 (± 0.00)			
Cycle 2, Week 24	0.0 (± 0.00)			
Cycle 2, EOT	0.0 (± 0.00)			
Cycle 3, Week 0	0.0 (± 0.00)			
Cycle 3, Week 1	0.0 (± 0.00)			
Cycle 3, Week 2	0.0 (± 0.00)			
Cycle 3, EOT	0.0 (± 0.00)			
Overall EOT	0.0 (± 0.00)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first dose of study drug until follow-up visit (4 weeks after EOT/ET [up to 47.3-51.3 weeks])

Adverse event reporting additional description:

Safety Analysis Set included all participants who received at least 1 dose of study teduglutide.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26.0

Reporting groups

Reporting group title	Teduglutide

Reporting group description:

Participants received teduglutide 0.05 milligram per kilogram (mg/kg) (0.025 mg/kg for participants with moderate or greater renal impairment) SC injection once daily for 24 weeks followed by no treatment period for 4 weeks or a maximum of 3 cycles (cycle length=24 weeks.

Serious adverse events	Teduglutide		
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 3 (100.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
General disorders and administration site conditions			
Catheter site pruritus			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular device occlusion			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Bacteraemia			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Device related infection			

subjects affected / exposed	2 / 3 (66.67%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 0		
Product issues			
Device breakage			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Teduglutide		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 3 (100.00%)		
Investigations			
Blood iron increased			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
General disorders and administration site conditions			
Catheter site rash			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Gastrointestinal disorders			
Enterocolitis			
subjects affected / exposed	2 / 3 (66.67%)		
occurrences (all)	2		
Hepatobiliary disorders			
Liver disorder			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Upper respiratory tract inflammation			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Renal and urinary disorders			

Oliguria subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1		
Infections and infestations COVID-19 subjects affected / exposed occurrences (all) Parainfluenzae virus infection subjects affected / exposed occurrences (all) Skin candida subjects affected / exposed occurrences (all) Respiratory syncytial virus infection subjects affected / exposed occurrences (all)	 2 / 3 (66.67%) 2 1 / 3 (33.33%) 1 1 / 3 (33.33%) 1 2 / 3 (66.67%) 2		
Metabolism and nutrition disorders Lactic acidosis subjects affected / exposed occurrences (all)	 1 / 3 (33.33%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
01 December 2021	The following changes were implemented based on Amendment 1: 1. Changed the screening period. 2. Added the expected maximum duration of treatment (approximately 18 months). 3. Added a description to the estimated glomerular filtration rate criteria. 4. Amended the errors related to the change of screening period for another treatment cycle. 5. Removed "enteral glutamine" from exclusion criteria with considering the clinical settings in Japan. 6. Added a description to allow the participants who develop renal impairment during the study to continue the dosing. 7. Added a description to avoid the situation that teduglutide is administered twice a day with more than 12 hours separation. 8. Error modifications and description adjustments where applicable.
19 May 2022	The following changes were implemented based on Amendment 2: 1. Added a study procedure "evaluation of escape criteria" at Week 24. 2. Added the maximum duration of treatment. 3. Corrected a criterion of participants' body weight, who develop renal impairment to continue the dosing during the study for consistency with the inclusion criterion 4. 4. Added a description to clarify that estimated glomerular filtration rates are calculated with the quintic equation. 5. Corrected typographical errors.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported