



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 Serious Adverse Events (SAEs)

| | |
|-----------------|--------------------------------------------------------------------------|
| End point title | Number of Participants With Serious Adverse Events (SAEs) ^[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 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:

[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 | 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) ^[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 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:

[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 | 0 | | | |

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 (\pm 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 (\pm 0.4101) | | | |

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:

[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 | 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 Stool Output Reported as an Adverse Event

| | |
|-----------------|--------------------------------------------------------------------------------------------------|
| End point title | Number of Participants With a Change in Stool Output Reported as an Adverse Event ^[9] |
|-----------------|--------------------------------------------------------------------------------------------------|

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:

[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 | 3 | | | |
| Units: participants | 0 | | | |

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.

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|----------------|-----------|
| 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

| 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) | 2 / 3 (66.67%) 2 | | |
| Parainfluenzae virus infection subjects affected / exposed occurrences (all) | 1 / 3 (33.33%) 1 | | |
| Skin candida subjects affected / exposed occurrences (all) | 1 / 3 (33.33%) 1 | | |
| Respiratory syncytial virus infection subjects affected / exposed occurrences (all) | 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