

**Clinical trial results:****A 12-Week Pharmacokinetic, Safety, and Pharmacodynamic Study of Teduglutide in Pediatric Subjects Aged 1 Year through 17 Years, with Short Bowel Syndrome who are Dependent on Parenteral Support****Summary**

|                          |                 |
|--------------------------|-----------------|
| EudraCT number           | 2013-004588-30  |
| Trial protocol           | SE GB           |
| Global end of trial date | 09 January 2015 |

**Results information**

|                                |               |
|--------------------------------|---------------|
| Result version number          | v1 (current)  |
| This version publication date  | 28 April 2016 |
| First version publication date | 28 April 2016 |

**Trial information****Trial identification**

|                       |             |
|-----------------------|-------------|
| Sponsor protocol code | TED-C13-003 |
|-----------------------|-------------|

**Additional study identifiers**

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT01952080 |
| WHO universal trial number (UTN)   | -           |

Notes:

**Sponsors**

|                              |   |
|------------------------------|---|
| Sponsor organisation name    | NPS Pharmaceuticals, Inc. (Since 21 February 2015, NPS Pharmaceuticals, Inc. has been a member of the Shire Group of companies) |
| Sponsor organisation address | 300 Shire Way, Lexington, United States, 02421  |
| Public contact               | Shire Development LLC, Study Physician , +1 8668425335,   |
| Scientific contact           | Shire Development LLC, Study Physician, +1 8668425335,  |

Notes:

**Paediatric regulatory details**

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

Notes:

## Results analysis stage

|  |                 |
|--|-----------------|
| Analysis stage                                       | Final           |
| Date of interim/final analysis                       | 09 January 2015 |
| Is this the analysis of the primary completion data? | No              |
| Global end of trial reached?                         | Yes             |
| Global end of trial date                             | 09 January 2015 |
| Was the trial ended prematurely?                     | No              |

Notes:

## General information about the trial

Main objective of the trial:

The objective of this clinical study was to evaluate the pharmacokinetic (PK) profile, safety and tolerability, and pharmacodynamic effects of teduglutide compared with standard of care in pediatric subjects (aged 1 year through 17 years) with short bowel syndrome (SBS) who are dependent on parenteral support.

Protection of trial subjects:

This protocol was conducted in accordance with the current applicable International Conference on Harmonisation (ICH) Guidelines, Good Clinical Practice, and the World Medical Association Declaration of Helsinki and its amendments concerning medical research in humans at the time of the study was conducted.

Background therapy: -

Evidence for comparator: -

|   |                  |
|---|------------------|
| Actual start date of recruitment                          | 14 November 2013 |
| Long term follow-up planned                               | No               |
| Independent data monitoring committee (IDMC) involvement? | Yes              |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |                   |
|--------------------------------------|-------------------|
| Country: Number of subjects enrolled | United Kingdom: 3 |
| Country: Number of subjects enrolled | United States: 39 |
| Worldwide total number of subjects   | 42                |
| EEA total number of subjects         | 3                 |

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)  | 4  |
| Children (2-11 years)                     | 35 |
| Adolescents (12-17 years)                 | 3  |
| Adults (18-64 years)                      | 0  |
| From 65 to 84 years                       | 0  |



## Subject disposition

### Recruitment

Recruitment details:

Subjects were recruited to participate at 17 sites in 2 countries (United Kingdom and United States of America)

### Pre-assignment

Screening details:

Subjects were screened for eligibility for a minimum of 2 weeks.

### 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 |
|------------------------------|-----|

|                  |                  |
|------------------|------------------|
| <b>Arm title</b> | Standard of care |
|------------------|------------------|

Arm description:

Subjects received the standard of care

|          |                 |
|----------|-----------------|
| Arm type | No intervention |
|----------|-----------------|

No investigational medicinal product assigned in this arm

|                  |                              |
|------------------|------------------------------|
| <b>Arm title</b> | Teduglutide 0.0125 mg/kg/Day |
|------------------|------------------------------|

Arm description:

Cohort 1 - Teduglutide 0.0125 mg/kg/Day

|          |              |
|----------|--------------|
| Arm type | Experimental |
|----------|--------------|

|  |             |
|--|-------------|
| Investigational medicinal product name | Teduglutide |
|--|-------------|

|  |  |
|--|--|
| Investigational medicinal product code |  |
|--|--|

|            |                             |
|------------|-----------------------------|
| Other name | ALX-0600, Gattex, Revestive |
|------------|-----------------------------|

|                      |   |
|----------------------|---|
| Pharmaceutical forms | Powder and solvent for solution for injection |
|----------------------|---|

|                          |                  |
|--------------------------|------------------|
| Routes of administration | Subcutaneous use |
|--------------------------|------------------|

Dosage and administration details:

Subjects received teduglutide 0.0125 mg/kg/day of a 10 mg/mL, 5 mg/mL, or 2.5 mg/mL solution in the morning for 12 weeks. The dose calculation was based on body weight measured at the Baseline Visit (Visit 2). No adjustments to dose were made during the study period. Teduglutide was administered by subcutaneous injection into 1 of the 4 quadrants of the abdomen (in subjects without a stoma) or either thigh or arm.

|                  |                             |
|------------------|-----------------------------|
| <b>Arm title</b> | Teduglutide 0.025 mg/kg/Day |
|------------------|-----------------------------|

Arm description:

Cohort 2 -Teduglutide 0.025mg/kg/Day

|          |              |
|----------|--------------|
| Arm type | Experimental |
|----------|--------------|

|  |             |
|--|-------------|
| Investigational medicinal product name | Teduglutide |
|--|-------------|

|  |  |
|--|--|
| Investigational medicinal product code |  |
|--|--|

|            |                             |
|------------|-----------------------------|
| Other name | ALX-0600, Gattex, Revestive |
|------------|-----------------------------|

|                      |   |
|----------------------|---|
| Pharmaceutical forms | Powder and solvent for solution for injection |
|----------------------|---|

|                          |                  |
|--------------------------|------------------|
| Routes of administration | Subcutaneous use |
|--------------------------|------------------|

Dosage and administration details:

Subjects received teduglutide 0.025 mg/kg/day of a 10 mg/mL, 5 mg/mL, or 2.5 mg/mL solution in the morning for 12 weeks. The dose calculation was based on body weight measured at the Baseline Visit (Visit 2). No adjustments to dose were made during the study period. Teduglutide was administered by subcutaneous injection into 1 of the 4 quadrants of the abdomen (in subjects without a stoma) or either thigh or arm.

|   |   |
|---|---|
| <b>Arm title</b>  | Teduglutide 0.05 mg/kg/Day                    |
| Arm description:<br>Cohort 3 - Teduglutide 0.05 mg/kg/Day |   |
| Arm type  | Experimental                                  |
| Investigational medicinal product name                    | Teduglutide                                   |
| Investigational medicinal product code                    |   |
| Other name  | ALX-0600, Gattex, Revestive                   |
| Pharmaceutical forms                                      | Powder and solvent for solution for injection |
| Routes of administration                                  | Subcutaneous use                              |

Dosage and administration details:

Subjects received teduglutide 0.05 mg/kg/day of a 10 mg/mL, 5 mg/mL, or 2.5 mg/mL solution in the morning for 12 weeks. The dose calculation was based on body weight measured at the Baseline Visit (Visit 2). No adjustments to dose were made during the study period. Teduglutide was administered by subcutaneous injection into 1 of the 4 quadrants of the abdomen (in subjects without a stoma) or either thigh or arm.

| <b>Number of subjects in period 1</b> | Standard of care | Teduglutide 0.0125 mg/kg/Day | Teduglutide 0.025 mg/kg/Day |
|---------------------------------------|------------------|------------------------------|-----------------------------|
| Started                               | 5                | 8                            | 14                          |
| Completed                             | 5                | 7                            | 14                          |
| Not completed                         | 0                | 1                            | 0                           |
| Protocol non-compliance               | -                | 1                            | -                           |
| Withdrawal by subject                 | -                | -                            | -                           |

| <b>Number of subjects in period 1</b> | Teduglutide 0.05 mg/kg/Day |
|---------------------------------------|----------------------------|
| Started                               | 15                         |
| Completed                             | 14                         |
| Not completed                         | 1                          |
| Protocol non-compliance               | -                          |
| Withdrawal by subject                 | 1                          |

## Baseline characteristics

### Reporting groups

|   |                              |
|---|------------------------------|
| Reporting group title   | Standard of care             |
| Reporting group description:<br>Subjects received the standard of care  |                              |
| Reporting group title   | Teduglutide 0.0125 mg/kg/Day |
| Reporting group description:<br>Cohort 1 - Teduglutide 0.0125 mg/kg/Day |                              |
| Reporting group title   | Teduglutide 0.025 mg/kg/Day  |
| Reporting group description:<br>Cohort 2 -Teduglutide 0.025mg/kg/Day    |                              |
| Reporting group title   | Teduglutide 0.05 mg/kg/Day   |
| Reporting group description:<br>Cohort 3 - Teduglutide 0.05 mg/kg/Day   |                              |

| Reporting group values                  | Standard of care | Teduglutide 0.0125 mg/kg/Day | Teduglutide 0.025 mg/kg/Day |
|---|------------------|------------------------------|-----------------------------|
| Number of subjects                      | 5                | 8                            | 14                          |
| Age categorical<br>Units: Subjects      |                  |                              |                             |
| 1 to 3 years                            | 5                | 4                            | 6                           |
| 4 to 12 years                           | 0                | 3                            | 7                           |
| 13 to 17 years                          | 0                | 1                            | 1                           |
| Age continuous<br>Units: years          |                  |                              |                             |
| arithmetic mean                         | 2.2              | 5.1                          | 4.6                         |
| standard deviation                      | ± 0.45           | ± 4.55                       | ± 3.43                      |
| Gender categorical<br>Units: Subjects   |                  |                              |                             |
| Female                                  | 2                | 2                            | 3                           |
| Male                                    | 3                | 6                            | 11                          |
| Region of enrollment<br>Units: Subjects |                  |                              |                             |
| United States                           | 5                | 8                            | 14                          |
| United Kingdom                          | 0                | 0                            | 0                           |

| Reporting group values             | Teduglutide 0.05 mg/kg/Day | Total |  |
|------------------------------------|----------------------------|-------|--|
| Number of subjects                 | 15                         | 42    |  |
| Age categorical<br>Units: Subjects |                            |       |  |
| 1 to 3 years                       | 7                          | 22    |  |
| 4 to 12 years                      | 7                          | 17    |  |
| 13 to 17 years                     | 1                          | 3     |  |
| Age continuous<br>Units: years     |                            |       |  |
| arithmetic mean                    | 4.5                        | -     |  |
| standard deviation                 | ± 3.16                     | -     |  |

|                      |    |    |  |
|----------------------|----|----|--|
| Gender categorical   |    |    |  |
| Units: Subjects      |    |    |  |
| Female               | 7  | 14 |  |
| Male                 | 8  | 28 |  |
| Region of enrollment |    |    |  |
| Units: Subjects      |    |    |  |
| United States        | 12 | 39 |  |
| United Kingdom       | 3  | 3  |  |

## End points

### End points reporting groups

|   |                              |
|---|------------------------------|
| Reporting group title   | Standard of care             |
| Reporting group description:<br>Subjects received the standard of care  |                              |
| Reporting group title   | Teduglutide 0.0125 mg/kg/Day |
| Reporting group description:<br>Cohort 1 - Teduglutide 0.0125 mg/kg/Day |                              |
| Reporting group title   | Teduglutide 0.025 mg/kg/Day  |
| Reporting group description:<br>Cohort 2 -Teduglutide 0.025mg/kg/Day    |                              |
| Reporting group title   | Teduglutide 0.05 mg/kg/Day   |
| Reporting group description:<br>Cohort 3 - Teduglutide 0.05 mg/kg/Day   |                              |

### Primary: Percent Change in Parenteral Support (Parenteral Nutrition [PN]/Intravenous [IV]) Volume at Week 12

|  |  |
|--|--|
| End point title  | Percent Change in Parenteral Support (Parenteral Nutrition [PN]/Intravenous [IV]) Volume at Week 12 <sup>[1]</sup> |
| End point description:<br>Percent change in PN/IV from the Baseline Visit to Week 12 Visit.<br>Percent change in PN/IV volume from baseline to Visit timepoints based on prescribed data - Intent-to-Treat Population, defined as subjects who were enrolled in the study. |  |
| End point type   | Primary  |
| End point timeframe:<br>Baseline, Week 12  |  |

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: The small sample size resulting from the small study population required the use of descriptive statistics with a goal of summarizing the sample.

| End point values                     | Standard of care | Teduglutide 0.0125 mg/kg/Day | Teduglutide 0.025 mg/kg/Day | Teduglutide 0.05 mg/kg/Day |
|--------------------------------------|------------------|------------------------------|-----------------------------|----------------------------|
| Subject group type                   | Reporting group  | Reporting group              | Reporting group             | Reporting group            |
| Number of subjects analysed          | 5                | 7                            | 13                          | 14                         |
| Units: percent change                |                  |                              |                             |                            |
| arithmetic mean (standard deviation) | 7.38 (± 12.756)  | -9.95 (± 21.625)             | -37.34 (± 26.422)           | -39.11 (± 40.792)          |

### Statistical analyses

No statistical analyses for this end point

### Primary: Percent Change in Parenteral Support (PN/IV) Volume at End of Treatment

|                 |  |
|-----------------|--|
| End point title | Percent Change in Parenteral Support (PN/IV) Volume at End of Treatment <sup>[2]</sup> |
|-----------------|--|

End point description:

Percent change in PN/IV from the Baseline Visit to End of Treatment Visit.

Percent change in PN/IV volume from baseline to End of Treatment based on prescribed data - Intent-to-Treat Population.

End point type Primary

End point timeframe:

Baseline, End of Treatment

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: The small sample size resulting from the small study population required the use of descriptive statistics with a goal of summarizing the sample.

| End point values                     | Standard of care | Teduglutide 0.0125 mg/kg/Day | Teduglutide 0.025 mg/kg/Day | Teduglutide 0.05 mg/kg/Day |
|--------------------------------------|------------------|------------------------------|-----------------------------|----------------------------|
| Subject group type                   | Reporting group  | Reporting group              | Reporting group             | Reporting group            |
| Number of subjects analysed          | 5                | 8                            | 14                          | 15                         |
| Units: percent change                |                  |                              |                             |                            |
| arithmetic mean (standard deviation) | 7.38 (± 12.756)  | -8.6 (± 20.38)               | -35.61 (± 26.198)           | -36.5 (± 40.585)           |

## Statistical analyses

No statistical analyses for this end point

### Primary: Percent Change in Parenteral Support (PN/IV) Volume at Week 16

End point title Percent Change in Parenteral Support (PN/IV) Volume at Week 16<sup>[3]</sup>

End point description:

Percent change in PN/IV from the Baseline Visit to Week 16 Visit.

Percent change in PN/IV volume from baseline to Week 16 based on prescribed data - Intent-to-Treat Population.

End point type Primary

End point timeframe:

Baseline, Week 16

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: The small sample size resulting from the small study population required the use of descriptive statistics with a goal of summarizing the sample.

| End point values                     | Standard of care | Teduglutide 0.0125 mg/kg/Day | Teduglutide 0.025 mg/kg/Day | Teduglutide 0.05 mg/kg/Day |
|--------------------------------------|------------------|------------------------------|-----------------------------|----------------------------|
| Subject group type                   | Reporting group  | Reporting group              | Reporting group             | Reporting group            |
| Number of subjects analysed          | 5                | 7                            | 14                          | 14                         |
| Units: percent change                |                  |                              |                             |                            |
| arithmetic mean (standard deviation) | 3.92 (± 16.616)  | -11.25 (± 21.196)            | -33.85 (± 27.017)           | -31.8 (± 39.264)           |

## Statistical analyses

No statistical analyses for this end point

### Primary: Absolute Change in Parenteral Support (PN/IV) Volume at Week 12

|                 |  |
|-----------------|--|
| End point title | Absolute Change in Parenteral Support (PN/IV) Volume at Week 12 <sup>[4]</sup> |
|-----------------|--|

End point description:

Absolute change in PN/IV from the Baseline Visit to Week 12 Visit.

Absolute change in PN/IV volume from baseline to Week 12 based on prescribed data - Intent-to-Treat Population.

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Baseline, Week 12

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: The small sample size resulting from the small study population required the use of descriptive statistics with a goal of summarizing the sample.

| End point values                     | Standard of care | Teduglutide 0.0125 mg/kg/Day | Teduglutide 0.025 mg/kg/Day | Teduglutide 0.05 mg/kg/Day |
|--------------------------------------|------------------|------------------------------|-----------------------------|----------------------------|
| Subject group type                   | Reporting group  | Reporting group              | Reporting group             | Reporting group            |
| Number of subjects analysed          | 5                | 7                            | 13                          | 14                         |
| Units: Litres/week                   |                  |                              |                             |                            |
| arithmetic mean (standard deviation) | 0.43 (± 0.746)   | -0.5 (± 0.91)                | -2.78 (± 1.985)             | -2.57 (± 3.564)            |

## Statistical analyses

No statistical analyses for this end point

### Primary: Absolute Change in Parenteral Support (PN/IV) Volume at End of Treatment

|                 |   |
|-----------------|---|
| End point title | Absolute Change in Parenteral Support (PN/IV) Volume at End of Treatment <sup>[5]</sup> |
|-----------------|---|

End point description:

Absolute change in PN/IV from the Baseline Visit to End of Treatment Visit.

Absolute change in PN/IV volume from baseline to End of Treatment based on prescribed data - Intent-to-Treat Population.

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Baseline, End of Treatment

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: The small sample size resulting from the small study population required the use of descriptive statistics with a goal of summarizing the sample.

| <b>End point values</b>              | Standard of care | Teduglutide 0.0125 mg/kg/Day | Teduglutide 0.025 mg/kg/Day | Teduglutide 0.05 mg/kg/Day |
|--------------------------------------|------------------|------------------------------|-----------------------------|----------------------------|
| Subject group type                   | Reporting group  | Reporting group              | Reporting group             | Reporting group            |
| Number of subjects analysed          | 5                | 8                            | 14                          | 15                         |
| Units: Litres/week                   |                  |                              |                             |                            |
| arithmetic mean (standard deviation) | 0.43 (± 0.746)   | -0.43 (± 0.864)              | -2.73 (± 1.916)             | -2.4 (± 3.498)             |

### Statistical analyses

No statistical analyses for this end point

### Primary: Absolute Change in Parenteral Support (PN/IV) Volume at Week 16

|   |  |
|---|--|
| End point title   | Absolute Change in Parenteral Support (PN/IV) Volume at Week 16 <sup>[6]</sup> |
| End point description:<br>Absolute change in PN/IV from the Baseline Visit to Week 16 Visit.<br>Absolute change in PN/IV volume from baseline to Week 16 based on prescribed data - Intent-to-Treat Population. |  |
| End point type  | Primary  |
| End point timeframe:<br>Baseline, Week 16   |  |

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: The small sample size resulting from the small study population required the use of descriptive statistics with a goal of summarizing the sample.

| <b>End point values</b>              | Standard of care | Teduglutide 0.0125 mg/kg/Day | Teduglutide 0.025 mg/kg/Day | Teduglutide 0.05 mg/kg/Day |
|--------------------------------------|------------------|------------------------------|-----------------------------|----------------------------|
| Subject group type                   | Reporting group  | Reporting group              | Reporting group             | Reporting group            |
| Number of subjects analysed          | 5                | 7                            | 14                          | 14                         |
| Units: Litres/week                   |                  |                              |                             |                            |
| arithmetic mean (standard deviation) | 0.17 (± 1.027)   | -0.56 (± 0.885)              | -2.56 (± 1.917)             | -1.99 (± 3.092)            |

### Statistical analyses

No statistical analyses for this end point

### Other pre-specified: Percent Change in Enteral Support (EN) Volume From Baseline at Week 12

|  |  |
|--|--|
| End point title  | Percent Change in Enteral Support (EN) Volume From Baseline at Week 12 |
| End point description:<br>Percent change in enteral support requirements at Week 12 (litres/week).<br>Percent change of EN volume from baseline to Week 12 based on subject diary data - Intent-to-Treat Population. |  |
| End point type   | Other pre-specified  |

End point timeframe:

Baseline, Week 12

| <b>End point values</b>              | Standard of care      | Teduglutide 0.0125 mg/kg/Day | Teduglutide 0.025 mg/kg/Day | Teduglutide 0.05 mg/kg/Day |
|--------------------------------------|-----------------------|------------------------------|-----------------------------|----------------------------|
| Subject group type                   | Reporting group       | Reporting group              | Reporting group             | Reporting group            |
| Number of subjects analysed          | 3                     | 4                            | 12                          | 8                          |
| Units: percent change                |                       |                              |                             |                            |
| arithmetic mean (standard deviation) | 16.82 ( $\pm$ 14.921) | 23.5 ( $\pm$ 22.06)          | 50.93 ( $\pm$ 61.416)       | 57.96 ( $\pm$ 44.953)      |

### Statistical analyses

No statistical analyses for this end point

### Other pre-specified: Percent Change in Enteral Support (EN) Volume From Baseline at Week 16

|                 |  |
|-----------------|--|
| End point title | Percent Change in Enteral Support (EN) Volume From Baseline at Week 16 |
|-----------------|--|

End point description:

Percent change in enteral support requirements at Week 16 (litres/week).

Percent change of EN volume from baseline to Week 16 based on subject diary data - Intent-to-Treat Population.

"99999" indicates that no standard deviation (SD) is presented when only one subject had data for this time point.

|                |                     |
|----------------|---------------------|
| End point type | Other pre-specified |
|----------------|---------------------|

End point timeframe:

Baseline, Week 16

| <b>End point values</b>              | Standard of care      | Teduglutide 0.0125 mg/kg/Day | Teduglutide 0.025 mg/kg/Day | Teduglutide 0.05 mg/kg/Day |
|--------------------------------------|-----------------------|------------------------------|-----------------------------|----------------------------|
| Subject group type                   | Reporting group       | Reporting group              | Reporting group             | Reporting group            |
| Number of subjects analysed          | 4                     | 1                            | 11                          | 9                          |
| Units: percent change                |                       |                              |                             |                            |
| arithmetic mean (standard deviation) | 52.06 ( $\pm$ 66.194) | 60.3 ( $\pm$ 99999)          | 43.98 ( $\pm$ 78.599)       | 58.93 ( $\pm$ 63.927)      |

### Statistical analyses

No statistical analyses for this end point

### Other pre-specified: Absolute Change in Enteral Support (EN) Volume From Baseline at Week 12

|  |   |
|--|---|
| End point title  | Absolute Change in Enteral Support (EN) Volume From Baseline at Week 12 |
| End point description:<br>Absolute change in enteral support requirements at Week 12 (litres/week).<br>Absolute change of EN volume from baseline to Week 12 based on subject diary data - Intent-to-Treat Population. |   |
| End point type   | Other pre-specified   |
| End point timeframe:<br>Baseline, Week 12  |   |

| End point values                     | Standard of care | Teduglutide 0.0125 mg/kg/Day | Teduglutide 0.025 mg/kg/Day | Teduglutide 0.05 mg/kg/Day |
|--------------------------------------|------------------|------------------------------|-----------------------------|----------------------------|
| Subject group type                   | Reporting group  | Reporting group              | Reporting group             | Reporting group            |
| Number of subjects analysed          | 4                | 7                            | 12                          | 12                         |
| Units: Litres/week                   |                  |                              |                             |                            |
| arithmetic mean (standard deviation) | 0.69 (± 0.715)   | 2.67 (± 4.412)               | 2.64 (± 3.22)               | 0.97 (± 1.127)             |

### Statistical analyses

No statistical analyses for this end point

### Other pre-specified: Absolute Change in Enteral Support (EN) Volume From Baseline at Week 16

|  |   |
|--|---|
| End point title  | Absolute Change in Enteral Support (EN) Volume From Baseline at Week 16 |
| End point description:<br>Absolute change in enteral support requirements at Week 16 (litres/week).<br>Absolute change of EN volume from baseline to Week 16 based on subject diary data - Intent-to-Treat Population. |   |
| End point type   | Other pre-specified   |
| End point timeframe:<br>Baseline, Week 16  |   |

| End point values                     | Standard of care | Teduglutide 0.0125 mg/kg/Day | Teduglutide 0.025 mg/kg/Day | Teduglutide 0.05 mg/kg/Day |
|--------------------------------------|------------------|------------------------------|-----------------------------|----------------------------|
| Subject group type                   | Reporting group  | Reporting group              | Reporting group             | Reporting group            |
| Number of subjects analysed          | 5                | 3                            | 11                          | 13                         |
| Units: Litres/week                   |                  |                              |                             |                            |
| arithmetic mean (standard deviation) | 0.84 (± 0.624)   | 4.56 (± 5.384)               | 2.47 (± 3.403)              | 0.91 (± 0.968)             |

### Statistical analyses

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No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Adverse event data were collected from the first patient consent to the time of the last visit for a duration of 421 days.

Adverse event reporting additional description:

This section reports "treatment-emergent" adverse events. Serious adverse events may be included in the 5% NSAE section.

|                 |                |
|-----------------|----------------|
| Assessment type | Non-systematic |
|-----------------|----------------|

### Dictionary used

|                 |        |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

|                    |      |
|--------------------|------|
| Dictionary version | 12.0 |
|--------------------|------|

### Reporting groups

|                       |                  |
|-----------------------|------------------|
| Reporting group title | Standard of care |
|-----------------------|------------------|

Reporting group description:

Subjects received the standard of care

|                       |                              |
|-----------------------|------------------------------|
| Reporting group title | Teduglutide 0.0125 mg/kg/Day |
|-----------------------|------------------------------|

Reporting group description:

Cohort 1 - Teduglutide 0.0125 mg/kg/Day

|                       |                             |
|-----------------------|-----------------------------|
| Reporting group title | Teduglutide 0.025 mg/kg/Day |
|-----------------------|-----------------------------|

Reporting group description:

Cohort 2 - Teduglutide 0.025mg/kg/Day

|                       |                            |
|-----------------------|----------------------------|
| Reporting group title | Teduglutide 0.05 mg/kg/Day |
|-----------------------|----------------------------|

Reporting group description:

Cohort 3 - Teduglutide 0.05 mg/kg/Day

| <b>Serious adverse events</b>                     | Standard of care | Teduglutide 0.0125 mg/kg/Day | Teduglutide 0.025 mg/kg/Day |
|---|------------------|------------------------------|-----------------------------|
| Total subjects affected by serious adverse events |                  |                              |                             |
| subjects affected / exposed                       | 3 / 5 (60.00%)   | 3 / 8 (37.50%)               | 6 / 14 (42.86%)             |
| number of deaths (all causes)                     | 0                | 0                            | 0                           |
| number of deaths resulting from adverse events    | 0                | 0                            | 0                           |
| Investigations                                    |                  |                              |                             |
| Blood creatinine increased                        |                  |                              |                             |
| subjects affected / exposed                       | 0 / 5 (0.00%)    | 0 / 8 (0.00%)                | 1 / 14 (7.14%)              |
| occurrences causally related to treatment / all   | 0 / 0            | 0 / 0                        | 0 / 1                       |
| deaths causally related to treatment / all        | 0 / 0            | 0 / 0                        | 0 / 0                       |
| Vascular disorders                                |                  |                              |                             |
| Hypovolaemic shock                                |                  |                              |                             |
| subjects affected / exposed                       | 0 / 5 (0.00%)    | 0 / 8 (0.00%)                | 1 / 14 (7.14%)              |
| occurrences causally related to treatment / all   | 0 / 0            | 0 / 0                        | 0 / 1                       |
| deaths causally related to treatment / all        | 0 / 0            | 0 / 0                        | 0 / 0                       |

|  |                |               |                 |
|--|----------------|---------------|-----------------|
| Nervous system disorders                             |                |               |                 |
| Depressed level of consciousness                     |                |               |                 |
| subjects affected / exposed                          | 0 / 5 (0.00%)  | 0 / 8 (0.00%) | 0 / 14 (0.00%)  |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0           |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0         | 0 / 0           |
| Grand mal convulsion                                 |                |               |                 |
| subjects affected / exposed                          | 0 / 5 (0.00%)  | 0 / 8 (0.00%) | 1 / 14 (7.14%)  |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 1           |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0         | 0 / 0           |
| Blood and lymphatic system disorders                 |                |               |                 |
| Pancytopenia   |                |               |                 |
| subjects affected / exposed                          | 0 / 5 (0.00%)  | 0 / 8 (0.00%) | 0 / 14 (0.00%)  |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0           |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0         | 0 / 0           |
| General disorders and administration site conditions |                |               |                 |
| Pyrexia  |                |               |                 |
| subjects affected / exposed                          | 2 / 5 (40.00%) | 0 / 8 (0.00%) | 1 / 14 (7.14%)  |
| occurrences causally related to treatment / all      | 0 / 2          | 0 / 0         | 0 / 1           |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0         | 0 / 0           |
| Catheter related complication                        |                |               |                 |
| subjects affected / exposed                          | 1 / 5 (20.00%) | 0 / 8 (0.00%) | 2 / 14 (14.29%) |
| occurrences causally related to treatment / all      | 0 / 1          | 0 / 0         | 0 / 2           |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0         | 0 / 0           |
| Fatigue  |                |               |                 |
| subjects affected / exposed                          | 0 / 5 (0.00%)  | 0 / 8 (0.00%) | 0 / 14 (0.00%)  |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0           |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0         | 0 / 0           |
| Irritability   |                |               |                 |
| subjects affected / exposed                          | 0 / 5 (0.00%)  | 0 / 8 (0.00%) | 0 / 14 (0.00%)  |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0           |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0         | 0 / 0           |
| Immune system disorders                              |                |               |                 |
| Anaphylactic reaction                                |                |               |                 |

|   |               |                |                 |
|---|---------------|----------------|-----------------|
| subjects affected / exposed                     | 0 / 5 (0.00%) | 0 / 8 (0.00%)  | 0 / 14 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0           |
| <b>Gastrointestinal disorders</b>               |               |                |                 |
| Abdominal distension                            |               |                |                 |
| subjects affected / exposed                     | 0 / 5 (0.00%) | 0 / 8 (0.00%)  | 1 / 14 (7.14%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0           |
| Frequent bowel movements                        |               |                |                 |
| subjects affected / exposed                     | 0 / 5 (0.00%) | 0 / 8 (0.00%)  | 0 / 14 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0           |
| Haematochezia                                   |               |                |                 |
| subjects affected / exposed                     | 0 / 5 (0.00%) | 0 / 8 (0.00%)  | 1 / 14 (7.14%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0           |
| <b>Skin and subcutaneous tissue disorders</b>   |               |                |                 |
| Rash  |               |                |                 |
| subjects affected / exposed                     | 0 / 5 (0.00%) | 0 / 8 (0.00%)  | 1 / 14 (7.14%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0           |
| <b>Infections and infestations</b>              |               |                |                 |
| Central line infection                          |               |                |                 |
| subjects affected / exposed                     | 0 / 5 (0.00%) | 0 / 8 (0.00%)  | 3 / 14 (21.43%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 5           |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0           |
| Parainfluenzae virus infection                  |               |                |                 |
| subjects affected / exposed                     | 0 / 5 (0.00%) | 0 / 8 (0.00%)  | 1 / 14 (7.14%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0           |
| Adenovirus infection                            |               |                |                 |
| subjects affected / exposed                     | 0 / 5 (0.00%) | 1 / 8 (12.50%) | 0 / 14 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 1          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0           |

|   |                |                |                |
|---|----------------|----------------|----------------|
| Catheter related infection                      |                |                |                |
| subjects affected / exposed                     | 0 / 5 (0.00%)  | 1 / 8 (12.50%) | 0 / 14 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Catheter sepsis                                 |                |                |                |
| subjects affected / exposed                     | 0 / 5 (0.00%)  | 0 / 8 (0.00%)  | 0 / 14 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Influenza                                       |                |                |                |
| subjects affected / exposed                     | 0 / 5 (0.00%)  | 1 / 8 (12.50%) | 0 / 14 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Rhinovirus infection                            |                |                |                |
| subjects affected / exposed                     | 0 / 5 (0.00%)  | 0 / 8 (0.00%)  | 1 / 14 (7.14%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Fungaemia                                       |                |                |                |
| subjects affected / exposed                     | 1 / 5 (20.00%) | 0 / 8 (0.00%)  | 0 / 14 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Viral infection                                 |                |                |                |
| subjects affected / exposed                     | 1 / 5 (20.00%) | 0 / 8 (0.00%)  | 0 / 14 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Gastroenteritis viral                           |                |                |                |
| subjects affected / exposed                     | 1 / 5 (20.00%) | 0 / 8 (0.00%)  | 0 / 14 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Metabolism and nutrition disorders              |                |                |                |
| Dehydration                                     |                |                |                |
| subjects affected / exposed                     | 0 / 5 (0.00%)  | 0 / 8 (0.00%)  | 0 / 14 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |

| <b>Serious adverse events</b>                        | Teduglutide 0.05 mg/kg/Day |  |  |
|--|----------------------------|--|--|
| Total subjects affected by serious adverse events    |                            |  |  |
| subjects affected / exposed                          | 8 / 15 (53.33%)            |  |  |
| number of deaths (all causes)                        | 0                          |  |  |
| number of deaths resulting from adverse events       | 0                          |  |  |
| Investigations                                       |                            |  |  |
| Blood creatinine increased                           |                            |  |  |
| subjects affected / exposed                          | 0 / 15 (0.00%)             |  |  |
| occurrences causally related to treatment / all      | 0 / 0                      |  |  |
| deaths causally related to treatment / all           | 0 / 0                      |  |  |
| Vascular disorders                                   |                            |  |  |
| Hypovolaemic shock                                   |                            |  |  |
| subjects affected / exposed                          | 0 / 15 (0.00%)             |  |  |
| occurrences causally related to treatment / all      | 0 / 0                      |  |  |
| deaths causally related to treatment / all           | 0 / 0                      |  |  |
| Nervous system disorders                             |                            |  |  |
| Depressed level of consciousness                     |                            |  |  |
| subjects affected / exposed                          | 1 / 15 (6.67%)             |  |  |
| occurrences causally related to treatment / all      | 0 / 1                      |  |  |
| deaths causally related to treatment / all           | 0 / 0                      |  |  |
| Grand mal convulsion                                 |                            |  |  |
| subjects affected / exposed                          | 0 / 15 (0.00%)             |  |  |
| occurrences causally related to treatment / all      | 0 / 0                      |  |  |
| deaths causally related to treatment / all           | 0 / 0                      |  |  |
| Blood and lymphatic system disorders                 |                            |  |  |
| Pancytopenia   |                            |  |  |
| subjects affected / exposed                          | 1 / 15 (6.67%)             |  |  |
| occurrences causally related to treatment / all      | 0 / 1                      |  |  |
| deaths causally related to treatment / all           | 0 / 0                      |  |  |
| General disorders and administration site conditions |                            |  |  |
| Pyrexia  |                            |  |  |
| subjects affected / exposed                          | 3 / 15 (20.00%)            |  |  |
| occurrences causally related to treatment / all      | 0 / 3                      |  |  |
| deaths causally related to treatment / all           | 0 / 0                      |  |  |
| Catheter related complication                        |                            |  |  |

|   |                |  |  |
|---|----------------|--|--|
| subjects affected / exposed                     | 1 / 15 (6.67%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| <b>Fatigue</b>                                  |                |  |  |
| subjects affected / exposed                     | 1 / 15 (6.67%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| <b>Irritability</b>                             |                |  |  |
| subjects affected / exposed                     | 1 / 15 (6.67%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| <b>Immune system disorders</b>                  |                |  |  |
| <b>Anaphylactic reaction</b>                    |                |  |  |
| subjects affected / exposed                     | 1 / 15 (6.67%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| <b>Gastrointestinal disorders</b>               |                |  |  |
| <b>Abdominal distension</b>                     |                |  |  |
| subjects affected / exposed                     | 0 / 15 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| <b>Frequent bowel movements</b>                 |                |  |  |
| subjects affected / exposed                     | 1 / 15 (6.67%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| <b>Haematochezia</b>                            |                |  |  |
| subjects affected / exposed                     | 0 / 15 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| <b>Skin and subcutaneous tissue disorders</b>   |                |  |  |
| <b>Rash</b>                                     |                |  |  |
| subjects affected / exposed                     | 0 / 15 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |

|   |                |  |  |
|---|----------------|--|--|
| Infections and infestations                     |                |  |  |
| Central line infection                          |                |  |  |
| subjects affected / exposed                     | 1 / 15 (6.67%) |  |  |
| occurrences causally related to treatment / all | 0 / 2          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Parainfluenzae virus infection                  |                |  |  |
| subjects affected / exposed                     | 1 / 15 (6.67%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Adenovirus infection                            |                |  |  |
| subjects affected / exposed                     | 0 / 15 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Catheter related infection                      |                |  |  |
| subjects affected / exposed                     | 0 / 15 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Catheter sepsis                                 |                |  |  |
| subjects affected / exposed                     | 1 / 15 (6.67%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Influenza                                       |                |  |  |
| subjects affected / exposed                     | 0 / 15 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Rhinovirus infection                            |                |  |  |
| subjects affected / exposed                     | 0 / 15 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Fungaemia                                       |                |  |  |
| subjects affected / exposed                     | 0 / 15 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Viral infection                                 |                |  |  |

|   |                |  |  |
|---|----------------|--|--|
| subjects affected / exposed                     | 0 / 15 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Gastroenteritis viral                           |                |  |  |
| subjects affected / exposed                     | 0 / 15 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Metabolism and nutrition disorders              |                |  |  |
| Dehydration                                     |                |  |  |
| subjects affected / exposed                     | 1 / 15 (6.67%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |

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

| <b>Non-serious adverse events</b>                     | Standard of care | Teduglutide 0.0125 mg/kg/Day | Teduglutide 0.025 mg/kg/Day |
|---|------------------|------------------------------|-----------------------------|
| Total subjects affected by non-serious adverse events |                  |                              |                             |
| subjects affected / exposed                           | 5 / 5 (100.00%)  | 8 / 8 (100.00%)              | 14 / 14 (100.00%)           |
| Vascular disorders                                    |                  |                              |                             |
| Pallor  |                  |                              |                             |
| subjects affected / exposed                           | 1 / 5 (20.00%)   | 0 / 8 (0.00%)                | 0 / 14 (0.00%)              |
| occurrences (all)                                     | 1                | 0                            | 0                           |
| General disorders and administration site conditions  |                  |                              |                             |
| Catheter related complication                         |                  |                              |                             |
| subjects affected / exposed                           | 1 / 5 (20.00%)   | 3 / 8 (37.50%)               | 4 / 14 (28.57%)             |
| occurrences (all)                                     | 1                | 4                            | 4                           |
| Fatigue   |                  |                              |                             |
| subjects affected / exposed                           | 0 / 5 (0.00%)    | 0 / 8 (0.00%)                | 1 / 14 (7.14%)              |
| occurrences (all)                                     | 0                | 0                            | 1                           |
| Injection site haemorrhage                            |                  |                              |                             |
| subjects affected / exposed                           | 0 / 5 (0.00%)    | 0 / 8 (0.00%)                | 0 / 14 (0.00%)              |
| occurrences (all)                                     | 0                | 0                            | 0                           |
| Pyrexia   |                  |                              |                             |
| subjects affected / exposed                           | 2 / 5 (40.00%)   | 0 / 8 (0.00%)                | 2 / 14 (14.29%)             |
| occurrences (all)                                     | 3                | 0                            | 2                           |

|   |  |   |  |
|---|--|---|--|
| Irritability<br>subjects affected / exposed<br>occurrences (all)  | 1 / 5 (20.00%)<br>1  | 0 / 8 (0.00%)<br>0  | 0 / 14 (0.00%)<br>0  |
| Immune system disorders<br>Drug hypersensitivity<br>subjects affected / exposed<br>occurrences (all)  | 0 / 5 (0.00%)<br>0   | 0 / 8 (0.00%)<br>0  | 2 / 14 (14.29%)<br>2   |
| Respiratory, thoracic and mediastinal disorders<br>Cough<br>subjects affected / exposed<br>occurrences (all)<br><br>Rhinorrhoea<br>subjects affected / exposed<br>occurrences (all)<br><br>Tonsillar hypertrophy<br>subjects affected / exposed<br>occurrences (all)  | 1 / 5 (20.00%)<br>1<br><br>0 / 5 (0.00%)<br>0<br><br>0 / 5 (0.00%)<br>0  | 1 / 8 (12.50%)<br>3<br><br>0 / 8 (0.00%)<br>0<br><br>0 / 8 (0.00%)<br>0   | 2 / 14 (14.29%)<br>3<br><br>1 / 14 (7.14%)<br>1<br><br>2 / 14 (14.29%)<br>2  |
| Investigations<br>Alanine aminotransferase increased<br>subjects affected / exposed<br>occurrences (all)<br><br>Aspartate aminotransferase increased<br>subjects affected / exposed<br>occurrences (all)<br><br>Bacteria urine<br>subjects affected / exposed<br>occurrences (all)<br><br>Blood bicarbonate decreased<br>subjects affected / exposed<br>occurrences (all)<br><br>Blood urine present<br>subjects affected / exposed<br>occurrences (all)<br><br>Protein urine present<br>subjects affected / exposed<br>occurrences (all) | 0 / 5 (0.00%)<br>0<br><br>0 / 5 (0.00%)<br>0<br><br>1 / 5 (20.00%)<br>1<br><br>2 / 5 (40.00%)<br>2<br><br>0 / 5 (0.00%)<br>0<br><br>0 / 5 (0.00%)<br>0 | 0 / 8 (0.00%)<br>0<br><br>0 / 8 (0.00%)<br>0<br><br>0 / 8 (0.00%)<br>0<br><br>1 / 8 (12.50%)<br>1<br><br>0 / 8 (0.00%)<br>0<br><br>0 / 8 (0.00%)<br>0 | 1 / 14 (7.14%)<br>1<br><br>1 / 14 (7.14%)<br>1<br><br>0 / 14 (0.00%)<br>0<br><br>1 / 14 (7.14%)<br>1<br><br>0 / 14 (0.00%)<br>0<br><br>0 / 14 (0.00%)<br>0 |

|   |                     |                     |                      |
|---|---------------------|---------------------|----------------------|
| Red blood cells urine positive<br>subjects affected / exposed<br>occurrences (all)  | 0 / 5 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  | 0 / 14 (0.00%)<br>0  |
| Weight decreased<br>subjects affected / exposed<br>occurrences (all)  | 0 / 5 (0.00%)<br>0  | 1 / 8 (12.50%)<br>1 | 1 / 14 (7.14%)<br>1  |
| White blood cells urine positive<br>subjects affected / exposed<br>occurrences (all)  | 0 / 5 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  | 0 / 14 (0.00%)<br>0  |
| C-reactive protein increased<br>subjects affected / exposed<br>occurrences (all)  | 1 / 5 (20.00%)<br>1 | 0 / 8 (0.00%)<br>0  | 0 / 14 (0.00%)<br>0  |
| Urine leukocyte esterase positive<br>subjects affected / exposed<br>occurrences (all)   | 1 / 5 (20.00%)<br>1 | 0 / 8 (0.00%)<br>0  | 0 / 14 (0.00%)<br>0  |
| White blood cell count increased<br>subjects affected / exposed<br>occurrences (all)  | 1 / 5 (20.00%)<br>1 | 0 / 8 (0.00%)<br>0  | 0 / 14 (0.00%)<br>0  |
| Injury, poisoning and procedural<br>complications   |                     |                     |                      |
| Feeding tube complication<br>subjects affected / exposed<br>occurrences (all)   | 0 / 5 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  | 2 / 14 (14.29%)<br>2 |
| Gastrointestinal stoma complication<br>subjects affected / exposed <sup>[1]</sup><br>occurrences (all)                          | 0 / 5 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0   |
| Additional description: Only 1 subject in each of the 3 dosing cohorts had a stoma and no standard of care subject had a stoma. |                     |                     |                      |
| Incision site erythema<br>subjects affected / exposed<br>occurrences (all)  | 0 / 5 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  | 1 / 14 (7.14%)<br>1  |
| Cardiac disorders   |                     |                     |                      |
| Tachycardia<br>subjects affected / exposed<br>occurrences (all)   | 1 / 5 (20.00%)<br>1 | 0 / 8 (0.00%)<br>0  | 1 / 14 (7.14%)<br>1  |
| Nervous system disorders  |                     |                     |                      |
| Dizziness<br>subjects affected / exposed<br>occurrences (all)   | 0 / 5 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  | 1 / 14 (7.14%)<br>1  |

|   |                     |                     |                      |
|---|---------------------|---------------------|----------------------|
| Headache<br>subjects affected / exposed<br>occurrences (all)  | 0 / 5 (0.00%)<br>0  | 1 / 8 (12.50%)<br>5 | 2 / 14 (14.29%)<br>2 |
| Blood and lymphatic system disorders<br>Neutropenia<br>subjects affected / exposed<br>occurrences (all) | 0 / 5 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  | 2 / 14 (14.29%)<br>2 |
| Thrombocytopenia<br>subjects affected / exposed<br>occurrences (all)                                    | 0 / 5 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  | 2 / 14 (14.29%)<br>2 |
| Eye disorders<br>Eyes sunken<br>subjects affected / exposed<br>occurrences (all)                        | 0 / 5 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  | 0 / 14 (0.00%)<br>0  |
| Gastrointestinal disorders<br>Abdominal distension<br>subjects affected / exposed<br>occurrences (all)  | 0 / 5 (0.00%)<br>0  | 1 / 8 (12.50%)<br>2 | 1 / 14 (7.14%)<br>1  |
| Abdominal pain<br>subjects affected / exposed<br>occurrences (all)                                      | 1 / 5 (20.00%)<br>1 | 1 / 8 (12.50%)<br>1 | 1 / 14 (7.14%)<br>5  |
| Constipation<br>subjects affected / exposed<br>occurrences (all)  | 1 / 5 (20.00%)<br>2 | 0 / 8 (0.00%)<br>0  | 0 / 14 (0.00%)<br>0  |
| Diarrhoea<br>subjects affected / exposed<br>occurrences (all)   | 1 / 5 (20.00%)<br>1 | 0 / 8 (0.00%)<br>0  | 1 / 14 (7.14%)<br>1  |
| Faecal volume increased<br>subjects affected / exposed<br>occurrences (all)                             | 0 / 5 (0.00%)<br>0  | 1 / 8 (12.50%)<br>1 | 1 / 14 (7.14%)<br>1  |
| Haematochezia<br>subjects affected / exposed<br>occurrences (all)                                       | 0 / 5 (0.00%)<br>0  | 2 / 8 (25.00%)<br>2 | 1 / 14 (7.14%)<br>1  |
| Nausea<br>subjects affected / exposed<br>occurrences (all)  | 0 / 5 (0.00%)<br>0  | 1 / 8 (12.50%)<br>3 | 2 / 14 (14.29%)<br>2 |
| Painful defecation  |                     |                     |                      |

|  |                     |                     |                      |
|--|---------------------|---------------------|----------------------|
| subjects affected / exposed<br>occurrences (all)                           | 0 / 5 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  | 0 / 14 (0.00%)<br>0  |
| Retching<br>subjects affected / exposed<br>occurrences (all)               | 0 / 5 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  | 2 / 14 (14.29%)<br>2 |
| Vomiting<br>subjects affected / exposed<br>occurrences (all)               | 0 / 5 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  | 5 / 14 (35.71%)<br>8 |
| Flatulence<br>subjects affected / exposed<br>occurrences (all)             | 0 / 5 (0.00%)<br>0  | 2 / 8 (25.00%)<br>2 | 1 / 14 (7.14%)<br>1  |
| <b>Skin and subcutaneous tissue disorders</b>                              |                     |                     |                      |
| Dermatitis diaper<br>subjects affected / exposed<br>occurrences (all)      | 1 / 5 (20.00%)<br>1 | 0 / 8 (0.00%)<br>0  | 1 / 14 (7.14%)<br>1  |
| Rash<br>subjects affected / exposed<br>occurrences (all)                   | 0 / 5 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  | 1 / 14 (7.14%)<br>3  |
| Rash erythematous<br>subjects affected / exposed<br>occurrences (all)      | 1 / 5 (20.00%)<br>1 | 0 / 8 (0.00%)<br>0  | 0 / 14 (0.00%)<br>0  |
| <b>Musculoskeletal and connective tissue disorders</b>                     |                     |                     |                      |
| Pain in extremity<br>subjects affected / exposed<br>occurrences (all)      | 0 / 5 (0.00%)<br>0  | 1 / 8 (12.50%)<br>1 | 0 / 14 (0.00%)<br>0  |
| <b>Infections and infestations</b>   |                     |                     |                      |
| Central line infection<br>subjects affected / exposed<br>occurrences (all) | 0 / 5 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  | 3 / 14 (21.43%)<br>5 |
| Gastroenteritis viral<br>subjects affected / exposed<br>occurrences (all)  | 1 / 5 (20.00%)<br>1 | 1 / 8 (12.50%)<br>1 | 0 / 14 (0.00%)<br>0  |
| Influenza<br>subjects affected / exposed<br>occurrences (all)              | 0 / 5 (0.00%)<br>0  | 1 / 8 (12.50%)<br>1 | 1 / 14 (7.14%)<br>1  |
| Nasopharyngitis  |                     |                     |                      |

|  |                     |                     |                      |
|--|---------------------|---------------------|----------------------|
| subjects affected / exposed<br>occurrences (all)   | 0 / 5 (0.00%)<br>0  | 2 / 8 (25.00%)<br>2 | 0 / 14 (0.00%)<br>0  |
| Overgrowth bacterial<br>subjects affected / exposed<br>occurrences (all)                 | 0 / 5 (0.00%)<br>0  | 2 / 8 (25.00%)<br>2 | 0 / 14 (0.00%)<br>0  |
| Parainfluenzae virus infection<br>subjects affected / exposed<br>occurrences (all)       | 0 / 5 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  | 1 / 14 (7.14%)<br>1  |
| Rhinovirus infection<br>subjects affected / exposed<br>occurrences (all)                 | 0 / 5 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  | 2 / 14 (14.29%)<br>2 |
| Upper respiratory tract infection<br>subjects affected / exposed<br>occurrences (all)    | 2 / 5 (40.00%)<br>2 | 2 / 8 (25.00%)<br>3 | 4 / 14 (28.57%)<br>6 |
| Gastrointestinal bacterial infection<br>subjects affected / exposed<br>occurrences (all) | 1 / 5 (20.00%)<br>1 | 0 / 8 (0.00%)<br>0  | 0 / 14 (0.00%)<br>0  |
| Viral infection<br>subjects affected / exposed<br>occurrences (all)                      | 1 / 5 (20.00%)<br>1 | 0 / 8 (0.00%)<br>0  | 0 / 14 (0.00%)<br>0  |
| Fungaemia<br>subjects affected / exposed<br>occurrences (all)                            | 1 / 5 (20.00%)<br>2 | 0 / 8 (0.00%)<br>0  | 0 / 14 (0.00%)<br>0  |
| Metabolism and nutrition disorders   |                     |                     |                      |
| Anorexia<br>subjects affected / exposed<br>occurrences (all)                             | 0 / 5 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  | 0 / 14 (0.00%)<br>0  |
| Dehydration<br>subjects affected / exposed<br>occurrences (all)                          | 1 / 5 (20.00%)<br>1 | 1 / 8 (12.50%)<br>1 | 0 / 14 (0.00%)<br>0  |
| Hypoglycaemia<br>subjects affected / exposed<br>occurrences (all)                        | 0 / 5 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  | 1 / 14 (7.14%)<br>1  |

|  |                               |  |  |
|--|-------------------------------|--|--|
| <b>Non-serious adverse events</b>                        | Teduglutide 0.05<br>mg/kg/Day |  |  |
| Total subjects affected by non-serious<br>adverse events |                               |  |  |

|  |                   |  |  |
|--|-------------------|--|--|
| subjects affected / exposed                          | 15 / 15 (100.00%) |  |  |
| Vascular disorders                                   |                   |  |  |
| Pallor   |                   |  |  |
| subjects affected / exposed                          | 1 / 15 (6.67%)    |  |  |
| occurrences (all)                                    | 1                 |  |  |
| General disorders and administration site conditions |                   |  |  |
| Catheter related complication                        |                   |  |  |
| subjects affected / exposed                          | 2 / 15 (13.33%)   |  |  |
| occurrences (all)                                    | 3                 |  |  |
| Fatigue  |                   |  |  |
| subjects affected / exposed                          | 4 / 15 (26.67%)   |  |  |
| occurrences (all)                                    | 11                |  |  |
| Injection site haemorrhage                           |                   |  |  |
| subjects affected / exposed                          | 3 / 15 (20.00%)   |  |  |
| occurrences (all)                                    | 4                 |  |  |
| Pyrexia  |                   |  |  |
| subjects affected / exposed                          | 7 / 15 (46.67%)   |  |  |
| occurrences (all)                                    | 8                 |  |  |
| Irritability   |                   |  |  |
| subjects affected / exposed                          | 1 / 15 (6.67%)    |  |  |
| occurrences (all)                                    | 1                 |  |  |
| Immune system disorders                              |                   |  |  |
| Drug hypersensitivity                                |                   |  |  |
| subjects affected / exposed                          | 0 / 15 (0.00%)    |  |  |
| occurrences (all)                                    | 0                 |  |  |
| Respiratory, thoracic and mediastinal disorders      |                   |  |  |
| Cough  |                   |  |  |
| subjects affected / exposed                          | 4 / 15 (26.67%)   |  |  |
| occurrences (all)                                    | 5                 |  |  |
| Rhinorrhoea  |                   |  |  |
| subjects affected / exposed                          | 1 / 15 (6.67%)    |  |  |
| occurrences (all)                                    | 1                 |  |  |
| Tonsillar hypertrophy                                |                   |  |  |
| subjects affected / exposed                          | 0 / 15 (0.00%)    |  |  |
| occurrences (all)                                    | 0                 |  |  |
| Investigations                                       |                   |  |  |

|  |                      |  |  |
|--|----------------------|--|--|
| Alanine aminotransferase increased<br>subjects affected / exposed<br>occurrences (all)   | 1 / 15 (6.67%)<br>1  |  |  |
| Aspartate aminotransferase increased<br>subjects affected / exposed<br>occurrences (all) | 1 / 15 (6.67%)<br>1  |  |  |
| Bacteria urine<br>subjects affected / exposed<br>occurrences (all)                       | 2 / 15 (13.33%)<br>2 |  |  |
| Blood bicarbonate decreased<br>subjects affected / exposed<br>occurrences (all)          | 3 / 15 (20.00%)<br>4 |  |  |
| Blood urine present<br>subjects affected / exposed<br>occurrences (all)                  | 2 / 15 (13.33%)<br>2 |  |  |
| Protein urine present<br>subjects affected / exposed<br>occurrences (all)                | 2 / 15 (13.33%)<br>2 |  |  |
| Red blood cells urine positive<br>subjects affected / exposed<br>occurrences (all)       | 2 / 15 (13.33%)<br>2 |  |  |
| Weight decreased<br>subjects affected / exposed<br>occurrences (all)                     | 1 / 15 (6.67%)<br>1  |  |  |
| White blood cells urine positive<br>subjects affected / exposed<br>occurrences (all)     | 2 / 15 (13.33%)<br>2 |  |  |
| C-reactive protein increased<br>subjects affected / exposed<br>occurrences (all)         | 1 / 15 (6.67%)<br>1  |  |  |
| Urine leukocyte esterase positive<br>subjects affected / exposed<br>occurrences (all)    | 1 / 15 (6.67%)<br>1  |  |  |
| White blood cell count increased   |                      |  |  |

|  |                       |   |  |
|--|-----------------------|---|--|
| subjects affected / exposed<br>occurrences (all)   | 0 / 15 (0.00%)<br>0   |   |  |
| Injury, poisoning and procedural complications   |                       |   |  |
| Feeding tube complication<br>subjects affected / exposed<br>occurrences (all)                          | 0 / 15 (0.00%)<br>0   |   |  |
| Gastrointestinal stoma complication<br>subjects affected / exposed <sup>[1]</sup><br>occurrences (all) | 1 / 1 (100.00%)<br>5  | Additional description: Only 1 subject in each of the 3 dosing cohorts had a stoma and no standard of care subject had a stoma. |  |
| Incision site erythema<br>subjects affected / exposed<br>occurrences (all)                             | 1 / 15 (6.67%)<br>1   |   |  |
| Cardiac disorders  |                       |   |  |
| Tachycardia<br>subjects affected / exposed<br>occurrences (all)  | 1 / 15 (6.67%)<br>1   |   |  |
| Nervous system disorders   |                       |   |  |
| Dizziness<br>subjects affected / exposed<br>occurrences (all)  | 2 / 15 (13.33%)<br>3  |   |  |
| Headache<br>subjects affected / exposed<br>occurrences (all)   | 2 / 15 (13.33%)<br>10 |   |  |
| Blood and lymphatic system disorders   |                       |   |  |
| Neutropenia<br>subjects affected / exposed<br>occurrences (all)  | 0 / 15 (0.00%)<br>0   |   |  |
| Thrombocytopenia<br>subjects affected / exposed<br>occurrences (all)                                   | 0 / 15 (0.00%)<br>0   |   |  |
| Eye disorders  |                       |   |  |
| Eyes sunken<br>subjects affected / exposed<br>occurrences (all)  | 2 / 15 (13.33%)<br>2  |   |  |
| Gastrointestinal disorders   |                       |   |  |

|  |                 |  |  |
|--|-----------------|--|--|
| Abdominal distension                   |                 |  |  |
| subjects affected / exposed            | 1 / 15 (6.67%)  |  |  |
| occurrences (all)                      | 2               |  |  |
| Abdominal pain                         |                 |  |  |
| subjects affected / exposed            | 4 / 15 (26.67%) |  |  |
| occurrences (all)                      | 15              |  |  |
| Constipation                           |                 |  |  |
| subjects affected / exposed            | 2 / 15 (13.33%) |  |  |
| occurrences (all)                      | 2               |  |  |
| Diarrhoea                              |                 |  |  |
| subjects affected / exposed            | 3 / 15 (20.00%) |  |  |
| occurrences (all)                      | 6               |  |  |
| Faecal volume increased                |                 |  |  |
| subjects affected / exposed            | 2 / 15 (13.33%) |  |  |
| occurrences (all)                      | 2               |  |  |
| Haematochezia                          |                 |  |  |
| subjects affected / exposed            | 0 / 15 (0.00%)  |  |  |
| occurrences (all)                      | 0               |  |  |
| Nausea                                 |                 |  |  |
| subjects affected / exposed            | 2 / 15 (13.33%) |  |  |
| occurrences (all)                      | 8               |  |  |
| Painful defecation                     |                 |  |  |
| subjects affected / exposed            | 2 / 15 (13.33%) |  |  |
| occurrences (all)                      | 2               |  |  |
| Retching                               |                 |  |  |
| subjects affected / exposed            | 0 / 15 (0.00%)  |  |  |
| occurrences (all)                      | 0               |  |  |
| Vomiting                               |                 |  |  |
| subjects affected / exposed            | 7 / 15 (46.67%) |  |  |
| occurrences (all)                      | 29              |  |  |
| Flatulence                             |                 |  |  |
| subjects affected / exposed            | 0 / 15 (0.00%)  |  |  |
| occurrences (all)                      | 0               |  |  |
| Skin and subcutaneous tissue disorders |                 |  |  |
| Dermatitis diaper                      |                 |  |  |

|  |                      |  |  |
|--|----------------------|--|--|
| subjects affected / exposed<br>occurrences (all)   | 1 / 15 (6.67%)<br>1  |  |  |
| Rash<br>subjects affected / exposed<br>occurrences (all)   | 2 / 15 (13.33%)<br>3 |  |  |
| Rash erythematous<br>subjects affected / exposed<br>occurrences (all)  | 0 / 15 (0.00%)<br>0  |  |  |
| Musculoskeletal and connective tissue disorders<br>Pain in extremity<br>subjects affected / exposed<br>occurrences (all) | 1 / 15 (6.67%)<br>1  |  |  |
| Infections and infestations<br>Central line infection<br>subjects affected / exposed<br>occurrences (all)                | 1 / 15 (6.67%)<br>2  |  |  |
| Gastroenteritis viral<br>subjects affected / exposed<br>occurrences (all)  | 2 / 15 (13.33%)<br>2 |  |  |
| Influenza<br>subjects affected / exposed<br>occurrences (all)  | 0 / 15 (0.00%)<br>0  |  |  |
| Nasopharyngitis<br>subjects affected / exposed<br>occurrences (all)  | 1 / 15 (6.67%)<br>1  |  |  |
| Overgrowth bacterial<br>subjects affected / exposed<br>occurrences (all)   | 0 / 15 (0.00%)<br>0  |  |  |
| Parainfluenzae virus infection<br>subjects affected / exposed<br>occurrences (all)                                       | 1 / 15 (6.67%)<br>1  |  |  |
| Rhinovirus infection<br>subjects affected / exposed<br>occurrences (all)   | 0 / 15 (0.00%)<br>0  |  |  |
| Upper respiratory tract infection  |                      |  |  |

|                                      |                 |  |  |
|--------------------------------------|-----------------|--|--|
| subjects affected / exposed          | 4 / 15 (26.67%) |  |  |
| occurrences (all)                    | 4               |  |  |
| Gastrointestinal bacterial infection |                 |  |  |
| subjects affected / exposed          | 0 / 15 (0.00%)  |  |  |
| occurrences (all)                    | 0               |  |  |
| Viral infection                      |                 |  |  |
| subjects affected / exposed          | 1 / 15 (6.67%)  |  |  |
| occurrences (all)                    | 1               |  |  |
| Fungaemia                            |                 |  |  |
| subjects affected / exposed          | 0 / 15 (0.00%)  |  |  |
| occurrences (all)                    | 0               |  |  |
| Metabolism and nutrition disorders   |                 |  |  |
| Anorexia                             |                 |  |  |
| subjects affected / exposed          | 2 / 15 (13.33%) |  |  |
| occurrences (all)                    | 2               |  |  |
| Dehydration                          |                 |  |  |
| subjects affected / exposed          | 1 / 15 (6.67%)  |  |  |
| occurrences (all)                    | 1               |  |  |
| Hypoglycaemia                        |                 |  |  |
| subjects affected / exposed          | 1 / 15 (6.67%)  |  |  |
| occurrences (all)                    | 1               |  |  |

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: Only 1 subject in each of the 3 dosing cohorts had a stoma and no standard of care subject had a stoma.

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date         | Amendment  |
|--------------|--|
| 11 July 2014 | <p>The following substantial changes were made for implementation at all study sites:</p> <ol style="list-style-type: none"><li>1) Inclusion Criterion 5 was clarified to provide further specific definition of stable PN/IV support.</li><li>2) Exclusion Criterion 17 was clarified to provide further details regarding prestudy hospital admissions.</li><li>3) The details surrounding the storage conditions of the study medication were clarified.</li><li>4) Details for dose interruption of individual subjects and study termination were included in the protocol.</li><li>5) Changes from local Amendments 1 and 2 were incorporated for all sites.</li></ol> <p>Local Amendment 1:</p> <ol style="list-style-type: none"><li>1) The observation time after the first SC injection was increased to 4 hours to allow for monitoring of hypersensitivity reactions.</li><li>2) The definition of true abstinence was added for females of child bearing potential in order to clarify study requirements.</li></ol> <p>Local Amendment 2:</p> <ol style="list-style-type: none"><li>1) A rationale for the study design was added to provide risk/benefit information for PN/IV support in relation to the protocol design.</li><li>2) Additional safety visits were added after EOT and before End of Study for 3 consecutive weeks to provide follow-up safety monitoring.</li><li>3) Post-treatment guidance was added to ensure that subjects were returned to their previous standard of care.</li><li>4) The time frame of 5 years was added to Exclusion Criterion 8 for history of cancer or clinically significant lymphoproliferative disease.</li><li>5) The duration of record retention was extended to 10 years.</li></ol> |

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported