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

85 years and over	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
Arm title	Standard of care

Arm description:

Subjects received the standard of care

Arm type	No intervention

No investigational medicinal product assigned in this arm

Arm title	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.

Arm title	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.

Arm title	Teduglutide 0.05 mg/kg/Day

Arm description:

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.

Number of subjects in period 1	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	-	-	-

Number of subjects in period 1	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:	
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	

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 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 Units: years			
arithmetic mean	2.2	5.1	4.6
standard deviation	± 0.45	± 4.55	± 3.43
Gender categorical Units: Subjects			
Female	2	2	3
Male	3	6	11
Region of enrollment 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 Units: Subjects			
1 to 3 years	7	22	
4 to 12 years	7	17	
13 to 17 years	1	3	
Age continuous 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: 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	

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[1]

End point description:

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

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[2]

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[3]

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[4]

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[5]

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.

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: 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[6]

End point description:

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

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.

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: 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:

Percent change in enteral support requirements at Week 12 (litres/week).
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

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	3	4	12	8
Units: percent change				
arithmetic mean (standard deviation)	16.82 (± 14.921)	23.5 (± 22.06)	50.93 (± 61.416)	57.96 (± 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

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	1	11	9
Units: percent change				
arithmetic mean (standard deviation)	52.06 (± 66.194)	60.3 (± 99999)	43.98 (± 78.599)	58.93 (± 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:

Absolute change in enteral support requirements at Week 12 (litres/week).
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:

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:

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

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

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

Serious adverse events	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
Gastrointestinal disorders			
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
Skin and subcutaneous tissue disorders			
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
Infections and infestations			
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

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

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

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

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

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

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

Non-serious adverse events	Teduglutide 0.05 mg/kg/Day		
Total subjects affected by non-serious 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				
subjects affected / exposed	1 / 15 (6.67%)			
occurrences (all)	1			
Aspartate aminotransferase increased				
subjects affected / exposed	1 / 15 (6.67%)			
occurrences (all)	1			
Bacteria urine				
subjects affected / exposed	2 / 15 (13.33%)			
occurrences (all)	2			
Blood bicarbonate decreased				
subjects affected / exposed	3 / 15 (20.00%)			
occurrences (all)	4			
Blood urine present				
subjects affected / exposed	2 / 15 (13.33%)			
occurrences (all)	2			
Protein urine present				
subjects affected / exposed	2 / 15 (13.33%)			
occurrences (all)	2			
Red blood cells urine positive				
subjects affected / exposed	2 / 15 (13.33%)			
occurrences (all)	2			
Weight decreased				
subjects affected / exposed	1 / 15 (6.67%)			
occurrences (all)	1			
White blood cells urine positive				
subjects affected / exposed	2 / 15 (13.33%)			
occurrences (all)	2			
C-reactive protein increased				
subjects affected / exposed	1 / 15 (6.67%)			
occurrences (all)	1			
Urine leukocyte esterase positive				
subjects affected / exposed	1 / 15 (6.67%)			
occurrences (all)	1			
White blood cell count increased				

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

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

subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Rash			
subjects affected / exposed	2 / 15 (13.33%)		
occurrences (all)	3		
Rash erythematous			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Infections and infestations			
Central line infection			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	2		
Gastroenteritis viral			
subjects affected / exposed	2 / 15 (13.33%)		
occurrences (all)	2		
Influenza			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Nasopharyngitis			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Overgrowth bacterial			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Parainfluenzae virus infection			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Rhinovirus infection			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	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	The following substantial changes were made for implementation at all study sites: 1) Inclusion Criterion 5 was clarified to provide further specific definition of stable PN/IV support. 2) Exclusion Criterion 17 was clarified to provide further details regarding prestudy hospital admissions. 3) The details surrounding the storage conditions of the study medication were clarified. 4) Details for dose interruption of individual subjects and study termination were included in the protocol. 5) Changes from local Amendments 1 and 2 were incorporated for all sites. Local Amendment 1: 1) The observation time after the first SC injection was increased to 4 hours to allow for monitoring of hypersensitivity reactions. 2) The definition of true abstinence was added for females of child bearing potential in order to clarify study requirements. Local Amendment 2: 1) A rationale for the study design was added to provide risk/benefit information for PN/IV support in relation to the protocol design. 2) Additional safety visits were added after EOT and before End of Study for 3 consecutive weeks to provide follow-up safety monitoring. 3) Post-treatment guidance was added to ensure that subjects were returned to their previous standard of care. 4) The time frame of 5 years was added to Exclusion Criterion 8 for history of cancer or clinically significant lymphoproliferative disease. 5) The duration of record retention was extended to 10 years.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported