Clinical trial results:
A phase 2 trial testing ZP1848 in patients with SBS

A proof-of-concept, dose-finding, controlled, single-center, randomized, cross-over, double-blind, fixed dose trial

Summary

EudraCT number	2015-002826-38
Trial protocol	DK
Global end of trial date	04 May 2017

Results information

Result version number	v1 (current)
This version publication date	01 June 2018
First version publication date	01 June 2018

Trial information

Trial identification

Sponsor protocol code	ZP1848-15073

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02690025
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Zealand Pharma A/S
Sponsor organisation address	Smedeland 36, Glostrup, Denmark, 2600
Public contact	Gertrud Koefoed Rasmussen, Zealand Pharma A/S, 0045 50603773, gkr@zealandpharma.com
Scientific contact	Gertrud Koefoed Rasmussen, Zealand Pharma A/S, 0045 50603773, gkr@zealandpharma.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	04 May 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	04 May 2017
Global end of trial reached?	Yes
Global end of trial date	04 May 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective is to evaluate the effect of three different doses of ZP1848 on intestinal absorption in SBS patients after three week treatment periods.

Protection of trial subjects:

The trial was conducted in accordance of the World Medical Association Declaration of Helsinki, current guidelines for GCP and local regulations.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	05 February 2016
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Denmark: 18
Worldwide total number of subjects	18
EEA total number of subjects	18

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)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	12
From 65 to 84 years	6
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

22 patients were screened at one Danish site. The first patient was screened on 5 Feb 2016 and the last patient was enrolled on 25 Jan 2017. 18 Patients were randomized in the trial and 16 patients completed the trial.

Pre-assignment

Screening details:

4 patients failed screening. 18 patients were randomized and received treatment. 2 patients dropped out during their first treatment period (did not start the second treatment period). Hence, totally 34 treatment periods were started/32 were completed. The screening assessments occurred up to 27 days prior to baseline assessments.

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Monitor, Data analyst, Subject

Arms

Are arms mutually exclusive?	No
Arm title	0.1 mg/day

Arm description: -

Arm type	Experimental
Investigational medicinal product name	ZP1848
Investigational medicinal product code	
Other name	glepaglutide
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

0.1 mg injected daily subcutaneously in abdomen or thighs for 3 weeks

Arm title	1 mg/day

Arm description: -

Arm type	Experimental
Investigational medicinal product name	ZP1848
Investigational medicinal product code	
Other name	glepaglutide
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

1 mg injected daily subcutaneously in abdomen or thighs for 3 weeks

Arm title	10 mg/day

Arm description: -

Arm type	Experimental
Investigational medicinal product name	ZP1848
Investigational medicinal product code	
Other name	glepaglutide
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:
10 mg injected daily subcutaneously in abdomen or thighs for 3 weeks

Number of subjects in period 1	0.1 mg/day	1 mg/day	10 mg/day
Started	11	11	12
Completed	10	11	11
Not completed	1	0	1
Consent withdrawn by subject	1	-	-
Adverse event, non-fatal	-	-	1

Baseline characteristics

Reporting groups

Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	18	18	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	12	12	
From 65-84 years	6	6	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	9	9	
Male	9	9	

Subject analysis sets

Subject analysis set title	FAS
Subject analysis set type	Full analysis

Subject analysis set description:

The full analysis set comprises all randomized patients delivering post-baseline efficacy data

Reporting group values	FAS		
Number of subjects	16		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	0		
Children (2-11 years)	0		
Adolescents (12-17 years)	0		
Adults (18-64 years)	11		
From 65-84 years	5		
85 years and over	0		

Gender categorical Units: Subjects			
Female	8		
Male	8		

End points

End points reporting groups

Reporting group title	0.1 mg/day
Reporting group description: -	
Reporting group title	1 mg/day
Reporting group description: -	
Reporting group title	10 mg/day
Reporting group description: -	
Subject analysis set title	FAS
Subject analysis set type	Full analysis
Subject analysis set description:	
The full analysis set comprises all randomized patients delivering post-baseline efficacy data	

Primary: Absolute change from baseline to the end of the 3-week treatment periods of wet weight output or diarrhea

End point title	Absolute change from baseline to the end of the 3-week treatment periods of wet weight output or diarrhea
End point description:	
End point type	Primary
End point timeframe:	
Change measured between baseline and end of the 3-week treatment period	

End point values	0.1 mg/day	1 mg/day	10 mg/day	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10	11	11	
Units: g per day				
least squares mean (confidence interval 95%)	173 (-160 to 506)	-592 (-913 to -272)	-833 (-1152 to -515)	

Statistical analyses

Statistical analysis title	Test 1 Effect in the pooled 10 and 1 mg dose group
Statistical analysis description:	
Effect in the pooled medium and high dose groups	
Comparison groups	10 mg/day v 1 mg/day
Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	other[1]
P-value	< 0.0001
Method	ANCOVA

Notes:

[1] - The primary endpoint was analyzed using a linear model having period (1,2) and treatment doses (0.1, 1 and 10.0 mg) as fixed effects and patient as random effect, adjusting for the baseline value within each dosing period, the total oral intake (solid and liquid combined in grams) and the PS volume. The model was analyzed using a mixed-effects analysis of covariance (ANCOVA).

Statistical analysis title	Test 2 Effect in the 10 mg dose

Statistical analysis description:

Effect in the high dose group

Comparison groups	10 mg/day v 1 mg/day
Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	other[2]
P-value	= 0.0002 [3]
Method	ANCOVA

Notes:

[2] - The primary endpoint was analyzed using a linear model having period (1,2) and treatment doses (0.1, 1 and 10.0 mg) as fixed effects and patient as random effect, adjusting for the baseline value within each dosing period, the total oral intake (solid and liquid combined in grams) and the PS volume. The model was analyzed using a mixed-effects analysis of covariance (ANCOVA).

[3] - The primary hypotheses were tested sequentially in a hierarchical testing procedure.

Statistical analysis title	Test 3 Effect in the 1 mg dose group

Statistical analysis description:

Effect of the medium dose

Comparison groups	1 mg/day v 0.1 mg/day
Number of subjects included in analysis	21
Analysis specification	Pre-specified
Analysis type	other[4]
P-value	= 0.0021 [5]
Method	ANCOVA

Notes:

[4] - The primary endpoint was analyzed using a linear model having period (1,2) and treatment doses (0.1, 1 and 10.0 mg) as fixed effects and patient as random effect, adjusting for the baseline value within each dosing period, the total oral intake (solid and liquid combined in grams) and the PS volume. The model was analyzed using a mixed-effects analysis of covariance (ANCOVA).

[5] - The primary hypotheses were tested sequentially in a hierarchical testing procedure.

Statistical analysis title	Test 4 Effect in the 0.1 mg dose group
Comparison groups	0.1 mg/day v 1 mg/day
Number of subjects included in analysis	21
Analysis specification	Pre-specified
Analysis type	other[6]
P-value	= 0.2743 [7]
Method	ANCOVA

Notes:

[6] - The primary endpoint was analyzed using a linear model having period (1,2) and treatment doses (0.1, 1 and 10.0 mg) as fixed effects and patient as random effect, adjusting for the baseline value within each dosing period, the total oral intake (solid and liquid combined in grams) and the PS volume. The model was analyzed using a mixed-effects analysis of covariance (ANCOVA).

[7] - The primary hypotheses were tested sequentially in a hierarchical testing procedure. The test procedure stopped at test 4

Secondary: Relative change from baseline to the end of treatment of wet weight of ostomy output or diarrhea

End point title	Relative change from baseline to the end of treatment of wet weight of ostomy output or diarrhea

End point description:

End point type	Secondary

End point timeframe:

Change measured between baseline and end of the 3 week treatment period

End point values	0.1 mg/day	1 mg/day	10 mg/day	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10	11	11	
Units: percent				
least squares mean (confidence interval 95%)	10 (-3 to 22)	-23 (-35 to -11)	-30 (-42 to -19)	

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute change from baseline to the end of treatment of urine weight

End point title	Absolute change from baseline to the end of treatment of urine weight

End point description:

End point type	Secondary

End point timeframe:

Change measured between baseline and end of the 3 week treatment period

End point values	0.1 mg/day	1 mg/day	10 mg/day	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10	11	11	
Units: g per day				
least squares mean (confidence interval 95%)	90 (-208 to 389)	530 (245 to 816)	368 (82 to 654)	

Statistical analyses

No statistical analyses for this end point

Secondary: Relative change from baseline to the end of treatment of urine weight

End point title	Relative change from baseline to the end of treatment of urine weight

End point description:

End point type	Secondary

End point timeframe:

Change measured between baseline and end of the 3 week treatment period

End point values	0.1 mg/day	1 mg/day	10 mg/day	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10	11	11	
Units: percent				
least squares mean (confidence interval 95%)	11 (-11 to 34)	40 (18 to 61)	32 (11 to 54)	

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute change from baseline to the end of treatment of wet weight absorption (measured by oral intake minus fecal excretion)

End point title	Absolute change from baseline to the end of treatment of wet weight absorption (measured by oral intake minus fecal excretion)

End point description:

End point type	Secondary

End point timeframe:

Change measured between baseline and end of the 3 week treatment period

End point values	0.1 mg/day	1 mg/day	10 mg/day	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10	11	11	
Units: g per day				
least squares mean (confidence interval 95%)	-211 (-487 to 64)	650 (385 to 914)	786 (523 to 1049)	

Statistical analyses

No statistical analyses for this end point

Secondary: Relative change from baseline to the end of treatment of wet weight absorption (measured by oral intake minus fecal excretion)

End point title	Relative change from baseline to the end of treatment of wet

	weight absorption (measured by oral intake minus fecal excretion)

End point description:

End point type	Secondary

End point timeframe:

Change measured between baseline and end of the 3 week treatment period

End point values	0.1 mg/day	1 mg/day	10 mg/day	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10	11	11	
Units: percent				
least squares mean (confidence interval 95%)	-34 (-228 to 159)	21 (-165 to 207)	87 (-98 to 272)	

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute change from baseline to the end of treatment of urine weight minus oral intake

End point title	Absolute change from baseline to the end of treatment of urine weight minus oral intake

End point description:

End point type	Secondary

End point timeframe:

Change measured between baseline and end of the 3 week treatment period

End point values	0.1 mg/day	1 mg/day	10 mg/day	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10	11	11	
Units: g per day				
least squares mean (confidence interval 95%)	118 (-244 to 479)	487 (140 to 833)	411 (65 to 758)	

Statistical analyses

No statistical analyses for this end point

Secondary: Relative change from baseline to the end of treatment of urine weight minus oral intake

End point title	Relative change from baseline to the end of treatment of urine weight minus oral intake

End point description:

End point type	Secondary

End point timeframe:

Change measured between baseline and end of the 3 week treatment period

End point values	0.1 mg/day	1 mg/day	10 mg/day	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10	11	11	
Units: percent				
least squares mean (confidence interval 95%)	-4 (-39 to 31)	-45 (-79 to -11)	-50 (-84 to -16)	

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute change from baseline to the end of treatment of the intestinal absorption (oral intake minus fecal excretion) of sodium

End point title	Absolute change from baseline to the end of treatment of the intestinal absorption (oral intake minus fecal excretion) of sodium

End point description:

End point type	Secondary

End point timeframe:

Change measured between baseline and end of the 3 week treatment period

End point values	0.1 mg/day	1 mg/day	10 mg/day	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10	11	11	
Units: mmol per day				
least squares mean (confidence interval 95%)	-17 (-58 to 24)	47 (7 to 86)	40 (1 to 80)	

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute change from baseline to the end of treatment of the intestinal

absorption (oral intake minus fecal excretion) of magnesium	
End point title	Absolute change from baseline to the end of treatment of the intestinal absorption (oral intake minus fecal excretion) of magnesium

End point description:

End point type	Secondary

End point timeframe:

Change measured between baseline and end of the 3 week treatment period

End point values	0.1 mg/day	1 mg/day	10 mg/day	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10	11	11	
Units: mmol per day				
least squares mean (confidence interval 95%)	-3 (-6 to -1)	1 (-2 to 3)	-1 (-4 to 1)	

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute change from baseline to the end of treatment of the intestinal absorption (oral intake minus fecal excretion) of calcium	
End point title	Absolute change from baseline to the end of treatment of the intestinal absorption (oral intake minus fecal excretion) of calcium

End point description:

End point type	Secondary

End point timeframe:

Change measured between baseline and end of the 3 week treatment period

End point values	0.1 mg/day	1 mg/day	10 mg/day	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10	11	11	
Units: mmol per day				
least squares mean (confidence interval 95%)	-5 (-9 to -1)	0 (-4 to 4)	0 (-4 to 4)	

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute change from baseline to the end of treatment of the intestinal absorption (oral intake minus fecal excretion) of potassium

End point title	Absolute change from baseline to the end of treatment of the intestinal absorption (oral intake minus fecal excretion) of potassium

End point description:

End point type	Secondary

End point timeframe:

Change measured between baseline and end of the 3 week treatment period

End point values	0.1 mg/day	1 mg/day	10 mg/day	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10	11	11	
Units: mmol per day				
least squares mean (confidence interval 95%)	0 (-16 to 17)	16 (0 to 31)	10 (-5 to 25)	

Statistical analyses

No statistical analyses for this end point

Secondary: Relative change from baseline to the end of treatment of the intestinal absorption (oral intake minus fecal excretion) of sodium

End point title	Relative change from baseline to the end of treatment of the intestinal absorption (oral intake minus fecal excretion) of sodium

End point description:

End point type	Secondary

End point timeframe:

Change measured between baseline and end of the 3 week treatment period

End point values	0.1 mg/day	1 mg/day	10 mg/day	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10	11	11	
Units: percent				
least squares mean (confidence interval 95%)	13 (-235 to 260)	60 (-176 to 295)	131 (-102 to 364)	

Statistical analyses

No statistical analyses for this end point

Secondary: Relative change from baseline to the end of treatment of the intestinal absorption (oral intake minus fecal excretion) of magnesium

End point title	Relative change from baseline to the end of treatment of the intestinal absorption (oral intake minus fecal excretion) of magnesium

End point description:

End point type	Secondary

End point timeframe:

Change measured between baseline and end of the 3 week treatment period

End point values	0.1 mg/day	1 mg/day	10 mg/day	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10	11	11	
Units: percent				
least squares mean (confidence interval 95%)	128 (-200 to 457)	-90 (-403 to 223)	-109 (-418 to 200)	

Statistical analyses

No statistical analyses for this end point

Secondary: Relative change from baseline to the end of treatment of the intestinal absorption (oral intake minus fecal excretion) of calcium

End point title	Relative change from baseline to the end of treatment of the intestinal absorption (oral intake minus fecal excretion) of calcium

End point description:

End point type	Secondary

End point timeframe:

Change measured between baseline and end of the 3 week treatment period

End point values	0.1 mg/day	1 mg/day	10 mg/day	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10	11	11	
Units: percent				
least squares mean (confidence interval 95%)	-242 (-453 to -30)	-17 (-220 to 186)	74 (-127 to 276)	

Statistical analyses

No statistical analyses for this end point

Secondary: Relative change from baseline to the end of treatment of the intestinal absorption (oral intake minus fecal excretion) of potassium

End point title	Relative change from baseline to the end of treatment of the intestinal absorption (oral intake minus fecal excretion) of potassium

End point description:

End point type	Secondary

End point timeframe:

Change measured between baseline and end of the 3 week treatment period

End point values	0.1 mg/day	1 mg/day	10 mg/day	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10	11	11	
Units: percent				
least squares mean (confidence interval 95%)	-90 (-326 to 146)	-80 (-306 to 146)	57 (-164 to 279)	

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute change from baseline to the end of treatment of intestinal absorption (oral intake minus fecal excretion) of energy assessed by bomb calorimetry

End point title	Absolute change from baseline to the end of treatment of intestinal absorption (oral intake minus fecal excretion) of energy assessed by bomb calorimetry

End point description:

End point type	Secondary

End point timeframe:

Change measured between baseline and end of the 3 week treatment period

End point values	0.1 mg/day	1 mg/day	10 mg/day	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10	11	11	
Units: kJ per day				
least squares mean (confidence interval 95%)	-377 (-1234 to 481)	435 (-393 to 1263)	588 (-227 to 1403)	

Statistical analyses

No statistical analyses for this end point

Secondary: Relative change from baseline to the end of treatment of intestinal absorption (oral intake minus fecal excretion) of energy assessed by bomb calorimetry

End point title	Relative change from baseline to the end of treatment of intestinal absorption (oral intake minus fecal excretion) of energy assessed by bomb calorimetry

End point description:

End point type	Secondary

End point timeframe:

Change measured between baseline and end of the 3 week treatment period

End point values	0.1 mg/day	1 mg/day	10 mg/day	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10	11	11	
Units: percent				
least squares mean (confidence interval 95%)	6 (-66 to 78)	24 (-46 to 94)	21 (-48 to 90)	

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute change from baseline to the end of treatment of intestinal absorption (oral intake minus fecal excretion) of lipids

End point title	Absolute change from baseline to the end of treatment of intestinal absorption (oral intake minus fecal excretion) of lipids

End point description:

End point type	Secondary

End point timeframe:

Change measured between baseline and end of the 3 week treatment period

End point values	0.1 mg/day	1 mg/day	10 mg/day	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10	11	11	
Units: kJ per day				
least squares mean (confidence interval 95%)	-330 (-864 to 205)	516 (3 to 1029)	103 (-407 to 612)	

Statistical analyses

No statistical analyses for this end point

Secondary: Relative change from baseline to the end of treatment of intestinal absorption (oral intake minus fecal excretion) of lipids

End point title	Relative change from baseline to the end of treatment of intestinal absorption (oral intake minus fecal excretion) of lipids

End point description:

End point type	Secondary

End point timeframe:

Change measured between baseline and end of the 3 week treatment period

End point values	0.1 mg/day	1 mg/day	10 mg/day	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10	11	11	
Units: percent				
least squares mean (confidence interval 95%)	-31 (-72 to 10)	48 (9 to 87)	0 (-38 to 39)	

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute change from baseline to the end of treatment of intestinal absorption (oral intake minus fecal excretion) of nitrogen (a marker of proteins)

End point title	Absolute change from baseline to the end of treatment of intestinal absorption (oral intake minus fecal excretion) of nitrogen (a marker of proteins)

End point description:

End point type	Secondary

End point timeframe:

Change measured between baseline and end of the 3 week treatment period

End point values	0.1 mg/day	1 mg/day	10 mg/day	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10	11	11	
Units: g per day				
least squares mean (confidence interval 95%)	-1 (-3 to 1)	2 (0 to 3)	1 (-1 to 2)	

Statistical analyses

No statistical analyses for this end point

Secondary: Relative change from baseline to the end of treatment of intestinal absorption (oral intake minus fecal excretion) of nitrogen (a marker of proteins)

End point title	Relative change from baseline to the end of treatment of intestinal absorption (oral intake minus fecal excretion) of nitrogen (a marker of proteins)

End point description:

End point type	Secondary

End point timeframe:

Change measured between baseline and end of the 3 week treatment period

End point values	0.1 mg/day	1 mg/day	10 mg/day	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10	11	11	
Units: percent				
least squares mean (confidence interval 95%)	-83 (-220 to 55)	-63 (-196 to 70)	-42 (-173 to 89)	

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute change from baseline to the end of treatment of intestinal absorption (oral intake minus fecal excretion) of carbohydrates

End point title	Absolute change from baseline to the end of treatment of intestinal absorption (oral intake minus fecal excretion) of carbohydrates

End point description:

End point type	Secondary

End point timeframe:

Change measured between baseline and end of the 3 week treatment period

End point values	0.1 mg/day	1 mg/day	10 mg/day	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10	11	11	
Units: kJ per day				
least squares mean (confidence interval 95%)	-11 (-399 to 377)	368 (-6 to 743)	336 (-31 to 703)	

Statistical analyses

No statistical analyses for this end point

Secondary: Mean score change in mental component score (MCS)

End point title	Mean score change in mental component score (MCS)

End point description:

SF-36v2 1 week-recall version

End point type	Secondary

End point timeframe:

Change measured between baseline and end of the 3 week treatment period

End point values	0.1 mg/day	1 mg/day	10 mg/day	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10	11	11	
Units: Score				
arithmetic mean (standard deviation)	2.7 (± 9.5)	1.8 (± 7.0)	-4.8 (± 13.7)	

Statistical analyses

No statistical analyses for this end point

Secondary: Relative change from baseline to the end of treatment of intestinal absorption (oral intake minus fecal excretion) of carbohydrates

End point title	Relative change from baseline to the end of treatment of intestinal absorption (oral intake minus fecal excretion) of carbohydrates

End point description:

End point type	Secondary

End point timeframe:

Change measured between baseline and end of the 3 week treatment period

End point values	0.1 mg/day	1 mg/day	10 mg/day	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10	11	11	
Units: percent				
least squares mean (confidence interval 95%)	-2 (-20 to 17)	18 (-1 to 36)	21 (3 to 39)	

Statistical analyses

No statistical analyses for this end point

Secondary: Mean score change in physical component score (PCS)

End point title	Mean score change in physical component score (PCS)

End point description:

SF-36v2 1-week recall version used

End point type	Secondary

End point timeframe:

Change measured between baseline and end of the 3 week treatment period

End point values	0.1 mg/day	1 mg/day	10 mg/day	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10	11	11	
Units: Score				
arithmetic mean (standard deviation)	1.3 (± 6.1)	2.5 (± 5.6)	-2.5 (± 6.8)	

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Absolute change from baseline to the end of treatment of intestinal absorption (oral intake minus fecal excretion) of energy calculated as the sum of the energy content

End point title	Absolute change from baseline to the end of treatment of intestinal absorption (oral intake minus fecal excretion) of energy calculated as the sum of the energy content

End point description:

Energy was calculated as the sum of the energy content from lipids, nitrogen (as a marker for proteins) and carbohydrates and used as an approximation

End point type	Other pre-specified

End point timeframe:

Change measured between baseline and end of the 3 week treatment period

End point values	0.1 mg/day	1 mg/day	10 mg/day	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10	10	10	
Units: kJ per day				
least squares mean (confidence interval 95%)	-491 (-1402 to 419)	1099 (223 to 1976)	544 (-317 to 1406)	

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Relative change from baseline to the end of treatment of intestinal absorption (oral intake minus fecal excretion) of energy calculated as the sum of the energy content

End point title	Relative change from baseline to the end of treatment of intestinal absorption (oral intake minus fecal excretion) of energy calculated as the sum of the energy content

End point description:

Energy was calculated as the sum of the energy content from lipids, nitrogen (as a marker for proteins) and carbohydrates and used as an approximation

End point type	Other pre-specified

End point timeframe:

Change measured between baseline and end of the 3 week treatment period

End point values	0.1 mg/day	1 mg/day	10 mg/day	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10	11	11	
Units: percent				
least squares mean (confidence interval 95%)	-10 (-33 to 13)	25 (3 to 47)	11 (-11 to 34)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Adverse event reporting was done from informed consent was signed and until the follow up visit	
Adverse event reporting additional description:	
Due to the size of the trial population any event reported would result in >5% frequency	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	18.1

Reporting groups	
Reporting group title	0.1 mg/day
Reporting group description: -	
Reporting group title	Safety analysis set
Reporting group description: -	
Reporting group title	10 mg/day
Reporting group description: -	
Reporting group title	1 mg/day
Reporting group description: -	

Serious adverse events	0.1 mg/day	Safety analysis set	10 mg/day
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 12 (16.67%)	7 / 18 (38.89%)	6 / 12 (50.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0		0
Injury, poisoning and procedural complications			
Stoma obstruction			
subjects affected / exposed	1 / 12 (8.33%)	1 / 18 (5.56%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	2 / 2	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Thrombophlebitis superficial			
subjects affected / exposed	0 / 12 (0.00%)	1 / 18 (5.56%)	1 / 12 (8.33%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Catheter removal			

subjects affected / exposed	0 / 12 (0.00%)	1 / 18 (5.56%)	1 / 12 (8.33%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Transient ischaemic attack			
subjects affected / exposed	0 / 12 (0.00%)	1 / 18 (5.56%)	1 / 12 (8.33%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	0 / 12 (0.00%)	1 / 18 (5.56%)	1 / 12 (8.33%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain			
subjects affected / exposed	1 / 12 (8.33%)	1 / 18 (5.56%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	2 / 2	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mechanical ileus			
subjects affected / exposed	0 / 12 (0.00%)	1 / 18 (5.56%)	1 / 12 (8.33%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Device related sepsis	Additional description: Cross-over design.One patient in group 0.1 mg is the same patient as in the 10 mg group, hence this patient experienced 2 events both of them assessed not related.		
subjects affected / exposed	2 / 12 (16.67%)	2 / 18 (11.11%)	1 / 12 (8.33%)
occurrences causally related to treatment / all	1 / 2	1 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	1 / 12 (8.33%)	1 / 18 (5.56%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infection			

subjects affected / exposed	1 / 12 (8.33%)	2 / 18 (11.11%)	1 / 12 (8.33%)
occurrences causally related to treatment / all	1 / 1	2 / 2	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 12 (0.00%)	1 / 18 (5.56%)	1 / 12 (8.33%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	1 mg/day		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 12 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Injury, poisoning and procedural complications			
Stoma obstruction			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Thrombophlebitis superficial			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Surgical and medical procedures			
Catheter removal			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Transient ischaemic attack			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal pain upper			

subjects affected / exposed	0 / 12 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Abdominal pain			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Mechanical ileus			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Device related sepsis	Additional description: Cross-over design.One patient in group 0.1 mg is the same patient as in the 10 mg group, hence this patient experienced 2 events both of them assessed not related.		
subjects affected / exposed	0 / 12 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Sepsis			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infection			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	0.1 mg/day	Safety analysis set	10 mg/day
Total subjects affected by non-serious adverse events			
subjects affected / exposed	11 / 12 (91.67%)	18 / 18 (100.00%)	12 / 12 (100.00%)
Vascular disorders			
Hot flush			
subjects affected / exposed	0 / 12 (0.00%)	3 / 18 (16.67%)	3 / 12 (25.00%)
occurrences (all)	0	4	4
Peripheral coldness			
subjects affected / exposed	1 / 12 (8.33%)	1 / 18 (5.56%)	0 / 12 (0.00%)
occurrences (all)	1	1	0
Hypertension			
subjects affected / exposed	0 / 12 (0.00%)	1 / 18 (5.56%)	0 / 12 (0.00%)
occurrences (all)	0	1	1
Surgical and medical procedures			
Enterostomy			
subjects affected / exposed	0 / 12 (0.00%)	1 / 18 (5.56%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			
Injection site reaction	Additional description: This was a cross-over design, hence subjects may appear in 2 groups. Injection site reactions (ISRs) were captured separately from AEs. ISRs were recorded on a symptom level: itching, redness, induration/infiltration, pain, edema and other		
subjects affected / exposed	2 / 12 (16.67%)	11 / 18 (61.11%)	8 / 12 (66.67%)
occurrences (all)	11	498	327
Oedema peripheral			
subjects affected / exposed	2 / 12 (16.67%)	10 / 18 (55.56%)	5 / 12 (41.67%)
occurrences (all)	3	21	9
Fatigue			
subjects affected / exposed	1 / 12 (8.33%)	6 / 18 (33.33%)	4 / 12 (33.33%)
occurrences (all)	1	7	4
Malaise			
subjects affected / exposed	2 / 12 (16.67%)	3 / 18 (16.67%)	2 / 12 (16.67%)
occurrences (all)	3	5	2
Thirst			
subjects affected / exposed	0 / 12 (0.00%)	1 / 18 (5.56%)	1 / 12 (8.33%)
occurrences (all)	0	2	2
Impaired healing			

subjects affected / exposed	1 / 12 (8.33%)	1 / 18 (5.56%)	0 / 12 (0.00%)
occurrences (all)	1	1	0
Device occlusion			
subjects affected / exposed	1 / 12 (8.33%)	1 / 18 (5.56%)	0 / 12 (0.00%)
occurrences (all)	1	1	0
Chills			
subjects affected / exposed	0 / 12 (0.00%)	1 / 18 (5.56%)	1 / 12 (8.33%)
occurrences (all)	0	1	1
Reproductive system and breast disorders			
Oedema genital			
subjects affected / exposed	0 / 12 (0.00%)	2 / 18 (11.11%)	2 / 12 (16.67%)
occurrences (all)	0	2	2
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 12 (8.33%)	4 / 18 (22.22%)	2 / 12 (16.67%)
occurrences (all)	1	4	2
Oropharyngeal pain			
subjects affected / exposed	2 / 12 (16.67%)	2 / 18 (11.11%)	1 / 12 (8.33%)
occurrences (all)	2	3	1
Dyspnoea exertional			
subjects affected / exposed	0 / 12 (0.00%)	1 / 18 (5.56%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			
Restlessness			
subjects affected / exposed	0 / 12 (0.00%)	2 / 18 (11.11%)	0 / 12 (0.00%)
occurrences (all)	0	2	0
Irritability			
subjects affected / exposed	0 / 12 (0.00%)	1 / 18 (5.56%)	1 / 12 (8.33%)
occurrences (all)	0	1	1
Insomnia			
subjects affected / exposed	0 / 12 (0.00%)	1 / 18 (5.56%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Depressed mood			
subjects affected / exposed	1 / 12 (8.33%)	1 / 18 (5.56%)	0 / 12 (0.00%)
occurrences (all)	1	1	0
Investigations			

Gastrointestinal stoma output increased			
subjects affected / exposed	0 / 12 (0.00%)	3 / 18 (16.67%)	3 / 12 (25.00%)
occurrences (all)	0	4	4
Weight increased			
subjects affected / exposed	0 / 12 (0.00%)	1 / 18 (5.56%)	1 / 12 (8.33%)
occurrences (all)	0	1	1
Weight decreased			
subjects affected / exposed	1 / 12 (8.33%)	1 / 18 (5.56%)	0 / 12 (0.00%)
occurrences (all)	1	1	0
Urine output increased			
subjects affected / exposed	0 / 12 (0.00%)	1 / 18 (5.56%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Serum ferritin decreased			
subjects affected / exposed	0 / 12 (0.00%)	1 / 18 (5.56%)	1 / 12 (8.33%)
occurrences (all)	0	1	1
International normalised ratio abnormal			
subjects affected / exposed	0 / 12 (0.00%)	1 / 18 (5.56%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Haemoglobin decreased			
subjects affected / exposed	0 / 12 (0.00%)	1 / 18 (5.56%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal stoma output decreased			
subjects affected / exposed	0 / 12 (0.00%)	1 / 18 (5.56%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Injury, poisoning and procedural complications			
Stoma complication			
subjects affected / exposed	2 / 12 (16.67%)	13 / 18 (72.22%)	10 / 12 (83.33%)
occurrences (all)	2	20	12
Gastrointestinal stoma complication			
subjects affected / exposed	3 / 12 (25.00%)	13 / 18 (72.22%)	10 / 12 (83.33%)
occurrences (all)	3	19	10
Stoma obstruction			
subjects affected / exposed	1 / 12 (8.33%)	1 / 18 (5.56%)	0 / 12 (0.00%)
occurrences (all)	1	1	0

Procedural pain			
subjects affected / exposed	2 / 12 (16.67%)	3 / 18 (16.67%)	1 / 12 (8.33%)
occurrences (all)	2	3	1
Stoma site haemorrhage			
subjects affected / exposed	1 / 12 (8.33%)	1 / 18 (5.56%)	0 / 12 (0.00%)
occurrences (all)	2	2	0
Stoma site oedema			
subjects affected / exposed	0 / 12 (0.00%)	1 / 18 (5.56%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Stoma site erythema			
subjects affected / exposed	0 / 12 (0.00%)	1 / 18 (5.56%)	1 / 12 (8.33%)
occurrences (all)	0	1	1
Ligament sprain			
subjects affected / exposed	1 / 12 (8.33%)	1 / 18 (5.56%)	0 / 12 (0.00%)
occurrences (all)	1	1	0
Scar			
subjects affected / exposed	1 / 12 (8.33%)	1 / 18 (5.56%)	0 / 12 (0.00%)
occurrences (all)	1	1	0
Excoriation			
subjects affected / exposed	0 / 12 (0.00%)	1 / 18 (5.56%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Accidental overdose			
subjects affected / exposed	1 / 12 (8.33%)	1 / 18 (5.56%)	0 / 12 (0.00%)
occurrences (all)	1	1	0
Cardiac disorders			
Tachycardia			
subjects affected / exposed	1 / 12 (8.33%)	3 / 18 (16.67%)	2 / 12 (16.67%)
occurrences (all)	1	5	3
Palpitations			
subjects affected / exposed	1 / 12 (8.33%)	1 / 18 (5.56%)	1 / 12 (8.33%)
occurrences (all)	2	3	1
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 12 (8.33%)	3 / 18 (16.67%)	2 / 12 (16.67%)
occurrences (all)	2	13	5
Dizziness			

subjects affected / exposed	2 / 12 (16.67%)	5 / 18 (27.78%)	3 / 12 (25.00%)
occurrences (all)	4	8	4
Migraine			
subjects affected / exposed	0 / 12 (0.00%)	2 / 18 (11.11%)	1 / 12 (8.33%)
occurrences (all)	0	3	1
Paraesthesia			
subjects affected / exposed	0 / 12 (0.00%)	1 / 18 (5.56%)	0 / 12 (0.00%)
occurrences (all)	0	2	0
Restless legs syndrome			
subjects affected / exposed	0 / 12 (0.00%)	1 / 18 (5.56%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Hypoaesthesia			
subjects affected / exposed	1 / 12 (8.33%)	1 / 18 (5.56%)	0 / 12 (0.00%)
occurrences (all)	1	1	0
Eye disorders			
Conjunctival haemorrhage			
subjects affected / exposed	0 / 12 (0.00%)	1 / 18 (5.56%)	1 / 12 (8.33%)
occurrences (all)	0	1	1
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	4 / 12 (33.33%)	8 / 18 (44.44%)	6 / 12 (50.00%)
occurrences (all)	6	21	14
Abdominal pain			
subjects affected / exposed	5 / 12 (41.67%)	7 / 18 (38.89%)	2 / 12 (16.67%)
occurrences (all)	12	17	3
Gastrointestinal sounds abnormal			
subjects affected / exposed	1 / 12 (8.33%)	1 / 18 (5.56%)	0 / 12 (0.00%)
occurrences (all)	10	11	0
Abdominal pain upper			
subjects affected / exposed	2 / 12 (16.67%)	4 / 18 (22.22%)	3 / 12 (25.00%)
occurrences (all)	2	8	5
Vomiting			
subjects affected / exposed	3 / 12 (25.00%)	5 / 18 (27.78%)	3 / 12 (25.00%)
occurrences (all)	3	8	4
Abdominal distension			

subjects affected / exposed	3 / 12 (25.00%)	5 / 18 (27.78%)	2 / 12 (16.67%)
occurrences (all)	3	7	2
Dry mouth			
subjects affected / exposed	0 / 12 (0.00%)	2 / 18 (11.11%)	2 / 12 (16.67%)
occurrences (all)	0	2	2
Rectal haemorrhage			
subjects affected / exposed	1 / 12 (8.33%)	1 / 18 (5.56%)	0 / 12 (0.00%)
occurrences (all)	1	1	0
Abdominal pain lower			
subjects affected / exposed	1 / 12 (8.33%)	1 / 18 (5.56%)	0 / 12 (0.00%)
occurrences (all)	1	1	0
Abdominal tenderness			
subjects affected / exposed	1 / 12 (8.33%)	1 / 18 (5.56%)	0 / 12 (0.00%)
occurrences (all)	1	1	0
Abdominal discomfort			
subjects affected / exposed	1 / 12 (8.33%)	1 / 18 (5.56%)	0 / 12 (0.00%)
occurrences (all)	1	1	0
Skin and subcutaneous tissue disorders			
Erythema			
subjects affected / exposed	0 / 12 (0.00%)	1 / 18 (5.56%)	1 / 12 (8.33%)
occurrences (all)	0	1	1
Renal and urinary disorders			
Polyuria			
subjects affected / exposed	1 / 12 (8.33%)	6 / 18 (33.33%)	3 / 12 (25.00%)
occurrences (all)	1	7	3
Pollakiuria			
subjects affected / exposed	0 / 12 (0.00%)	2 / 18 (11.11%)	2 / 12 (16.67%)
occurrences (all)	0	2	2
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 12 (8.33%)	3 / 18 (16.67%)	1 / 12 (8.33%)
occurrences (all)	1	4	1
Myalgia			
subjects affected / exposed	1 / 12 (8.33%)	2 / 18 (11.11%)	1 / 12 (8.33%)
occurrences (all)	1	2	1
Muscular weakness			

subjects affected / exposed	1 / 12 (8.33%)	1 / 18 (5.56%)	0 / 12 (0.00%)
occurrences (all)	1	1	0
Fistula discharge			
subjects affected / exposed	0 / 12 (0.00%)	1 / 18 (5.56%)	1 / 12 (8.33%)
occurrences (all)	0	1	1
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	1 / 12 (8.33%)	3 / 18 (16.67%)	2 / 12 (16.67%)
occurrences (all)	1	5	2
Influenza			
subjects affected / exposed	1 / 12 (8.33%)	3 / 18 (16.67%)	1 / 12 (8.33%)
occurrences (all)	1	3	1
Infection			
subjects affected / exposed	1 / 12 (8.33%)	1 / 18 (5.56%)	0 / 12 (0.00%)
occurrences (all)	1	1	0
Upper respiratory tract infection			
subjects affected / exposed	2 / 12 (16.67%)	2 / 18 (11.11%)	0 / 12 (0.00%)
occurrences (all)	2	2	0
Tooth infection			
subjects affected / exposed	0 / 12 (0.00%)	1 / 18 (5.56%)	1 / 12 (8.33%)
occurrences (all)	0	1	1
Pneumonia			
subjects affected / exposed	0 / 12 (0.00%)	1 / 18 (5.56%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Nasopharyngitis			
subjects affected / exposed	0 / 12 (0.00%)	1 / 18 (5.56%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Rhinitis			
subjects affected / exposed	0 / 12 (0.00%)	1 / 18 (5.56%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 12 (8.33%)	4 / 18 (22.22%)	2 / 12 (16.67%)
occurrences (all)	1	4	2
Iron deficiency			

subjects affected / exposed	0 / 12 (0.00%)	1 / 18 (5.56%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Hypokalaemia			
subjects affected / exposed	1 / 12 (8.33%)	1 / 18 (5.56%)	0 / 12 (0.00%)
occurrences (all)	1	1	0
Abnormal weight gain			
subjects affected / exposed	0 / 12 (0.00%)	1 / 18 (5.56%)	1 / 12 (8.33%)
occurrences (all)	0	1	1
Vitamin D deficiency			
subjects affected / exposed	0 / 12 (0.00%)	1 / 18 (5.56%)	1 / 12 (8.33%)
occurrences (all)	0	1	1

Non-serious adverse events	1 mg/day		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	11 / 12 (91.67%)		
Vascular disorders			
Hot flush			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Peripheral coldness			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Hypertension			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Surgical and medical procedures			
Enterostomy			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
General disorders and administration site conditions			
Injection site reaction	Additional description: This was a cross-over design, hence subjects may appear in 2 groups. Injection site reactions (ISRs) were captured separately from AEs. ISRs were recorded on a symptom level: itching, redness, induration/infiltration, pain, edema and other		
subjects affected / exposed	7 / 12 (58.33%)		
occurrences (all)	160		
Oedema peripheral			

subjects affected / exposed occurrences (all)	6 / 12 (50.00%) 9		
Fatigue subjects affected / exposed occurrences (all)	2 / 12 (16.67%) 2		
Malaise subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0		
Thirst subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0		
Impaired healing subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0		
Device occlusion subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0		
Chills subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0		
Reproductive system and breast disorders			
Oedema genital subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0		
Respiratory, thoracic and mediastinal disorders			
Cough subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1		
Oropharyngeal pain subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0		
Dyspnoea exertional subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1		
Psychiatric disorders			

Restlessness			
subjects affected / exposed	2 / 12 (16.67%)		
occurrences (all)	2		
Irritability			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Insomnia			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Depressed mood			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Investigations			
Gastrointestinal stoma output increased			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Weight increased			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Weight decreased			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Urine output increased			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Serum ferritin decreased			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
International normalised ratio abnormal			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Haemoglobin decreased			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Gastrointestinal stoma output decreased			

subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			
Stoma complication			
subjects affected / exposed	6 / 12 (50.00%)		
occurrences (all)	6		
Gastrointestinal stoma complication			
subjects affected / exposed	6 / 12 (50.00%)		
occurrences (all)	6		
Stoma obstruction			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Procedural pain			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Stoma site haemorrhage			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Stoma site oedema			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Stoma site erythema			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Ligament sprain			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Scar			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Excoriation			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Accidental overdose			

subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Cardiac disorders			
Tachycardia			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Palpitations			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	6		
Dizziness			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Migraine			
subjects affected / exposed	2 / 12 (16.67%)		
occurrences (all)	2		
Paraesthesia			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	2		
Restless legs syndrome			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Hypoaesthesia			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Eye disorders			
Conjunctival haemorrhage			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Abdominal pain			

subjects affected / exposed	2 / 12 (16.67%)		
occurrences (all)	2		
Gastrointestinal sounds abnormal			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Abdominal pain upper			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Vomiting			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Abdominal distension			
subjects affected / exposed	2 / 12 (16.67%)		
occurrences (all)	2		
Dry mouth			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Rectal haemorrhage			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Abdominal pain lower			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Abdominal tenderness			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Abdominal discomfort			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Skin and subcutaneous tissue disorders			
Erythema			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Renal and urinary disorders			
Polyuria			

subjects affected / exposed	3 / 12 (25.00%)		
occurrences (all)	3		
Pollakiuria			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 12 (16.67%)		
occurrences (all)	2		
Myalgia			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Muscular weakness			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Fistula discharge			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	2		
Influenza			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Infection			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Upper respiratory tract infection			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Tooth infection			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Pneumonia			

subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Nasopharyngitis			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Rhinitis			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Iron deficiency			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Hypokalaemia			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Abnormal weight gain			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Vitamin D deficiency			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported