Clinical trial results:
A Phase II, multicentre, randomised, double-blind, placebo controlled, proof of concept study of efficacy and safety of Rifamycin SV-MMX® 600 mg tablets administered three or two times daily to patients with diarrhoea-predominant irritable bowel syndrome (IBS-D)

Summary

EudraCT number	2016-004977-42
Trial protocol	BE ES DE IT
Global end of trial date	10 September 2020

Results information

Result version number	v1 (current)
This version publication date	04 October 2022
First version publication date	04 October 2022
Summary attachment (see zip file)	Protocol (20180220-c130-csp-f-3-0.pdf)

Trial information

Trial identification

Sponsor protocol code	CB-01-11/28

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03099785
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Cosmo Technologies
Sponsor organisation address	Riverside 2, 49 Sir John Rogerson's Quay, Grand Canal Dock, Dublin,, Dublin, Italy, D02 KV60
Public contact	Cristina Banyai, Cosmo Technologies Ltd, +353 867015703, cbanyai@cosmopharma.com
Scientific contact	Luigi Longo, Cosmo Technologies Ltd, +353 867015703, cbanyai@cosmopharma.com
Sponsor organisation name	Cosmo Technologies
Sponsor organisation address	Riverside 2, 49 Sir John Rogerson's Quay, Grand Canal Dock , Dublin, Ireland, D02 KV60
Public contact	Cristina Banyai, Luigi Longo, cbanyai@cosmopharma.com
Scientific contact	Cristina Banyai, Luigi Longo, LLongo@cosmopharma.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	No

1901/2006 apply to this trial?	

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	01 April 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	10 September 2020
Global end of trial reached?	Yes
Global end of trial date	10 September 2020
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To compare two dose regimens of Rifamycin SV-MMX® 600 mg tablets versus matching placebo in terms of proportion of subjects with adequate relief of the composite of abdominal pain and stool consistency.

Protection of trial subjects:

Subjects were followed for safety and tolerability assessments: Treatment-emergent adverse events (TEAEs); vital signs (blood pressure, heart rate, body temperature, body weight), physical examinations; laboratory tests; electrocardiogram (ECG).

Background therapy:

There were no additional treatments or comparators used in this study across all arms/groups of the study.

Evidence for comparator:

The present proof of concept trial is designed to preliminarily investigate the efficacy of rifamycin SV in the indicated pathology versus matching placebo. Moreover, the efficacy will be also compared between two different rifamycin SV dose regimens. There were no comparators used in the study.

Actual start date of recruitment	09 November 2017
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	Spain: 60
Country: Number of subjects enrolled	Belgium: 50
Country: Number of subjects enrolled	Germany: 136
Country: Number of subjects enrolled	Italy: 33
Worldwide total number of subjects	279
EEA total number of subjects	279

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)	244
From 65 to 84 years	35
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

342 subjects were planned to be enrolled. The study was prematurely terminate on 31OCT20, due to also the pandemic situation. The enrolment stopped with the randomisation of 279 subjects. First patient enrolled 09Nov2017. There were study 25 centres/4 countries including Spain, Belgium, Italy and Germany.

Pre-assignment

Screening details:

The study protocol foresaw a screening phase including a baseline symptom evaluation period, followed by a treatment period of 2 weeks (visits 2, 3 and 4) and by a follow-up period of 10 weeks (visits 5 to 7, telephonic follow-ups 1 to 7). Screening window Day-21 till Day-15.

Period 1

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

Blinding implementation details:

The code for specific subjects will be documented in the source, in the eCRF and in the clinical study report. Breaking of an individual randomisation code by the investigator during the study is allowed only when knowledge of the code is essential for the subject's health. In these cases, the investigator will access the individual code of the concerned subject in the integrated eCRF system, where the unblinding action will be audit trailed.

Arms

Are arms mutually exclusive?	Yes
Arm title	Treatment group 1: dose regimen 1

Arm description:

Rifamycin SV-MMX® 600 mg modified release tablets, three times daily (t.i.d.)
Morning: one 600 mg tablet
Afternoon: one 600 mg tablet
Evening: one 600 mg tablet

Arm type	Active comparator
Investigational medicinal product name	Rifamycin SV-MMX® 600 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Rifamycin SV-MMX® 600 mg modified release tablets, three times daily (t.i.d.)
Morning: one 600 mg tablet
Afternoon: one 600 mg tablet
Evening: one 600 mg tablet
All the subjects will take the assigned tablets t.i.d., ideally at the following times: 07:30±2 h, 15:30±2 h and 23:30±2 h, for 14 days.

Arm title	Treatment group 2: dose regimen 2

Arm description:

Rifamycin SV-MMX® 600 mg modified release tablets, two times daily (b.i.d.) + matching placebo daily (q.d.)
Morning. one 600 mg tablet
Afternoon: one matching placebo tablet
Evening: one 600 mg tablet

Arm type	Active comparator

Investigational medicinal product name	Rifamycin SV-MMX®
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Ocular use

Dosage and administration details:

Rifamycin SV-MMX® 600mg

Arm title	Treatment group 3: matching placebo

Arm description:

Rifamycin SV-MMX® matching placebo tablets, t.i.d.
Morning. one matching placebo tablet
Afternoon: one matching placebo tablet
Evening: one matching placebo tablet

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Matching Placebo tablets

Number of subjects in period 1	Treatment group 1: dose regimen 1	Treatment group 2: dose regimen 2	Treatment group 3: matching placebo
Started	87	95	97
Completed	79	88	91
Not completed	8	7	6
Consent withdrawn by subject	1	2	2
Physician decision	1	-	-
Early termination due to holiday	1	-	-
Adverse event, non-fatal	1	1	1
Incompliant with study drug and the visits	-	-	1
Shouldn't be randomised	-	1	-
Lost to follow-up	2	2	-
Discontinued before treatment	2	1	1
Lack of efficacy	-	-	1

Baseline characteristics

Reporting groups

Reporting group title	Treatment period- overall study

Reporting group description: -

Reporting group values	Treatment period- overall study	Total	
Number of subjects	279	279	
Age categorical Units: Subjects			
Adults (18-64 years)	257	257	
From 65-84 years	22	22	
85 years and over	0	0	
Age continuous Units: years			
arithmetic mean	40.6		
standard deviation	± 14.7	-	
Gender categorical Units: Subjects			
Female	169	169	
Male	110	110	
Race Units: Subjects			
White	274	274	
Other	2	2	
Black	2	2	
Asian	1	1	
BW Units: kg			
arithmetic mean	74.01		
standard deviation	± 16.55	-	
Height Units: cm			
arithmetic mean	170.2		
standard deviation	± 9.4	-	

Subject analysis sets

Subject analysis set title	The intent-to-treat (ITT)
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Intention-To-Treat Set (ITT): all randomised subjects. This analysis set was used for sensitivity analyses

Subject analysis set title	Full Analysis Set (FAS)
Subject analysis set type	Full analysis

Subject analysis set description:

All randomised subjects, who receive at least one dose of the investigational medicinal product and have at least one post randomisation assessment of the primary efficacy data. This analysis set will be used for the primary efficacy analysis

Subject analysis set title	Per Protocol Set (PP)

Subject analysis set type	Per protocol

Subject analysis set description:

Per Protocol Set (PP): all randomised subjects who fulfil the study protocol requirements in terms of IMP intake and collection of primary efficacy data and with no major deviations that may affect study results. This analysis set will be used for sensitivity analyses

Subject analysis set title	Safety Set
Subject analysis set type	Safety analysis

Subject analysis set description:

All subjects who receive at least one dose of the IMP. This analysis set will be used for the safety analyses

Subject analysis set title	mFAS
Subject analysis set type	Sub-group analysis

Subject analysis set description:

The modified FAS (mFAS) is a subset of the FAS including all the subjects who fulfilled the protocol in terms of treatment compliance in the first week of treatment and had at least 6 (out of 7) daily assessments of abdominal pain score and stool consistency in both the last available week of screening and the first week of treatment and with no major deviations that could affect primary efficacy analysis

Subject analysis set title	Dose Regimen 1 (Full Analysis Set)
Subject analysis set type	Full analysis

Subject analysis set description:

Dose Regimen 1 (Full Analysis Set)

Subject analysis set title	Dose Regimen 2 (Full Analysis Set)
Subject analysis set type	Full analysis

Subject analysis set description:

Dose Regimen 2 (Full Analysis Set)

Subject analysis set title	Dose Regimen 3 (Full Analysis Set)
Subject analysis set type	Full analysis

Subject analysis set description:

Dose Regimen 3 (Full Analysis Set)

Subject analysis set title	Dose Regimen 1 (IIT)
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Dose Regimen 1 (Intention to Treat)

Subject analysis set title	Dose Regimen 2 (IIT)
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Dose Regimen 2 (Intention to Treat)

Subject analysis set title	Dose Regimen 3 (IIT)
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Dose Regimen 3 (Intention to Treat)

Subject analysis set title	Dose Regimen 1 (Per Protocol Set)
Subject analysis set type	Per protocol

Subject analysis set description:

Dose Regimen 1 (Per Protocol Set)

Subject analysis set title	Dose Regimen 2 (Per Protocol Set)
Subject analysis set type	Per protocol

Subject analysis set description:

Dose Regimen 2 (Per Protocol Set)

Subject analysis set title	Dose Regimen 3 (Per Protocol Set)
Subject analysis set type	Per protocol

Subject analysis set description:

Dose Regimen 3 (Per Protocol Set)

Subject analysis set title	Dose Regimen 1 (mFAS)
Subject analysis set type	Modified intention-to-treat
Subject analysis set description: Dose Regimen 1 (modified Full Analysis Set)	
Subject analysis set title	Dose Regimen 2 (mFAS)
Subject analysis set type	Modified intention-to-treat
Subject analysis set description: Dose Regimen 2 (modified Full Analysis Set)	
Subject analysis set title	Dose Regimen 3 (mFAS)
Subject analysis set type	Modified intention-to-treat
Subject analysis set description: Dose Regimen 3 (modified Full Analysis Set)	

Reporting group values	The intent-to-treat (ITT)	Full Analysis Set (FAS)	Per Protocol Set (PP)
Number of subjects	279	264	207
Age categorical Units: Subjects			
Adults (18-64 years)	257	243	192
From 65-84 years	22	21	15
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	40.6	40.5	40.2
standard deviation	± 14.7	± 14.6	± 14.5
Gender categorical Units: Subjects			
Female	169	162	117
Male	110	102	90
Race Units: Subjects			
White	274	259	202
Other	2	2	2
Black	2	2	2
Asian	1	1	1
BW Units: kg			
arithmetic mean	74.01	74.07	74.83
standard deviation	± 16.55	± 16.77	± 16.70
Height Units: cm			
arithmetic mean	170.2	170.2	170.5
standard deviation	± 9.4	± 9.5	± 9.8

Reporting group values	Safety Set	mFAS	Dose Regimen 1 (Full Analysis Set)
Number of subjects	275	235	81
Age categorical Units: Subjects			
Adults (18-64 years)	254	218	74
From 65-84 years	21	17	7
85 years and over	0	0	0

Age continuous Units: years			
arithmetic mean	40.5	40.1	40.6
standard deviation	± 14.6	± 14.4	± 15.6
Gender categorical Units: Subjects			
Female	167	140	48
Male	108	95	33
Race Units: Subjects			
White	270	230	79
Other	2	2	1
Black	2	2	0
Asian	1	1	1
BW Units: kg			
arithmetic mean	74.12	74.39	74.20
standard deviation	± 16.59	± 17.02	± 17.06
Height Units: cm			
arithmetic mean	170.1	170.2	170.3
standard deviation	± 9.5	± 9.7	± 9.1

Reporting group values	Dose Regimen 2 (Full Analysis Set)	Dose Regimen 3 (Full Analysis Set)	Dose Regimen 1 (IIT)
Number of subjects	88	95	87
Age categorical Units: Subjects			
Adults (18-64 years)	82	87	80
From 65-84 years	6	8	7
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	41.1	39.9	40.1
standard deviation	± 13.4	± 15.0	± 15.3
Gender categorical Units: Subjects			
Female	55	59	52
Male	33	36	35
Race Units: Subjects			
White	87	93	85
Other	0	1	1
Black	1	1	0
Asian	0	0	1
BW Units: kg			
arithmetic mean	75.40	72.72	73.70
standard deviation	± 16.64	± 16.71	± 16.91
Height Units: cm			
arithmetic mean	170.5	169.8	170.2

standard deviation	± 9.2	± 10.2	± 9.1

Reporting group values	Dose Regimen 2 (IIT)	Dose Regimen 3 (IIT)	Dose Regimen 1 (Per Protocol Set)
Number of subjects	95	97	63
Age categorical Units: Subjects			
Adults (18-64 years)	88	89	58
From 65-84 years	7	8	5
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	41.5	40.2	40.8
standard deviation	± 13.7	± 15.1	± 15.9
Gender categorical Units: Subjects			
Female	58	59	33
Male	37	38	30
Race Units: Subjects			
White	94	95	61
Other	0	1	1
Black	1	1	0
Asian	0	0	1
BW Units: kg			
arithmetic mean	75.55	72.77	74.16
standard deviation	± 16.21	± 16.61	± 15.59
Height Units: cm			
arithmetic mean	170.4	169.9	170.9
standard deviation	± 9.1	± 10.2	± 8.9

Reporting group values	Dose Regimen 2 (Per Protocol Set)	Dose Regimen 3 (Per Protocol Set)	Dose Regimen 1 (mFAS)
Number of subjects	65	79	74
Age categorical Units: Subjects			
Adults (18-64 years)	60	74	68
From 65-84 years	5	5	6
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	41.8	38.5	40.2
standard deviation	± 13.1	± 14.5	± 15.7
Gender categorical Units: Subjects			
Female	36	48	42
Male	29	31	32

Race Units: Subjects			
White	64	77	72
Other	0	1	1
Black	1	1	0
Asian	0	0	1
BW Units: kg			
arithmetic mean	77.97	72.76	74.46
standard deviation	± 17.13	± 17.02	± 17.69
Height Units: cm			
arithmetic mean	170.9	169.9	170.5
standard deviation	± 10.0	± 10.3	± 9.1

Reporting group values	Dose Regimen 2 (mFAS)	Dose Regimen 3 (mFAS)	
Number of subjects	75	86	
Age categorical Units: Subjects			
Adults (18-64 years)	70	80	
From 65-84 years	5	6	
85 years and over	0	0	
Age continuous Units: years			
arithmetic mean	41.2	38.9	
standard deviation	± 13.2	± 14.4	
Gender categorical Units: Subjects			
Female	44	54	
Male	31	32	
Race Units: Subjects			
White	74	84	
Other	0	1	
Black	1	1	
Asian	0	0	
BW Units: kg			
arithmetic mean	76.23	72.70	
standard deviation	± 16.79	± 16.65	
Height Units: cm			
arithmetic mean	170.5	169.6	
standard deviation	± 9.7	± 10.2	

End points

End points reporting groups

Reporting group title	Treatment group 1: dose regimen 1
Reporting group description:	
Rifamycin SV-MMX® 600 mg modified release tablets, three times daily (t.i.d.) Morning: one 600 mg tablet Afternoon: one 600 mg tablet Evening: one 600 mg tablet	
Reporting group title	Treatment group 2: dose regimen 2
Reporting group description:	
Rifamycin SV-MMX® 600 mg modified release tablets, two times daily (b.i.d.) + matching placebo daily (q.d.) Morning. one 600 mg tablet Afternoon: one matching placebo tablet Evening: one 600 mg tablet	
Reporting group title	Treatment group 3: matching placebo
Reporting group description:	
Rifamycin SV-MMX® matching placebo tablets, t.i.d. Morning. one matching placebo tablet Afternoon: one matching placebo tablet Evening: one matching placebo tablet	
Subject analysis set title	The intent-to-treat (ITT)
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Intention-To-Treat Set (ITT): all randomised subjects. This analysis set was used for sensitivity analyses	
Subject analysis set title	Full Analysis Set (FAS)
Subject analysis set type	Full analysis
Subject analysis set description:	
All randomised subjects, who receive at least one dose of the investigational medicinal product and have at least one post randomisation assessment of the primary efficacy data. This analysis set will be used for the primary efficacy analysis	
Subject analysis set title	Per Protocol Set (PP)
Subject analysis set type	Per protocol
Subject analysis set description:	
Per Protocol Set (PP): all randomised subjects who fulfil the study protocol requirements in terms of IMP intake and collection of primary efficacy data and with no major deviations that may affect study results. This analysis set will be used for sensitivity analyses	
Subject analysis set title	Safety Set
Subject analysis set type	Safety analysis
Subject analysis set description:	
All subjects who receive at least one dose of the IMP. This analysis set will be used for the safety analyses	
Subject analysis set title	mFAS
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
The modified FAS (mFAS) is a subset of the FAS including all the subjects who fulfilled the protocol in terms of treatment compliance in the first week of treatment and had at least 6 (out of 7) daily assessments of abdominal pain score and stool consistency in both the last available week of screening and the first week of treatment and with no major deviations that could affect primary efficacy analysis	
Subject analysis set title	Dose Regimen 1 (Full Analysis Set)
Subject analysis set type	Full analysis
Subject analysis set description:	
Dose Regimen 1 (Full Analysis Set)	
Subject analysis set title	Dose Regimen 2 (Full Analysis Set)
Subject analysis set type	Full analysis

Subject analysis set description: Dose Regimen 2 (Full Analysis Set)	
Subject analysis set title	Dose Regimen 3 (Full Analysis Set)
Subject analysis set type	Full analysis
Subject analysis set description: Dose Regimen 3 (Full Analysis Set)	
Subject analysis set title	Dose Regimen 1 (IIT)
Subject analysis set type	Intention-to-treat
Subject analysis set description: Dose Regimen 1 (Intention to Treat)	
Subject analysis set title	Dose Regimen 2 (IIT)
Subject analysis set type	Intention-to-treat
Subject analysis set description: Dose Regimen 2 (Intention to Treat)	
Subject analysis set title	Dose Regimen 3 (IIT)
Subject analysis set type	Intention-to-treat
Subject analysis set description: Dose Regimen 3 (Intention to Treat)	
Subject analysis set title	Dose Regimen 1 (Per Protocol Set)
Subject analysis set type	Per protocol
Subject analysis set description: Dose Regimen 1 (Per Protocol Set)	
Subject analysis set title	Dose Regimen 2 (Per Protocol Set)
Subject analysis set type	Per protocol
Subject analysis set description: Dose Regimen 2 (Per Protocol Set)	
Subject analysis set title	Dose Regimen 3 (Per Protocol Set)
Subject analysis set type	Per protocol
Subject analysis set description: Dose Regimen 3 (Per Protocol Set)	
Subject analysis set title	Dose Regimen 1 (mFAS)
Subject analysis set type	Modified intention-to-treat
Subject analysis set description: Dose Regimen 1 (modified Full Analysis Set)	
Subject analysis set title	Dose Regimen 2 (mFAS)
Subject analysis set type	Modified intention-to-treat
Subject analysis set description: Dose Regimen 2 (modified Full Analysis Set)	
Subject analysis set title	Dose Regimen 3 (mFAS)
Subject analysis set type	Modified intention-to-treat
Subject analysis set description: Dose Regimen 3 (modified Full Analysis Set)	

Primary: Proportion of weekly responders with adequate relief of the composite of abdominal pain and stool consistency in the 1st week of treatment

End point title	Proportion of weekly responders with adequate relief of the composite of abdominal pain and stool consistency in the 1st week of treatment

End point description:

Relief of abdominal pain is defined as a decrease in the weekly average of abdominal pain score of at least 30% compared with baseline and relief of stool consistency is defined as a 50% or greater reduction in the number of days per week with at least one stool that has a consistency of Type 6 or 7 compared with baseline.

End point type	Primary
End point timeframe: 1st week of treatment	

End point values	Treatment group 1: dose regimen 1	Treatment group 2: dose regimen 2	Treatment group 3: matching placebo	Dose Regimen 1 (Full Analysis Set)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	87	95	97	81
Units: subjects	10	22	9	10

End point values	Dose Regimen 2 (Full Analysis Set)	Dose Regimen 3 (Full Analysis Set)	Dose Regimen 1 (IIT)	Dose Regimen 2 (IIT)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	88	95	87	95
Units: subjects	22	9	10	22

End point values	Dose Regimen 3 (IIT)	Dose Regimen 1 (Per Protocol Set)	Dose Regimen 2 (Per Protocol Set)	Dose Regimen 3 (Per Protocol Set)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	97	63	65	79
Units: subjects	9	7	18	7

End point values	Dose Regimen 1 (mFAS)	Dose Regimen 2 (mFAS)	Dose Regimen 3 (mFAS)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	74	75	86	
Units: subjects	9	21	9	

Statistical analyses

Statistical analysis title	DOSE REGIMEN 1 vs. DOSE REGIMEN 3 (FAS)
Statistical analysis description: Odds Ratio and 95% CI of DOSE REGIMEN 1 vs. DOSE REGIMEN 3 (Full Analysis Set)	
Comparison groups	Dose Regimen 1 (Full Analysis Set) v Dose Regimen 3 (Full Analysis Set)

Number of subjects included in analysis	176
Analysis specification	Pre-specified
Analysis type	superiority[1]
P-value	= 0.5892
Method	Wald Chi-Square
Parameter estimate	Odds ratio (OR)
Point estimate	1.35
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.52
upper limit	3.49

Notes:

[1] - Subjects with missing data on primary endpoint are defined as non-responders according to EMA guidance

Statistical analysis title	DOSE REGIMEN 1 vs. DOSE REGIMEN 3 (mFAS)

Statistical analysis description:

Odds Ratio and 95% CI of DOSE REGIMEN 1 vs. DOSE REGIMEN 3 (mFAS)

Comparison groups	Dose Regimen 1 (mFAS) v Dose Regimen 3 (mFAS)
Number of subjects included in analysis	160
Analysis specification	Pre-specified
Analysis type	superiority[2]
P-value	= 0.4758
Method	Wald Chi-Square
Parameter estimate	Odds ratio (OR)
Point estimate	1.18
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.44
upper limit	3.16

Notes:

[2] - Subjects with missing data on primary endpoint are defined as non-responders according to EMA guidance

Statistical analysis title	DOSE REGIMEN 1 vs. DOSE REGIMEN 3 (IIT)

Statistical analysis description:

Odds Ratio and 95% CI of DOSE REGIMEN 1 vs. DOSE REGIMEN 3 (IIT)

Comparison groups	Dose Regimen 1 (IIT) v Dose Regimen 3 (IIT)
Number of subjects included in analysis	184
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.593
Method	Wald Chi-Square
Parameter estimate	Odds ratio (OR)
Point estimate	1.33
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.51
upper limit	3.45

Statistical analysis title	DOSE REGIMEN 2 vs. DOSE REGIMEN 3 (FAS)
Statistical analysis description:	
Odds Ratio and 95% CI of DOSE REGIMEN 2 vs. DOSE REGIMEN 3 (Full Analysis Set)	
Comparison groups	Dose Regimen 3 (Full Analysis Set) v Dose Regimen 2 (Full Analysis Set)
Number of subjects included in analysis	183
Analysis specification	Pre-specified
Analysis type	superiority[3]
P-value	= 0.0066
Method	Wald Chi-Square
Parameter estimate	Odds ratio (OR)
Point estimate	3.19
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.38
upper limit	7.37

Notes:

[3] - Subjects with missing data on primary endpoint are defined as non-responders according to EMA guidance

Statistical analysis title	DOSE REGIMEN 1 vs. DOSE REGIMEN 2 (FAS)
Statistical analysis description:	
Odds Ratio and 95% CI of DOSE REGIMEN 1 vs. DOSE REGIMEN 2 (Full Analysis Set)	
Comparison groups	Dose Regimen 1 (Full Analysis Set) v Dose Regimen 2 (Full Analysis Set)
Number of subjects included in analysis	169
Analysis specification	Pre-specified
Analysis type	superiority[4]
P-value	= 0.0314
Method	Wald Chi-Square
Parameter estimate	Odds ratio (OR)
Point estimate	0.42
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.19
upper limit	0.96

Notes:

[4] - Subjects with missing data on primary endpoint are defined as non-responders according to EMA guidance

Statistical analysis title	DOSE REGIMEN 2 vs. DOSE REGIMEN 3 (mFAS)
Statistical analysis description:	
Odds Ratio and 95% CI of DOSE REGIMEN 2 vs. DOSE REGIMEN 3 (mFAS)	
Comparison groups	Dose Regimen 3 (mFAS) v Dose Regimen 2 (mFAS)

Number of subjects included in analysis	161
Analysis specification	Pre-specified
Analysis type	superiority[5]
P-value	= 0.0015
Method	Wald Chi-Square
Parameter estimate	Odds ratio (OR)
Point estimate	3.33
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.42
upper limit	7.82

Notes:

[5] - Subjects with missing data on primary endpoint are defined as non-responders according to EMA guidance

Statistical analysis title	DOSE REGIMEN 1 vs. DOSE REGIMEN 2 (mFAS)

Statistical analysis description:

Odds Ratio and 95% CI of DOSE REGIMEN 1 vs. DOSE REGIMEN 2 (mFAS)

Comparison groups	Dose Regimen 2 (mFAS) v Dose Regimen 1 (mFAS)
Number of subjects included in analysis	149
Analysis specification	Pre-specified
Analysis type	superiority[6]
P-value	= 0.0124
Method	Wald Chi-Square
Parameter estimate	Odds ratio (OR)
Point estimate	0.36
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.15
upper limit	0.84

Notes:

[6] - Subjects with missing data on primary endpoint are defined as non-responders according to EMA guidance

Statistical analysis title	DOSE REGIMEN 2 vs. DOSE REGIMEN 3 (IIT)

Statistical analysis description:

Odds Ratio and 95% CI of DOSE REGIMEN 2 vs. DOSE REGIMEN 3 (IIT)

Comparison groups	Dose Regimen 3 (IIT) v Dose Regimen 2 (IIT)
Number of subjects included in analysis	192
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0101
Method	Wald Chi-Square
Parameter estimate	Odds ratio (OR)
Point estimate	3.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.32
upper limit	7.07

Statistical analysis title	DOSE REGIMEN 1 vs. DOSE REGIMEN 2 (IIT)
Statistical analysis description:	
Odds Ratio and 95% CI of DOSE REGIMEN 1 vs. DOSE REGIMEN 2 (IIT)	
Comparison groups	Dose Regimen 2 (IIT) v Dose Regimen 1 (IIT)
Number of subjects included in analysis	182
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0438
Method	Wald Chi-Square
Parameter estimate	Odds ratio (OR)
Point estimate	0.44
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.19
upper limit	0.99

Statistical analysis title	DOSE REGIMEN 1 vs. DOSE REGIMEN 3 (PP)
Statistical analysis description:	
Odds Ratio and 95% CI of DOSE REGIMEN 1 vs. DOSE REGIMEN 3 (PP Analysis Set)	
Comparison groups	Dose Regimen 3 (Per Protocol Set) v Dose Regimen 1 (Per Protocol Set)
Number of subjects included in analysis	142
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7975
Method	Wald Chi-Square
Parameter estimate	Odds ratio (OR)
Point estimate	1.29
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.43
upper limit	3.88

Statistical analysis title	DOSE REGIMEN 2 vs. DOSE REGIMEN 3 (PP)
Statistical analysis description:	
Odds Ratio and 95% CI of DOSE REGIMEN 1 vs. DOSE REGIMEN 3 (PP Analysis Set)	
Comparison groups	Dose Regimen 3 (Per Protocol Set) v Dose Regimen 2 (Per Protocol Set)

Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.004
Method	Wald Chi-Square
Parameter estimate	Odds ratio (OR)
Point estimate	3.94
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.53
upper limit	10.16

Statistical analysis title	DOSE REGIMEN 1 vs. DOSE REGIMEN 2 (PP)
Statistical analysis description:	
Odds Ratio and 95% CI of DOSE REGIMEN 1 vs. DOSE REGIMEN 2 (PP Analysis Set)	
Comparison groups	Dose Regimen 2 (Per Protocol Set) v Dose Regimen 1 (Per Protocol Set)
Number of subjects included in analysis	128
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.011
Method	Wald Chi-Square
Parameter estimate	Odds ratio (OR)
Point estimate	0.33
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.13
upper limit	0.85

Secondary: Proportion of subjects with adequate relief of global IBS symptoms for at least 2 (consecutive or not) of the 10 weeks during the follow-up period

End point title	Proportion of subjects with adequate relief of global IBS symptoms for at least 2 (consecutive or not) of the 10 weeks during the follow-up period

End point description:

Adequate relief of global IBS symptoms is defined as a response of "yes" to the following question, which was asked weekly (every 7 days):
"In regard to all your symptoms of IBS, as compared to the way you felt before you started study medication, have you, in the past 7 days, had adequate relief of your IBS symptoms? [Yes/No]"

End point type	Secondary

End point timeframe:

Weeks 3-12

End point values	Treatment group 1: dose regimen 1	Treatment group 2: dose regimen 2	Treatment group 3: matching placebo	Dose Regimen 1 (Full Analysis Set)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	87	95	97	81
Units: Subjects	45	59	55	43

End point values	Dose Regimen 2 (Full Analysis Set)	Dose Regimen 3 (Full Analysis Set)	Dose Regimen 1 (IIT)	Dose Regimen 2 (IIT)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	88	95	87	95
Units: Subjects	58	54	45	59

End point values	Dose Regimen 3 (IIT)	Dose Regimen 1 (Per Protocol Set)	Dose Regimen 2 (Per Protocol Set)	Dose Regimen 3 (Per Protocol Set)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	97	63	65	79
Units: Subjects	55	38	45	46

Statistical analyses

Statistical analysis title	Dose regimen 1 vs. Dose Regimen 3 (FAS)
Statistical analysis description:	
Odds ratios and their 95% confidence intervals for Dose Regimen 1 vs Dose Regimen 3 (FAS)	
Comparison groups	Dose Regimen 1 (Full Analysis Set) v Dose Regimen 3 (Full Analysis Set)
Number of subjects included in analysis	176
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	1.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.53
upper limit	2.04

Statistical analysis title	Dose regimen 2 vs. Dose Regimen 3 (FAS)
Statistical analysis description:	
Odds ratios and their 95% confidence intervals for Dose Regimen 2 vs Dose Regimen 3 (FAS)	
Comparison groups	Dose Regimen 3 (Full Analysis Set) v Dose Regimen 2 (Full

	Analysis Set)
Number of subjects included in analysis	183
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	1.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.86
upper limit	3.36

Statistical analysis title	Dose regimen 1 vs. Dose Regimen 2 (FAS)
Statistical analysis description:	
Odds ratios and their 95% confidence intervals for Dose Regimen 1 vs Dose Regimen 2 (FAS)	
Comparison groups	Dose Regimen 2 (Full Analysis Set) v Dose Regimen 1 (Full Analysis Set)
Number of subjects included in analysis	169
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	0.61
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.3
upper limit	1.26

Statistical analysis title	Dose regimen 1 vs. Dose Regimen 3 (ITT)
Statistical analysis description:	
Odds ratios and their 95% confidence intervals for Dose Regimen 1 vs Dose Regimen 3 (ITT)	
Comparison groups	Dose Regimen 1 (IIT) v Dose Regimen 3 (IIT)
Number of subjects included in analysis	184
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	1.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.53
upper limit	1.99

Statistical analysis title	Dose regimen 2 vs. Dose Regimen 3 (ITT)

Statistical analysis description:	
Odds ratios and their 95% confidence intervals for Dose Regimen 2 vs Dose Regimen 3 (ITT)	
Comparison groups	Dose Regimen 3 (IIT) v Dose Regimen 2 (IIT)
Number of subjects included in analysis	192
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	1.61
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.82
upper limit	3.16

Statistical analysis title	Dose regimen 1 vs. Dose Regimen 2 (ITT)
Statistical analysis description:	
Odds ratios and their 95% confidence intervals for Dose Regimen 1 vs Dose Regimen 2 (ITT)	
Comparison groups	Dose Regimen 2 (IIT) v Dose Regimen 1 (IIT)
Number of subjects included in analysis	182
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	0.64
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.31
upper limit	1.29

Statistical analysis title	Dose regimen 1 vs. Dose Regimen 3 (PP)
Statistical analysis description:	
Odds ratios and their 95% confidence intervals for Dose Regimen 1 vs Dose Regimen 3 (PP)	
Comparison groups	Dose Regimen 1 (Per Protocol Set) v Dose Regimen 3 (Per Protocol Set)
Number of subjects included in analysis	142
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	1.29
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.62
upper limit	2.67

Statistical analysis title	Dose regimen 2 vs. Dose Regimen 3 (PP)
Statistical analysis description: Odds ratios and their 95% confidence intervals for Dose Regimen 2 vs Dose Regimen 3 (PP)	
Comparison groups	Dose Regimen 3 (Per Protocol Set) v Dose Regimen 2 (Per Protocol Set)
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	1.83
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.86
upper limit	3.86

Statistical analysis title	Dose regimen 1 vs. Dose Regimen 2 (PP)
Statistical analysis description: Odds ratios and their 95% confidence intervals for Dose Regimen 1 vs Dose Regimen 2 (PP)	
Comparison groups	Dose Regimen 2 (Per Protocol Set) v Dose Regimen 1 (Per Protocol Set)
Number of subjects included in analysis	128
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.31
upper limit	1.58

Secondary: Proportion of subjects with adequate relief of global IBS symptoms during at least 2 weeks (consecutive or not) per month (“monthly response”) during month 1, during month 1 through 2 and during month 1 through 3

End point title	Proportion of subjects with adequate relief of global IBS symptoms during at least 2 weeks (consecutive or not) per month (“monthly response”) during month 1, during month 1 through 2 and during month 1 through 3

End point description:

Adequate relief of global IBS symptoms is defined as a response of "yes" to the following question, which was asked weekly (every 7 days):
"In regard to all your symptoms of IBS, as compared to the way you felt before you started study medication, have you, in the past 7 days, had adequate relief of your IBS symptoms? [Yes/No]"

End point type	Secondary

End point timeframe:
during month 1, during month 1 through 2 and during month 1 through 3

End point values	Treatment group 1: dose regimen 1	Treatment group 2: dose regimen 2	Treatment group 3: matching placebo	Dose Regimen 1 (Full Analysis Set)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	87	95	97	81
Units: Subjects				
Month 1	42	53	34	41
Month 1 through 2	34	49	36	34
Month 1 through 3	28	40	33	28

End point values	Dose Regimen 2 (Full Analysis Set)	Dose Regimen 3 (Full Analysis Set)	Dose Regimen 1 (IIT)	Dose Regimen 2 (IIT)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	88	95	87	95
Units: Subjects				
Month 1	50	34	42	53
Month 1 through 2	48	36	34	49
Month 1 through 3	39	33	28	40

End point values	Dose Regimen 3 (IIT)	Dose Regimen 1 (Per Protocol Set)	Dose Regimen 2 (Per Protocol Set)	Dose Regimen 3 (Per Protocol Set)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	97	63	65	79
Units: Subjects				
Month 1	34	34	38	28
Month 1 through 2	36	27	37	32
Month 1 through 3	33	23	29	30

Statistical analyses

Statistical analysis title	Dose Regimen 1 vs. Dose Regimen 3 (FAS)

Statistical analysis description:
Odds ratios and their 95% confidence intervals for Dose Regimen 1 vs Dose Regimen 3 (FAS)

Comparison groups	Dose Regimen 1 (Full Analysis Set) v Dose Regimen 3 (Full Analysis Set)

Number of subjects included in analysis	176
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	95
Confidence interval	
level	90 %
sides	1-sided
lower limit	90

Statistical analysis title	Dose Regimen 2 vs. Dose Regimen 3 (FAS)
Statistical analysis description:	
Odds ratios and their 95% confidence intervals for Dose Regimen 2 vs Dose Regimen 3 (FAS)	
Comparison groups	Dose Regimen 3 (Full Analysis Set) v Dose Regimen 2 (Full Analysis Set)
Number of subjects included in analysis	183
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	1.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.86
upper limit	3.36

Statistical analysis title	Dose Regimen 1 vs. Dose Regimen 2 (FAS)
Statistical analysis description:	
Odds ratios and their 95% confidence intervals for Dose Regimen 1 vs Dose Regimen 2 (FAS)	
Comparison groups	Dose Regimen 2 (Full Analysis Set) v Dose Regimen 1 (Full Analysis Set)
Number of subjects included in analysis	169
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	0.61
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.3
upper limit	1.26

Statistical analysis title	Dose Regimen 1 vs. Dose Regimen 3 (ITT)

Statistical analysis description:	
Odds ratios and their 95% confidence intervals for Dose Regimen 1 vs Dose Regimen 3 (ITT)	
Comparison groups	Dose Regimen 1 (IIT) v Dose Regimen 3 (IIT)
Number of subjects included in analysis	184
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	1.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.53
upper limit	1.99

Statistical analysis title	Dose Regimen 2 vs. Dose Regimen 3 (ITT)
Statistical analysis description:	
Odds ratios and their 95% confidence intervals for Dose Regimen 2 vs Dose Regimen 3 (ITT)	
Comparison groups	Dose Regimen 3 (IIT) v Dose Regimen 2 (IIT)
Number of subjects included in analysis	192
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	1.61
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.82
upper limit	3.16

Statistical analysis title	Dose Regimen 1 vs. Dose Regimen 2 (ITT)
Statistical analysis description:	
Odds ratios and their 95% confidence intervals for Dose Regimen 1 vs Dose Regimen 2 (ITT)	
Comparison groups	Dose Regimen 2 (IIT) v Dose Regimen 1 (IIT)
Number of subjects included in analysis	182
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	0.64
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.31
upper limit	1.29

Statistical analysis title	Dose Regimen 1 vs. Dose Regimen 3 (PP)
Statistical analysis description:	
Odds ratios and their 95% confidence intervals for Dose Regimen 1 vs Dose Regimen 3 (PP)	
Comparison groups	Dose Regimen 1 (Per Protocol Set) v Dose Regimen 3 (Per Protocol Set)
Number of subjects included in analysis	142
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	1.29
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.62
upper limit	2.67

Statistical analysis title	Dose Regimen 2 vs. Dose Regimen 3 (PP)
Statistical analysis description:	
Odds ratios and their 95% confidence intervals for Dose Regimen 2 vs Dose Regimen 3 (PP)	
Comparison groups	Dose Regimen 3 (Per Protocol Set) v Dose Regimen 2 (Per Protocol Set)
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	1.83
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.86
upper limit	3.86

Statistical analysis title	Dose Regimen 1 vs. Dose Regimen 2 (PP)
Statistical analysis description:	
Odds ratios and their 95% confidence intervals for Dose Regimen 1 vs Dose Regimen 2 (PP)	
Comparison groups	Dose Regimen 2 (Per Protocol Set) v Dose Regimen 1 (Per Protocol Set)
Number of subjects included in analysis	128
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.31
upper limit	1.58

Secondary: Proportion of subjects with adequate relief of IBS-related bloating for at least 2 (consecutive or not) of the 10 weeks during the follow-up period (i.e., weeks 3 through 12).

End point title	Proportion of subjects with adequate relief of IBS-related bloating for at least 2 (consecutive or not) of the 10 weeks during the follow-up period (i.e., weeks 3 through 12).

End point description:

Adequate relief of bloating is defined as a response of "yes" to the following question, which was asked weekly (every 7 days):
"In regard to your symptom of bloating, as compared to the way you felt before you started study medication, have you, in the past 7 days, had adequate relief of your IBS symptom of bloating? [Yes/No]."

End point type	Secondary

End point timeframe:

Weeks 3 through 12

End point values	Treatment group 1: dose regimen 1	Treatment group 2: dose regimen 2	Treatment group 3: matching placebo	Dose Regimen 1 (Full Analysis Set)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	87	95	97	81
Units: Subjects	48	59	54	47

End point values	Dose Regimen 2 (Full Analysis Set)	Dose Regimen 3 (Full Analysis Set)	Dose Regimen 1 (IIT)	Dose Regimen 2 (IIT)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	88	95	87	95
Units: Subjects	57	53	48	59

End point values	Dose Regimen 3 (IIT)	Dose Regimen 1 (Per Protocol Set)	Dose Regimen 2 (Per Protocol Set)	Dose Regimen 3 (Per Protocol Set)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	97	63	65	79
Units: Subjects	54	39	44	46

Statistical analyses

Statistical analysis title	Dose Regimen 1 vs Dose Regimen 3 (FAS)
Statistical analysis description:	
Odds ratios and their 95% confidence intervals for Dose Regimen 1 vs Dose Regimen 3 (FAS)	
Comparison groups	Dose Regimen 1 (Full Analysis Set) v Dose Regimen 3 (Full Analysis Set)
Number of subjects included in analysis	176
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	1.45
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.72
upper limit	2.89

Statistical analysis title	Dose Regimen 2 vs Dose Regimen 3 (FAS)
Statistical analysis description:	
Odds ratios and their 95% confidence intervals for Dose Regimen 2 vs Dose Regimen 3 (FAS)	
Comparison groups	Dose Regimen 3 (Full Analysis Set) v Dose Regimen 2 (Full Analysis Set)
Number of subjects included in analysis	183
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	1.67
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.85
upper limit	3.27

Statistical analysis title	Dose Regimen 1 vs Dose Regimen 2 (FAS)
Statistical analysis description:	
Odds ratios and their 95% confidence intervals for Dose Regimen 1 vs Dose Regimen 2 (FAS)	
Comparison groups	Dose Regimen 2 (Full Analysis Set) v Dose Regimen 1 (Full Analysis Set)
Number of subjects included in analysis	169
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	0.87
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.42
upper limit	1.81

Statistical analysis title	Dose Regimen 1 vs Dose Regimen 3 (ITT)
Statistical analysis description: Odds ratios and their 95% confidence intervals for Dose Regimen 1 vs Dose Regimen 3 (ITT)	
Comparison groups	Dose Regimen 1 (IIT) v Dose Regimen 3 (IIT)
Number of subjects included in analysis	184
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	1.31
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.67
upper limit	2.58

Statistical analysis title	Dose Regimen 2 vs Dose Regimen 3 (ITT)
Statistical analysis description: Odds ratios and their 95% confidence intervals for Dose Regimen 2 vs Dose Regimen 3 (ITT)	
Comparison groups	Dose Regimen 3 (IIT) v Dose Regimen 2 (IIT)
Number of subjects included in analysis	192
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	1.61
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.83
upper limit	3.14

Statistical analysis title	Dose Regimen 1 vs Dose Regimen 2 (ITT)
Statistical analysis description: Odds ratios and their 95% confidence intervals for Dose Regimen 1 vs Dose Regimen 2(ITT)	
Comparison groups	Dose Regimen 2 (IIT) v Dose Regimen 1 (IIT)
Number of subjects included in analysis	182
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	0.81

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.4
upper limit	1.66

Statistical analysis title	Dose Regimen 1 vs Dose Regimen 3 (PP)
Statistical analysis description:	
Odds ratios and their 95% confidence intervals for Dose Regimen 1 vs Dose Regimen 3(PP)	
Comparison groups	Dose Regimen 1 (Per Protocol Set) v Dose Regimen 3 (Per Protocol Set)
Number of subjects included in analysis	142
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	1.48
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.7
upper limit	3.13

Statistical analysis title	Dose Regimen 2 vs Dose Regimen 3 (PP)
Statistical analysis description:	
Odds ratios and their 95% confidence intervals for Dose Regimen 2 vs Dose Regimen 3(PP)	
Comparison groups	Dose Regimen 3 (Per Protocol Set) v Dose Regimen 2 (Per Protocol Set)
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	1.67
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.8
upper limit	3.51

Statistical analysis title	Dose Regimen 1 vs Dose Regimen 2 (PP)
Statistical analysis description:	
Odds ratios and their 95% confidence intervals for Dose Regimen 1 vs Dose Regimen 2(PP)	
Comparison groups	Dose Regimen 2 (Per Protocol Set) v Dose Regimen 1 (Per Protocol Set)

Number of subjects included in analysis	128
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	0.89
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.39
upper limit	2

Secondary: Proportion of subjects with relief (weekly responders) determined from the subjects' daily assessments of IBS symptoms, bloating, and abdominal pain

End point title	Proportion of subjects with relief (weekly responders) determined from the subjects' daily assessments of IBS symptoms, bloating, and abdominal pain

End point description:

Relief of IBS symptoms and bloating is defined as a score of either 0 (not at all) or 1 (hardly) for at least 50% of the days in a given week or a score of 0 (not at all), 1 (hardly), or 2 (somewhat) for 100% of the days in a given week for at least 2 (consecutive or not) of the 4 weeks during a given month. Relief of abdominal pain is defined as a decrease by ≥30% from baseline in weekly mean rating of IBS-related abdominal pain.

End point type	Secondary

End point timeframe:

During treatment and follow up period

End point values	Treatment group 1: dose regimen 1	Treatment group 2: dose regimen 2	Treatment group 3: matching placebo	Dose Regimen 1 (Full Analysis Set)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	87	95	97	81
Units: Subjects				
IBS Symptoms	22	29	19	21
Bloating	22	33	16	20
Abdominal Pain	46	52	55	44

End point values	Dose Regimen 2 (Full Analysis Set)	Dose Regimen 3 (Full Analysis Set)	Dose Regimen 1 (IIT)	Dose Regimen 2 (IIT)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	88	95	87	95
Units: Subjects				
IBS Symptoms	29	19	22	29
Bloating	32	16	22	33
Abdominal Pain	51	55	46	52

End point values	Dose Regimen 3 (IIT)	Dose Regimen 1 (Per Protocol Set)	Dose Regimen 2 (Per Protocol Set)	Dose Regimen 3 (Per Protocol Set)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	97	63	65	79
Units: Subjects				
IBS Symptoms	19	17	24	16
Bloating	16	17	26	13
Abdominal Pain	55	34	40	47

Statistical analyses

Statistical analysis title	Dose Regimen 1 vs Dose Regimen 3(FAS)-IBS Symptoms
Statistical analysis description:	
Odds ratio and 95% CI: Dose Regimen 1 vs Dose Regimen 3 (FAS) - IBS Symptoms	
Comparison groups	Dose Regimen 1 (Full Analysis Set) v Dose Regimen 3 (Full Analysis Set)
Number of subjects included in analysis	176
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	1.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.69
upper limit	2.84

Statistical analysis title	Dose Regimen 2 vs Dose Regimen 3(FAS)-IBS Symptoms
Statistical analysis description:	
Odds ratio and 95% CI: Dose Regimen 2 vs Dose Regimen 3 (FAS) - IBS Symptoms	
Comparison groups	Dose Regimen 3 (Full Analysis Set) v Dose Regimen 2 (Full Analysis Set)
Number of subjects included in analysis	183
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	1.97
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.01
upper limit	3.85

Statistical analysis title	Dose Regimen 1 vs Dose Regimen 2(FAS)-IBS Symptoms
Statistical analysis description: Odds ratio and 95% CI: Dose Regimen 1 vs Dose Regimen 2 (FAS) - IBS Symptoms	
Comparison groups	Dose Regimen 2 (Full Analysis Set) v Dose Regimen 1 (Full Analysis Set)
Number of subjects included in analysis	169
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	0.71
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.37
upper limit	1.39

Statistical analysis title	Dose Regimen 1 vs Dose Regimen 3(ITT)-IBS Symptom
Statistical analysis description: Odds ratio and 95% CI: Dose Regimen 1 vs Dose Regimen 3 (ITT)-IBS Symptoms	
Comparison groups	Dose Regimen 1 (IIT) v Dose Regimen 3 (IIT)
Number of subjects included in analysis	184
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	1.44
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.71
upper limit	2.89

Statistical analysis title	Dose Regimen 2 vs Dose Regimen 3(ITT)-IBS Symptoms
Statistical analysis description: Odds ratio and 95% CI: Dose Regimen 2 vs Dose Regimen 3 (ITT) - IBS Symptoms	
Comparison groups	Dose Regimen 3 (IIT) v Dose Regimen 2 (IIT)
Number of subjects included in analysis	192
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	1.87

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.96
upper limit	3.64

Statistical analysis title	Dose Regimen 1 vs Dose Regimen 2(ITT)-IBS Symptoms
Statistical analysis description:	
Odds ratio and 95% CI: Dose Regimen 1 vs Dose Regimen 2 (ITT) - IBS Symptoms	
Comparison groups	Dose Regimen 2 (IIT) v Dose Regimen 1 (IIT)
Number of subjects included in analysis	182
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	0.77
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.4
upper limit	1.49

Statistical analysis title	Dose Regimen 1 vs Dose Regimen 3 (PP)-IBS Symptoms
Statistical analysis description:	
Odds ratio and 95% CI: Dose Regimen 1 vs Dose Regimen 3 (PP Set) - IBS Symptoms	
Comparison groups	Dose Regimen 1 (Per Protocol Set) v Dose Regimen 3 (Per Protocol Set)
Number of subjects included in analysis	142
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	1.46
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.67
upper limit	3.18

Statistical analysis title	Dose Regimen 2 vs Dose Regimen 3(PP)-IBS Symptoms
Statistical analysis description:	
Odds ratio and 95% CI: Dose Regimen 2 vs Dose Regimen 3 (PP Set) - IBS Symptoms	
Comparison groups	Dose Regimen 3 (Per Protocol Set) v Dose Regimen 2 (Per Protocol Set)

Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	2.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.09
upper limit	4.85

Statistical analysis title	Dose Regimen 1 vs Dose Regimen 2(PP)-IBS Symptoms
Statistical analysis description:	
Odds ratio and 95% CI: Dose Regimen 1 vs Dose Regimen 2 (PP Set) - IBS Symptoms	
Comparison groups	Dose Regimen 2 (Per Protocol Set) v Dose Regimen 1 (Per Protocol Set)
Number of subjects included in analysis	128
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	0.63
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.3
upper limit	1.34

Statistical analysis title	Dose Regimen 1 vs Dose Regimen 3 (FAS) - Bloating
Statistical analysis description:	
Odds ratio and 95% CI: Dose Regimen 1 vs Dose Regimen 3 (FAS) - Bloating	
Comparison groups	Dose Regimen 3 (Full Analysis Set) v Dose Regimen 1 (Full Analysis Set)
Number of subjects included in analysis	176
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	1.62
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.77
upper limit	3.38

Statistical analysis title	Dose Regimen 2 vs Dose Regimen 3 (FAS) - Bloating

Statistical analysis description:	
Odds ratio and 95% CI: Dose Regimen 2 vs Dose Regimen 3 (FAS) - Bloating	
Comparison groups	Dose Regimen 3 (Full Analysis Set) v Dose Regimen 2 (Full Analysis Set)
Number of subjects included in analysis	183
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	2.82
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.41
upper limit	5.63

Statistical analysis title	Dose Regimen 1 vs Dose Regimen 2 (FAS) - Bloating
Statistical analysis description:	
Odds ratio and 95% CI: Dose Regimen 1 vs Dose Regimen 2 (FAS) - Bloating	
Comparison groups	Dose Regimen 2 (Full Analysis Set) v Dose Regimen 1 (Full Analysis Set)
Number of subjects included in analysis	169
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	0.57
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.29
upper limit	1.12

Statistical analysis title	Dose Regimen 1 vs Dose Regimen 3 (ITT) -Bloating
Statistical analysis description:	
Odds ratio and 95% CI: Dose Regimen 1 vs Dose Regimen 3 (ITT) - Bloating	
Comparison groups	Dose Regimen 1 (IIT) v Dose Regimen 3 (IIT)
Number of subjects included in analysis	184
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	1.77
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.86
upper limit	3.66

Statistical analysis title	Dose Regimen 2 vs Dose Regimen 3 (ITT) - Bloating
Statistical analysis description: Odds ratio and 95% CI: Dose Regimen 2 vs Dose Regimen 3 (ITT) - Bloating	
Comparison groups	Dose Regimen 3 (IIT) v Dose Regimen 2 (IIT)
Number of subjects included in analysis	192
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	2.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.41
upper limit	5.55

Statistical analysis title	Dose Regimen 1 vs Dose Regimen 2 (ITT) - Bloating
Statistical analysis description: Odds ratio and 95% CI: Dose Regimen 1 vs Dose Regimen 2 (ITT) - Bloating	
Comparison groups	Dose Regimen 2 (IIT) v Dose Regimen 1 (IIT)
Number of subjects included in analysis	182
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	0.63
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.33
upper limit	1.21

Statistical analysis title	Dose Regimen 1 vs Dose Regimen 3 (PP) - Bloating
Statistical analysis description: Odds ratio and 95% CI: Dose Regimen 1 vs Dose Regimen 3 (PP Set) - Bloating	
Comparison groups	Dose Regimen 1 (Per Protocol Set) v Dose Regimen 3 (Per Protocol Set)
Number of subjects included in analysis	142
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	1.88

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.83
upper limit	4.24

Statistical analysis title	Dose Regimen 2 vs Dose Regimen 3 (PP) - Bloating
Statistical analysis description:	
Odds ratio and 95% CI: Dose Regimen 2 vs Dose Regimen 3 (PP Set) - Bloating	
Comparison groups	Dose Regimen 3 (Per Protocol Set) v Dose Regimen 2 (Per Protocol Set)
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	3.38
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.56
upper limit	7.34

Statistical analysis title	Dose Regimen 1 vs Dose Regimen 2 (PP) - Bloating
Statistical analysis description:	
Odds ratio and 95% CI: Dose Regimen 1 vs Dose Regimen 2 (PP Set) - Bloating	
Comparison groups	Dose Regimen 2 (Per Protocol Set) v Dose Regimen 1 (Per Protocol Set)
Number of subjects included in analysis	128
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	0.55
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.26
upper limit	1.17

Statistical analysis title	Dose Regimen 1 vs Dose Regimen 3 (FAS)-Abdom. Pain
Statistical analysis description:	
Odds ratio and 95% CI: Dose Regimen 1 vs Dose Regimen 3 (FAS) - Abdominal Pain	
Comparison groups	Dose Regimen 1 (Full Analysis Set) v Dose Regimen 3 (Full Analysis Set)

Number of subjects included in analysis	176
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	0.86
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.48
upper limit	1.57

Statistical analysis title	Dose Regimen 2 vs Dose Regimen 3 (FAS)-Abdom. Pain
Statistical analysis description:	
Odds ratio and 95% CI: Dose Regimen 2 vs Dose Regimen 3 (FAS) - Abdominal Pain	
Comparison groups	Dose Regimen 3 (Full Analysis Set) v Dose Regimen 2 (Full Analysis Set)
Number of subjects included in analysis	183
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.56
upper limit	1.8

Statistical analysis title	Dose Regimen 1 vs Dose Regimen 2 (FAS)-Abdom. Pain
Statistical analysis description:	
Odds ratio and 95% CI: Dose Regimen 1 vs Dose Regimen 2 (FAS) - Abdominal Pain	
Comparison groups	Dose Regimen 1 (Full Analysis Set) v Dose Regimen 2 (Full Analysis Set)
Number of subjects included in analysis	169
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	0.86
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.47
upper limit	1.59

Statistical analysis title	Dose Regimen 1 vs Dose Regimen 3 (ITT)-Abdom. Pain

Statistical analysis description: Odds ratio and 95% CI: Dose Regimen 1 vs Dose Regimen 3 (ITT) - Abdominal Pain	
Comparison groups	Dose Regimen 1 (IIT) v Dose Regimen 3 (IIT)
Number of subjects included in analysis	184
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.5
upper limit	1.63

Statistical analysis title	Dose Regimen 2 vs Dose Regimen 3 (ITT)-Abdom. Pain
Statistical analysis description: Odds ratio and 95% CI: Dose Regimen 2 vs Dose Regimen 3 (ITT) - Abdominal Pain	
Comparison groups	Dose Regimen 3 (IIT) v Dose Regimen 2 (IIT)
Number of subjects included in analysis	192
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	0.97
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.54
upper limit	1.73

Statistical analysis title	Dose Regimen 1 vs Dose Regimen 2 (ITT)-Abdom. Pain
Statistical analysis description: Odds ratio and 95% CI: Dose Regimen 1 vs Dose Regimen 2 (ITT) - Abdominal Pain	
Comparison groups	Dose Regimen 2 (IIT) v Dose Regimen 1 (IIT)
Number of subjects included in analysis	182
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	0.93
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.51
upper limit	1.69

Statistical analysis title	Dose Regimen 1 vs Dose Regimen 3 (PP)-Abdom. Pain
Statistical analysis description:	
Odds ratio and 95% CI: Dose Regimen 1 vs Dose Regimen 3 (PP Set) - Abdominal Pain	
Comparison groups	Dose Regimen 1 (Per Protocol Set) v Dose Regimen 3 (Per Protocol Set)
Number of subjects included in analysis	142
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.41
upper limit	1.56

Statistical analysis title	Dose Regimen 2 vs Dose Regimen 3 (PP)-Abdom. Pain
Statistical analysis description:	
Odds ratio and 95% CI: Dose Regimen2 vs Dose Regimen 3 (PP Set) - Abdominal Pain	
Comparison groups	Dose Regimen 2 (Per Protocol Set) v Dose Regimen 3 (Per Protocol Set)
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	1.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.56
upper limit	2.13

Statistical analysis title	Dose Regimen 1 vs Dose Regimen 2 (PP)-Abdom. Pain
Statistical analysis description:	
Odds ratio and 95% CI: Dose Regimen 1 vs Dose Regimen 2 (PP Set) - Abdominal Pain	
Comparison groups	Dose Regimen 2 (Per Protocol Set) v Dose Regimen 1 (Per Protocol Set)
Number of subjects included in analysis	128
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	0.73
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.36
upper limit	1.48

Secondary: Change from baseline to week 12 in daily IBS symptoms, bloating and abdominal pain.

End point title	Change from baseline to week 12 in daily IBS symptoms, bloating and abdominal pain.

End point description:

Values at week 12 were calculated as:
- IBS symptoms, bloating, abdominal pain, stool consistency: week 12 average of daily values,
- the sense of urgency is calculated as 100* (number of days with urgency/number of days with data).
The value at week 12 and change from baseline to week 12 in daily IBS symptoms, bloating and abdominal pain was summarised by treatment using descriptive statistics.

End point type	Secondary

End point timeframe:

From baseline to week 12

End point values	Dose Regimen 1 (Full Analysis Set)	Dose Regimen 2 (Full Analysis Set)	Dose Regimen 3 (Full Analysis Set)	Dose Regimen 1 (IIT)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	78	85	93	81
Units: Change in symptoms				
arithmetic mean (standard deviation)				
Global IBS Symptoms	-1.2 (± 1.6)	-1.3 (± 1.5)	-1.1 (± 1.4)	-1.1 (± 1.6)
IBS-Related Bloating	-0.9 (± 1.6)	-0.9 (± 1.6)	-0.8 (± 1.4)	-0.8 (± 1.5)
Abdominal Pain	-1.6 (± 2.2)	-1.9 (± 2.1)	-1.8 (± 2.1)	-1.5 (± 2.1)

End point values	Dose Regimen 2 (IIT)	Dose Regimen 3 (IIT)	Dose Regimen 1 (Per Protocol Set)	Dose Regimen 2 (Per Protocol Set)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	87	93	63	65
Units: Change in symptoms				
arithmetic mean (standard deviation)				
Global IBS Symptoms	-1.2 (± 1.5)	-1.0 (± 1.4)	-1.3 (± 1.6)	-1.2 (± 1.5)
IBS-Related Bloating	-0.9 (± 1.6)	-0.8 (± 1.4)	-0.9 (± 1.6)	-0.9 (± 1.6)
Abdominal Pain	-1.9 (± 2.1)	-1.7 (± 2.1)	-1.6 (± 2.2)	-1.8 (± 2.2)

End point values	Dose Regimen 3 (Per Protocol Set)			
Subject group type	Subject analysis set			
Number of subjects analysed	79			
Units: Change in symptoms				

arithmetic mean (standard deviation)				
Global IBS Symptoms	-1.1 (± 1.3)			
IBS-Related Bloating	-0.8 (± 1.4)			
Abdominal Pain	-1.7 (± 2.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of monthly responders during month 1, during month 1 through 2 and during month 1 through 3 determined from the subjects' daily assessments of IBS symptoms, bloating, and abdominal pain and stool consistency

End point title	Proportion of monthly responders during month 1, during month 1 through 2 and during month 1 through 3 determined from the subjects' daily assessments of IBS symptoms, bloating, and abdominal pain and stool consistency

End point description:

Relief of IBS symptoms and bloating is defined as a score of either 0 (not at all) or 1 (hardly) for at least 50% of the days in a given month or a score of 0 (not at all), 1 (hardly), or 2 (somewhat) for 100% of the days in a given month. Relief of abdominal pain is defined as a decrease by ≥30% from baseline in weekly mean rating of IBS-related abdominal pain. Relief of stool consistency is defined as a 50% or greater reduction in the number of days per month with at least one stool that has a consistency of Type 6 or 7 compared with baseline.

End point type	Secondary

End point timeframe:

During month 1, during month 1 through 2 and during month 1 through 3

End point values	Treatment group 1: dose regimen 1	Treatment group 2: dose regimen 2	Treatment group 3: matching placebo	Dose Regimen 1 (Full Analysis Set)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	87	95	97	81
Units: Subjects				
IBS Symptoms (Month 1)	10	17	8	9
IBS Symptoms (Month 1 through 2)	13	20	11	12
IBS Symptoms (Month 1 through 3)	12	19	13	12
Bloating (Month 1)	15	22	10	14
Bloating (Month 1 through 2)	13	25	14	13
Bloating (Month 1 through 3)	16	25	15	16
Abdominal Pain (Month 1)	40	55	51	38
Abdominal Pain (Month 1 through 2)	42	52	51	40
Abdominal Pain (Month 1 through 3)	41	55	52	39
Stool Consistency (Month 1)	50	61	54	48
Stool Consistency (Month 1 through 2)	53	57	52	51
Stool Consistency (Month 1 through 3)	51	56	55	50

End point values	Dose Regimen 2 (Full Analysis Set)	Dose Regimen 3 (Full Analysis Set)	Dose Regimen 1 (IIT)	Dose Regimen 2 (IIT)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	88	95	87	95
Units: Subjects				
IBS Symptoms (Month 1)	17	8	10	17
IBS Symptoms (Month 1 through 2)	19	11	13	20
IBS Symptoms (Month 1 through 3)	18	13	12	19
Bloating (Month 1)	18	10	15	18
Bloating (Month 1 through 2)	22	14	13	22
Bloating (Month 1 through 3)	24	15	16	25
Abdominal Pain (Month 1)	54	51	40	55
Abdominal Pain (Month 1 through 2)	51	51	42	52
Abdominal Pain (Month 1 through 3)	54	52	41	55
Stool Consistency (Month 1)	59	54	50	61
Stool Consistency (Month 1 through 2)	56	52	53	57
Stool Consistency (Month 1 through 3)	55	55	51	56

End point values	Dose Regimen 3 (IIT)	Dose Regimen 1 (Per Protocol Set)	Dose Regimen 2 (Per Protocol Set)	Dose Regimen 3 (Per Protocol Set)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	97	63	65	79
Units: Subjects				
IBS Symptoms (Month 1)	8	8	15	6
IBS Symptoms (Month 1 through 2)	11	10	15	10
IBS Symptoms (Month 1 through 3)	13	11	13	12
Bloating (Month 1)	10	12	16	9
Bloating (Month 1 through 2)	14	11	16	13
Bloating (Month 1 through 3)	15	14	18	13
Abdominal Pain (Month 1)	51	31	40	45
Abdominal Pain (Month 1 through 2)	51	34	38	48
Abdominal Pain (Month 1 through 3)	52	32	41	46
Stool Consistency (Month 1)	54	41	44	46
Stool Consistency (Month 1 through 2)	52	44	42	46
Stool Consistency (Month 1 through 3)	55	45	40	48

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline to each week during the 12 week follow up for daily IBS symptoms, bloating, abdominal pain, stool consistency and sense of urgency

End point title	Change from baseline to each week during the 12 week follow up for daily IBS symptoms, bloating, abdominal pain, stool consistency and sense of urgency

End point description:

Sense of urgency asked as "Have you felt or experienced a sense of urgency today? [Yes/No]" and calculated as 100x (number of days with urgency/number of days with data), and daily number of stools.

End point type	Secondary

End point timeframe:

From baseline to each week during the 12 week follow up

End point values	Treatment group 1: dose regimen 1	Treatment group 2: dose regimen 2	Treatment group 3: matching placebo	Dose Regimen 1 (Full Analysis Set)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	81	86	93	78
Units: Change in symptoms				
arithmetic mean (standard deviation)				
Global IBS Symptoms (Week 3)	-1.0 (± 1.2)	-1.2 (± 1.3)	-1.0 (± 1.3)	-1.0 (± 1.2)
Global IBS Symptoms (Week 4)	-0.9 (± 1.3)	-1.2 (± 1.4)	-0.9 (± 1.3)	-1.0 (± 1.3)
Global IBS Symptoms (Week 5)	-1.1 (± 1.2)	-1.2 (± 1.5)	-1.0 (± 1.3)	-1.2 (± 1.2)
Global IBS Symptoms (Week 6)	-1.1 (± 1.2)	-1.2 (± 1.5)	-1.0 (± 1.3)	-1.2 (± 1.2)
Global IBS Symptoms (Week 7)	-1.1 (± 1.4)	-1.3 (± 1.4)	-1.1 (± 1.2)	-1.2 (± 1.3)
Global IBS Symptoms (Week 8)	-1.1 (± 1.5)	-1.3 (± 1.5)	-1.0 (± 1.4)	-1.1 (± 1.4)
Global IBS Symptoms (Week 9)	-1.1 (± 1.5)	-1.3 (± 1.4)	-1.0 (± 1.4)	-1.1 (± 1.5)
Global IBS Symptoms (Week 10)	-1.2 (± 1.4)	-1.3 (± 1.5)	-1.1 (± 1.4)	-1.2 (± 1.4)
Global IBS Symptoms (Week 11)	-1.2 (± 1.6)	-1.3 (± 1.5)	-1.1 (± 1.4)	-1.3 (± 1.5)
Global IBS Symptoms (Week 12)	-1.1 (± 1.6)	-1.2 (± 1.5)	-1.0 (± 1.4)	-1.2 (± 1.6)
IBS-related bloating (Week 3)	-0.7 (± 1.3)	-0.9 (± 1.3)	-0.7 (± 1.3)	-0.7 (± 1.3)
IBS-related bloating (Week 4)	-0.6 (± 1.4)	-0.9 (± 1.4)	-0.9 (± 1.3)	-0.6 (± 1.4)
IBS-related bloating (Week 5)	-0.7 (± 1.4)	-0.9 (± 1.5)	-0.9 (± 1.3)	-0.8 (± 1.4)
IBS-related bloating (Week 6)	-0.8 (± 1.3)	-0.9 (± 1.5)	-1.0 (± 1.4)	-0.9 (± 1.4)
IBS-related bloating (Week 7)	-0.8 (± 1.5)	-0.9 (± 1.5)	-1.0 (± 1.4)	-0.8 (± 1.5)
IBS-related bloating (Week 8)	-0.8 (± 1.4)	-0.9 (± 1.6)	-1.0 (± 1.4)	-0.8 (± 1.4)
IBS-related bloating (Week 9)	-0.8 (± 1.4)	-1.0 (± 1.6)	-0.9 (± 1.4)	-0.9 (± 1.4)
IBS-related bloating (Week 10)	-0.9 (± 1.4)	-1.0 (± 1.6)	-0.9 (± 1.4)	-0.9 (± 1.4)
IBS-related bloating (Week 11)	-0.9 (± 1.4)	-1.0 (± 1.6)	-1.0 (± 1.4)	-0.9 (± 1.4)
IBS-related bloating (Week 12)	-0.8 (± 1.5)	-0.9 (± 1.6)	-0.8 (± 1.4)	-0.9 (± 1.6)
Abdominal Pain (Week 3)	-1.4 (± 1.7)	-1.9 (± 2.0)	-1.6 (± 1.9)	-1.4 (± 1.7)
Abdominal Pain (Week 4)	-1.3 (± 1.7)	-1.8 (± 2.1)	-1.7 (± 2.1)	-1.4 (± 1.7)
Abdominal Pain (Week 5)	-1.5 (± 1.7)	-1.9 (± 2.1)	-1.7 (± 2.1)	-1.6 (± 1.7)
Abdominal Pain (Week 6)	-1.5 (± 1.8)	-2.0 (± 2.1)	-1.6 (± 2.1)	-1.6 (± 1.8)
Abdominal Pain (Week 7)	-1.5 (± 2.0)	-2.1 (± 2.1)	-1.8 (± 2.0)	-1.6 (± 2.0)
Abdominal Pain (Week 8)	-1.5 (± 1.9)	-2.1 (± 2.2)	-1.8 (± 2.2)	-1.5 (± 1.9)
Abdominal Pain (Week 9)	-1.5 (± 2.0)	-2.1 (± 2.0)	-1.7 (± 2.3)	-1.5 (± 2.0)
Abdominal Pain (Week 10)	-1.6 (± 2.3)	-2.1 (± 2.1)	-1.9 (± 2.2)	-1.6 (± 2.2)
Abdominal Pain (Week 11)	-1.6 (± 2.1)	-2.1 (± 2.1)	-1.9 (± 2.2)	-1.6 (± 2.1)
Abdominal Pain (Week 12)	-1.5 (± 2.1)	-1.9 (± 2.1)	-1.7 (± 2.1)	-1.6 (± 2.2)
Sense of Urgency (Week 3)	-21.2 (± 33.7)	-28.9 (± 40.0)	-20.7 (± 34.9)	-21.3 (± 34.2)
Sense of Urgency (Week 4)	-18.2 (± 35.4)	-24.0 (± 40.1)	-22.4 (± 34.4)	-19.0 (± 35.8)
Sense of Urgency (Week 5)	-24.0 (± 34.6)	-31.2 (± 38.2)	-20.2 (± 34.5)	-23.9 (± 35.1)
Sense of Urgency (Week 6)	-21.2 (± 35.1)	-25.4 (± 39.3)	-21.0 (± 34.6)	-20.6 (± 35.5)

Sense of Urgency (Week 7)	-24.8 (± 35.4)	-29.5 (± 40.4)	-22.4 (± 35.2)	-24.6 (± 36.0)
Sense of Urgency (Week 8)	-24.8 (± 35.3)	-24.5 (± 39.7)	-22.1 (± 35.2)	-24.5 (± 35.9)
Sense of Urgency (Week 9)	-22.6 (± 35.0)	-28.4 (± 40.0)	-22.0 (± 35.2)	-22.7 (± 35.3)
Sense of Urgency (Week 10)	-24.2 (± 34.8)	-27.9 (± 39.1)	-22.8 (± 37.6)	-23.8 (± 35.3)
Sense of Urgency (Week 11)	-23.5 (± 36.1)	-29.9 (± 38.5)	-20.9 (± 37.6)	-23.6 (± 36.6)
Sense of Urgency (Week 12)	-25.6 (± 36.8)	-25.7 (± 40.6)	-21.9 (± 37.0)	-26.0 (± 37.4)
Stool Consistency (Week 3)	-1.1 (± 1.2)	-1.1 (± 1.2)	-1.0 (± 1.1)	-1.1 (± 1.1)
Stool Consistency (Week 4)	-1.0 (± 1.3)	-1.0 (± 1.2)	-1.0 (± 1.2)	-1.1 (± 1.3)
Stool Consistency (Week 5)	-1.1 (± 1.3)	-1.0 (± 1.0)	-0.9 (± 1.2)	-1.2 (± 1.3)
Stool Consistency (Week 6)	-1.1 (± 1.3)	-1.0 (± 1.1)	-0.9 (± 1.2)	-1.1 (± 1.3)
Stool Consistency (Week 7)	-1.0 (± 1.4)	-1.0 (± 1.2)	-0.9 (± 1.1)	-1.1 (± 1.3)
Stool Consistency (Week 8)	-1.0 (± 1.4)	-1.0 (± 1.3)	-1.1 (± 1.3)	-1.1 (± 1.4)
Stool Consistency (Week 9)	-0.9 (± 1.3)	-1.0 (± 1.3)	-1.2 (± 1.4)	-1.0 (± 1.2)
Stool Consistency (Week 10)	-1.0 (± 1.2)	-1.0 (± 1.0)	-1.2 (± 1.3)	-1.0 (± 1.2)
Stool Consistency (Week 11)	-1.0 (± 1.3)	-0.9 (± 1.0)	-1.0 (± 1.3)	-1.1 (± 1.3)
Stool Consistency (Week 12)	-1.0 (± 1.4)	-1.0 (± 1.1)	-1.0 (± 1.2)	-1.1 (± 1.4)
Bowel Movements (Week 3)	-0.5 (± 1.3)	-0.8 (± 1.3)	-0.8 (± 1.5)	-0.6 (± 1.3)
Bowel Movements (Week 4)	-0.6 (± 1.2)	-1.0 (± 1.4)	-0.7 (± 1.7)	-0.6 (± 1.2)
Bowel Movements (Week 5)	-0.6 (± 1.3)	-0.9 (± 1.3)	-0.7 (± 1.6)	-0.7 (± 1.3)
Bowel Movements (Week 6)	-0.5 (± 1.3)	-0.9 (± 1.4)	-0.7 (± 1.5)	-0.5 (± 1.4)
Bowel Movements (Week 7)	-0.5 (± 1.5)	-0.9 (± 1.4)	-0.7 (± 1.5)	-0.5 (± 1.5)
Bowel Movements (Week 8)	-0.6 (± 1.4)	-0.9 (± 1.4)	-0.8 (± 1.6)	-0.6 (± 1.4)
Bowel Movements (Week 9)	-0.4 (± 1.4)	-1.0 (± 1.3)	-0.8 (± 1.5)	-0.5 (± 1.4)
Bowel Movements (Week 10)	-0.5 (± 1.4)	-0.9 (± 1.4)	-0.8 (± 1.3)	-0.6 (± 1.4)
Bowel Movements (Week 11)	-0.6 (± 1.3)	-1.0 (± 1.4)	-0.8 (± 1.6)	0.6 (± 1.3)
Bowel Movements (Week 12)	-0.6 (± 1.4)	-0.9 (± 1.4)	-0.7 (± 1.4)	-0.7 (± 1.4)

End point values	Dose Regimen 2 (Full Analysis Set)	Dose Regimen 3 (Full Analysis Set)	Dose Regimen 1 (IIT)	Dose Regimen 2 (IIT)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	82	92	81	87
Units: Change in symptoms				
arithmetic mean (standard deviation)				
Global IBS Symptoms (Week 3)	-1.2 (± 1.3)	-1.0 (± 1.3)	-1.0 (± 1.2)	-1.2 (± 1.3)
Global IBS Symptoms (Week 4)	-1.2 (± 1.4)	-1.0 (± 1.3)	-0.9 (± 1.3)	-1.2 (± 1.4)
Global IBS Symptoms (Week 5)	-1.2 (± 1.5)	-1.0 (± 1.3)	-1.1 (± 1.2)	-1.2 (± 1.5)
Global IBS Symptoms (Week 6)	-1.3 (± 1.4)	-1.0 (± 1.3)	-1.1 (± 1.2)	-1.2 (± 1.5)
Global IBS Symptoms (Week 7)	-1.3 (± 1.4)	-1.1 (± 1.2)	-1.1 (± 1.4)	-1.3 (± 1.4)
Global IBS Symptoms (Week 8)	-1.3 (± 1.4)	-1.0 (± 1.4)	-1.1 (± 1.5)	-1.3 (± 1.5)
Global IBS Symptoms (Week 9)	-1.3 (± 1.4)	-1.0 (± 1.4)	-1.1 (± 1.5)	-1.3 (± 1.4)
Global IBS Symptoms (Week 10)	-1.3 (± 1.5)	-1.1 (± 1.4)	-1.2 (± 1.4)	-1.3 (± 1.5)
Global IBS Symptoms (Week 11)	-1.3 (± 1.5)	-1.1 (± 1.4)	-1.2 (± 1.6)	-1.3 (± 1.5)
Global IBS Symptoms (Week 12)	-1.3 (± 1.5)	-1.1 (± 1.4)	-1.1 (± 1.6)	-1.2 (± 1.5)
IBS-related bloating (Week 3)	-0.9 (± 1.4)	-0.7 (± 1.3)	-0.7 (± 1.3)	-0.9 (± 1.3)
IBS-related bloating (Week 4)	-0.9 (± 1.4)	-0.9 (± 1.3)	-0.6 (± 1.4)	-0.9 (± 1.4)
IBS-related bloating (Week 5)	-0.9 (± 1.5)	-0.9 (± 1.3)	-0.7 (± 1.4)	-0.9 (± 1.5)
IBS-related bloating (Week 6)	-1.0 (± 1.5)	-1.0 (± 1.4)	-0.8 (± 1.3)	-0.9 (± 1.5)
IBS-related bloating (Week 7)	-0.9 (± 1.5)	-1.0 (± 1.4)	-0.8 (± 1.5)	-0.9 (± 1.5)
IBS-related bloating (Week 8)	-0.9 (± 1.6)	-1.0 (± 1.4)	-0.8 (± 1.4)	-0.9 (± 1.6)

IBS-related bloating (Week 9)	-1.0 (± 1.6)	-0.9 (± 1.4)	-0.8 (± 1.4)	-1.0 (± 1.6)
IBS-related bloating (Week 10)	-1.0 (± 1.6)	-0.9 (± 1.4)	-0.9 (± 1.4)	-1.0 (± 1.6)
IBS-related bloating (Week 11)	-1.0 (± 1.6)	-1.0 (± 1.4)	-0.9 (± 1.4)	-1.0 (± 1.6)
IBS-related bloating (Week 12)	-0.9 (± 1.6)	-0.8 (± 1.4)	-0.8 (± 1.5)	-0.9 (± 1.6)
Abdominal Pain (Week 3)	-1.9 (± 1.9)	-1.6 (± 1.9)	-1.4 (± 1.7)	-1.9 (± 2.0)
Abdominal Pain (Week 4)	-1.8 (± 2.1)	-1.7 (± 2.1)	-1.3 (± 1.7)	-1.8 (± 2.1)
Abdominal Pain (Week 5)	-1.9 (± 2.0)	-1.7 (± 2.1)	-1.5 (± 1.7)	-1.9 (± 2.1)
Abdominal Pain (Week 6)	-2.1 (± 2.0)	-1.7 (± 2.1)	-1.5 (± 1.8)	-2.0 (± 2.1)
Abdominal Pain (Week 7)	-2.1 (± 2.0)	-1.8 (± 2.0)	-1.5 (± 2.0)	-2.1 (± 2.1)
Abdominal Pain (Week 8)	-2.1 (± 2.2)	-1.8 (± 2.2)	-1.5 (± 1.9)	-2.1 (± 2.2)
Abdominal Pain (Week 9)	-2.1 (± 1.9)	-1.7 (± 2.3)	-1.5 (± 2.0)	-2.1 (± 2.0)
Abdominal Pain (Week 10)	-2.1 (± 2.0)	-1.9 (± 2.2)	-1.6 (± 2.3)	-2.1 (± 2.1)
Abdominal Pain (Week 11)	-2.1 (± 2.0)	-1.9 (± 2.2)	-1.6 (± 2.1)	-2.1 (± 2.1)
Abdominal Pain (Week 12)	-1.9 (± 2.1)	-1.8 (± 2.1)	-1.5 (± 2.1)	-1.9 (± 2.1)
Sense of Urgency (Week 3)	-28.4 (± 40.0)	-20.5 (± 35.0)	-21.2 (± 33.7)	-28.9 (± 40.0)
Sense of Urgency (Week 4)	-23.8 (± 40.6)	-22.2 (± 34.5)	-18.2 (± 35.4)	-24.0 (± 40.1)
Sense of Urgency (Week 5)	-30.1 (± 37.5)	-20.1 (± 34.7)	-24.0 (± 34.6)	-31.2 (± 38.2)
Sense of Urgency (Week 6)	-24.1 (± 38.5)	-20.8 (± 34.7)	-21.2 (± 35.1)	-25.4 (± 39.3)
Sense of Urgency (Week 7)	-28.4 (± 39.8)	-22.2 (± 35.3)	-24.8 (± 35.4)	-29.5 (± 40.4)
Sense of Urgency (Week 8)	-23.7 (± 39.8)	-22.0 (± 35.4)	-24.8 (± 35.3)	-24.5 (± 39.7)
Sense of Urgency (Week 9)	-28.1 (± 40.1)	-21.9 (± 35.4)	-22.6 (± 35.0)	-28.4 (± 40.0)
Sense of Urgency (Week 10)	-27.7 (± 39.5)	-22.6 (± 37.8)	-24.2 (± 34.8)	-27.9 (± 39.1)
Sense of Urgency (Week 11)	-28.6 (± 37.5)	-20.6 (± 37.7)	-23.5 (± 36.1)	-29.9 (± 38.5)
Sense of Urgency (Week 12)	-25.1 (± 40.2)	-21.7 (± 37.1)	-25.6 (± 36.8)	-25.7 (± 40.6)
Stool Consistency (Week 3)	-1.1 (± 1.1)	-1.0 (± 1.1)	-1.1 (± 1.2)	-1.1 (± 1.2)
Stool Consistency (Week 4)	-1.0 (± 1.2)	-1.0 (± 1.2)	-1.0 (± 1.3)	-1.0 (± 1.2)
Stool Consistency (Week 5)	-1.0 (± 1.0)	-0.9 (± 1.3)	-1.1 (± 1.3)	-1.0 (± 1.0)
Stool Consistency (Week 6)	-1.0 (± 1.1)	-0.9 (± 1.2)	-1.1 (± 1.3)	-1.0 (± 1.1)
Stool Consistency (Week 7)	-1.0 (± 1.2)	-0.9 (± 1.1)	-1.0 (± 1.4)	-1.0 (± 1.2)
Stool Consistency (Week 8)	-1.0 (± 1.3)	-1.1 (± 1.3)	-1.0 (± 1.4)	-1.0 (± 1.3)
Stool Consistency (Week 9)	-1.1 (± 1.2)	-1.2 (± 1.4)	-0.9 (± 1.3)	-1.0 (± 1.3)
Stool Consistency (Week 10)	-1.0 (± 1.0)	-1.2 (± 1.3)	-1.0 (± 1.2)	-1.0 (± 1.0)
Stool Consistency (Week 11)	-1.0 (± 1.0)	-1.0 (± 1.3)	-1.0 (± 1.3)	-0.9 (± 1.0)
Stool Consistency (Week 12)	-1.0 (± 1.1)	-1.0 (± 1.2)	-1.0 (± 1.4)	-1.0 (± 1.1)
Bowel Movements (Week 3)	-0.8 (± 1.3)	-0.8 (± 1.5)	-0.5 (± 1.3)	-0.8 (± 1.3)
Bowel Movements (Week 4)	-0.9 (± 1.3)	-0.7 (± 1.7)	-0.6 (± 1.2)	-1.0 (± 1.4)
Bowel Movements (Week 5)	-0.9 (± 1.3)	-0.7 (± 1.6)	-0.6 (± 1.3)	-0.9 (± 1.3)
Bowel Movements (Week 6)	-0.9 (± 1.3)	-0.7 (± 1.5)	-0.5 (± 1.3)	-0.9 (± 1.4)
Bowel Movements (Week 7)	-0.9 (± 1.3)	-0.7 (± 1.5)	-0.5 (± 1.5)	-0.9 (± 1.4)
Bowel Movements (Week 8)	-0.9 (± 1.4)	-0.8 (± 1.6)	-0.6 (± 1.4)	-0.9 (± 1.4)
Bowel Movements (Week 9)	-1.0 (± 1.2)	-0.8 (± 1.6)	-0.4 (± 1.4)	-1.0 (± 1.3)
Bowel Movements (Week 10)	-0.9 (± 1.4)	0.8 (± 1.3)	-0.5 (± 1.4)	-0.9 (± 1.4)
Bowel Movements (Week 11)	-0.9 (± 1.4)	-0.8 (± 1.6)	-0.6 (± 1.3)	-1.0 (± 1.4)
Bowel Movements (Week 12)	-0.9 (± 1.4)	-0.7 (± 1.4)	-0.6 (± 1.4)	-0.9 (± 1.4)

End point values	Dose Regimen 3 (IIT)	Dose Regimen 1 (Per Protocol Set)	Dose Regimen 2 (Per Protocol Set)	Dose Regimen 3 (Per Protocol Set)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	94	63	63	78

Units: Change in symptoms				
arithmetic mean (standard deviation)				
Global IBS Symptoms (Week 3)	-1.0 (± 1.3)	-1.0 (± 1.2)	-1.1 (± 1.3)	-1.0 (± 1.2)
Global IBS Symptoms (Week 4)	-0.9 (± 1.3)	-1.1 (± 1.2)	-1.1 (± 1.4)	-1.0 (± 1.3)
Global IBS Symptoms (Week 5)	-1.0 (± 1.3)	-1.2 (± 1.2)	-1.2 (± 1.4)	-1.0 (± 1.4)
Global IBS Symptoms (Week 6)	-1.0 (± 1.3)	-1.2 (± 1.2)	-1.2 (± 1.4)	-1.0 (± 1.3)
Global IBS Symptoms (Week 7)	-1.1 (± 1.2)	-1.2 (± 1.3)	-1.3 (± 1.3)	-1.1 (± 1.2)
Global IBS Symptoms (Week 8)	-1.0 (± 1.4)	-1.3 (± 1.5)	-1.3 (± 1.4)	-1.1 (± 1.3)
Global IBS Symptoms (Week 9)	-1.0 (± 1.4)	-1.3 (± 1.5)	-1.2 (± 1.4)	-1.0 (± 1.4)
Global IBS Symptoms (Week 10)	-1.1 (± 1.4)	-1.3 (± 1.5)	-1.3 (± 1.5)	-1.1 (± 1.3)
Global IBS Symptoms (Week 11)	-1.1 (± 1.4)	-1.4 (± 1.5)	-1.3 (± 1.5)	-1.1 (± 1.3)
Global IBS Symptoms (Week 12)	-1.0 (± 1.4)	-1.3 (± 1.6)	-1.2 (± 1.5)	-1.1 (± 1.3)
IBS-related bloating (Week 3)	-0.7 (± 1.3)	-0.7 (± 1.3)	-0.9 (± 1.4)	-0.7 (± 1.2)
IBS-related bloating (Week 4)	-0.9 (± 1.3)	-0.7 (± 1.4)	-0.9 (± 1.5)	-0.9 (± 1.3)
IBS-related bloating (Week 5)	-0.9 (± 1.3)	-0.8 (± 1.4)	-0.9 (± 1.5)	-0.9 (± 1.3)
IBS-related bloating (Week 6)	-1.0 (± 1.4)	-0.9 (± 1.4)	-1.0 (± 1.5)	-1.0 (± 1.3)
IBS-related bloating (Week 7)	-1.0 (± 1.4)	-0.9 (± 1.5)	-0.9 (± 1.5)	-1.0 (± 1.4)
IBS-related bloating (Week 8)	-1.0 (± 1.4)	-1.0 (± 1.4)	-0.9 (± 1.7)	-1.0 (± 1.4)
IBS-related bloating (Week 9)	-0.9 (± 1.4)	-1.0 (± 1.4)	-1.0 (± 1.6)	-0.8 (± 1.4)
IBS-related bloating (Week 10)	-0.9 (± 1.4)	-1.0 (± 1.5)	-1.1 (± 1.6)	-0.9 (± 1.4)
IBS-related bloating (Week 11)	-1.0 (± 1.4)	-0.9 (± 1.5)	-1.0 (± 1.6)	-1.0 (± 1.4)
IBS-related bloating (Week 12)	-0.8 (± 1.4)	-0.9 (± 1.6)	-0.9 (± 1.6)	-0.8 (± 1.4)
Abdominal Pain (Week 3)	-1.6 (± 1.9)	-1.3 (± 1.7)	-1.8 (± 1.9)	-0.8 (± 1.9)
Abdominal Pain (Week 4)	-1.7 (± 2.1)	-1.5 (± 1.8)	-1.7 (± 2.0)	-1.9 (± 2.1)
Abdominal Pain (Week 5)	-1.7 (± 2.1)	-1.6 (± 1.7)	-1.9 (± 2.0)	-1.7 (± 2.2)
Abdominal Pain (Week 6)	-1.6 (± 2.1)	-1.6 (± 1.8)	-2.0 (± 2.1)	-1.8 (± 2.2)
Abdominal Pain (Week 7)	-1.8 (± 2.0)	-1.6 (± 1.9)	-2.0 (± 2.0)	-1.9 (± 2.0)
Abdominal Pain (Week 8)	-1.8 (± 2.2)	-1.6 (± 1.9)	-2.1 (± 2.2)	-2.0 (± 2.1)
Abdominal Pain (Week 9)	-1.7 (± 2.3)	-1.6 (± 2.1)	-2.0 (± 2.0)	-1.7 (± 2.3)
Abdominal Pain (Week 10)	-1.9 (± 2.2)	-1.6 (± 2.3)	-2.1 (± 2.1)	-1.9 (± 2.2)
Abdominal Pain (Week 11)	-1.9 (± 2.2)	-1.7 (± 2.2)	-2.0 (± 2.1)	-2.0 (± 2.3)
Abdominal Pain (Week 12)	-1.7 (± 2.1)	-1.6 (± 2.2)	-1.8 (± 2.2)	-1.7 (± 2.2)
Sense of Urgency (Week 3)	-20.7 (± 34.9)	-20.3 (± 34.6)	-30.0 (± 40.0)	-19.1 (± 33.4)
Sense of Urgency (Week 4)	-22.4 (± 34.4)	-19.4 (± 37.0)	-24.2 (± 42.0)	-21.5 (± 33.7)
Sense of Urgency (Week 5)	-20.2 (± 34.5)	-23.9 (± 35.8)	-27.9 (± 36.9)	-19.4 (± 34.7)
Sense of Urgency (Week 6)	-21.0 (± 34.6)	-20.5 (± 36.8)	-23.6 (± 37.3)	-20.1 (± 34.4)
Sense of Urgency (Week 7)	-22.4 (± 35.2)	-24.5 (± 35.9)	-26.5 (± 39.1)	-21.4 (± 33.8)
Sense of Urgency (Week 8)	-22.1 (± 35.2)	-25.7 (± 37.0)	-20.3 (± 38.4)	-22.7 (± 34.6)
Sense of Urgency (Week 9)	-22.0 (± 35.2)	-23.2 (± 35.9)	-25.2 (± 37.8)	-19.9 (± 34.0)
Sense of Urgency (Week 10)	-22.8 (± 37.6)	-25.4 (± 36.6)	-24.0 (± 39.6)	-20.3 (± 36.0)
Sense of Urgency (Week 11)	-20.9 (± 37.6)	-25.0 (± 37.4)	-25.7 (± 36.7)	-20.4 (± 37.1)
Sense of Urgency (Week 12)	-21.9 (± 37.0)	-28.3 (± 37.8)	-20.6 (± 39.5)	-19.8 (± 35.8)
Stool Consistency (Week 3)	-1.0 (± 1.1)	-1.2 (± 1.1)	-1.0 (± 1.1)	-1.0 (± 1.1)
Stool Consistency (Week 4)	-1.0 (± 1.2)	-1.1 (± 1.3)	-1.0 (± 1.3)	-1.0 (± 1.2)
Stool Consistency (Week 5)	-0.9 (± 1.2)	-1.2 (± 1.3)	-0.9 (± 1.0)	-0.9 (± 1.3)
Stool Consistency (Week 6)	-0.9 (± 1.2)	-1.2 (± 1.3)	-1.0 (± 1.2)	-0.9 (± 1.2)
Stool Consistency (Week 7)	-0.9 (± 1.1)	-1.0 (± 1.3)	-1.0 (± 1.1)	-0.9 (± 1.1)
Stool Consistency (Week 8)	-1.1 (± 1.3)	-1.1 (± 1.3)	-1.0 (± 1.2)	-1.1 (± 1.3)
Stool Consistency (Week 9)	-1.2 (± 1.4)	-1.0 (± 1.3)	-1.0 (± 1.1)	-1.1 (± 1.2)
Stool Consistency (Week 10)	-1.2 (± 1.3)	-1.0 (± 1.2)	-1.0 (± 1.0)	-1.1 (± 1.2)
Stool Consistency (Week 11)	-1.0 (± 1.3)	-1.1 (± 1.4)	-1.0 (± 1.0)	-0.9 (± 1.2)
Stool Consistency (Week 12)	-1.0 (± 1.2)	-1.1 (± 1.5)	-1.0 (± 1.1)	-1.0 (± 1.2)

Bowel Movements (Week 3)	-0.8 (± 1.5)	-0.6 (± 1.3)	-0.7 (± 1.1)	-0.8 (± 1.5)
Bowel Movements (Week 4)	-0.7 (± 1.7)	-0.6 (± 1.2)	-0.8 (± 1.2)	-0.8 (± 1.7)
Bowel Movements (Week 5)	-0.7 (± 1.6)	-0.7 (± 1.2)	-0.8 (± 1.2)	-0.8 (± 1.7)
Bowel Movements (Week 6)	-0.7 (± 1.5)	-0.6 (± 1.4)	-0.9 (± 1.2)	-0.8 (± 1.5)
Bowel Movements (Week 7)	-0.7 (± 1.5)	-0.6 (± 1.6)	-0.8 (± 1.1)	-0.8 (± 1.5)
Bowel Movements (Week 8)	-0.8 (± 1.6)	-0.7 (± 1.4)	-0.8 (± 1.3)	-1.0 (± 1.5)
Bowel Movements (Week 9)	-0.8 (± 1.5)	-0.6 (± 1.4)	-0.9 (± 1.0)	-0.8 (± 1.5)
Bowel Movements (Week 10)	-0.8 (± 1.3)	-0.6 (± 1.4)	-0.8 (± 1.2)	-0.8 (± 1.4)
Bowel Movements (Week 11)	-0.8 (± 1.6)	-0.6 (± 1.3)	-0.9 (± 1.2)	-0.9 (± 1.5)
Bowel Movements (Week 12)	-0.7 (± 1.4)	-0.7 (± 1.5)	-0.8 (± 1.2)	-0.7 (± 1.4)

Statistical analyses

No statistical analyses for this end point

Secondary: Number of weeks (consecutive or not) subjects achieved adequate relief of bloating during the follow up period.

End point title	Number of weeks (consecutive or not) subjects achieved adequate relief of bloating during the follow up period.

End point description:

Relief of IBS bloating is defined as a score of either 0 (not at all) or 1 (hardly) for at least 50% of the days in a given week or a score of 0 (not at all), 1 (hardly), or 2 (somewhat) for 100% of the days in a given week for at least 2 (consecutive or not) of the 4 weeks during a given month.

End point type	Secondary

End point timeframe:

Weeks 3 through 12

End point values	Treatment group 1: dose regimen 1	Treatment group 2: dose regimen 2	Treatment group 3: matching placebo	Dose Regimen 1 (Full Analysis Set)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	87	95	97	81
Units: Weeks				
median (full range (min-max))	2.0 (0 to 10)	4.0 (0 to 10)	3.0 (0 to 10)	2.0 (0 to 10)

End point values	Dose Regimen 2 (Full Analysis Set)	Dose Regimen 3 (Full Analysis Set)	Dose Regimen 1 (IIT)	Dose Regimen 2 (IIT)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	88	95	87	95
Units: Weeks				
median (full range (min-max))	4.0 (0 to 10)	3.0 (0 to 10)	2.0 (0 to 10)	4.0 (0 to 10)

End point values	Dose Regimen 3 (IIT)	Dose Regimen 1 (Per Protocol Set)	Dose Regimen 2 (Per Protocol Set)	Dose Regimen 3 (Per Protocol Set)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	97	63	65	79
Units: Weeks				
median (full range (min-max))	3.0 (0 to 10)	2.0 (0 to 10)	4.0 (0 to 10)	3.0 (0 to 10)

Statistical analyses

Statistical analysis title	Dose Regimen 1 vs Dose Regimen 3 (FAS)
Statistical analysis description:	
Comparison between treatment groups of the number of weeks subjects achieved adequate relief of bloating during follow-up phase (Full analysis set): Dose Regimen 1 vs Dose Regimen 3	
Comparison groups	Dose Regimen 1 (Full Analysis Set) v Dose Regimen 3 (Full Analysis Set)
Number of subjects included in analysis	176
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7582
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Wilcoxon Rank-Sum Statistics
Point estimate	6279.5
Confidence interval	
level	95 %
sides	1-sided
lower limit	90

Statistical analysis title	Dose Regimen 2 vs Dose Regimen 3 (FAS)
Statistical analysis description:	
Comparison between treatment groups of the number of weeks subjects achieved adequate relief of bloating during follow-up phase (Full analysis set): Dose Regimen 2 vs Dose Regimen 3	
Comparison groups	Dose Regimen 3 (Full Analysis Set) v Dose Regimen 2 (Full Analysis Set)
Number of subjects included in analysis	183
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2362
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Wilcoxon Rank-Sum Statistics
Point estimate	7561
Confidence interval	
level	95 %
sides	1-sided
lower limit	90

Statistical analysis title	Dose Regimen 1 vs Dose Regimen 2(FAS)
Statistical analysis description:	
Comparison between treatment groups of the number of weeks subjects achieved adequate relief of bloating during follow-up phase (Full analysis set): Dose Regimen 1 vs Dose Regimen 2	
Comparison groups	Dose Regimen 2 (Full Analysis Set) v Dose Regimen 1 (Full Analysis Set)
Number of subjects included in analysis	169
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3324
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Wilcoxon Rank-Sum Statistics
Point estimate	5686.5
Confidence interval	
level	95 %
sides	1-sided
lower limit	90

Statistical analysis title	Dose Regimen 1 vs Dose Regimen 3(IIT)
Statistical analysis description:	
Comparison between treatment groups of the number of weeks subjects achieved adequate relief of bloating during follow-up phase (ITT): Dose Regimen 1 vs Dose Regimen 3	
Comparison groups	Dose Regimen 1 (IIT) v Dose Regimen 3 (IIT)
Number of subjects included in analysis	184
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8789
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Wilcoxon Rank-Sum Statistics
Point estimate	6638.5
Confidence interval	
level	95 %
sides	1-sided
lower limit	90

Statistical analysis title	Dose Regimen 2 vs Dose Regimen 3(IIT)
Statistical analysis description:	
Comparison between treatment groups of the number of weeks subjects achieved adequate relief of bloating during follow-up phase (ITT): Dose Regimen 2 vs Dose Regimen 3	
Comparison groups	Dose Regimen 3 (IIT) v Dose Regimen 2 (IIT)
Number of subjects included in analysis	192
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2666
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Wilcoxon Rank-Sum Statistics
Point estimate	7981.5

Confidence interval	
level	95 %
sides	1-sided
lower limit	90

Statistical analysis title	Dose Regimen 1 vs Dose Regimen 2(IIT)
Statistical analysis description:	
Comparison between treatment groups of the number of weeks subjects achieved adequate relief of bloating during follow-up phase (ITT): Dose Regimen 1 vs Dose Regimen 2	
Comparison groups	Dose Regimen 2 (IIT) v Dose Regimen 1 (IIT)
Number of subjects included in analysis	182
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2915
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Wilcoxon Rank-Sum Statistics
Point estimate	6117.5
Confidence interval	
level	95 %
sides	1-sided
lower limit	90

Statistical analysis title	Dose Regimen 1 vs Dose Regimen 3(PP Set)
Statistical analysis description:	
Comparison between treatment groups of the number of weeks subjects achieved adequate relief of bloating during follow-up phase (PP Set): Dose Regimen 1 vs Dose Regimen 3	
Comparison groups	Dose Regimen 1 (Per Protocol Set) v Dose Regimen 3 (Per Protocol Set)
Number of subjects included in analysis	142
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.685
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Wilcoxon Rank-Sum Statistics
Point estimate	4434.5
Confidence interval	
level	95 %
sides	1-sided
lower limit	90

Statistical analysis title	Dose Regimen 2 vs Dose Regimen 3(PP Set)
Statistical analysis description:	
Comparison between treatment groups of the number of weeks subjects achieved adequate relief of bloating during follow-up phase (PP Set): Dose Regimen 2 vs Dose Regimen 3	
Comparison groups	Dose Regimen 3 (Per Protocol Set) v Dose Regimen 2 (Per

	Protocol Set)
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4077
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Wilcoxon Rank-Sum Statistics
Point estimate	4847
Confidence interval	
level	95 %
sides	1-sided
lower limit	90

Statistical analysis title	Dose Regimen 1 vs Dose Regimen 2(PP Set)
Statistical analysis description:	
Comparison between treatment groups of the number of weeks subjects achieved adequate relief of bloating during follow-up phase (PP Set): Dose Regimen 1 vs Dose Regimen 2	
Comparison groups	Dose Regimen 2 (Per Protocol Set) v Dose Regimen 1 (Per Protocol Set)
Number of subjects included in analysis	128
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5554
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Wilcoxon Rank-Sum Statistics
Point estimate	3846.5
Confidence interval	
level	95 %
sides	1-sided
lower limit	90

Secondary: Number of weeks (consecutive or not) subjects achieved adequate relief of IBS symptoms during the follow up period.

End point title	Number of weeks (consecutive or not) subjects achieved adequate relief of IBS symptoms during the follow up period.
End point description:	

End point type	Secondary
End point timeframe:	
Weeks 3 through 12	

End point values	Treatment group 1: dose regimen 1	Treatment group 2: dose regimen 2	Treatment group 3: matching placebo	Dose Regimen 1 (Full Analysis Set)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	87	95	97	81
Units: Weeks				
median (full range (min-max))	3.0 (0 to 10)	4.5 (0 to 10)	3.0 (0 to 10)	3.0 (0 to 10)

End point values	Dose Regimen 2 (Full Analysis Set)	Dose Regimen 3 (Full Analysis Set)	Dose Regimen 1 (IIT)	Dose Regimen 2 (IIT)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	88	95	87	95
Units: Weeks				
median (full range (min-max))	5.0 (0 to 10)	3.0 (0 to 10)	3.0 (0 to 10)	4.5 (0 to 10)

End point values	Dose Regimen 3 (IIT)	Dose Regimen 1 (Per Protocol Set)	Dose Regimen 2 (Per Protocol Set)	Dose Regimen 3 (Per Protocol Set)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	97	63	65	79
Units: Weeks				
median (full range (min-max))	3.0 (0 to 10)	3.0 (0 to 10)	4.0 (0 to 10)	3.0 (0 to 10)

Statistical analyses

Statistical analysis title	Dose Regimen 1 vs Dose Regimen 3 (FAS)

Statistical analysis description:

Comparison between treatment groups of the number of weeks subjects achieved adequate relief of IBS symptoms during follow-up phase (Full analysis set): Dose Regimen 1 vs Dose Regimen 3

Comparison groups	Dose Regimen 1 (Full Analysis Set) v Dose Regimen 3 (Full Analysis Set)
Number of subjects included in analysis	176
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8797
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Wilcoxon Rank-Sum Statistics
Point estimate	6233
Confidence interval	
level	95 %
sides	1-sided
lower limit	90

Statistical analysis title	Dose Regimen 2 vs Dose Regimen 3 (FAS)
Statistical analysis description:	
Comparison between treatment groups of the number of weeks subjects achieved adequate relief of IBS symptoms during follow-up phase (Full analysis set): Dose Regimen 2 vs Dose Regimen 3	
Comparison groups	Dose Regimen 3 (Full Analysis Set) v Dose Regimen 2 (Full Analysis Set)
Number of subjects included in analysis	183
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1965
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Wilcoxon Rank-Sum Statistics
Point estimate	7596.5
Confidence interval	
level	95 %
sides	1-sided
lower limit	90

Statistical analysis title	Dose Regimen 1 vs Dose Regimen 2 (FAS)
Statistical analysis description:	
Comparison between treatment groups of the number of weeks subjects achieved adequate relief of IBS symptoms during follow-up phase (Full analysis set): Dose Regimen 1 vs Dose Regimen 2	
Comparison groups	Dose Regimen 2 (Full Analysis Set) v Dose Regimen 1 (Full Analysis Set)
Number of subjects included in analysis	169
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2353
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Wilcoxon Rank-Sum Statistics
Point estimate	5624
Confidence interval	
level	95 %
sides	1-sided
lower limit	90

Statistical analysis title	Dose Regimen 1 vs Dose Regimen 3 (IIT)
Statistical analysis description:	
Comparison between treatment groups of the number of weeks subjects achieved adequate relief of IBS symptoms during follow-up phase (IIT): Dose Regimen 1 vs Dose Regimen 3	
Comparison groups	Dose Regimen 1 (IIT) v Dose Regimen 3 (IIT)
Number of subjects included in analysis	184
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9059
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Wilcoxon Rank-Sum Statistics
Point estimate	6628

Confidence interval	
level	95 %
sides	1-sided
lower limit	90

Statistical analysis title	Dose Regimen 2 vs Dose Regimen 3 (IIT)
Statistical analysis description:	
Comparison between treatment groups of the number of weeks subjects achieved adequate relief of IBS symptoms during follow-up phase (IIT): Dose Regimen 2 vs Dose Regimen 3	
Comparison groups	Dose Regimen 3 (IIT) v Dose Regimen 2 (IIT)
Number of subjects included in analysis	192
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2708
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Wilcoxon Rank-Sum Statistics
Point estimate	7979
Confidence interval	
level	95 %
sides	1-sided
lower limit	90

Statistical analysis title	Dose Regimen 1 vs Dose Regimen 2 (IIT)
Statistical analysis description:	
Comparison between treatment groups of the number of weeks subjects achieved adequate relief of IBS symptoms during follow-up phase (IIT): Dose Regimen 1 vs Dose Regimen 2	
Comparison groups	Dose Regimen 2 (IIT) v Dose Regimen 1 (IIT)
Number of subjects included in analysis	182
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2849
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Wilcoxon Rank-Sum Statistics
Point estimate	6112.5
Confidence interval	
level	95 %
sides	1-sided
lower limit	90

Statistical analysis title	Dose Regimen 1 vs Dose Regimen 3 (PP Set)
Statistical analysis description:	
Comparison between treatment groups of the number of weeks subjects achieved adequate relief of IBS symptoms during follow-up phase (PP Set): Dose Regimen 1 vs Dose Regimen 3	
Comparison groups	Dose Regimen 1 (Per Protocol Set) v Dose Regimen 3 (Per Protocol Set)

Number of subjects included in analysis	142
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5842
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Wilcoxon Rank-Sum Statistics
Point estimate	6233
Confidence interval	
level	95 %
sides	1-sided
lower limit	90
Variability estimate	Standard deviation

Statistical analysis title	Dose Regimen 2 vs Dose Regimen 3 (PP Set)
Statistical analysis description:	
Comparison between treatment groups of the number of weeks subjects achieved adequate relief of IBS symptoms during follow-up phase (PP Set): Dose Regimen 2 vs Dose Regimen 3	
Comparison groups	Dose Regimen 3 (Per Protocol Set) v Dose Regimen 2 (Per Protocol Set)
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4254
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Wilcoxon Rank-Sum Statistics
Point estimate	4840
Confidence interval	
level	95 %
sides	1-sided
lower limit	90

Statistical analysis title	Dose Regimen 1 vs Dose Regimen 2 (PP Set)
Statistical analysis description:	
Comparison between treatment groups of the number of weeks subjects achieved adequate relief of IBS symptoms during follow-up phase (PP Set): Dose Regimen 1 vs Dose Regimen 2	
Comparison groups	Dose Regimen 2 (Per Protocol Set) v Dose Regimen 1 (Per Protocol Set)
Number of subjects included in analysis	128
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8042
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Wilcoxon Rank-Sum Statistics
Point estimate	3916.5

Confidence interval	
level	95 %
sides	1-sided
lower limit	90

Secondary: Proportion of subjects with adequate relief of bloating during at least 2 weeks (consecutive or not) per month (“monthly response”)

End point title	Proportion of subjects with adequate relief of bloating during at least 2 weeks (consecutive or not) per month (“monthly response”)

End point description:

Adequate relief of bloating is defined as a response of "yes" to the following question, which was asked weekly (every 7 days):
"In regard to your symptom of bloating, as compared to the way you felt before you started study medication, have you, in the past 7 days, had adequate relief of your IBS symptom of bloating? [Yes/No]."

End point type	Secondary

End point timeframe:

Month 1 through Month 3

End point values	Treatment group 1: dose regimen 1	Treatment group 2: dose regimen 2	Treatment group 3: matching placebo	Dose Regimen 1 (Full Analysis Set)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	87	95	97	81
Units: Subjects				
Month 1	42	53	34	41
Month 1 through 2	34	49	36	34
Month 1 through 3	28	40	33	28

End point values	Dose Regimen 2 (Full Analysis Set)	Dose Regimen 3 (Full Analysis Set)	Dose Regimen 1 (IIT)	Dose Regimen 2 (IIT)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	88	95	87	95
Units: Subjects				
Month 1	50	34	42	53
Month 1 through 2	48	36	34	49
Month 1 through 3	39	33	28	40

End point values	Dose Regimen 3 (IIT)	Dose Regimen 1 (Per Protocol Set)	Dose Regimen 2 (Per Protocol Set)	Dose Regimen 3 (Per Protocol Set)

Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	97	63	65	79
Units: Subjects				
Month 1	34	34	38	28
Month 1 through 2	36	27	37	32
Month 1 through 3	33	23	29	30

Statistical analyses

Statistical analysis title	Dose regimen 1 vs. Dose Regimen 3 (FAS) -Month 1-2
Statistical analysis description:	
Odds Ratio and 95% CI of DOSE REGIMEN 1 vs. DOSE REGIMEN 3 (FAS) - Month 1 through 2	
Comparison groups	Dose Regimen 1 (Full Analysis Set) v Dose Regimen 3 (Full Analysis Set)
Number of subjects included in analysis	176
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	1.29
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.68
upper limit	2.43

Statistical analysis title	Dose regimen 2 vs. Dose Regimen 3 (FAS) -Month 1-2
Statistical analysis description:	
Odds Ratio and 95% CI of DOSE REGIMEN 2 vs. DOSE REGIMEN 3 (FAS) - Month 1 through 2	
Comparison groups	Dose Regimen 3 (Full Analysis Set) v Dose Regimen 2 (Full Analysis Set)
Number of subjects included in analysis	183
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	1.98
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.07
upper limit	3.67

Statistical analysis title	Dose regimen 1 vs. Dose Regimen 2 (FAS)-Month 1-2
Statistical analysis description:	
Odds Ratio and 95% CI of DOSE REGIMEN 1 vs. DOSE REGIMEN 2 (FAS) - Month 1 through 2	
Comparison groups	Dose Regimen 2 (Full Analysis Set) v Dose Regimen 1 (Full

	Analysis Set)
Number of subjects included in analysis	169
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	0.65
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.34
upper limit	1.24

Statistical analysis title	Dose regimen 1 vs. Dose Regimen 3 (ITT)-Month 1-2
Statistical analysis description:	
Odds Ratio and 95% CI of DOSE REGIMEN 1 vs. DOSE REGIMEN 3 (ITT) - Month 1 through 2	
Comparison groups	Dose Regimen 1 (IIT) v Dose Regimen 3 (IIT)
Number of subjects included in analysis	184
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	1.21
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.65
upper limit	2.27

Statistical analysis title	Dose regimen 2 vs. Dose Regimen 3 (ITT)-Month 1-2
Statistical analysis description:	
Odds Ratio and 95% CI of DOSE REGIMEN 2 vs. DOSE REGIMEN 3 (ITT) - Month 1 through 2	
Comparison groups	Dose Regimen 3 (IIT) v Dose Regimen 2 (IIT)
Number of subjects included in analysis	192
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	2
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.09
upper limit	3.69

Statistical analysis title	Dose regimen 1 vs. Dose Regimen 2 (ITT)-Month 1-2

Statistical analysis description:	
Odds Ratio and 95% CI of DOSE REGIMEN 1 vs. DOSE REGIMEN 2 (ITT) - Month 1 through 2	
Comparison groups	Dose Regimen 2 (IIT) v Dose Regimen 1 (IIT)
Number of subjects included in analysis	182
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.32
upper limit	1.14

Statistical analysis title	Dose regimen 1 vs. Dose Regimen 3 (PPS)-Month 1-2
Statistical analysis description:	
Odds Ratio and 95% CI of DOSE REGIMEN 1 vs. DOSE REGIMEN 3 (PP Set) - Month 1 through 2	
Comparison groups	Dose Regimen 1 (Per Protocol Set) v Dose Regimen 3 (Per Protocol Set)
Number of subjects included in analysis	142
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	1.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.59
upper limit	2.33

Statistical analysis title	Dose regimen 2 vs. Dose Regimen 3 (PPS)-Month 1-2
Statistical analysis description:	
Odds Ratio and 95% CI of DOSE REGIMEN 2 vs. DOSE REGIMEN 3 (PP Set) - Month 1 through 2	
Comparison groups	Dose Regimen 3 (Per Protocol Set) v Dose Regimen 2 (Per Protocol Set)
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	1.78
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.91
upper limit	3.47

Statistical analysis title	Dose regimen 1 vs. Dose Regimen 2 (PPS)-Month 1-2
Statistical analysis description:	
Odds Ratio and 95% CI of DOSE REGIMEN 1 vs. DOSE REGIMEN 2 (PP Set) - Month 1 through 2	
Comparison groups	Dose Regimen 2 (Per Protocol Set) v Dose Regimen 1 (Per Protocol Set)
Number of subjects included in analysis	128
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	0.66
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.32
upper limit	1.34

Statistical analysis title	Dose regimen 1 vs. Dose Regimen 3 (FAS)- Month 1
Statistical analysis description:	
Odds Ratio and 95% CI of DOSE REGIMEN 1 vs. DOSE REGIMEN 3 (FAS) - Month 1	
Comparison groups	Dose Regimen 1 (Full Analysis Set) v Dose Regimen 3 (Full Analysis Set)
Number of subjects included in analysis	176
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	1.98
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.05
upper limit	3.75

Statistical analysis title	Dose regimen 2 vs. Dose Regimen 3 (FAS) - Month 1
Statistical analysis description:	
Odds Ratio and 95% CI of DOSE REGIMEN 2 vs. DOSE REGIMEN 3 (FAS) - Month 1	
Comparison groups	Dose Regimen 3 (Full Analysis Set) v Dose Regimen 2 (Full Analysis Set)
Number of subjects included in analysis	183
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	2.59

Confidence interval	
level	95 %
sides	2-sided
lower limit	1.38
upper limit	4.86

Statistical analysis title	Dose regimen 1 vs. Dose Regimen 2 (FAS) - Month 1
Statistical analysis description:	
Odds Ratio and 95% CI of DOSE REGIMEN 1 vs. DOSE REGIMEN 2 (FAS) - Month 1	
Comparison groups	Dose Regimen 2 (Full Analysis Set) v Dose Regimen 1 (Full Analysis Set)
Number of subjects included in analysis	169
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	0.77
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.4
upper limit	1.47

Statistical analysis title	Dose regimen 1 vs. Dose Regimen 3 (ITT) - Month 1
Statistical analysis description:	
Odds Ratio and 95% CI of DOSE REGIMEN 1 vs. DOSE REGIMEN 3 (ITT) - Month 1	
Comparison groups	Dose Regimen 1 (IIT) v Dose Regimen 3 (IIT)
Number of subjects included in analysis	184
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	1.95
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.04
upper limit	3.65

Statistical analysis title	Dose regimen 2 vs. Dose Regimen 3 (ITT) - Month 1
Statistical analysis description:	
Odds Ratio and 95% CI of DOSE REGIMEN 2 vs. DOSE REGIMEN 3 (ITT) - Month 1	
Comparison groups	Dose Regimen 3 (IIT) v Dose Regimen 2 (IIT)

Number of subjects included in analysis	192
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	2.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.45
upper limit	5.03

Statistical analysis title	Dose regimen 1 vs. Dose Regimen 2 (ITT) - Month 1
Statistical analysis description:	
Odds Ratio and 95% CI of DOSE REGIMEN 1 vs. DOSE REGIMEN 2 (ITT) - Month 1	
Comparison groups	Dose Regimen 2 (IIT) v Dose Regimen 1 (IIT)
Number of subjects included in analysis	182
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	0.72
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.38
upper limit	1.36

Statistical analysis title	Dose regimen 1 vs. Dose Regimen 3(PP) - Month 1
Statistical analysis description:	
Odds Ratio and 95% CI of DOSE REGIMEN 1 vs. DOSE REGIMEN 3 (PP Set) - Month 1	
Comparison groups	Dose Regimen 1 (Per Protocol Set) v Dose Regimen 3 (Per Protocol Set)
Number of subjects included in analysis	142
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	2.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.05
upper limit	4.21

Statistical analysis title	Dose regimen 2 vs. Dose Regimen 3 (PP) - Month 1

Statistical analysis description:	
Odds Ratio and 95% CI of DOSE REGIMEN 2 vs. DOSE REGIMEN 3 (PP Set) - Month 1	
Comparison groups	Dose Regimen 3 (Per Protocol Set) v Dose Regimen 2 (Per Protocol Set)
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	2.54
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.27
upper limit	5.1

Statistical analysis title	Dose regimen 1 vs. Dose Regimen 2 (PP) - Month 1
Statistical analysis description:	
Odds Ratio and 95% CI of DOSE REGIMEN 1 vs. DOSE REGIMEN 2 (PP Set) - Month 1	
Comparison groups	Dose Regimen 2 (Per Protocol Set) v Dose Regimen 1 (Per Protocol Set)
Number of subjects included in analysis	128
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	0.83
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.4
upper limit	1.7

Statistical analysis title	Dose regimen 1 vs. Dose Regimen 3 (FAS) -Month 1-3
Statistical analysis description:	
Odds Ratio and 95% CI of DOSE REGIMEN 1 vs. DOSE REGIMEN 3 (FAS) - Month 1 through 3	
Comparison groups	Dose Regimen 1 (Full Analysis Set) v Dose Regimen 3 (Full Analysis Set)
Number of subjects included in analysis	176
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	1.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.53
upper limit	1.96

Statistical analysis title	Dose regimen 2 vs. Dose Regimen 3 (FAS)- Month 1-3
Statistical analysis description:	
Odds Ratio and 95% CI of DOSE REGIMEN 2 vs. DOSE REGIMEN 3 (FAS) - Month 1 through 3	
Comparison groups	Dose Regimen 3 (Full Analysis Set) v Dose Regimen 2 (Full Analysis Set)
Number of subjects included in analysis	183
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	1.58
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.84
upper limit	2.97

Statistical analysis title	Dose regimen 1 vs. Dose Regimen 2 (FAS) -Month 1-3
Statistical analysis description:	
Odds Ratio and 95% CI of DOSE REGIMEN 1 vs. DOSE REGIMEN 2 (FAS) - Month 1 through 3	
Comparison groups	Dose Regimen 2 (Full Analysis Set) v Dose Regimen 1 (Full Analysis Set)
Number of subjects included in analysis	169
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	0.65
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.33
upper limit	1.25

Statistical analysis title	Dose regimen 1 vs. Dose Regimen 3 (ITT)-Month 1-3
Statistical analysis description:	
Odds Ratio and 95% CI of DOSE REGIMEN 1 vs. DOSE REGIMEN 3 (ITT) - Month 1 through 3	
Comparison groups	Dose Regimen 1 (IIT) v Dose Regimen 3 (IIT)
Number of subjects included in analysis	184
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	0.97

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.51
upper limit	1.85

Statistical analysis title	Dose regimen 2 vs. Dose Regimen 3 (ITT)- Month 1-3
Statistical analysis description:	
Odds Ratio and 95% CI of DOSE REGIMEN 2 vs. DOSE REGIMEN 3 (ITT) - Month 1 through 3	
Comparison groups	Dose Regimen 3 (IIT) v Dose Regimen 2 (IIT)
Number of subjects included in analysis	192
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	1.61
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.86
upper limit	3.01

Statistical analysis title	Dose regimen 1 vs. Dose Regimen 2 (ITT)- Month 1-3
Statistical analysis description:	
Odds Ratio and 95% CI of DOSE REGIMEN 1 vs. DOSE REGIMEN 2 (ITT) - Month 1 through 3	
Comparison groups	Dose Regimen 2 (IIT) v Dose Regimen 1 (IIT)
Number of subjects included in analysis	182
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.31
upper limit	1.16

Statistical analysis title	Dose regimen 1 vs. Dose Regimen 3 (PP)- Month 1-3
Statistical analysis description:	
Odds Ratio and 95% CI of DOSE REGIMEN 1 vs. DOSE REGIMEN 3 (PP Set) - Month 1 through 3	
Comparison groups	Dose Regimen 1 (Per Protocol Set) v Dose Regimen 3 (Per Protocol Set)

Number of subjects included in analysis	142
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	0.95
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.47
upper limit	1.92

Statistical analysis title	Dose regimen 2 vs. Dose Regimen 3 (PP)- Month 1-3
Statistical analysis description:	
Odds Ratio and 95% CI of DOSE REGIMEN 2 vs. DOSE REGIMEN 3 (PP Set) - Month 1 through 3	
Comparison groups	Dose Regimen 3 (Per Protocol Set) v Dose Regimen 2 (Per Protocol Set)
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	1.35
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.68
upper limit	2.71

Statistical analysis title	Dose regimen 1 vs. Dose Regimen 2 (PP)-Month 1-3
Statistical analysis description:	
Odds Ratio and 95% CI of DOSE REGIMEN 1 vs. DOSE REGIMEN 2 (PP Set) - Month 1 through 3	
Comparison groups	Dose Regimen 2 (Per Protocol Set) v Dose Regimen 1 (Per Protocol Set)
Number of subjects included in analysis	128
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.34
upper limit	1.46

Secondary: Change from baseline in quality of life inquired as IBS-QoL

End point title	Change from baseline in quality of life inquired as IBS-QoL

End point description:

End point type	Secondary

End point timeframe:

At week 4, 8 and 12

End point values	Treatment group 1: dose regimen 1	Treatment group 2: dose regimen 2	Treatment group 3: matching placebo	Dose Regimen 1 (Full Analysis Set)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	68[7]	72[8]	80[9]	65[10]
Units: Change from Baseline in QoL scores				
arithmetic mean (standard deviation)				
Day 29	12.9 (± 15.5)	16.2 (± 15.5)	11.5 (± 14.6)	12.4 (± 15.7)
Day 57	13.4 (± 16.7)	16.1 (± 17.9)	12.0 (± 17.8)	12.8 (± 16.9)
Day 85	14.2 (± 20.0)	18.0 (± 18.3)	13.7 (± 15.8)	14.2 (± 20.3)

Notes:

[7] - Day 29: 68
Day 57: 68
Day 85: 55
[8] - Day 29: 72
Day 57: 73
Day 85: 62
[9] - Day 29: 80
Day 57: 78
Day 85: 68
[10] - Day 29: 65
Day 57: 65
Day 85: 53

End point values	Dose Regimen 2 (Full Analysis Set)	Dose Regimen 3 (Full Analysis Set)	Dose Regimen 1 (IIT)	Dose Regimen 2 (IIT)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	71[11]	80[12]	68[13]	72[14]
Units: Change from Baseline in QoL scores				
arithmetic mean (standard deviation)				
Day 29	16.0 (± 15.4)	11.5 (± 14.6)	12.9 (± 15.5)	16.2 (± 15.5)
Day 57	15.8 (± 17.9)	12.0 (± 17.8)	13.4 (± 16.7)	16.1 (± 17.9)
Day 85	18.0 (± 18.3)	13.7 (± 15.8)	14.2 (± 20.0)	18.0 (± 18.3)

Notes:

[11] - Day 29: 71
Day 57: 72
Day 85: 62
[12] - Day 29: 80
Day 57: 78
Day 85: 68
[13] - Day 29: 68
Day 57: 68
Day 85: 55
[14] - Day 29: 72
Day 57: 73

Day 85: 62

End point values	Dose Regimen 3 (IIT)	Dose Regimen 1 (Per Protocol Set)	Dose Regimen 2 (Per Protocol Set)	Dose Regimen 3 (Per Protocol Set)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	80[15]	54[16]	57[17]	70[18]
Units: Change from Baseline in QoL scores				
arithmetic mean (standard deviation)				
Day 29	11.5 (± 14.6)	13.6 (± 16.0)	15.3 (± 14.8)	12.4 (± 14.0)
Day 57	12.0 (± 17.8)	12.2 (± 15.6)	13.7 (± 15.5)	12.7 (± 18.0)
Day 85	13.7 (± 15.8)	14.5 (± 19.8)	15.6 (± 15.8)	13.9 (± 15.6)

Notes:

[15] - Day 29: 80
Day 57: 78
Day 85: 68
[16] - Day 29: 54
Day 57: 56
Day 85: 43
[17] - Day 29: 57
Day 57: 57
Day 85: 49
[18] - Day 29: 70
Day 57: 68
Day 85: 61

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Plasma levels of IL1β, IL6, IL8, IL12p70 and TNFα and those of the antibodies against vinculin and Campylobacter CdtB protein

End point title	Plasma levels of IL1β, IL6, IL8, IL12p70 and TNFα and those of the antibodies against vinculin and Campylobacter CdtB protein

End point description:

Immunomodulatory effect sub-study: To preliminarily investigate the potential anti-inflammatory and immunomodulatory effects of rifamycin SV in patients suffering from diarrhoea-predominant irritable bowel syndrome.
Unreported values are BLQL. BLQL below the LQL of 0.03 pg/mL for IL1β, 0.1 pg/mL for IL6, IL8 and IL12p70 and
0.3 pg/mL for TNFα.

End point type	Other pre-specified

End point timeframe:

Between Day -21 and Day 85

End point values	Treatment group 1: dose regimen 1	Treatment group 2: dose regimen 2	Treatment group 3: matching placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	13	20	15	
Units: Plasma concentration				
arithmetic mean (standard deviation)				

IL1B (pg/mL) - Day -21/-15	13 (± 0.023)	20 (± 0.008)	15 (± 0.100)	
IL1B (pg/mL) - Day 15	12 (± 0.043)	19 (± 0.019)	14 (± 0.020)	
IL1B (pg/mL) - Day 85	11 (± 0.036)	20 (± 0.016)	13 (± 0.020)	
IL6 (pg/mL) - Day -21/-15	13 (± 0.195)	20 (± 0.090)	15 (± 0.046)	
IL6 (pg/mL) - Day 15	12 (± 0.166)	19 (± 0.340)	14 (± 0.000)	
IL6 (pg/mL) - Day 85	11 (± 0.000)	20 (± 0.118)	13 (± 0.000)	
IL8 (pg/mL) - Day -21/-15	13 (± 0.152)	20 (± 0.133)	15 (± 0.140)	
IL8 (pg/mL) - Day 15	12 (± 0.201)	19 (± 0.174)	14 (± 0.264)	
IL8 (pg/mL) - Day 85	11 (± 0.187)	20 (± 0.235)	13 (± 0.152)	
IL12p70 (pg/mL) - Day -21/-15	13 (± 0.279)	20 (± 0.054)	15 (± 0.000)	
IL12p70 (pg/mL) - Day 15	12 (± 0.347)	19 (± 0.144)	14 (± 0.051)	
IL12p70 (pg/mL) - Day 85	11 (± 0.105)	20 (± 0.193)	13 (± 0.028)	
TNFa (pg/mL) - Day -21/-15	13 (± 0.368)	20 (± 0.104)	15 (± 0.113)	
TNFa (pg/mL) - Day 15	12 (± 0.298)	19 (± 0.352)	14 (± 0.131)	
TNFa (pg/mL) - Day 85	11 (± 0.379)	20 (± 0.384)	13 (± 0.182)	
Antibodies against vinculin (%) - Day -21/-15	13 (± 0.000)	20 (± 0.000)	15 (± 0.000)	
Antibodies against vinculin (%) - Day 15	12 (± 0.287)	19 (± 0.190)	14 (± 0.099)	
Antibodies against vinculin (%) - Day 85	11 (± 0.164)	20 (± 0.216)	13 (± 1.132)	
Antibodies against vinculin(OD at 450nm) -D-21/-15	0.631 (± 0.510)	0.617 (± 0.578)	0.342 (± 0.211)	
Antibodies against Campylobacter CdtB(%) -D-21/-15	13 (± 0.000)	20 (± 0.000)	15 (± 0.000)	
Antibodies against Campylobacter CdtB(%) -Day 15	12 (± 0.104)	19 (± 0.117)	14 (± 0.086)	
Antibodies against Campylobacter CdtB(%) -Day 85	11 (± 0.124)	20 (± 0.139)	13 (± 0.210)	
Campylobacter CdtB Antibodies(OD at450nm)-D-21/-15	13 (± 0.658)	20 (± 0.939)	15 (± 0.688)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: 09Nov2017 - 10Sep2020	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	20.0
Reporting groups	
Reporting group title	Dose Regimen 1
Reporting group description: Rifamycin SV 600 mg TD	
Reporting group title	Dose Regimen 2
Reporting group description: Rifamycin SV 600 mg BD	
Reporting group title	Dose Regimen 3
Reporting group description: Placebo	

Serious adverse events	Dose Regimen 1	Dose Regimen 2	Dose Regimen 3
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 85 (2.35%)	1 / 94 (1.06%)	1 / 96 (1.04%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Cardiac disorders			
Arteriosclerosis coronary artery	Additional description: Worsening of calcified atherosclerosis of the coronary		
subjects affected / exposed	0 / 85 (0.00%)	0 / 94 (0.00%)	1 / 96 (1.04%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Nephritis			
subjects affected / exposed	1 / 85 (1.18%)	0 / 94 (0.00%)	0 / 96 (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
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	1 / 85 (1.18%)	0 / 94 (0.00%)	0 / 96 (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

Erysipelas	Additional description: Erysipelas in the face left side		
subjects affected / exposed	0 / 85 (0.00%)	1 / 94 (1.06%)	0 / 96 (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

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

Non-serious adverse events	Dose Regimen 1	Dose Regimen 2	Dose Regimen 3
Total subjects affected by non-serious adverse events			
subjects affected / exposed	15 / 85 (17.65%)	45 / 94 (47.87%)	9 / 96 (9.38%)
Vascular disorders			
Flushing			
subjects affected / exposed	1 / 85 (1.18%)	0 / 94 (0.00%)	0 / 96 (0.00%)
occurrences (all)	1	0	0
Vaginal haemorrhage			
subjects affected / exposed	0 / 85 (0.00%)	0 / 94 (0.00%)	1 / 96 (1.04%)
occurrences (all)	0	0	1
Surgical and medical procedures			
Strabismus correction			
subjects affected / exposed	0 / 85 (0.00%)	1 / 94 (1.06%)	0 / 96 (0.00%)
occurrences (all)	0	1	0
Tooth extraction			
subjects affected / exposed	0 / 85 (0.00%)	0 / 94 (0.00%)	1 / 96 (1.04%)
occurrences (all)	0	0	1
Pregnancy, puerperium and perinatal conditions			
Pregnancy			
subjects affected / exposed	0 / 85 (0.00%)	1 / 94 (1.06%)	1 / 96 (1.04%)
occurrences (all)	0	1	1
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	2 / 85 (2.35%)	4 / 94 (4.26%)	2 / 96 (2.08%)
occurrences (all)	2	5	2
Pyrexia			
subjects affected / exposed	2 / 85 (2.35%)	3 / 94 (3.19%)	1 / 96 (1.04%)
occurrences (all)	2	3	1
General symptom			

subjects affected / exposed	0 / 85 (0.00%)	2 / 94 (2.13%)	1 / 96 (1.04%)
occurrences (all)	0	3	1
Asthenia			
subjects affected / exposed	0 / 85 (0.00%)	1 / 94 (1.06%)	0 / 96 (0.00%)
occurrences (all)	0	1	0
Discomfort			
subjects affected / exposed	0 / 85 (0.00%)	1 / 94 (1.06%)	0 / 96 (0.00%)
occurrences (all)	0	1	0
Malaise			
subjects affected / exposed	1 / 85 (1.18%)	0 / 94 (0.00%)	0 / 96 (0.00%)
occurrences (all)	1	0	0
Night sweats			
subjects affected / exposed	1 / 85 (1.18%)	0 / 94 (0.00%)	0 / 96 (0.00%)
occurrences (all)	1	0	0
Spinal pain			
subjects affected / exposed	0 / 85 (0.00%)	1 / 94 (1.06%)	0 / 96 (0.00%)
occurrences (all)	0	1	0
Temperature regulation disorder			
subjects affected / exposed	0 / 85 (0.00%)	1 / 94 (1.06%)	0 / 96 (0.00%)
occurrences (all)	0	2	0
Vaccination site pain			
subjects affected / exposed	1 / 85 (1.18%)	0 / 94 (0.00%)	0 / 96 (0.00%)
occurrences (all)	1	0	0
Withdrawal syndrome			
subjects affected / exposed	1 / 85 (1.18%)	0 / 94 (0.00%)	0 / 96 (0.00%)
occurrences (all)	1	0	0
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	1 / 85 (1.18%)	0 / 94 (0.00%)	3 / 96 (3.13%)
occurrences (all)	1	0	3
Allergy to arthropod bite			
subjects affected / exposed	0 / 85 (0.00%)	1 / 94 (1.06%)	0 / 96 (0.00%)
occurrences (all)	0	1	0
Rhinitis allergic			
subjects affected / exposed	0 / 85 (0.00%)	0 / 94 (0.00%)	1 / 96 (1.04%)
occurrences (all)	0	0	1

Reproductive system and breast disorders			
Dysmenorrhoea			
subjects affected / exposed	2 / 85 (2.35%)	1 / 94 (1.06%)	2 / 96 (2.08%)
occurrences (all)	2	1	3
Metrorrhagia			
subjects affected / exposed	2 / 85 (2.35%)	2 / 94 (2.13%)	0 / 96 (0.00%)
occurrences (all)	2	2	0
Hot flush			
subjects affected / exposed	0 / 85 (0.00%)	1 / 94 (1.06%)	0 / 96 (0.00%)
occurrences (all)	0	1	0
Menorrhagia			
subjects affected / exposed	0 / 85 (0.00%)	1 / 94 (1.06%)	0 / 96 (0.00%)
occurrences (all)	0	2	0
Ovulation pain			
subjects affected / exposed	0 / 85 (0.00%)	0 / 94 (0.00%)	1 / 96 (1.04%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	1 / 85 (1.18%)	3 / 94 (3.19%)	4 / 96 (4.17%)
occurrences (all)	1	3	4
Cough			
subjects affected / exposed	0 / 85 (0.00%)	2 / 94 (2.13%)	3 / 96 (3.13%)
occurrences (all)	0	2	3
Bronchiolitis			
subjects affected / exposed	0 / 85 (0.00%)	1 / 94 (1.06%)	0 / 96 (0.00%)
occurrences (all)	0	1	0
Chronic obstructive pulmonary disease			
subjects affected / exposed	1 / 85 (1.18%)	0 / 94 (0.00%)	0 / 96 (0.00%)
occurrences (all)	1	0	0
Dysphonia			
subjects affected / exposed	1 / 85 (1.18%)	0 / 94 (0.00%)	0 / 96 (0.00%)
occurrences (all)	1	0	0
Dyspnoea			
subjects affected / exposed	0 / 85 (0.00%)	1 / 94 (1.06%)	0 / 96 (0.00%)
occurrences (all)	0	1	0

Epistaxis			
subjects affected / exposed	1 / 85 (1.18%)	0 / 94 (0.00%)	0 / 96 (0.00%)
occurrences (all)	1	0	0
Nasal discomfort			
subjects affected / exposed	0 / 85 (0.00%)	1 / 94 (1.06%)	0 / 96 (0.00%)
occurrences (all)	0	1	0
Respiratory tract infection			
subjects affected / exposed	1 / 85 (1.18%)	0 / 94 (0.00%)	0 / 96 (0.00%)
occurrences (all)	1	0	0
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 85 (0.00%)	3 / 94 (3.19%)	0 / 96 (0.00%)
occurrences (all)	0	3	0
Insomnia			
subjects affected / exposed	1 / 85 (1.18%)	0 / 94 (0.00%)	1 / 96 (1.04%)
occurrences (all)	1	0	1
Anxiety			
subjects affected / exposed	0 / 85 (0.00%)	1 / 94 (1.06%)	0 / 96 (0.00%)
occurrences (all)	0	1	0
Emotional distress			
subjects affected / exposed	0 / 85 (0.00%)	1 / 94 (1.06%)	0 / 96 (0.00%)
occurrences (all)	0	1	0
Nervousness			
subjects affected / exposed	0 / 85 (0.00%)	0 / 94 (0.00%)	1 / 96 (1.04%)
occurrences (all)	0	0	1
Sleep disorder			
subjects affected / exposed	0 / 85 (0.00%)	0 / 94 (0.00%)	1 / 96 (1.04%)
occurrences (all)	0	0	1
Somnolence			
subjects affected / exposed	0 / 85 (0.00%)	1 / 94 (1.06%)	0 / 96 (0.00%)
occurrences (all)	0	1	0
Investigations			
Viral test negative			
subjects affected / exposed	1 / 85 (1.18%)	1 / 94 (1.06%)	0 / 96 (0.00%)
occurrences (all)	1	1	0
Hepatic enzyme increased			

subjects affected / exposed	1 / 85 (1.18%)	0 / 94 (0.00%)	0 / 96 (0.00%)
occurrences (all)	1	0	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 85 (0.00%)	0 / 94 (0.00%)	1 / 96 (1.04%)
occurrences (all)	0	0	1
Injury, poisoning and procedural complications			
Barotitis media			
subjects affected / exposed	1 / 85 (1.18%)	0 / 94 (0.00%)	0 / 96 (0.00%)
occurrences (all)	2	0	0
Burn of internal organs			
subjects affected / exposed	0 / 85 (0.00%)	0 / 94 (0.00%)	1 / 96 (1.04%)
occurrences (all)	0	0	1
Contusion			
subjects affected / exposed	0 / 85 (0.00%)	1 / 94 (1.06%)	0 / 96 (0.00%)
occurrences (all)	0	1	0
Congenital, familial and genetic disorders			
Congenital mitral valve incompetence			
subjects affected / exposed	1 / 85 (1.18%)	0 / 94 (0.00%)	0 / 96 (0.00%)
occurrences (all)	1	0	0
Cardiac disorders			
Arteriosclerosis coronary artery			
subjects affected / exposed	0 / 85 (0.00%)	0 / 94 (0.00%)	1 / 96 (1.04%)
occurrences (all)	0	0	1
Bradycardia			
subjects affected / exposed	1 / 85 (1.18%)	0 / 94 (0.00%)	0 / 96 (0.00%)
occurrences (all)	1	0	0
Palpitations			
subjects affected / exposed	0 / 85 (0.00%)	1 / 94 (1.06%)	0 / 96 (0.00%)
occurrences (all)	0	2	0
Tricuspid valve incompetence			
subjects affected / exposed	1 / 85 (1.18%)	0 / 94 (0.00%)	0 / 96 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			

Headache			
subjects affected / exposed	15 / 85 (17.65%)	19 / 94 (20.21%)	6 / 96 (6.25%)
occurrences (all)	21	31	9
Dizziness			
subjects affected / exposed	1 / 85 (1.18%)	2 / 94 (2.13%)	3 / 96 (3.13%)
occurrences (all)	1	3	3
Migraine			
subjects affected / exposed	2 / 85 (2.35%)	1 / 94 (1.06%)	1 / 96 (1.04%)
occurrences (all)	3	1	2
Tension headache			
subjects affected / exposed	0 / 85 (0.00%)	2 / 94 (2.13%)	2 / 96 (2.08%)
occurrences (all)	0	5	6
Cluster headache			
subjects affected / exposed	0 / 85 (0.00%)	2 / 94 (2.13%)	0 / 96 (0.00%)
occurrences (all)	0	3	0
Insomnia			
subjects affected / exposed	0 / 85 (0.00%)	2 / 94 (2.13%)	0 / 96 (0.00%)
occurrences (all)	0	2	0
Syncope			
subjects affected / exposed	2 / 85 (2.35%)	1 / 94 (1.06%)	0 / 96 (0.00%)
occurrences (all)	2	1	0
Migraine with aura			
subjects affected / exposed	0 / 85 (0.00%)	1 / 94 (1.06%)	0 / 96 (0.00%)
occurrences (all)	0	2	0
Somnambulism			
subjects affected / exposed	0 / 85 (0.00%)	0 / 94 (0.00%)	1 / 96 (1.04%)
occurrences (all)	0	0	1
Paraesthesia			
subjects affected / exposed	0 / 85 (0.00%)	0 / 94 (0.00%)	1 / 96 (1.04%)
occurrences (all)	0	0	1
Ear and labyrinth disorders			
Conductive deafness			
subjects affected / exposed	0 / 85 (0.00%)	1 / 94 (1.06%)	0 / 96 (0.00%)
occurrences (all)	0	1	0
Otitis media			

subjects affected / exposed	0 / 85 (0.00%)	1 / 94 (1.06%)	0 / 96 (0.00%)
occurrences (all)	0	1	0
Tinnitus			
subjects affected / exposed	0 / 85 (0.00%)	1 / 94 (1.06%)	0 / 96 (0.00%)
occurrences (all)	0	1	0
Eye disorders			
Cataract			
subjects affected / exposed	0 / 85 (0.00%)	1 / 94 (1.06%)	0 / 96 (0.00%)
occurrences (all)	0	1	0
Conjunctival haemorrhage			
subjects affected / exposed	0 / 85 (0.00%)	1 / 94 (1.06%)	0 / 96 (0.00%)
occurrences (all)	0	1	0
Conjunctivitis			
subjects affected / exposed	1 / 85 (1.18%)	0 / 94 (0.00%)	1 / 96 (1.04%)
occurrences (all)	1	0	1
Dry age-related macular degeneration			
subjects affected / exposed	0 / 85 (0.00%)	1 / 94 (1.06%)	0 / 96 (0.00%)
occurrences (all)	0	1	0
Eye pain			
subjects affected / exposed	0 / 85 (0.00%)	0 / 94 (0.00%)	1 / 96 (1.04%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	7 / 85 (8.24%)	9 / 94 (9.57%)	8 / 96 (8.33%)
occurrences (all)	9	13	10
Nausea			
subjects affected / exposed	4 / 85 (4.71%)	7 / 94 (7.45%)	4 / 96 (4.17%)
occurrences (all)	4	10	5
Abdominal distension			
subjects affected / exposed	5 / 85 (5.88%)	4 / 94 (4.26%)	3 / 96 (3.13%)
occurrences (all)	7	4	3
Abdominal pain upper			
subjects affected / exposed	2 / 85 (2.35%)	5 / 94 (5.32%)	3 / 96 (3.13%)
occurrences (all)	6	7	3
Diarrhoea			

subjects affected / exposed	4 / 85 (4.71%)	5 / 94 (5.32%)	1 / 96 (1.04%)
occurrences (all)	4	6	1
Irritable bowel syndrome			
subjects affected / exposed	3 / 85 (3.53%)	4 / 94 (4.26%)	2 / 96 (2.08%)
occurrences (all)	3	4	2
Gastrointestinal pain			
subjects affected / exposed	4 / 85 (4.71%)	1 / 94 (1.06%)	3 / 96 (3.13%)
occurrences (all)	5	1	4
Dyspepsia			
subjects affected / exposed	2 / 85 (2.35%)	4 / 94 (4.26%)	1 / 96 (1.04%)
occurrences (all)	2	4	1
Flatulence			
subjects affected / exposed	3 / 85 (3.53%)	1 / 94 (1.06%)	1 / 96 (1.04%)
occurrences (all)	5	1	1
Abdominal discomfort			
subjects affected / exposed	2 / 85 (2.35%)	2 / 94 (2.13%)	1 / 96 (1.04%)
occurrences (all)	2	2	1
Abnormal faeces			
subjects affected / exposed	2 / 85 (2.35%)	2 / 94 (2.13%)	0 / 96 (0.00%)
occurrences (all)	2	2	0
Gastroenteritis			
subjects affected / exposed	2 / 85 (2.35%)	1 / 94 (1.06%)	1 / 96 (1.04%)
occurrences (all)	2	1	1
Gastrooesophageal reflux disease			
subjects affected / exposed	2 / 85 (2.35%)	1 / 94 (1.06%)	1 / 96 (1.04%)
occurrences (all)	2	1	1
Haemorrhoids			
subjects affected / exposed	1 / 85 (1.18%)	0 / 94 (0.00%)	2 / 96 (2.08%)
occurrences (all)	1	0	2
Dry mouth			
subjects affected / exposed	1 / 85 (1.18%)	0 / 94 (0.00%)	1 / 96 (1.04%)
occurrences (all)	1	0	1
Frequent bowel movements			
subjects affected / exposed	1 / 85 (1.18%)	0 / 94 (0.00%)	1 / 96 (1.04%)
occurrences (all)	3	0	1
Gastroenteritis viral			

subjects affected / exposed	1 / 85 (1.18%)	0 / 94 (0.00%)	1 / 96 (1.04%)
occurrences (all)	2	0	1
Abdominal pain lower			
subjects affected / exposed	0 / 85 (0.00%)	1 / 94 (1.06%)	0 / 96 (0.00%)
occurrences (all)	0	1	0
Anal fissure			
subjects affected / exposed	2 / 85 (2.35%)	0 / 94 (0.00%)	0 / 96 (0.00%)
occurrences (all)	2	0	0
Anal haemorrhage			
subjects affected / exposed	1 / 85 (1.18%)	0 / 94 (0.00%)	0 / 96 (0.00%)
occurrences (all)	1	0	0
Aphthous ulcer			
subjects affected / exposed	0 / 85 (0.00%)	0 / 94 (0.00%)	1 / 96 (1.04%)
occurrences (all)	0	0	1
Change of bowel habit			
subjects affected / exposed	0 / 85 (0.00%)	1 / 94 (1.06%)	0 / 96 (0.00%)
occurrences (all)	0	1	0
Chapped lips			
subjects affected / exposed	0 / 85 (0.00%)	0 / 94 (0.00%)	1 / 96 (1.04%)
occurrences (all)	0	0	1
Colitis			
subjects affected / exposed	0 / 85 (0.00%)	0 / 94 (0.00%)	1 / 96 (1.04%)
occurrences (all)	0	0	1
Constipation			
subjects affected / exposed	0 / 85 (0.00%)	0 / 94 (0.00%)	1 / 96 (1.04%)
occurrences (all)	0	0	3
Dental pulp disorder			
subjects affected / exposed	0 / 85 (0.00%)	1 / 94 (1.06%)	0 / 96 (0.00%)
occurrences (all)	0	1	0
Epigastric discomfort			
subjects affected / exposed	1 / 85 (1.18%)	0 / 94 (0.00%)	0 / 96 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal hypermotility			
subjects affected / exposed	0 / 85 (0.00%)	0 / 94 (0.00%)	1 / 96 (1.04%)
occurrences (all)	0	0	1
Gastrointestinal somatic symptom			

disorder			
subjects affected / exposed	1 / 85 (1.18%)	0 / 94 (0.00%)	0 / 96 (0.00%)
occurrences (all)	2	0	0
Gingivitis			
subjects affected / exposed	0 / 85 (0.00%)	1 / 94 (1.06%)	1 / 96 (1.04%)
occurrences (all)	0	1	1
Haemorrhoidal haemorrhage			
subjects affected / exposed	0 / 85 (0.00%)	0 / 94 (0.00%)	1 / 96 (1.04%)
occurrences (all)	0	0	1
Hyperchlorhydria			
subjects affected / exposed	0 / 85 (0.00%)	1 / 94 (1.06%)	0 / 96 (0.00%)
occurrences (all)	0	1	0
Large intestine polyp			
subjects affected / exposed	1 / 85 (1.18%)	0 / 94 (0.00%)	0 / 96 (0.00%)
occurrences (all)	1	0	0
Loose tooth			
subjects affected / exposed	1 / 85 (1.18%)	0 / 94 (0.00%)	0 / 96 (0.00%)
occurrences (all)	1	0	0
Pulpitis dental			
subjects affected / exposed	0 / 85 (0.00%)	0 / 94 (0.00%)	1 / 96 (1.04%)
occurrences (all)	0	0	1
Vomiting			
subjects affected / exposed	0 / 85 (0.00%)	1 / 94 (1.06%)	0 / 96 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders			
Laceration			
subjects affected / exposed	0 / 85 (0.00%)	1 / 94 (1.06%)	1 / 96 (1.04%)
occurrences (all)	0	1	1
Pruritus generalised			
subjects affected / exposed	1 / 85 (1.18%)	1 / 94 (1.06%)	0 / 96 (0.00%)
occurrences (all)	1	1	0
Angular cheilitis			
subjects affected / exposed	1 / 85 (1.18%)	0 / 94 (0.00%)	0 / 96 (0.00%)
occurrences (all)	1	0	0
Erythema			

subjects affected / exposed	0 / 85 (0.00%)	0 / 94 (0.00%)	1 / 96 (1.04%)
occurrences (all)	0	0	1
Pruritus			
subjects affected / exposed	1 / 85 (1.18%)	0 / 94 (0.00%)	0 / 96 (0.00%)
occurrences (all)	1	0	0
Psoriasis			
subjects affected / exposed	1 / 85 (1.18%)	0 / 94 (0.00%)	0 / 96 (0.00%)
occurrences (all)	1	0	0
Rash			
subjects affected / exposed	0 / 85 (0.00%)	0 / 94 (0.00%)	2 / 96 (2.08%)
occurrences (all)	0	0	3
Skin lesion			
subjects affected / exposed	1 / 85 (1.18%)	0 / 94 (0.00%)	0 / 96 (0.00%)
occurrences (all)	1	0	0
Sunburn			
subjects affected / exposed	1 / 85 (1.18%)	0 / 94 (0.00%)	0 / 96 (0.00%)
occurrences (all)	1	0	0
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	1 / 85 (1.18%)	1 / 94 (1.06%)	0 / 96 (0.00%)
occurrences (all)	2	1	0
Cystitis			
subjects affected / exposed	0 / 85 (0.00%)	1 / 94 (1.06%)	0 / 96 (0.00%)
occurrences (all)	0	2	0
Dysuria			
subjects affected / exposed	1 / 85 (1.18%)	0 / 94 (0.00%)	0 / 96 (0.00%)
occurrences (all)	1	0	0
Leukocyturia			
subjects affected / exposed	0 / 85 (0.00%)	2 / 94 (2.13%)	0 / 96 (0.00%)
occurrences (all)	0	3	0
Micturition disorder			
subjects affected / exposed	0 / 85 (0.00%)	1 / 94 (1.06%)	0 / 96 (0.00%)
occurrences (all)	0	1	0
Micturition urgency			
subjects affected / exposed	0 / 85 (0.00%)	0 / 94 (0.00%)	1 / 96 (1.04%)
occurrences (all)	0	0	1

Nephritis			
subjects affected / exposed	1 / 85 (1.18%)	0 / 94 (0.00%)	0 / 96 (0.00%)
occurrences (all)	1	0	0
Polyuria			
subjects affected / exposed	0 / 85 (0.00%)	0 / 94 (0.00%)	1 / 96 (1.04%)
occurrences (all)	0	0	1
Renal colic			
subjects affected / exposed	1 / 85 (1.18%)	0 / 94 (0.00%)	0 / 96 (0.00%)
occurrences (all)	2	0	0
Urinary tract infection			
subjects affected / exposed	0 / 85 (0.00%)	1 / 94 (1.06%)	0 / 96 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 85 (0.00%)	6 / 94 (6.38%)	1 / 96 (1.04%)
occurrences (all)	0	7	2
Neck pain			
subjects affected / exposed	2 / 85 (2.35%)	1 / 94 (1.06%)	3 / 96 (3.13%)
occurrences (all)	2	1	4
Arthralgia			
subjects affected / exposed	0 / 85 (0.00%)	1 / 94 (1.06%)	3 / 96 (3.13%)
occurrences (all)	0	1	3
Muscle contracture			
subjects affected / exposed	1 / 85 (1.18%)	0 / 94 (0.00%)	2 / 96 (2.08%)
occurrences (all)	1	0	2
Muscle spasms			
subjects affected / exposed	1 / 85 (1.18%)	0 / 94 (0.00%)	1 / 96 (1.04%)
occurrences (all)	1	0	1
Ligament injury			
subjects affected / exposed	1 / 85 (1.18%)	0 / 94 (0.00%)	0 / 96 (0.00%)
occurrences (all)	1	0	0
Myalgia			
subjects affected / exposed	0 / 85 (0.00%)	0 / 94 (0.00%)	1 / 96 (1.04%)
occurrences (all)	0	0	1
Neuromuscular pain			

subjects affected / exposed	0 / 85 (0.00%)	0 / 94 (0.00%)	1 / 96 (1.04%)
occurrences (all)	0	0	1
Osteoarthritis			
subjects affected / exposed	1 / 85 (1.18%)	0 / 94 (0.00%)	0 / 96 (0.00%)
occurrences (all)	1	0	0
Pain in extremity			
subjects affected / exposed	0 / 85 (0.00%)	1 / 94 (1.06%)	0 / 96 (0.00%)
occurrences (all)	0	1	0
Tenosynovitis			
subjects affected / exposed	0 / 85 (0.00%)	1 / 94 (1.06%)	0 / 96 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal pain			
subjects affected / exposed	1 / 85 (1.18%)	0 / 94 (0.00%)	0 / 96 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
Influenza			
subjects affected / exposed	10 / 85 (11.76%)	2 / 94 (2.13%)	7 / 96 (7.29%)
occurrences (all)	11	2	8
Gastroenteritis			
subjects affected / exposed	4 / 85 (4.71%)	2 / 94 (2.13%)	4 / 96 (4.17%)
occurrences (all)	4	3	4
Vulvovaginal candidiasis			
subjects affected / exposed	2 / 85 (2.35%)	2 / 94 (2.13%)	2 / 96 (2.08%)
occurrences (all)	2	3	4
Urinary tract infection			
subjects affected / exposed	5 / 85 (5.88%)	1 / 94 (1.06%)	0 / 96 (0.00%)
occurrences (all)	5	1	0
Viral infection			
subjects affected / exposed	0 / 85 (0.00%)	3 / 94 (3.19%)	1 / 96 (1.04%)
occurrences (all)	0	3	1
Cystitis			
subjects affected / exposed	1 / 85 (1.18%)	1 / 94 (1.06%)	2 / 96 (2.08%)
occurrences (all)	1	1	2
Acute sinusitis			
subjects affected / exposed	0 / 85 (0.00%)	1 / 94 (1.06%)	1 / 96 (1.04%)
occurrences (all)	0	1	1

Oral herpes			
subjects affected / exposed	0 / 85 (0.00%)	2 / 94 (2.13%)	0 / 96 (0.00%)
occurrences (all)	0	2	0
Pharyngitis			
subjects affected / exposed	2 / 85 (2.35%)	0 / 94 (0.00%)	0 / 96 (0.00%)
occurrences (all)	2	0	0
Rhinitis			
subjects affected / exposed	1 / 85 (1.18%)	1 / 94 (1.06%)	0 / 96 (0.00%)
occurrences (all)	1	1	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 85 (0.00%)	1 / 94 (1.06%)	1 / 96 (1.04%)
occurrences (all)	0	1	2
Candida infection			
subjects affected / exposed	0 / 85 (0.00%)	0 / 94 (0.00%)	1 / 96 (1.04%)
occurrences (all)	0	0	1
Ear infection			
subjects affected / exposed	0 / 85 (0.00%)	1 / 94 (1.06%)	0 / 96 (0.00%)
occurrences (all)	0	1	0
Erysipelas			
subjects affected / exposed	0 / 85 (0.00%)	1 / 94 (1.06%)	0 / 96 (0.00%)
occurrences (all)	0	1	0
Groin abscess			
subjects affected / exposed	0 / 85 (0.00%)	1 / 94 (1.06%)	0 / 96 (0.00%)
occurrences (all)	0	1	0
H1N1 influenza			
subjects affected / exposed	0 / 85 (0.00%)	0 / 94 (0.00%)	1 / 96 (1.04%)
occurrences (all)	0	0	1
Infection			
subjects affected / exposed	0 / 85 (0.00%)	0 / 94 (0.00%)	1 / 96 (1.04%)
occurrences (all)	0	0	1
Laryngitis			
subjects affected / exposed	0 / 85 (0.00%)	0 / 94 (0.00%)	1 / 96 (1.04%)
occurrences (all)	0	0	1
Sinusitis			
subjects affected / exposed	0 / 85 (0.00%)	0 / 94 (0.00%)	2 / 96 (2.08%)
occurrences (all)	0	0	2

Tonsillitis			
subjects affected / exposed	0 / 85 (0.00%)	1 / 94 (1.06%)	0 / 96 (0.00%)
occurrences (all)	0	1	0
Vaginal infection			
subjects affected / exposed	0 / 85 (0.00%)	1 / 94 (1.06%)	0 / 96 (0.00%)
occurrences (all)	0	1	0
Viral pharyngitis			
subjects affected / exposed	0 / 85 (0.00%)	1 / 94 (1.06%)	1 / 96 (1.04%)
occurrences (all)	0	1	1
Cat scratch disease			
subjects affected / exposed	1 / 85 (1.18%)	0 / 94 (0.00%)	0 / 96 (0.00%)
occurrences (all)	1	0	0
Genitourinary tract infection			
subjects affected / exposed	0 / 85 (0.00%)	1 / 94 (1.06%)	0 / 96 (0.00%)
occurrences (all)	0	1	0
Metabolism and nutrition disorders			
Chondropathy			
subjects affected / exposed	0 / 85 (0.00%)	1 / 94 (1.06%)	0 / 96 (0.00%)
occurrences (all)	0	1	0
Contusion			
subjects affected / exposed	1 / 85 (1.18%)	0 / 94 (0.00%)	0 / 96 (0.00%)
occurrences (all)	1	0	0
Diabetes mellitus			
subjects affected / exposed	1 / 85 (1.18%)	0 / 94 (0.00%)	0 / 96 (0.00%)
occurrences (all)	1	0	0
Iron deficiency			
subjects affected / exposed	0 / 85 (0.00%)	1 / 94 (1.06%)	0 / 96 (0.00%)
occurrences (all)	0	1	0
Hypercholesterolaemia			
subjects affected / exposed	0 / 85 (0.00%)	1 / 94 (1.06%)	0 / 96 (0.00%)
occurrences (all)	0	1	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
27 February 2017	1) To complete all 14 days of treatment up to the evening of Day 14, the day of Visit 4 will be Day 15. To maintain 7-day intervals between subsequent visits, the day of Visits 3 to 7 and of all the Phone calls is rectified. 2) Since the bowel cleansing preparation and the colonoscopy may bias the baseline symptom data to be collected by the patients from Visit 1 to Day -1, the following changes are introduced to standardise the baseline data collection and to prevent any bias: the screening phase is extended to Day -21, the screening visit will be scheduled between Days -21 and -15, the colonoscopy, if needed, will be scheduled between Days -21 and -16, baseline data collected from Day -14 to Day -1 will be considered for the evaluation of inclusion criterion 4 at Visit 2 – Day 1. 3) Details of the co-ordinating site in Germany and of the CRO designated for monitoring and submissions in Belgium are added. 4) "Oral body temperature" is changed to "body temperature" to allow more measurement types since this parameter is not expected to vary critically during the study
20 February 2018	The aim of this substantial amendment is: 1) To replace the use of the electronic diary with the paper one. 2) To specify the permitted values of averages calculated for confirming the inclusion criterion 4 point b), when the values calculated is >4. 3) To specify the use the once-off medications related to the preparation or performance of the colonoscopy inside the study. 4) To amend the name of responsible person at ArisGlobal Ltd. (provider of EDC and randomisation system) 4) To integrate the Note to File 1 in the new protocol version. 5) To integrate the Amendment Nr. 01, Final version 1.0, 21JUL17 in the new protocol version. Sections affected: • Synopsis • Section 5.2, 5.3, 5.3.1 • Section 6.1.1 • Section 7.4.2, 7.4.3, 7.4.4, 7.4.5 • Section 7.6 • Section 8.1, 8.2 • Section 12.1 • Section 13.2 • Section 15.1 • Section 16.2.4.1 • Section 16.5

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
15 June 2020	Study was interrupted and completed earlier due to Covid-19 pandemic.	-

Notes:

Limitations and caveats

None reported