Clinical trial results:
A Double-Blind, Placebo-Controlled, Parallel-Group, Multicentre, Multiregional, One Year Study to Assess the Efficacy and Safety of Twice Daily Oral Rifaximin Delayed Release Tablets for Induction of Clinical Remission with Endoscopic Response at 16 Weeks followed by Clinical and Endoscopic Remission at 52 Weeks in Subjects with Active Moderate Crohn's Disease

Summary

EudraCT number	2014-001645-24
Trial protocol	HU CZ DE PL FR
Global end of trial date	06 October 2017

Results information

Result version number	v1 (current)
This version publication date	19 July 2019
First version publication date	19 July 2019

Trial information

Trial identification

Sponsor protocol code	RECD3126

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02240108
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Salix Pharmaceuticals, Inc
Sponsor organisation address	400 Somerset Corporate Blvd, Bridgewater, United States, NJ 08807
Public contact	Study Director, Clinical Affairs: John Lahey, Salix Pharmaceuticals, Inc, +1 908-541-8631, John.Lahey@bauschhealth.com
Scientific contact	Study Director, Clinical Affairs: John Lahey, Salix Pharmaceuticals, Inc, +1 908-541-8631, John.Lahey@bauschhealth.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	06 October 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	06 October 2017
Global end of trial reached?	Yes
Global end of trial date	06 October 2017
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To determine the efficacy of Rifaximin EIR (extended intestinal release) 800 mg twice daily (BID) vs. placebo for the induction of clinical remission and endoscopic response following 16 weeks of treatment in subjects presenting with active moderate Crohn’s disease.

Protection of trial subjects:

This study was conducted in compliance with the study protocol and in accordance with Declaration of Helsinki on Ethical Principles for Medical Research Involving Human Subjects, and with Good Clinical Practice (GCP), as required by the US Code of Federal Regulations applicable to clinical studies (21 CFR Parts 11, 50, 54, 56 and 312, 42 USC 282(j), International Conference on Harmonization, Harmonized Tripartite Guideline E6 (R1): GCP and E2A: Safety Data Management, and applicable local regulations.

To ensure the safety of patients on placebo, subjects were allowed to continue stable doses of oral 5-ASA, mercaptopurine, azathioprine, and/or methotrexate as concomitant therapies throughout the study.

Background therapy:

No background therapy was specified. Subjects were allowed to continue stable doses of oral 5-ASA, mercaptopurine, azathioprine, and/or methotrexate as concomitant therapies throughout the study.

Evidence for comparator:

The comparator in this study was an inactive placebo.

Actual start date of recruitment	28 October 2014
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	Czech Republic: 10
Country: Number of subjects enrolled	France: 4
Country: Number of subjects enrolled	Hungary: 2
Country: Number of subjects enrolled	United States: 64
Worldwide total number of subjects	80
EEA total number of subjects	16

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)	73
From 65 to 84 years	7
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Men and women aged ≥18 years, with moderate, non-fistulising Crohn's disease in ileum or colon with a Crohn's Disease Activity Index (CDAI) score of ≥220 and ≤450 points prior to randomisation; and a Simple Endoscopic Score for Crohn's Disease (SES-CD) score of ≥7. Exclusion criteria: ulcerative or indeterminate colitis, celiac disease.

Pre-assignment

Screening details:

During Screening, eligible subjects had an average daily score of >1.5 for abdominal pain (CDAI Item 2) and average daily count of >1.5 for liquid/very soft stools (CDAI Item 1).

Period 1

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

Blinding implementation details:

Rifaximin EIR was supplied as pink, coated, oval, biconvex tablets. Matching placebo was supplied as tablets that were identical in appearance to Rifaximin EIR tablets with inactive ingredients.
Subjects were assigned to treatment groups by the means of a centralised electronic randomization system in a 1:1 allocation to either rifaximin or matching placebo.

Arms

Are arms mutually exclusive?	Yes
Arm title	Rifaximin EIR 800 mg

Arm description:

Two x 400 mg tablets twice a day (total daily dose 800 mg)

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

Dosage and administration details:

800 mg rifaximin EIR twice a day for up to 52 weeks

Arm title	Placebo

Arm description:

Placebo comparator arm

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

Dosage and administration details:

Placebo matching rifaximin EIR tablets administered twice daily for up to 52 weeks

Number of subjects in period 1	Rifaximin EIR 800 mg	Placebo
Started	35	45
Completed	21	21
Not completed	14	24
Consent withdrawn by subject	5	10
Physician decision	3	2
Adverse event, non-fatal	1	9
Not reported	2	1
Pregnancy	1	-
Lost to follow-up	1	1
Lack of efficacy	1	1

Baseline characteristics

Reporting groups	
Reporting group title	Rifaximin EIR 800 mg
Reporting group description:	
Two x 400 mg tablets twice a day (total daily dose 800 mg)	
Reporting group title	Placebo
Reporting group description:	
Placebo comparator arm	

Reporting group values	Rifaximin EIR 800 mg	Placebo	Total
Number of subjects	35	45	80
Age categorical			
Units: Subjects			
In utero			0
Preterm newborn infants (gestational age < 37 wks)			0
Newborns (0-27 days)			0
Infants and toddlers (28 days-23 months)			0
Children (2-11 years)			0
Adolescents (12-17 years)			0
Adults (18-64 years)			0
From 65-84 years			0
85 years and over			0
Age continuous			
Units: years			
arithmetic mean	43.5	43.2	
standard deviation	± 14.85	± 12.97	-
Gender categorical			
Units: Subjects			
Female	19	24	43
Male	16	21	37
CDAI score			
Crohn's Disease Activity Index at baseline			
Units: Score			
arithmetic mean	305.4	300.0	
standard deviation	± 69.51	± 56.39	-
SES-CD score			
Simple endoscopic score for Crohn's disease at baseline.			
Units: Score			
arithmetic mean	12.0	11.7	
standard deviation	± 5.01	± 4.61	-
Duration of disease			
Duration of Crohn's disease at baseline.			
Units: Years			
arithmetic mean	10.5	9.6	
standard deviation	± 8.57	± 9.53	-

End points

End points reporting groups

Reporting group title	Rifaximin EIR 800 mg
Reporting group description:	
Two x 400 mg tablets twice a day (total daily dose 800 mg)	
Reporting group title	Placebo
Reporting group description:	
Placebo comparator arm	

Primary: Change in CDAI Item 1 (Week 16)

End point title	Change in CDAI Item 1 (Week 16)[1]
End point description:	
Clinical symptom remission defined by (1) the total number of liquid/very soft stools for the 7 days prior to the Week 16 visit being ≤ 10 (from CDAI Item 1).	
End point type	Primary
End point timeframe:	
From baseline to Week 16.	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis is presented because the study was terminated prematurely, at which point there were only 80 patients randomised (rather than the 660 overall).

End point values	Rifaximin EIR 800 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	35	45		
Units: Subjects				
≤ 10 liquid/ very soft stools	6	8		

Statistical analyses

No statistical analyses for this end point

Primary: Abdominal pain rating (Week 16)

End point title	Abdominal pain rating (Week 16)[2]
End point description:	
An abdominal pain rating of ≤ 1 on each day for the 7 days prior to the Week 16 visit	
End point type	Primary
End point timeframe:	
From baseline to Week 16.	

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis is presented because the study was terminated prematurely, at which point there were only 80 patients randomised (rather than the 660 planned overall).

End point values	Rifaximin EIR 800 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	35	45		
Units: Subjects				
pain rating of ≤ 1	19	15		

Statistical analyses

No statistical analyses for this end point

Primary: Change in CDAI Item 1 and abdominal pain rating (Week 16)

End point title	Change in CDAI Item 1 and abdominal pain rating (Week 16)[3]

End point description:

Number of liquid/very soft stools for the 7 days prior to the week 16 visit being ≤ 10 and an abdominal pain rating of ≤ 1 on each day for the 7 days prior to the week 16 visit.

End point type	Primary

End point timeframe:

From baseline to Week 16.

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis is presented because the study was terminated prematurely, at which point there were only 80 patients randomised (rather than the 660 planned overall).

End point values	Rifaximin EIR 800 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	35	45		
Units: Subjects				
≤ 10 liquid/ soft stools and pain rating of ≤ 1	5	7		

Statistical analyses

No statistical analyses for this end point

Primary: Endoscopic response (Week 16)

End point title	Endoscopic response (Week 16)[4]

End point description:

Endoscopic response defined as a ≥ 3-point decrease in the SES-CD from baseline to the SES-CD score obtained between Week 16 and Week 17.

End point type	Primary

End point timeframe:

From baseline up to Week 16/17.

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis is presented because the study was terminated prematurely, at which point there were only 80 patients randomised (rather than the 660 overall).

End point values	Rifaximin EIR 800 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	35	45		
Units: Subjects				
≥ 3-point decrease in SES-CD	10	10		

Statistical analyses

No statistical analyses for this end point

Primary: Change in CDAI Item 1 (Week 52)

End point title	Change in CDAI Item 1 (Week 52)[5]

End point description:

Clinical symptom remission defined by (1) the total number of liquid/very soft stools for the 7 days prior to the Week 52 visit being ≤ 10 (from CDAI Item 1).

End point type	Primary

End point timeframe:

From baseline to Week 52.

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis is presented because the study was terminated prematurely, at which point there were only 80 patients randomised (rather than the 660 planned overall).

End point values	Rifaximin EIR 800 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	35	45		
Units: Subjects				
≤ 10 liquid/ very soft stools	7	3		

Statistical analyses

No statistical analyses for this end point

Primary: Abdominal pain rating (Week 52)

End point title	Abdominal pain rating (Week 52)[6]

End point description:

An abdominal pain rating of ≤ 1 on each day for the 7 days prior to the Week 52 visit.

End point type	Primary

End point timeframe:

From baseline to Week 52.

Notes:

[6] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis is presented because the study was terminated prematurely, at which point there were only 80 patients randomised (rather than the 660 planned overall).

End point values	Rifaximin EIR 800 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	35	45		
Units: Subjects				
pain rating of ≤ 1	9	5		

Statistical analyses

No statistical analyses for this end point

Primary: Change in CDAI Item 1 and abdominal pain rating (Week 52)

End point title	Change in CDAI Item 1 and abdominal pain rating (Week 52)[7]

End point description:

Number of liquid/very soft stools for the 7 days prior to the Week 52 visit being ≤ 10 and an abdominal pain rating of ≤ 1 on each day for the 7 days prior to the Week 52 visit.

End point type	Primary

End point timeframe:

From baseline to Week 52.

Notes:

[7] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis is presented because the study was terminated prematurely, at which point there were only 80 patients randomised (rather than the 660 planned overall).

End point values	Rifaximin EIR 800 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	35	45		
Units: Subjects				
≤ 10 liquid/ soft stools and pain rating of ≤ 1	6	1		

Statistical analyses

No statistical analyses for this end point

Primary: Endoscopic response (Week 52)

End point title	Endoscopic response (Week 52)[8]

End point description:

Endoscopic response defined as a ≥ 3-point decrease in the SES-CD2 from baseline to the SES-CD score obtained at Week 52.

End point type	Primary

End point timeframe:

From baseline to Week 52.

Notes:

[8] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis is presented because the study was terminated prematurely, at which point there were only 80 patients randomised (rather than the 660 overall).

End point values	Rifaximin EIR 800 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	35	45		
Units: Subjects				
≥ 3-point decrease in SES-CD	9	15		

Statistical analyses

No statistical analyses for this end point

Secondary: Induction of Clinical Remission (Week 16)

End point title	Induction of Clinical Remission (Week 16)

End point description:

Induction of clinical remission defined as a CDAI score of less than 150 points at Week 16.

End point type	Secondary

End point timeframe:

From baseline to Week 16.

End point values	Rifaximin EIR 800 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	35	45		
Units: Subjects				
CDAI score < 150 points	17	12		

Statistical analyses

No statistical analyses for this end point

Secondary: Total number of liquid/very soft stools and daily abdominal pain score (Week 52)

End point title	Total number of liquid/very soft stools and daily abdominal pain score (Week 52)

End point description:

The total number of liquid/very soft stools being ≤ 10 and a daily abdominal pain score of ≤ 1 for the 7 days prior to the visit in ≥ 80% of the study visits during the 52-week treatment period.

End point type	Secondary

End point timeframe:

From baseline to Week 52.

End point values	Rifaximin EIR 800 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	35	45		
Units: Subjects				
≤ 10 liquid/very soft stools and pain score of ≤ 1	2	3		

Statistical analyses

No statistical analyses for this end point

Secondary: SES-CD Score of 0 at Week 52

End point title	SES-CD Score of 0 at Week 52

End point description:

Proportion of Subjects with SES-CD Score of 0 at Week 52

End point type	Secondary

End point timeframe:

At Week 52.

End point values	Rifaximin EIR 800 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	35	45		
Units: Subjects				
Score of 0	0	3		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were reported from time of signing informed consent until the end of the follow-up period (2 weeks after last treatment).

Adverse event reporting additional description:

Occurrences of AEs or SAEs were reported during each study visit or by the subject outside of scheduled visits.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21.0

Reporting groups

Reporting group title	Rifaximin EIR 800mg

Reporting group description:

Two x 400 mg tablets twice a day (total daily dose 800 mg).

Reporting group title	Placebo

Reporting group description:

Inactive placebo tablets matching rifaximin EIR twice daily.

Serious adverse events	Rifaximin EIR 800mg	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 35 (17.14%)	9 / 45 (20.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Hodgkin's disease			
subjects affected / exposed	0 / 35 (0.00%)	1 / 45 (2.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung adenocarcinoma			
subjects affected / exposed	1 / 35 (2.86%)	0 / 45 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Overdose			

subjects affected / exposed	1 / 35 (2.86%)	0 / 45 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary retention postoperative			
subjects affected / exposed	0 / 35 (0.00%)	1 / 45 (2.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Peripheral ischaemia			
subjects affected / exposed	0 / 35 (0.00%)	1 / 45 (2.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Coronary artery disease			
subjects affected / exposed	1 / 35 (2.86%)	0 / 45 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			
subjects affected / exposed	1 / 35 (2.86%)	0 / 45 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Seizure			
subjects affected / exposed	1 / 35 (2.86%)	0 / 45 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pregnancy, puerperium and perinatal conditions			
Pregnancy			
subjects affected / exposed	1 / 35 (2.86%)	0 / 45 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			

subjects affected / exposed	1 / 35 (2.86%)	0 / 45 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	1 / 35 (2.86%)	0 / 45 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 35 (0.00%)	1 / 45 (2.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Barrett's oesophagus			
subjects affected / exposed	0 / 35 (0.00%)	1 / 45 (2.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis			
subjects affected / exposed	0 / 35 (0.00%)	1 / 45 (2.22%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Crohn's disease			
subjects affected / exposed	0 / 35 (0.00%)	3 / 45 (6.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea haemorrhagic			
subjects affected / exposed	0 / 35 (0.00%)	1 / 45 (2.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 35 (0.00%)	1 / 45 (2.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Nausea			
subjects affected / exposed	0 / 35 (0.00%)	1 / 45 (2.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Odynophagia			
subjects affected / exposed	0 / 35 (0.00%)	1 / 45 (2.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis acute			
subjects affected / exposed	0 / 35 (0.00%)	1 / 45 (2.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal obstruction			
subjects affected / exposed	0 / 35 (0.00%)	1 / 45 (2.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	0 / 35 (0.00%)	2 / 45 (4.44%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Prostatitis			
subjects affected / exposed	0 / 35 (0.00%)	1 / 45 (2.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	0 / 35 (0.00%)	1 / 45 (2.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration			

subjects affected / exposed	1 / 35 (2.86%)	1 / 45 (2.22%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Rifaximin EIR 800mg	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	25 / 35 (71.43%)	25 / 45 (55.56%)	
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	2 / 35 (5.71%)	0 / 45 (0.00%)	
occurrences (all)	4	0	
Nervous system disorders			
Headache			
subjects affected / exposed	3 / 35 (8.57%)	5 / 45 (11.11%)	
occurrences (all)	3	5	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	3 / 35 (8.57%)	1 / 45 (2.22%)	
occurrences (all)	3	1	
Lymphadenopathy			
subjects affected / exposed	2 / 35 (5.71%)	0 / 45 (0.00%)	
occurrences (all)	3	0	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	2 / 35 (5.71%)	2 / 45 (4.44%)	
occurrences (all)	2	2	
Pain			
subjects affected / exposed	2 / 35 (5.71%)	0 / 45 (0.00%)	
occurrences (all)	2	0	
Pyrexia			
subjects affected / exposed	2 / 35 (5.71%)	2 / 45 (4.44%)	
occurrences (all)	2	2	
Gastrointestinal disorders			

Abdominal pain			
subjects affected / exposed	2 / 35 (5.71%)	7 / 45 (15.56%)	
occurrences (all)	2	7	
Abdominal pain upper			
subjects affected / exposed	4 / 35 (11.43%)	2 / 45 (4.44%)	
occurrences (all)	4	3	
Crohn's disease			
subjects affected / exposed	3 / 35 (8.57%)	7 / 45 (15.56%)	
occurrences (all)	3	8	
Diarrhoea			
subjects affected / exposed	4 / 35 (11.43%)	5 / 45 (11.11%)	
occurrences (all)	5	6	
Nausea			
subjects affected / exposed	3 / 35 (8.57%)	4 / 45 (8.89%)	
occurrences (all)	3	4	
Rectal haemorrhage			
subjects affected / exposed	0 / 35 (0.00%)	4 / 45 (8.89%)	
occurrences (all)	0	4	
Vomiting			
subjects affected / exposed	4 / 35 (11.43%)	4 / 45 (8.89%)	
occurrences (all)	4	4	
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	2 / 35 (5.71%)	0 / 45 (0.00%)	
occurrences (all)	2	0	
Rash			
subjects affected / exposed	2 / 35 (5.71%)	4 / 45 (8.89%)	
occurrences (all)	2	5	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	3 / 35 (8.57%)	3 / 45 (6.67%)	
occurrences (all)	3	3	
Back pain			
subjects affected / exposed	3 / 35 (8.57%)	2 / 45 (4.44%)	
occurrences (all)	3	3	
Pain in extremity			

subjects affected / exposed	2 / 35 (5.71%)	0 / 45 (0.00%)	
occurrences (all)	2	0	
Infections and infestations			
Gastroenteritis viral			
subjects affected / exposed	2 / 35 (5.71%)	0 / 45 (0.00%)	
occurrences (all)	2	0	
Nasopharyngitis			
subjects affected / exposed	4 / 35 (11.43%)	1 / 45 (2.22%)	
occurrences (all)	7	1	
Pharyngitis streptococcal			
subjects affected / exposed	2 / 35 (5.71%)	0 / 45 (0.00%)	
occurrences (all)	2	0	
Sinusitis			
subjects affected / exposed	2 / 35 (5.71%)	0 / 45 (0.00%)	
occurrences (all)	2	0	
Upper respiratory tract infection			
subjects affected / exposed	2 / 35 (5.71%)	2 / 45 (4.44%)	
occurrences (all)	2	2	
Urinary tract infection			
subjects affected / exposed	0 / 35 (0.00%)	3 / 45 (6.67%)	
occurrences (all)	0	3	
Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	1 / 35 (2.86%)	3 / 45 (6.67%)	
occurrences (all)	1	3	
Type 2 diabetes mellitus			
subjects affected / exposed	2 / 35 (5.71%)	0 / 45 (0.00%)	
occurrences (all)	2	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
06 October 2017	The trial was prematurely discontinued due to difficulty in enrollment and lack of clinical study drug access.	-

Notes:

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

The study was terminated early due to difficulty in enrollment and lack of clinical study drug access. The efficacy results are not considered definitive and are considered for exploratory purposes only.

Notes: