Clinical trial results:
A Phase 2, Multi-Center, Open-Label Induction Trial with Extension Period to Assess Endoscopic Improvement and Changes in Intestinal and Serum Biomarkers in Patients with Moderately to Severely Active Crohn's Disease Receiving Oral RPC1063 as Induction Therapy

Summary

EudraCT number	2015-002025-19
Trial protocol	HU PL IT
Global end of trial date	28 November 2019

Results information

Result version number	v1 (current)
This version publication date	06 December 2020
First version publication date	06 December 2020

Trial information

Trial identification

Sponsor protocol code	RPC01-2201

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02531113
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Bristol-Myers Squibb
Sponsor organisation address	Chaussée de la Hulpe 185, Brussels, Belgium, 1170
Public contact	EU Study Start-Up Unit, Bristol-Myers Squibb International Corporation, Clinical.Trials@bms.com
Scientific contact	Bristol-Myers Squibb Study Director, Bristol-Myers Squibb, Clinical.Trials@bms.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	28 November 2019
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	28 November 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess endoscopic improvement following treatment with ozanimod

Protection of trial subjects:

Patient Confidentiality, Informed Consent and Archival of Essential Documents

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	09 October 2015
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	37 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Canada: 1
Country: Number of subjects enrolled	Hungary: 3
Country: Number of subjects enrolled	Poland: 10
Country: Number of subjects enrolled	Ukraine: 17
Country: Number of subjects enrolled	United States: 38
Worldwide total number of subjects	69
EEA total number of subjects	13

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)	67

From 65 to 84 years	2
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Sixty-nine adult participants were enrolled from 28 sites located in Europe and North America.

Pre-assignment

Screening details:

Eligible participants must have had a Crohn’s Disease Activity Index (CDAI) score of 220 to 450 inclusive with an Simple Endoscopic Score for Crohn’s Disease (SES-CD) score of ≥ 6 and an average daily stool score ≥ 4 points and/or an average daily abdominal pain score of ≥ 2 points.

Period 1

Period 1 title	Induction Period: Week 0 to 12
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Ozanimod Hydrochloride (HCl) 1 mg

Arm description:

Participants received ozanimod 1 mg capsules daily for the first 12 weeks of the induction period (an initial 7-day dose escalation regimen that consisted of 4 days of ozanimod HCl 0.25 mg (equivalent to ozanimod 0.23 mg) daily followed by 3 days of ozanimod HCl 0.5 mg (equivalent to ozanimod 0.46 mg) daily, with the final dose of ozanimod HCl 1 mg (equivalent to ozanimod 0.92 mg) daily dose reached on Day 8. Participants who completed the induction period had the opportunity at Week 12 to continue to receive ozanimod 1 mg capsules daily during the extension period up to an additional 148 weeks, provided that the investigator determined that the participant should continue. Participants in the extension period continued to receive ozanimod 1 mg capsules daily through Week 160. Participants who completed the Week 160 visit had the option to continue open-label ozanimod 1 mg capsules by immediately entering the open-label extension Phase 3 Crohn's Disease Study RPC01-3204 (NCT03467958).

Arm type	Experimental
Investigational medicinal product name	RPC1063
Investigational medicinal product code	
Other name	Ozanimod
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

0.25 mg, 1 mg

Number of subjects in period 1	Ozanimod Hydrochloride (HCl) 1 mg
Started	69
Completed	58
Not completed	11
Consent withdrawn by subject	3
Adverse event, non-fatal	4
Lack of efficacy	4

Period 2

Period 2 title	Extension Period: Week 12 up to Week 160
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Ozanimod Hydrochloride (HCl) 1 mg

Arm description:

Participants received ozanimod 1 mg capsules daily for the first 12 weeks of the induction period (an initial 7-day dose escalation regimen that consisted of 4 days of ozanimod HCl 0.25 mg (equivalent to ozanimod 0.23 mg) daily followed by 3 days of ozanimod HCl 0.5 mg (equivalent to ozanimod 0.46 mg) daily, with the final dose of ozanimod HCl 1 mg (equivalent to ozanimod 0.92 mg) daily dose reached on Day 8. Participants who completed the induction period had the opportunity at Week 12 to continue to receive ozanimod 1 mg capsules daily during the extension period up to an additional 148 weeks, provided that the investigator determined that the participant should continue. Participants in the extension period continued to receive ozanimod 1 mg capsules daily through Week 160. Participants who completed the Week 160 visit had the option to continue open-label ozanimod 1 mg capsules by immediately entering the open-label extension Phase 3 Crohn's Disease Study RPC01-3204 (NCT03467958).

Arm type	Experimental
Investigational medicinal product name	RPC1063
Investigational medicinal product code	
Other name	Ozanimod
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

0.25 mg, 1 mg

Number of subjects in period 2[1]	Ozanimod Hydrochloride (HCl) 1 mg
Started	52
Completed	14
Not completed	38
Physician decision	2
Consent withdrawn by subject	11
Adverse event, non-fatal	5
Pregnancy	1
Lack of efficacy	19

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: 6 participants completed Induction Period, but did not proceed to Extension Period due to lack of efficacy

Baseline characteristics

Reporting groups	
Reporting group title	Ozanimod Hydrochloride (HCl) 1 mg

Reporting group description:

Participants received ozanimod 1 mg capsules daily for the first 12 weeks of the induction period (an initial 7-day dose escalation regimen that consisted of 4 days of ozanimod HCl 0.25 mg (equivalent to ozanimod 0.23 mg) daily followed by 3 days of ozanimod HCl 0.5 mg (equivalent to ozanimod 0.46 mg) daily, with the final dose of ozanimod HCl 1 mg (equivalent to ozanimod 0.92 mg) daily dose reached on Day 8. Participants who completed the induction period had the opportunity at Week 12 to continue to receive ozanimod 1 mg capsules daily during the extension period up to an additional 148 weeks, provided that the investigator determined that the participant should continue. Participants in the extension period continued to receive ozanimod 1 mg capsules daily through Week 160. Participants who completed the Week 160 visit had the option to continue open-label ozanimod 1 mg capsules by immediately entering the open-label extension Phase 3 Crohn's Disease Study RPC01-3204 (NCT03467958).

Reporting group values	Ozanimod Hydrochloride (HCl) 1 mg	Total	
Number of subjects	69	69	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	67	67	
From 65-84 years	2	2	
85 years and over	0	0	
Age Continuous Units: Years			
arithmetic mean	37.7		
standard deviation	± 11.97	-	
Sex: Female, Male Units: Participants			
Female	36	36	
Male	33	33	
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	5	5	
Not Hispanic or Latino	64	64	
Unknown or Not Reported	0	0	
Race/Ethnicity, Customized Units: Subjects			
Asian	1	1	
Black or African American	7	7	
Other	1	1	
White	60	60	

Prior Corticosteroid Use Units: Subjects			
Prior Use of Corticosteroids	62	62	
No Prior Use of Corticosteroids	7	7	
Prior Use of Immunomodulator Units: Subjects			
Prior Use of Immunomodulator	38	38	
No Prior Use of Immunomodulator	31	31	
Disease Location Units: Subjects			
Ileum Only	11	11	
Colon Only	26	26	
Ileocolonic (Ileum and Colon)	32	32	
Years Since Crohn's Disease Diagnosis Units: Years			
arithmetic mean	8.9		
standard deviation	± 8.53	-	
Crohn’s Disease Activity Index (CDAI) Score at Baseline			
The CDAI is a composite score that was used to measure the clinical activity of Crohn’s disease. The CDAI used a questionnaire with responses scored numerically and weighted. Scores range from 0 to approximately 600, with higher scores indicating greater disease activity.			
Units: Units on a Scale			
arithmetic mean	322.8		
standard deviation	± 59.19	-	
Daily Stool Frequency (SF) at Baseline			
SF = the average daily stool score = average of the number of liquid/soft stools for the available days in the 7-day window, using the most recent 7 days prior to the visit.			
Units: Stools/day			
arithmetic mean	6.15		
standard deviation	± 2.792	-	
Daily Abdominal Pain Score at Baseline			
The daily abdominal pain score was defined as the average of the abdominal pain level for the available days in the 7-day window, using the most recent 7 days prior to the visit date. Abdominal pain is scored on a scale 0-3.			
Units: Units on a Scale			
arithmetic mean	2.05		
standard deviation	± 0.526	-	
Simple Endoscopic Score for Crohn's Disease (SES-CD) at Baseline			
The SES-CD assesses the degree of inflammation on the basis of 4 components: size of ulcers, ulcerated surface, affected surface, and presence of narrowing. Each of these components was scored on a scale of 0 to 3 (worst). In the SES-CD, each of these 4 components were assessed in the five segments of the ileum and colon: ileum, right, transverse, left (descending and sigmoid), and rectum. The SES-CD is the sum of the individual scores of each of the components across the five segments, with higher scores indicating greater disease activity.			
Units: Units on a Scale			
arithmetic mean	13.28		
standard deviation	± 6.584	-	
Fecal Calprotectin at Baseline Units: µg/g			
arithmetic mean	1158.17		
standard deviation	± 1231.267	-	
C-reactive Protein (mg/L) at Baseline Units: (mg/L)			

arithmetic mean standard deviation	18.2 ± 25.36	-	

End points

End points reporting groups

Reporting group title	Ozanimod Hydrochloride (HCl) 1 mg

Reporting group description:

Participants received ozanimod 1 mg capsules daily for the first 12 weeks of the induction period (an initial 7-day dose escalation regimen that consisted of 4 days of ozanimod HCl 0.25 mg (equivalent to ozanimod 0.23 mg) daily followed by 3 days of ozanimod HCl 0.5 mg (equivalent to ozanimod 0.46 mg) daily, with the final dose of ozanimod HCl 1 mg (equivalent to ozanimod 0.92 mg) daily dose reached on Day 8. Participants who completed the induction period had the opportunity at Week 12 to continue to receive ozanimod 1 mg capsules daily during the extension period up to an additional 148 weeks, provided that the investigator determined that the participant should continue. Participants in the extension period continued to receive ozanimod 1 mg capsules daily through Week 160. Participants who completed the Week 160 visit had the option to continue open-label ozanimod 1 mg capsules by immediately entering the open-label extension Phase 3 Crohn's Disease Study RPC01-3204 (NCT03467958).

Reporting group title	Ozanimod Hydrochloride (HCl) 1 mg

Reporting group description:

Participants received ozanimod 1 mg capsules daily for the first 12 weeks of the induction period (an initial 7-day dose escalation regimen that consisted of 4 days of ozanimod HCl 0.25 mg (equivalent to ozanimod 0.23 mg) daily followed by 3 days of ozanimod HCl 0.5 mg (equivalent to ozanimod 0.46 mg) daily, with the final dose of ozanimod HCl 1 mg (equivalent to ozanimod 0.92 mg) daily dose reached on Day 8. Participants who completed the induction period had the opportunity at Week 12 to continue to receive ozanimod 1 mg capsules daily during the extension period up to an additional 148 weeks, provided that the investigator determined that the participant should continue. Participants in the extension period continued to receive ozanimod 1 mg capsules daily through Week 160. Participants who completed the Week 160 visit had the option to continue open-label ozanimod 1 mg capsules by immediately entering the open-label extension Phase 3 Crohn's Disease Study RPC01-3204 (NCT03467958).

Primary: Change in Simple Endoscopic Score for Crohn's Disease (SES-CD) (Paired Segments) from Baseline at Week 12 as Determined by a Blinded Central Reader.

End point title	Change in Simple Endoscopic Score for Crohn's Disease (SES-CD) (Paired Segments) from Baseline at Week 12 as Determined by a Blinded Central Reader.[1]

End point description:

The simple endoscopy score (SES-CD) assesses the degree of inflammation. The SES-CD assesses the following 4 components: size of ulcers, ulcerated surface, affected surface, and presence of narrowing. Each of these components are scored on a scale of 0 to 3. In the SES-CD, each of these 4 components are assessed in the five segments of the ileum and colon: ileum, right, transverse, left (descending and sigmoid), and rectum. The SES-CD is the sum of the individual scores of each of the components across the five segments. The range of SES-CD scores is 0 – 12 for each segment, and 0 – 56 for the overall SES-CD score, with larger scores indicating greater severity of disease.

End point type	Primary

End point timeframe:

Baseline to Week 12

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only summary statistics were planned for this endpoint

End point values	Ozanimod Hydrochloride (HCl) 1 mg			
Subject group type	Reporting group			
Number of subjects analysed	56			
Units: Units on a Scale				
arithmetic mean (standard deviation)	-2.3 (± 6.20)			

Statistical analyses

No statistical analyses for this end point

Secondary: The Number of Participants with Treatment Emergent Adverse Events (TEAE) During the Induction and Extension Period

End point title	The Number of Participants with Treatment Emergent Adverse Events (TEAE) During the Induction and Extension Period

End point description:

A TEAE = any event with an onset date on or after the first dose date, or any ongoing event on the first dose date that worsens in severity or after the first dose date and until 90 days following the last dose of study drug treatment. An AE = untoward medical occurrence in a patient or clinical investigation patient administered a pharmaceutical product, which that does not necessarily have a causal relationship with the investigational treatment. An AE can be any unfavorable or unintended sign, symptom, or disease temporally associated with the use of an investigational medicinal product, whether or not considered related to the investigational medicinal product. A serious AE (experience) or reaction is any untoward medical occurrence that at any dose: Results in death, Is life-threatening, Requires inpatient hospitalization or prolongation of existing hospitalization, Results in persistent or significant disability/incapacity, or Is a congenital abnormality/birth defect

End point type	Secondary

End point timeframe:

From the first day of ozanimod up to 90 days after the last dose of ozanimod; mean duration of exposure of study drug was 1.305 years

End point values	Ozanimod Hydrochloride (HCl) 1 mg			
Subject group type	Reporting group			
Number of subjects analysed	69			
Units: Participants				
≥ 1 TEAE	59			
≥ 1 Moderate or Severe TEAE	43			
≥ 1 Severe TEAE	15			
≥ 1 Possible, Probable or Related TEAE	24			
≥ 1 Related TEAE	7			
≥ 1 Serious TEAE	18			
≥ 1 Possible, Probable or Related Serious TEAE	4			
≥ 1 Related Serious TEAE	1			
≥ 1 TEAE Leading to Discontinuation of Ozanimod	11			
≥ 1 TEAE Leading to Study Withdrawal	11			
Death	1			

Death Possible, Probable or Related to Ozanimod	1			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change in the Crohn's Disease Activity Index (CDAI) Score from Baseline at Week 12

End point title	Change in the Crohn's Disease Activity Index (CDAI) Score from Baseline at Week 12

End point description:

The Crohn's Disease Activity Index is a composite score that is used to measure the clinical activity of Crohn's disease. The CDAI includes uses 8 components: Number of liquid or soft stools for 7 days, Abdominal pain for 7 days, General well-being for 7 days, Presence of complications, Taking diarrhea medication, Abdominal mass, Hematocrit and Percentage deviation from standard weight. Scores range from 0 to approximately 600, with higher scores indicating greater disease activity. Baseline was defined as the last non-missing record on or before the first dose of study drug.

End point type	Other pre-specified

End point timeframe:

Baseline to Week 12

End point values	Ozanimod Hydrochloride (HCl) 1 mg			
Subject group type	Reporting group			
Number of subjects analysed	54			
Units: Units on a Scale				
arithmetic mean (standard deviation)	-141.5 (± 99.42)			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Percentage of Participants with Clinical Remission Based on the Crohn's Disease Activity Index (CDAI) at Week 12

End point title	Percentage of Participants with Clinical Remission Based on the Crohn's Disease Activity Index (CDAI) at Week 12

End point description:

Clinical Remission is defined as a CDAI score of < 150. The Crohn's Disease Activity Index is a composite score that is used to measure the clinical activity of Crohn's disease. The CDAI includes uses 8 components: Number of liquid or soft stools for 7 days, Abdominal pain for 7 days, General well-being for 7 days, Presence of complications, Taking diarrhea medication, Abdominal mass, Hematocrit and Percentage deviation from standard weight. Scores range from 0 to approximately 600, with higher scores indicating greater disease activity. 95% confidence interval (CI) was created using the Clopper-Pearson Exact Method.

End point type	Other pre-specified

End point timeframe:

Week 12

End point values	Ozanimod Hydrochloride (HCl) 1 mg			
Subject group type	Reporting group			
Number of subjects analysed	69			
Units: Percentage of Participants				
number (confidence interval 95%)	33.3 (22.44 to 45.71)			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Percentage of Participants who Achieved a Clinical Response Based on Crohn's Disease Activity Index (CDAI) at Week 12

End point title	Percentage of Participants who Achieved a Clinical Response Based on Crohn's Disease Activity Index (CDAI) at Week 12

End point description:

Clinical Response is defined as a CDAI reduction from baseline of ≥ 100 points. The Crohn's Disease Activity Index is a composite score that is used to measure the clinical activity of Crohn's disease. The CDAI includes uses 8 components: Number of liquid or soft stools for 7 days, Abdominal pain for 7 days, General well-being for 7 days, Presence of complications, Taking diarrhea medication, Abdominal mass, Hematocrit and Percentage deviation from standard weight. Scores range from 0 to approximately 600, with higher scores indicating greater disease activity. 95% confidence interval (CI) was created using the Clopper-Pearson Exact Method.

End point type	Other pre-specified

End point timeframe:

Week 12

End point values	Ozanimod Hydrochloride (HCl) 1 mg			
Subject group type	Reporting group			
Number of subjects analysed	69			
Units: Percentage of Participants				
number (confidence interval 95%)	50.7 (38.41 to 62.98)			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Percentage of Participants Who Achieved Clinical Remission Based on Patient-Reported Outcome (PRO2) Measure Definitions at Week 12

End point title	Percentage of Participants Who Achieved Clinical Remission Based on Patient-Reported Outcome (PRO2) Measure Definitions at Week 12

End point description:

The PRO2 is a composite score based on 2 components of the CDAI, the number of liquid or soft stools/day for 7 days, stool frequency (SF) and abdominal pain (AP) (rated on a scale of 0-3) assessed for 7 days. Clinical Remission (SF and AP remission) was defined as the average daily stool score ≤3 points AND average daily abdominal pain score ≤1 point. 95% confidence interval (CI) was created using the Clopper-Pearson Exact Method.

End point type	Other pre-specified

End point timeframe:

Week 12

End point values	Ozanimod Hydrochloride (HCl) 1 mg			
Subject group type	Reporting group			
Number of subjects analysed	69			
Units: Percentage of Participants				
number (confidence interval 95%)	20.3 (11.56 to 31.69)			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Percentage of Participants who Achieved a Clinical Response Based on Patient Reported Outcome (PRO2) Measures from Baseline at Week 12

End point title	Percentage of Participants who Achieved a Clinical Response Based on Patient Reported Outcome (PRO2) Measures from Baseline at Week 12

End point description:

Clinical response based on PRO2 was defined as PRO2 decrease of ≥50% from baseline. The PRO2 is a composite score based on 2 components of the Crohn's Disease Activity Index, the number of liquid or soft stools/day for 7 days and the abdominal pain (rated on a scale of 0-3) assessed for 7 days. 95% confidence interval (CI) was created using the Clopper-Pearson Exact Method.

End point type	Other pre-specified

End point timeframe:

Week 12

End point values	Ozanimod Hydrochloride (HCl) 1 mg			
Subject group type	Reporting group			
Number of subjects analysed	69			
Units: Percentage of Participants				
number (confidence interval 95%)	29.0 (18.69 to 41.16)			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Percentage of Participants of Participants who Achieved Endoscopic Remission Based on Simple Endoscopic Score for Crohn's Disease (SES-CD) Definitions at Week 12 (Paired Segments)

End point title	Percentage of Participants of Participants who Achieved Endoscopic Remission Based on Simple Endoscopic Score for Crohn's Disease (SES-CD) Definitions at Week 12 (Paired Segments)

End point description:

Endoscopic remission is defined as SES-CD ≤ 4 points and a SES-CD decrease ≥ 2 points with no SES-CD sub-score >1point. The SES-CD assesses the degree of inflammation. The SES-CD assesses the following 4 components: size of ulcers, ulcerated surface, affected surface, and presence of narrowing. Each of these components are scored on a scale of 0 to 3. In the SES-CD, each of these 4 components are assessed in the five segments of the ileum and colon: ileum, right, transverse, left (descending and sigmoid), and rectum. The SES-CD is the sum of the individual scores of each of the components across the five segments. The range of SES-CD scores is 0 – 12 for each segment, and 0 – 56 for the overall SES-CD score, with larger scores indicating greater severity of disease. 95% confidence interval (CI) was created using the Clopper-Pearson Exact Method.

End point type	Other pre-specified

End point timeframe:

Week 12

End point values	Ozanimod Hydrochloride (HCl) 1 mg			
Subject group type	Reporting group			
Number of subjects analysed	69			
Units: Percentage of Participants				
number (confidence interval 95%)	10.1 (4.18 to 19.79)			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Percentage of Participants who Achieved an Endoscopic Response-50 (Paired Segment) Based on Based on Simple Endoscopic Score for

Crohn's Disease (SES-CD) Definitions at Week 12

End point title	Percentage of Participants who Achieved an Endoscopic Response-50 (Paired Segment) Based on Based on Simple Endoscopic Score for Crohn's Disease (SES-CD) Definitions at Week 12

End point description:

Endoscopic Response is defined as a SES-CD decrease from baseline of ≥ 50%. The SES-CD assesses the degree of inflammation. The SES-CD assesses the following 4 components: size of ulcers, ulcerated surface, affected surface, and presence of narrowing. Each of these components are scored on a scale of 0 to 3. In the SES-CD, each of these 4 components are assessed in the five segments of the ileum and colon: ileum, right, transverse, left (descending and sigmoid), and rectum. The SES-CD is the sum of the individual scores of each of the components across the five segments. The range of SES-CD scores is 0 – 12 for each segment, and 0 – 56 for the overall SES-CD score, with larger scores indicating greater severity of disease. 95% confidence interval (CI) was created using the Clopper-Pearson Exact Method.

End point type	Other pre-specified

End point timeframe:

Week 12

End point values	Ozanimod Hydrochloride (HCl) 1 mg			
Subject group type	Reporting group			
Number of subjects analysed	69			
Units: Percentage of Participants				
number (confidence interval 95%)	23.2 (13.87 to 34.91)			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change in Roberts Intestinal Histopathology Index from Baseline (Paired Segments) at Week 12

End point title	Change in Roberts Intestinal Histopathology Index from Baseline (Paired Segments) at Week 12

End point description:

Changes in intestinal mucosa histopathologic features and disease activity were assessed by blinded pathologists. Robarts Histopathology Index (RHI) had a maximum total score of 165, with higher scores indicating more severe histological disease. Baseline was defined as the last non-missing record on or before the first dose of study drug.

End point type	Other pre-specified

End point timeframe:

Week 12

End point values	Ozanimod Hydrochloride (HCl) 1 mg			
Subject group type	Reporting group			
Number of subjects analysed	51			
Units: Units on a Scale				
arithmetic mean (standard deviation)	-10.2 (± 25.83)			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Improvement in Perianal and Enterocutaneous Fistulas

End point title	Improvement in Perianal and Enterocutaneous Fistulas

End point description:

The assessment is based on two parameters: whether the fistula is draining and whether it’s open or closed. This is assessment was only on participants that had a fistula at baseline.

End point type	Other pre-specified

End point timeframe:

Week 12

End point values	Ozanimod Hydrochloride (HCl) 1 mg			
Subject group type	Reporting group			
Number of subjects analysed	0[2]			
Units: change from baseline				
number (not applicable)				

Notes:

[2] - Too few participants with perianal or enterocutaneous fistulas at baseline for meaningful evaluation

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Percentage of Participants who Achieved Endoscopic Remission Based on Simple Endoscopic Score for Crohn's Disease (SES-CD) Definitions at Week 52 - Observed Cases

End point title	Percentage of Participants who Achieved Endoscopic Remission Based on Simple Endoscopic Score for Crohn's Disease (SES-CD) Definitions at Week 52 - Observed Cases

End point description:

Endoscopic remission is defined as SES-CD ≤ 4 points and a SES-CD decrease ≥ 2 points with no SES-CD sub-score >1point. The SES-CD assesses the degree of inflammation. The SES-CD assesses the following 4 components: size of ulcers, ulcerated surface, affected surface, and presence of narrowing. Each of these components are scored on a scale of 0 to 3. In the SES-CD, each of these 4 components are assessed in the five segments of the ileum and colon: ileum, right, transverse, left (descending and sigmoid), and rectum. The SES-CD is the sum of the individual scores of each of the components across the five segments. The range of SES-CD scores is 0 – 12 for each segment, and 0 – 56 for the overall

SES-CD score, with larger scores indicating greater severity of disease. 95% confidence interval (CI) was created using the Clopper-Pearson Exact Method.

End point type	Other pre-specified

End point timeframe:

Week 52

End point values	Ozanimod Hydrochloride (HCl) 1 mg			
Subject group type	Reporting group			
Number of subjects analysed	30			
Units: Percentage of Participants				
number (confidence interval 95%)	16.7 (5.64 to 34.72)			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Percentage of Participants who Achieved an Endoscopic Response-50 Based on Simple Endoscopic Score for Crohn's Disease (SES-CD) Definitions at Week 52

End point title	Percentage of Participants who Achieved an Endoscopic Response-50 Based on Simple Endoscopic Score for Crohn's Disease (SES-CD) Definitions at Week 52

End point description:

Endoscopic Response is defined as a SES-CD decrease from baseline of ≥ 50%. The SES-CD assesses the degree of inflammation. The SES-CD assesses the following 4 components: size of ulcers, ulcerated surface, affected surface, and presence of narrowing. Each of these components are scored on a scale of 0 to 3. In the SES-CD, each of these 4 components are assessed in the five segments of the ileum and colon: ileum, right, transverse, left (descending and sigmoid), and rectum. The SES-CD is the sum of the individual scores of each of the components across the five segments. The range of SES-CD scores is 0 – 12 for each segment, and 0 – 56 for the overall SES-CD score, with larger scores indicating greater severity of disease. 95% confidence interval (CI) was created using the Clopper-Pearson Exact Method..

End point type	Other pre-specified

End point timeframe:

Week 52

End point values	Ozanimod Hydrochloride (HCl) 1 mg			
Subject group type	Reporting group			
Number of subjects analysed	30			
Units: Percentage of Participants				
number (confidence interval 95%)	30.0 (14.73 to 49.40)			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Percentage of Participants who Achieved Clinical Remission Based on the Crohn's Disease Activity Index (CDAI) at Week 52

End point title	Percentage of Participants who Achieved Clinical Remission Based on the Crohn's Disease Activity Index (CDAI) at Week 52

End point description:

Clinical Remission is defined as a CDAI score of < 150. The CDAI includes uses 8 components: Number of liquid or soft stools for 7 days, Abdominal pain for 7 days, General well-being for 7 days, Presence of complications, Taking diarrhea medication, Abdominal mass, Hematocrit and Percentage deviation from standard weight. Scores range from 0 to approximately 600, with higher scores indicating greater disease activity. 95% confidence interval (CI) was created using the Clopper-Pearson Exact Method.

End point type	Other pre-specified

End point timeframe:

Week 52

End point values	Ozanimod Hydrochloride (HCl) 1 mg			
Subject group type	Reporting group			
Number of subjects analysed	32			
Units: Percentage of Participants				
number (confidence interval 95%)	65.6 (46.81 to 81.43)			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Percentage of Participants who Achieved a Clinical Response Based on CDAI at Week 52

End point title	Percentage of Participants who Achieved a Clinical Response Based on CDAI at Week 52

End point description:

Clinical Response is defined as a CDAI reduction from baseline of ≥ 100 points. The CDAI includes uses 8 components: Number of liquid or soft stools for 7 days, Abdominal pain for 7 days, General well-being for 7 days, Presence of complications, Taking diarrhea medication, Abdominal mass, Hematocrit and Percentage deviation from standard weight. Scores range from 0 to approximately 600, with higher scores indicating greater disease activity. 95% confidence interval (CI) was created using the Clopper-Pearson Exact Method.

End point type	Other pre-specified

End point timeframe:

Week 52

End point values	Ozanimod Hydrochloride (HCl) 1 mg			
Subject group type	Reporting group			
Number of subjects analysed	32			
Units: Percentage of Participants				
number (confidence interval 95%)	93.8 (79.19 to 99.23)			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Percentage of Participants Who Achieved Clinical Remission Based on Patient-Reported Outcome (PRO2) Measure Definitions at Week 52

End point title	Percentage of Participants Who Achieved Clinical Remission Based on Patient-Reported Outcome (PRO2) Measure Definitions at Week 52

End point description:

Clinical Remission is defined as the participants with the average daily stool score ≤3 points AND average daily abdominal pain score ≤1 point. The PRO2 is a composite score based on 2 components of the CDAI, the number of liquid or soft stools/day for 7 days and the abdominal pain (rated on a scale of 0-3) assessed for 7 days.

End point type	Other pre-specified

End point timeframe:

Week 52

End point values	Ozanimod Hydrochloride (HCl) 1 mg			
Subject group type	Reporting group			
Number of subjects analysed	32			
Units: Percentage of Participants				
number (confidence interval 95%)	53.1 (34.74 to 70.91)			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Percentage of Participants who Achieved a Clinical Response Based on Patient Reported Outcome (PRO2) Measures from Baseline at Week 52

End point title	Percentage of Participants who Achieved a Clinical Response Based on Patient Reported Outcome (PRO2) Measures from Baseline at Week 52

End point description:

Clinical response based on PRO2 was defined as PRO2 decrease of ≥50% from baseline. The PRO2 is a composite score based on 2 components of the Crohn's Disease Activity Index, the number of liquid or soft stools/day for 7 days and the abdominal pain (rated on a scale of 0-3) assessed for 7 days. 95% confidence interval (CI) was created using the Clopper-Pearson Exact Method.

End point type	Other pre-specified

End point timeframe:

Week 52

End point values	Ozanimod Hydrochloride (HCl) 1 mg			
Subject group type	Reporting group			
Number of subjects analysed	32			
Units: Percentage of Participants				
number (confidence interval 95%)	65.6 (46.81 to 81.43)			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Percentage of Participants in Clinical Remission Based on CDAI and PRO2 Definitions who were off Corticosteroids at Week 52 of Those on Corticosteroids

End point title	Percentage of Participants in Clinical Remission Based on CDAI and PRO2 Definitions who were off Corticosteroids at Week 52 of Those on Corticosteroids

End point description:

Clinical Remission is defined as CDAI score of < 150. The CDAI is a composite score that is used to measure the clinical activity of Crohn's disease. The CDAI uses a questionnaire with responses scored numerically and weighted. The weighted sum of the 8 components: Number of liquid or soft stools for 7 days, Abdominal pain for 7 days, general well-being for 7 days, presence of complications, taking diarrhea medication, abdominal mass, hematocrit and percentage deviation from standard weight. The typical range of CDAI score is 0 to > 600. 95% confidence interval (CI) was created using the Clopper-Pearson Exact Method.

End point type	Other pre-specified

End point timeframe:

Week 52

End point values	Ozanimod Hydrochloride (HCl) 1 mg			
Subject group type	Reporting group			
Number of subjects analysed	16			
Units: Percentage of Participants				
number (confidence interval 95%)	18.8 (4.05 to 45.65)			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Percentage of Participants with Clinical Remission Based on the Crohn's Disease Activity Index (CDAI) at Weeks 4 and 8

End point title	Percentage of Participants with Clinical Remission Based on the Crohn's Disease Activity Index (CDAI) at Weeks 4 and 8

End point description:

Clinical Remission is defined as a CDAI score of < 150. The CDAI is a composite score that is used to measure the clinical activity of Crohn's disease. The CDAI includes uses 8 components: Number of liquid or soft stools for 7 days, Abdominal pain for 7 days, General well-being for 7 days, Presence of complications, Taking diarrhea medication, Abdominal mass, Hematocrit and Percentage deviation from standard weight. Scores range from 0 to approximately 600, with higher scores indicating greater disease activity. 95% confidence interval (CI) was created using the Clopper-Pearson Exact Method.

End point type	Other pre-specified

End point timeframe:

Weeks 4 and 8

End point values	Ozanimod Hydrochloride (HCl) 1 mg			
Subject group type	Reporting group			
Number of subjects analysed	69			
Units: Percentage of Participants				
number (not applicable)				
Week 4	15.9			
Week 8	23.2			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Percentage of Participants who Achieved a Clinical Response Based on CDAI at Weeks 4 and 8

End point title	Percentage of Participants who Achieved a Clinical Response Based on CDAI at Weeks 4 and 8

End point description:

Clinical Response is defined as a CDAI reduction from baseline of ≥ 100 points. The CDAI includes uses

8 components: Number of liquid or soft stools for 7 days, Abdominal pain for 7 days, General well-being for 7 days, Presence of complications, Taking diarrhea medication, Abdominal mass, Hematocrit and Percentage deviation from standard weight. Scores range from 0 to approximately 600, with higher scores indicating greater disease activity. 95% CI was created using the Clopper-Pearson Exact Method.

End point type	Other pre-specified

End point timeframe:

Weeks 4 and 8

End point values	Ozanimod Hydrochloride (HCl) 1 mg			
Subject group type	Reporting group			
Number of subjects analysed	69			
Units: Percentage of Participants				
number (not applicable)				
Weeks 4	37.7			
Weeks 8	52.2			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Percentage of Participants Who Achieved Clinical Remission Based on Patient-Reported Outcome (PRO2) Measure Definitions at Weeks 4 and 8

End point title	Percentage of Participants Who Achieved Clinical Remission Based on Patient-Reported Outcome (PRO2) Measure Definitions at Weeks 4 and 8

End point description:

The PRO2 is a composite score based on 2 components of the CDAI, the number of liquid or soft stools/day for 7 days, stool frequency (SF) and abdominal pain (AP) (rated on a scale of 0-3) assessed for 7 days. Clinical Remission (SF and AP remission) was defined as the average daily stool score ≤3 points AND average daily abdominal pain score ≤1 point. 95% confidence interval (CI) was created using the Clopper-Pearson Exact Method.

End point type	Other pre-specified

End point timeframe:

Weeks 4 and 8

End point values	Ozanimod Hydrochloride (HCl) 1 mg			
Subject group type	Reporting group			
Number of subjects analysed	69			
Units: Percentage of Participants				
number (not applicable)				
Week 4	11.6			
Week 8	26.1			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Percentage of Participants who Achieved a Clinical Response Based on Patient Reported Outcome (PRO2) Measures at Weeks 4 and 8

End point title	Percentage of Participants who Achieved a Clinical Response Based on Patient Reported Outcome (PRO2) Measures at Weeks 4 and 8

End point description:

Clinical response based on PRO2 was defined as PRO2 decrease of ≥50%. The PRO2 is a composite score based on 2 components of the Crohn's Disease Activity Index, the number of liquid or soft stools/day for 7 days and the abdominal pain (rated on a scale of 0-3) assessed for 7 days. 95% confidence interval (CI) was created using the Clopper-Pearson Exact Method.

End point type	Other pre-specified

End point timeframe:

Weeks 4 and Week 8

End point values	Ozanimod Hydrochloride (HCl) 1 mg			
Subject group type	Reporting group			
Number of subjects analysed	69			
Units: Percentage of Participants				
number (not applicable)				
Week 4	20.3			
Week 8	33.3			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Percentage of Participants with RHI Healing at Week 52

End point title	Percentage of Participants with RHI Healing at Week 52

End point description:

Changes in intestinal mucosa histopathologic features and disease activity were assessed by blinded pathologists. Robarts Histopathology Index (RHI) had a maximum total score of 165, with higher scores indicating more severe histological disease. Baseline was defined as the last non-missing record on or before the first dose of study drug.

The Robarts Histopathology Index (RHI) is a recently validated instrument that measures histological disease activity in ulcerative colitis.

RHI Mucosal Healing was defined as a composite endpoint of being a responder for endoscopic remission

and RHI remission.

End point type	Other pre-specified

End point timeframe:

Week 52

End point values	Ozanimod Hydrochloride (HCl) 1 mg			
Subject group type	Reporting group			
Number of subjects analysed	28			
Units: Percentage of Participants				
number (confidence interval 95%)	14.3 (4.03 to 32.67)			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change in Fecal Calprotectin (Observed Cases) at Weeks 12 and 52

End point title	Change in Fecal Calprotectin (Observed Cases) at Weeks 12 and 52

End point description:

Change in fecal calprotectin (observed cases) determined by comparing measurements at weeks 12 and 52 to baseline measurement.

End point type	Other pre-specified

End point timeframe:

Baseline to Weeks 12 and Week 52

End point values	Ozanimod Hydrochloride (HCl) 1 mg			
Subject group type	Reporting group			
Number of subjects analysed	46			
Units: µg/g				
median (full range (min-max))				
Week 12	-41.0 (-3518 to 4791)			
Week 52	-103.3 (-4450 to 19534)			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change in Serum C-Reactive Protein (CRP) Levels from Baseline (Observed Cases) at Weeks 12 and 52

End point title	Change in Serum C-Reactive Protein (CRP) Levels from Baseline (Observed Cases) at Weeks 12 and 52

End point description:

Change in Serum C-Reactive Protein was determined by comparing to baseline.

End point type	Other pre-specified

End point timeframe:

Baseline to Weeks 12 and 52

End point values	Ozanimod Hydrochloride (HCl) 1 mg			
Subject group type	Reporting group			
Number of subjects analysed	53			
Units: mg/L				
median (full range (min-max))				
Week 12	1.0 (-56 to 72)			
Week 52	-0.5 (-59 to 41)			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Changes in Biomarkers: Percentage of Participants with CRP Response-10 - Non-responder Imputation

End point title	Changes in Biomarkers: Percentage of Participants with CRP Response-10 - Non-responder Imputation

End point description:

The percentage of participants with a CRP Response-10 was assessed. CRP Response-10 is defined as C-reactive protein < 10 mg/L.

If any scores are missing then non-responder imputation is applied.

End point type	Other pre-specified

End point timeframe:

Week 12, Week 52

End point values	Ozanimod Hydrochloride (HCl) 1 mg			
Subject group type	Reporting group			
Number of subjects analysed	69			
Units: Percentage of participants				
number (confidence interval 95%)				
Week 12	39.1 (27.60 to 51.63)			
Week 52	23.2 (13.87 to 34.91)			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Changes in Biomarkers: Percentage of Participants with FCP Response-250 - Non-responder Imputation

End point title	Changes in Biomarkers: Percentage of Participants with FCP Response-250 - Non-responder Imputation

End point description:

The percentage of participants with a FCP Response-250 was assessed. FCP Response-250 is defined as Fecal calprotectin < 250 ug/g.

If any Fecal Calprotectin are missing then non-responder imputation is applied.

End point type	Other pre-specified

End point timeframe:

Week 12, Week 52

End point values	Ozanimod Hydrochloride (HCl) 1 mg			
Subject group type	Reporting group			
Number of subjects analysed	69			
Units: Percentage of participants				
number (confidence interval 95%)				
Week 12	30.4 (19.92 to 42.69)			
Week 52	11.6 (5.14 to 21.57)			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Improvement in Perianal and Enterocutaneous Fistulas in Participants with Fistula's from Baseline at Weeks 4 and 8

End point title	Improvement in Perianal and Enterocutaneous Fistulas in

	Participants with Fistula's from Baseline at Weeks 4 and 8

End point description:

The assessment is based on two parameters: whether the fistula is draining and whether it’s open or closed. This is assessment was only on participants that had a fistula at baseline.

End point type	Other pre-specified

End point timeframe:

Baseline to Week 4 and 8

End point values	Ozanimod Hydrochloride (HCl) 1 mg			
Subject group type	Reporting group			
Number of subjects analysed	0[3]			
Units: Change from baseline				
number (not applicable)				

Notes:

[3] - Too few participants with perianal or enterocutaneous fistulas at baseline for meaningful evaluation

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Pharmacokinetic Plasma Concentration of Ozanimod

End point title	Pharmacokinetic Plasma Concentration of Ozanimod

End point description:

Pharmacokinetic structure and variability using the population modeling approach.

End point type	Other pre-specified

End point timeframe:

Population PK based estimate for day 1 and steady state Caverage: Day 1 predose and prior to discharge (approximately 6 – 8 hour postdose), and at predose on week 4, 8 and 12 visits

End point values	Ozanimod Hydrochloride (HCl) 1 mg			
Subject group type	Reporting group			
Number of subjects analysed	68			
Units: mean pM				
number (not applicable)				
Day 1 Steady State	76.10 683.42			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Pharmacokinetic (PK) Plasma Concentration of Active Metabolite CC112273

End point title	Pharmacokinetic (PK) Plasma Concentration of Active Metabolite CC112273

End point description:

PK structure and variability parameters estimated using the population modeling approach. Metabolite measured is CC112273.

End point type	Other pre-specified

End point timeframe:

Population PK based estimate for day 1 and steady state Caverage: Day 1 predose and prior to discharge (approximately 6 – 8 hour postdose), and at predose on week 4, 8 and 12 visits

End point values	Ozanimod Hydrochloride (HCl) 1 mg			
Subject group type	Reporting group			
Number of subjects analysed	68			
Units: mean pM				
number (not applicable)				
Day 1 - Male (32 total)	173.6754			
Day 1 - Female (36 toal)	202.2904			
Steady State - Male (32 total)	8295.396			
Steady State - Female (36 total)	10988.31			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change from Baseline in Absolute Lymphocyte Count (ALC) Derived from Hematology Laboratory Results at Weeks 4, 8 and 12

End point title	Change from Baseline in Absolute Lymphocyte Count (ALC) Derived from Hematology Laboratory Results at Weeks 4, 8 and 12

End point description:

Change in Absolute Lymphocyte Count (ALC) from baseline was determined by compared to baseline.

End point type	Other pre-specified

End point timeframe:

Baseline up to Weeks 4, 8 and 12

End point values	Ozanimod Hydrochloride (HCl) 1 mg			
Subject group type	Reporting group			
Number of subjects analysed	65			
Units: 10 ^9 cells/L				
arithmetic mean (standard deviation)				

Week 4	-0.946 (± 0.783)			
Week 8	-1.086 (± 0.778)			
Week 12	-1.092 (± 0.783)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From the first day of ozanimod up to 90 days after the last dose of ozanimod; mean duration of exposure of study drug was 1.305 years

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18.1

Reporting groups

Reporting group title	RPC1063 1.0 mg

Reporting group description:

Participants received ozanimod 1 mg capsules daily for the first 12 weeks of the induction period (an initial 7-day dose escalation regimen that consisted of 4 days of ozanimod HCl 0.25 mg (equivalent to ozanimod 0.23 mg) daily followed by 3 days of ozanimod HCl 0.5 mg (equivalent to ozanimod 0.46 mg) daily, with the final dose of ozanimod HCl 1 mg (equivalent to ozanimod 0.92 mg) daily dose reached on Day 8. Participants who completed the induction period had the opportunity at Week 12 to continue to receive ozanimod 1 mg capsules daily during the extension period up to an additional 148 weeks, provided that the investigator determined that the participant should continue. Participants in the extension period continued to receive ozanimod 1 mg capsules daily through Week 160. Participants who completed the Week 160 visit had the option to continue open-label ozanimod 1 mg capsules by immediately entering the open-label extension Phase 3 Crohn's Disease Study RPC01-3204 (NCT03467958).

Serious adverse events	RPC1063 1.0 mg		
Total subjects affected by serious adverse events			
subjects affected / exposed	18 / 69 (26.09%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Pancreatic carcinoma			
subjects affected / exposed	1 / 69 (1.45%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 69 (1.45%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal pain upper			

subjects affected / exposed	1 / 69 (1.45%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Anal fistula				
subjects affected / exposed	1 / 69 (1.45%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Crohn's disease				
subjects affected / exposed	6 / 69 (8.70%)			
occurrences causally related to treatment / all	0 / 6			
deaths causally related to treatment / all	0 / 0			
Enterocolonic fistula				
subjects affected / exposed	1 / 69 (1.45%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Enterocutaneous fistula				
subjects affected / exposed	1 / 69 (1.45%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Fistula of small intestine				
subjects affected / exposed	1 / 69 (1.45%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Intestinal fistula				
subjects affected / exposed	1 / 69 (1.45%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Intestinal obstruction				
subjects affected / exposed	1 / 69 (1.45%)			
occurrences causally related to treatment / all	0 / 5			
deaths causally related to treatment / all	0 / 0			
Pancreatitis acute				

subjects affected / exposed	1 / 69 (1.45%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Small intestinal obstruction				
subjects affected / exposed	2 / 69 (2.90%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Renal and urinary disorders				
Renal colic				
subjects affected / exposed	1 / 69 (1.45%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Abdominal abscess				
subjects affected / exposed	2 / 69 (2.90%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Anal abscess				
subjects affected / exposed	1 / 69 (1.45%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Campylobacter infection				
subjects affected / exposed	1 / 69 (1.45%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Diverticulitis				
subjects affected / exposed	1 / 69 (1.45%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Sepsis				
subjects affected / exposed	1 / 69 (1.45%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Metabolism and nutrition disorders				

Dehydration			
subjects affected / exposed	1 / 69 (1.45%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	RPC1063 1.0 mg		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	47 / 69 (68.12%)		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	6 / 69 (8.70%)		
occurrences (all)	6		
Aspartate aminotransferase increased			
subjects affected / exposed	5 / 69 (7.25%)		
occurrences (all)	5		
C-reactive protein increased			
subjects affected / exposed	4 / 69 (5.80%)		
occurrences (all)	9		
Gamma-glutamyltransferase increased			
subjects affected / exposed	5 / 69 (7.25%)		
occurrences (all)	7		
Nervous system disorders			
Dizziness			
subjects affected / exposed	4 / 69 (5.80%)		
occurrences (all)	4		
Headache			
subjects affected / exposed	4 / 69 (5.80%)		
occurrences (all)	4		
Paraesthesia			
subjects affected / exposed	4 / 69 (5.80%)		
occurrences (all)	6		
Blood and lymphatic system disorders			

Anaemia			
subjects affected / exposed	5 / 69 (7.25%)		
occurrences (all)	5		
Lymphopenia			
subjects affected / exposed	9 / 69 (13.04%)		
occurrences (all)	12		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	10 / 69 (14.49%)		
occurrences (all)	13		
Abdominal pain lower			
subjects affected / exposed	4 / 69 (5.80%)		
occurrences (all)	8		
Abdominal pain upper			
subjects affected / exposed	6 / 69 (8.70%)		
occurrences (all)	6		
Crohn's disease			
subjects affected / exposed	15 / 69 (21.74%)		
occurrences (all)	25		
Diarrhoea			
subjects affected / exposed	5 / 69 (7.25%)		
occurrences (all)	5		
Nausea			
subjects affected / exposed	9 / 69 (13.04%)		
occurrences (all)	16		
Vomiting			
subjects affected / exposed	5 / 69 (7.25%)		
occurrences (all)	5		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	9 / 69 (13.04%)		
occurrences (all)	13		
Infections and infestations			
Sinusitis			
subjects affected / exposed	5 / 69 (7.25%)		
occurrences (all)	7		

Upper respiratory tract infection subjects affected / exposed occurrences (all) Urinary tract infection subjects affected / exposed occurrences (all)	 5 / 69 (7.25%) 6 5 / 69 (7.25%) 6		
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	 4 / 69 (5.80%) 4		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 July 2015	• Addition of clinically relevant cardiovascular condition to exclusion criterion (Exclusion Criterion 12) • Added section for Un-weighted Stool Frequency and Abdominal Pain • Added section for planned Data Safety Monitoring Board
09 June 2017	• The extension period was extended by 48 weeks for a total trialstudy period of 160 weeks • The complete PE was to be performed at Week 160 rather than Week 112 • An additional PFT and OCT assessment was added at Week 112
29 May 2018	• A 75-day (±10 days) Safety Follow-up Visit was added. • Added the option for subjects who complete the Week 160 visit to enter the open label extension Phase 3 Crohn's disease Study RPC01-3204.
24 May 2019	• Change to safety follow up from 75 days to 90-day (±10 days) Safety Follow-up Visit

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported