Clinical trial results:
A Phase 3, Multicenter, Randomized, Double-blind, Placebo-controlled Trial of Oral RPC1063 as Induction and Maintenance Therapy for Moderate to Severe Ulcerative Colitis

Summary

EudraCT number	2015-000319-41
Trial protocol	DE SK HU CZ NL GB BE BG PL HR LV AT GR ES IT
Global end of trial date	17 June 2020

Results information

Result version number	v1 (current)
This version publication date	03 July 2021
First version publication date	03 July 2021

Trial information

Trial identification

Sponsor protocol code	RPC01-3101

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Bristol-Myers Squibb
Sponsor organisation address	Chaussee de la Hulpe 185, Brussels, Belgium, 1170
Public contact	Bristol-Myers Squibb International Corporation, EU Study Start-up Unit, 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	04 August 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	17 June 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The objective of the RPC1063 clinical development program in UC is to demonstrate that RPC1063 administered orally is safe and effective in inducing and maintaining remission in patients with moderate to severe UC.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Conference on Harmonization Good Clinical Practice Guidelines. All the local regulatory requirements pertinent to safety of trial subjects were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	13 October 2014
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 9
Country: Number of subjects enrolled	Israel: 25
Country: Number of subjects enrolled	Korea, Republic of: 48
Country: Number of subjects enrolled	Belarus: 18
Country: Number of subjects enrolled	Bulgaria: 22
Country: Number of subjects enrolled	Croatia: 6
Country: Number of subjects enrolled	Czechia: 33
Country: Number of subjects enrolled	Georgia: 30
Country: Number of subjects enrolled	Hungary: 26
Country: Number of subjects enrolled	Moldova, Republic of: 21
Country: Number of subjects enrolled	Poland: 76
Country: Number of subjects enrolled	Romania: 21
Country: Number of subjects enrolled	Russian Federation: 102
Country: Number of subjects enrolled	Serbia: 64
Country: Number of subjects enrolled	Slovakia: 4
Country: Number of subjects enrolled	Ukraine: 99
Country: Number of subjects enrolled	Canada: 33
Country: Number of subjects enrolled	United States: 214
Country: Number of subjects enrolled	South Africa: 9

Country: Number of subjects enrolled	Argentina: 3
Country: Number of subjects enrolled	Germany: 33
Country: Number of subjects enrolled	Italy: 60
Country: Number of subjects enrolled	Netherlands: 17
Country: Number of subjects enrolled	United Kingdom: 13
Country: Number of subjects enrolled	Belgium: 19
Country: Number of subjects enrolled	Greece: 1
Country: Number of subjects enrolled	Latvia: 4
Country: Number of subjects enrolled	New Zealand: 1
Country: Number of subjects enrolled	Austria: 1
Worldwide total number of subjects	1012
EEA total number of subjects	323

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)	958
From 65 to 84 years	54
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

1012 randomized and treated

Period 1

Period 1 title	Induction Period
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	RPC1063 Cohort 1 (Induction Period)

Arm description:

- Blinded
-On Days 1 to 4, RPC1063/ozanimod HCl 0.25 mg (equivalent to ozanimod 0.23 mg) or matching placebo once daily (one 0.25 mg capsule) -On Days 5 to 7, RPC1063/ozanimod HCl 0.5 mg (equivalent to ozanimod 0.46 mg) or matching placebo once daily (two 0.25 mg capsules) -On Day 8, patients will receive the final dose RPC1063/ozanimod HCl 1 mg (equivalent to ozanimod 0.92 mg) or matching placebo once daily for 9 weeks (one 1 mg capsule)

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

Dosage and administration details:

0.25mg

Investigational medicinal product name	Ozanimod HCl
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

0.5mg (2 x 0.25mg)

Investigational medicinal product name	Ozanimod HCl
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

1mg

Arm title	Placebo (Induction Period)

Arm description:

Placebo Blinded

Arm type	Placebo

Investigational medicinal product name	placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

0.25mg

Investigational medicinal product name	placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

1mg

Investigational medicinal product name	placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

0.5mg

Arm title	RPC1063 Cohort 2 (Induction Period)

Arm description:

- Open Label
-On Days 1 to 4, RPC1063/ozanimod HCl 0.25 mg (equivalent to ozanimod 0.23 mg) or matching placebo once daily (one 0.25 mg capsule) -On Days 5 to 7, RPC1063/ozanimod HCl 0.5 mg (equivalent to ozanimod 0.46 mg) or matching placebo once daily (two 0.25 mg capsules) -On Day 8, patients will receive the final dose RPC1063/ozanimod HCl 1 mg (equivalent to ozanimod 0.92 mg) or matching placebo once daily for 9 weeks (one 1 mg capsule)

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

Dosage and administration details:

0.25mg

Investigational medicinal product name	Ozanimod HCl
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

0.5mg (2 x 0.25mg)

Investigational medicinal product name	Ozanimod HCl
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

1mg

Number of subjects in period 1	RPC1063 Cohort 1 (Induction Period)	Placebo (Induction Period)	RPC1063 Cohort 2 (Induction Period)
Started	429	216	367
Transition to Maintenance Period	233 [1]	69 [2]	224 [3]
Treated in Maintenance Period	0 [4]	69 [5]	0 [6]
Completed	401	192	324
Not completed	28	24	43
Consent withdrawn by subject	10	8	20
Physician decision	-	-	1
non compliance with protocol	2	-	1
Adverse event, non-fatal	11	6	12
Other Reason	1	-	-
Lack of efficacy	4	10	9

Notes:

[1] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Subjects from this arm were re randomized to the maintenance period

[2] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Subjects from this arm either were re randomized to the maintenance period, or continued in this arm throughout the study

[3] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Subjects from this arm were re randomized to the maintenance period

[4] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Subjects from this arm were re randomized to the maintenance period

[5] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Subjects from this arm were re randomized to the maintenance period

[6] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Subjects from this arm were re randomized to the maintenance period

Period 2

Period 2 title	Maintenance Period
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Blinding implementation details:

This population was re-randomized and blinded from subjects which were treated in the induction period.

Arms	
Are arms mutually exclusive?	No
Arm title	RPC01063 Maintenance Period

Arm description:

-Blinded
RPC1063/ozanimod HCl 1 mg (equivalent to ozanimod 0.92 mg) once daily for 42 weeks (one 1 mg capsule)

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

Dosage and administration details:

1mg

Arm title	Placebo Maintenance Period

Arm description:

Placebo
Blinded

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

Dosage and administration details:

1mg

Arm title	Placebo

Arm description:

Subjects from Induction period placebo arm who continued on placebo during maintenance

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

Dosage and administration details:

1mg

Number of subjects in period 2	RPC01063 Maintenance Period	Placebo Maintenance Period	Placebo
Started	230	227	69
Completed	184	124	45
Not completed	46	103	24
discontinued treatment	12	22	2
entered open label extension	34	81	22

Baseline characteristics

Reporting groups	
Reporting group title	RPC1063 Cohort 1 (Induction Period)
Reporting group description:	
- Blinded -On Days 1 to 4, RPC1063/ozanimod HCl 0.25 mg (equivalent to ozanimod 0.23 mg) or matching placebo once daily (one 0.25 mg capsule) -On Days 5 to 7, RPC1063/ozanimod HCl 0.5 mg (equivalent to ozanimod 0.46 mg) or matching placebo once daily (two 0.25 mg capsules) -On Day 8, patients will receive the final dose RPC1063/ozanimod HCl 1 mg (equivalent to ozanimod 0.92 mg) or matching placebo once daily for 9 weeks (one 1 mg capsule)	
Reporting group title	Placebo (Induction Period)
Reporting group description:	
Placebo Blinded	
Reporting group title	RPC1063 Cohort 2 (Induction Period)
Reporting group description:	
- Open Label -On Days 1 to 4, RPC1063/ozanimod HCl 0.25 mg (equivalent to ozanimod 0.23 mg) or matching placebo once daily (one 0.25 mg capsule) -On Days 5 to 7, RPC1063/ozanimod HCl 0.5 mg (equivalent to ozanimod 0.46 mg) or matching placebo once daily (two 0.25 mg capsules) -On Day 8, patients will receive the final dose RPC1063/ozanimod HCl 1 mg (equivalent to ozanimod 0.92 mg) or matching placebo once daily for 9 weeks (one 1 mg capsule)	

Reporting group values	RPC1063 Cohort 1 (Induction Period)	Placebo (Induction Period)	RPC1063 Cohort 2 (Induction Period)
Number of subjects	429	216	367
Age categorical Units: Subjects			
Adults (18-64 years)	410	202	346
From 65-84 years	19	14	21
Age Continuous Units: Years			
arithmetic mean	41.4	41.9	42.1
standard deviation	± 13.54	± 13.64	± 13.72
Sex: Female, Male Units: Participants			
Female	184	73	153
Male	245	143	214
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	36	17	12
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	14	4	10
White	370	192	336
Unknown or Not Reported	9	3	9
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	26	8	16
Not Hispanic or Latino	403	208	351
Unknown or Not Reported	0	0	0

Reporting group values	Total		
Number of subjects	1012		
Age categorical Units: Subjects			
Adults (18-64 years)	958		
From 65-84 years	54		
Age Continuous Units: Years			
arithmetic mean			
standard deviation	-		
Sex: Female, Male Units: Participants			
Female	410		
Male	602		
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0		
Asian	65		
Native Hawaiian or Other Pacific Islander	0		
Black or African American	28		
White	898		
Unknown or Not Reported	21		
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	50		
Not Hispanic or Latino	962		
Unknown or Not Reported	0		

End points

End points reporting groups

Reporting group title	RPC1063 Cohort 1 (Induction Period)
Reporting group description:	
- Blinded -On Days 1 to 4, RPC1063/ozanimod HCl 0.25 mg (equivalent to ozanimod 0.23 mg) or matching placebo once daily (one 0.25 mg capsule) -On Days 5 to 7, RPC1063/ozanimod HCl 0.5 mg (equivalent to ozanimod 0.46 mg) or matching placebo once daily (two 0.25 mg capsules) -On Day 8, patients will receive the final dose RPC1063/ozanimod HCl 1 mg (equivalent to ozanimod 0.92 mg) or matching placebo once daily for 9 weeks (one 1 mg capsule)	

Reporting group title	Placebo (Induction Period)
Reporting group description:	
Placebo Blinded	

Reporting group title	RPC1063 Cohort 2 (Induction Period)
Reporting group description:	
- Open Label -On Days 1 to 4, RPC1063/ozanimod HCl 0.25 mg (equivalent to ozanimod 0.23 mg) or matching placebo once daily (one 0.25 mg capsule) -On Days 5 to 7, RPC1063/ozanimod HCl 0.5 mg (equivalent to ozanimod 0.46 mg) or matching placebo once daily (two 0.25 mg capsules) -On Day 8, patients will receive the final dose RPC1063/ozanimod HCl 1 mg (equivalent to ozanimod 0.92 mg) or matching placebo once daily for 9 weeks (one 1 mg capsule)	

Reporting group title	RPC01063 Maintenance Period
Reporting group description:	
-Blinded RPC1063/ozanimod HCl 1 mg (equivalent to ozanimod 0.92 mg) once daily for 42 weeks (one 1 mg capsule)	

Reporting group title	Placebo Maintenance Period
Reporting group description:	
Placebo Blinded	

Reporting group title	Placebo
Reporting group description:	
Subjects from Induction period placebo arm who continued on placebo during maintenance	

Primary: Percentage of Participants in Clinical Remission at 10 weeks

End point title	Percentage of Participants in Clinical Remission at 10 weeks
End point description:	
Percentage of participants that are in Clinical remission at 10 weeks	

End point type	Primary
End point timeframe:	
At 10 Weeks	

End point values	RPC1063 Cohort 1 (Induction Period)	Placebo (Induction Period)	RPC1063 Cohort 2 (Induction Period)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	429	216	367	
Units: Percentage				
number (not applicable)	18.4	6.0	21.0	

Statistical analyses

Statistical analysis title	RPC1063 vs Placebo in Induction Period
Comparison groups	Placebo (Induction Period) v RPC1063 Cohort 1 (Induction Period)
Number of subjects included in analysis	645
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	3.586
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.938
upper limit	6.636

Primary: Percentage of Participants in Clinical Remission at 52 weeks

End point title	Percentage of Participants in Clinical Remission at 52 weeks
End point description:	
Percentage of participants that are in Clinical remission at 52 weeks	
End point type	Primary
End point timeframe:	
At 52 Weeks	

End point values	RPC01063 Maintenance Period	Placebo Maintenance Period	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	230	227	69	
Units: Percentage				
number (not applicable)	37.0	18.5	24.6	

Statistical analyses

Statistical analysis title	SAP of RPC01063 vs Placebo in Maintenance Period
Comparison groups	RPC01063 Maintenance Period v Placebo Maintenance Period
Number of subjects included in analysis	457
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	2.755
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.767
upper limit	4.294

Secondary: Percentage of Participants with clinical response at 10 weeks

End point title	Percentage of Participants with clinical response at 10 weeks
End point description:	
Percentage of participants that are in Clinical response at 10 weeks	
End point type	Secondary
End point timeframe:	
At 10 Weeks	

End point values	RPC1063 Cohort 1 (Induction Period)	Placebo (Induction Period)	RPC1063 Cohort 2 (Induction Period)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	429	216	367	
Units: Percentage				
number (not applicable)	47.8	25.9	52.6	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with endoscopic improvement at 10 weeks

End point title	Percentage of Participants with endoscopic improvement at 10 weeks
End point description:	
Percentage of participants with endoscopic improvement at 10 weeks	
End point type	Secondary

End point timeframe:
At 10 Weeks

End point values	RPC1063 Cohort 1 (Induction Period)	Placebo (Induction Period)	RPC1063 Cohort 2 (Induction Period)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	429	216	367	
Units: Percentage				
number (not applicable)	27.3	12.0	27.2	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with mucosal healing at 10 weeks

End point title	Percentage of Participants with mucosal healing at 10 weeks

End point description:
Percentage of participants with mucosal healing at 10 weeks

End point type	Secondary

End point timeframe:
At 10 Weeks

End point values	RPC1063 Cohort 1 (Induction Period)	Placebo (Induction Period)	RPC1063 Cohort 2 (Induction Period)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	429	216	367	
Units: Percentage				
number (not applicable)	12.6	3.7	11.4	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants in Clinical Response at 52 weeks

End point title	Percentage of Participants in Clinical Response at 52 weeks

End point description:
Percentage of participants that are in Clinical response at 52 weeks

End point type	Secondary

End point timeframe:

At 52 Weeks

End point values	RPC01063 Maintenance Period	Placebo Maintenance Period	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	230	227	69	
Units: Percentage				
number (not applicable)	60.0	41.0	39.1	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with endoscopic improvement at 52 weeks

End point title	Percentage of participants with endoscopic improvement at 52 weeks

End point description:

Percentage of participants with endoscopic improvement at 52 weeks

End point type	Secondary

End point timeframe:

At 52 Weeks

End point values	RPC01063 Maintenance Period	Placebo Maintenance Period	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	230	227	69	
Units: Percentage				
number (not applicable)	45.7	26.4	29.0	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants in clinical remission at week 52 who were in remission at week 10

End point title	Percentage of participants in clinical remission at week 52 who were in remission at week 10

End point description:

Percentage of participants in clinical remission at week 52 who were in clinical remission at week 10

End point type	Secondary

End point timeframe:

At 52 Weeks

End point values	RPC01063 Maintenance Period	Placebo Maintenance Period	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	230	227	69	
Units: Percentage				
number (not applicable)	51.9	29.3	41.7	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with corticosteroid free remission at 52 weeks

End point title	Percentage of participants with corticosteroid free remission at 52 weeks

End point description:

Percentage of participants with corticosteroid free remission at 52 weeks

End point type	Secondary

End point timeframe:

At 52 Weeks

End point values	RPC01063 Maintenance Period	Placebo Maintenance Period	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	230	227	69	
Units: Percentage				
number (not applicable)	31.7	16.7	24.6	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with Mucosal Healing at 52 weeks

End point title	Percentage of participants with Mucosal Healing at 52 weeks

End point description:

Percentage of participants with Mucosal Healing at 52 weeks

End point type	Secondary

End point timeframe:
At 52 Weeks

End point values	RPC01063 Maintenance Period	Placebo Maintenance Period	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	230	227	69	
Units: Percentage				
number (not applicable)	29.6	14.1	10.1	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with durable clinical remission at 52 weeks

End point title	Percentage of participants with durable clinical remission at 52 weeks

End point description:
Percentage of participants with durable clinical remission at 52 weeks

End point type	Secondary

End point timeframe:
At 52 Weeks

End point values	RPC01063 Maintenance Period	Placebo Maintenance Period	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	230	227	69	
Units: Percentage				
number (not applicable)	17.8	9.7	7.2	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Approximately up to 52 Weeks

Adverse event reporting additional description:

Participant overlap due to re randomization occuring before maintenance phase

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	22.1

Reporting groups

Reporting group title	Cohort 1 (Induction Period): RPC1063 1mg

Reporting group description:

- Blinded
-On Days 1 to 4, RPC1063/ozanimod HCl 0.25 mg (equivalent to ozanimod 0.23 mg) or matching placebo once daily (one 0.25 mg capsule) -On Days 5 to 7, RPC1063/ozanimod HCl 0.5 mg (equivalent to ozanimod 0.46 mg) or matching placebo once daily (two 0.25 mg capsules) -On Day 8, patients will receive the final dose RPC1063/ozanimod HCl 1 mg (equivalent to ozanimod 0.92 mg) or matching placebo once daily for 9 weeks (one 1 mg capsule)

Reporting group title	Cohort 1: Placebo

Reporting group description:

Placebo Blinded

Reporting group title	Cohort 2 (Induction Period): RPC1063 1mg

Reporting group description:

- Open Label
-On Days 1 to 4, RPC1063/ozanimod HCl 0.25 mg (equivalent to ozanimod 0.23 mg) or matching placebo once daily (one 0.25 mg capsule) -On Days 5 to 7, RPC1063/ozanimod HCl 0.5 mg (equivalent to ozanimod 0.46 mg) or matching placebo once daily (two 0.25 mg capsules) -On Day 8, patients will receive the final dose RPC1063/ozanimod HCl 1 mg (equivalent to ozanimod 0.92 mg) or matching placebo once daily for 9 weeks (one 1 mg capsule)

Reporting group title	RPC01063 Maintenance Period

Reporting group description:

-Blinded
RPC1063/ozanimod HCl 1 mg (equivalent to ozanimod 0.92 mg) once daily for 42 weeks (one 1 mg capsule)

Reporting group title	Placebo (Maintenance Period): Placebo

Reporting group description:

Placebo Blinded

Serious adverse events	Cohort 1 (Induction Period): RPC1063 1mg	Cohort 1: Placebo	Cohort 2 (Induction Period): RPC1063 1mg
Total subjects affected by serious adverse events			
subjects affected / exposed	17 / 429 (3.96%)	11 / 216 (5.09%)	23 / 367 (6.27%)
number of deaths (all causes)	0	0	1
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma of colon			

subjects affected / exposed	0 / 429 (0.00%)	0 / 216 (0.00%)	0 / 367 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Breast cancer			
subjects affected / exposed	0 / 429 (0.00%)	0 / 216 (0.00%)	0 / 367 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cervix carcinoma stage 0			
subjects affected / exposed	0 / 429 (0.00%)	0 / 216 (0.00%)	1 / 367 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal adenocarcinoma			
subjects affected / exposed	0 / 429 (0.00%)	0 / 216 (0.00%)	0 / 367 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypertensive crisis			
subjects affected / exposed	0 / 429 (0.00%)	0 / 216 (0.00%)	0 / 367 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 429 (0.00%)	1 / 216 (0.46%)	0 / 367 (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
Immune system disorders			
Food allergy			
subjects affected / exposed	0 / 429 (0.00%)	0 / 216 (0.00%)	0 / 367 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Acute respiratory distress syndrome			

subjects affected / exposed	0 / 429 (0.00%)	0 / 216 (0.00%)	1 / 367 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Investigations			
Respiratory syncytial virus test positive			
subjects affected / exposed	0 / 429 (0.00%)	0 / 216 (0.00%)	1 / 367 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Accidental overdose			
subjects affected / exposed	1 / 429 (0.23%)	0 / 216 (0.00%)	0 / 367 (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
Concussion			
subjects affected / exposed	0 / 429 (0.00%)	0 / 216 (0.00%)	1 / 367 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Contusion			
subjects affected / exposed	0 / 429 (0.00%)	0 / 216 (0.00%)	1 / 367 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neck injury			
subjects affected / exposed	0 / 429 (0.00%)	0 / 216 (0.00%)	1 / 367 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Road traffic accident			
subjects affected / exposed	0 / 429 (0.00%)	0 / 216 (0.00%)	1 / 367 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Toxicity to various agents			
subjects affected / exposed	0 / 429 (0.00%)	0 / 216 (0.00%)	0 / 367 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 429 (0.00%)	0 / 216 (0.00%)	1 / 367 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery stenosis			
subjects affected / exposed	0 / 429 (0.00%)	0 / 216 (0.00%)	1 / 367 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericarditis			
subjects affected / exposed	0 / 429 (0.00%)	0 / 216 (0.00%)	0 / 367 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 429 (0.23%)	0 / 216 (0.00%)	0 / 367 (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
Ischaemic stroke			
subjects affected / exposed	1 / 429 (0.23%)	0 / 216 (0.00%)	0 / 367 (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
Syncope			
subjects affected / exposed	0 / 429 (0.00%)	0 / 216 (0.00%)	0 / 367 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	4 / 429 (0.93%)	0 / 216 (0.00%)	1 / 367 (0.27%)
occurrences causally related to treatment / all	0 / 5	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Cataract			

subjects affected / exposed	0 / 429 (0.00%)	0 / 216 (0.00%)	0 / 367 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Photophobia			
subjects affected / exposed	1 / 429 (0.23%)	0 / 216 (0.00%)	0 / 367 (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
Gastrointestinal disorders			
Colitis ulcerative			
subjects affected / exposed	6 / 429 (1.40%)	5 / 216 (2.31%)	9 / 367 (2.45%)
occurrences causally related to treatment / all	0 / 6	2 / 5	0 / 9
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	0 / 429 (0.00%)	1 / 216 (0.46%)	0 / 367 (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
Diarrhoea haemorrhagic			
subjects affected / exposed	0 / 429 (0.00%)	1 / 216 (0.46%)	0 / 367 (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
Enterocolitis			
subjects affected / exposed	0 / 429 (0.00%)	1 / 216 (0.46%)	0 / 367 (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
Gastritis			
subjects affected / exposed	1 / 429 (0.23%)	0 / 216 (0.00%)	0 / 367 (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
Haemorrhoids			
subjects affected / exposed	0 / 429 (0.00%)	0 / 216 (0.00%)	1 / 367 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Melaena			

subjects affected / exposed	0 / 429 (0.00%)	0 / 216 (0.00%)	1 / 367 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Proctitis ulcerative			
subjects affected / exposed	0 / 429 (0.00%)	0 / 216 (0.00%)	0 / 367 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 429 (0.00%)	0 / 216 (0.00%)	0 / 367 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	0 / 429 (0.00%)	0 / 216 (0.00%)	0 / 367 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholelithiasis			
subjects affected / exposed	0 / 429 (0.00%)	0 / 216 (0.00%)	0 / 367 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Calculus urinary			
subjects affected / exposed	0 / 429 (0.00%)	1 / 216 (0.46%)	0 / 367 (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
Nephrolithiasis			
subjects affected / exposed	1 / 429 (0.23%)	0 / 216 (0.00%)	0 / 367 (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
Urethral stenosis			
subjects affected / exposed	0 / 429 (0.00%)	0 / 216 (0.00%)	0 / 367 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue			

disorders			
Arthralgia			
subjects affected / exposed	1 / 429 (0.23%)	0 / 216 (0.00%)	0 / 367 (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
Myalgia			
subjects affected / exposed	1 / 429 (0.23%)	0 / 216 (0.00%)	0 / 367 (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			
Appendicitis			
subjects affected / exposed	1 / 429 (0.23%)	0 / 216 (0.00%)	2 / 367 (0.54%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	0 / 429 (0.00%)	1 / 216 (0.46%)	0 / 367 (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
Clostridium difficile infection			
subjects affected / exposed	0 / 429 (0.00%)	0 / 216 (0.00%)	0 / 367 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Complicated appendicitis			
subjects affected / exposed	0 / 429 (0.00%)	0 / 216 (0.00%)	0 / 367 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 429 (0.00%)	0 / 216 (0.00%)	2 / 367 (0.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis norovirus			
subjects affected / exposed	0 / 429 (0.00%)	0 / 216 (0.00%)	0 / 367 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Large intestine infection			
subjects affected / exposed	0 / 429 (0.00%)	1 / 216 (0.46%)	0 / 367 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Measles			
subjects affected / exposed	0 / 429 (0.00%)	0 / 216 (0.00%)	0 / 367 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nasopharyngitis			
subjects affected / exposed	1 / 429 (0.23%)	0 / 216 (0.00%)	0 / 367 (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
Pneumonia influenzal			
subjects affected / exposed	0 / 429 (0.00%)	0 / 216 (0.00%)	1 / 367 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Pyelonephritis			
subjects affected / exposed	1 / 429 (0.23%)	0 / 216 (0.00%)	0 / 367 (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
Urinary tract infection			
subjects affected / exposed	0 / 429 (0.00%)	0 / 216 (0.00%)	1 / 367 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vestibular neuronitis			
subjects affected / exposed	1 / 429 (0.23%)	0 / 216 (0.00%)	0 / 367 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Yersinia infection			
subjects affected / exposed	0 / 429 (0.00%)	0 / 216 (0.00%)	0 / 367 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			

Dehydration			
subjects affected / exposed	0 / 429 (0.00%)	1 / 216 (0.46%)	1 / 367 (0.27%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	RPC01063 Maintenance Period	Placebo (Maintenance Period): Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	12 / 230 (5.22%)	18 / 227 (7.93%)	
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)			
Adenocarcinoma of colon			
subjects affected / exposed	0 / 230 (0.00%)	1 / 227 (0.44%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast cancer			
subjects affected / exposed	0 / 230 (0.00%)	1 / 227 (0.44%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cervix carcinoma stage 0			
subjects affected / exposed	0 / 230 (0.00%)	0 / 227 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal adenocarcinoma			
subjects affected / exposed	1 / 230 (0.43%)	0 / 227 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Hypertensive crisis			
subjects affected / exposed	1 / 230 (0.43%)	1 / 227 (0.44%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Pyrexia			

subjects affected / exposed	0 / 230 (0.00%)	0 / 227 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Food allergy			
subjects affected / exposed	1 / 230 (0.43%)	0 / 227 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Acute respiratory distress syndrome			
subjects affected / exposed	0 / 230 (0.00%)	0 / 227 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Respiratory syncytial virus test positive			
subjects affected / exposed	0 / 230 (0.00%)	0 / 227 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Accidental overdose			
subjects affected / exposed	0 / 230 (0.00%)	0 / 227 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Concussion			
subjects affected / exposed	0 / 230 (0.00%)	0 / 227 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Contusion			
subjects affected / exposed	0 / 230 (0.00%)	0 / 227 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neck injury			

subjects affected / exposed	0 / 230 (0.00%)	0 / 227 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Road traffic accident			
subjects affected / exposed	0 / 230 (0.00%)	0 / 227 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Toxicity to various agents			
subjects affected / exposed	1 / 230 (0.43%)	0 / 227 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 230 (0.00%)	0 / 227 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery stenosis			
subjects affected / exposed	0 / 230 (0.00%)	0 / 227 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericarditis			
subjects affected / exposed	1 / 230 (0.43%)	0 / 227 (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			
Headache			
subjects affected / exposed	0 / 230 (0.00%)	0 / 227 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic stroke			
subjects affected / exposed	0 / 230 (0.00%)	0 / 227 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			

subjects affected / exposed	1 / 230 (0.43%)	0 / 227 (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 / 230 (0.43%)	0 / 227 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Cataract			
subjects affected / exposed	1 / 230 (0.43%)	0 / 227 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Photophobia			
subjects affected / exposed	0 / 230 (0.00%)	0 / 227 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Colitis ulcerative			
subjects affected / exposed	1 / 230 (0.43%)	9 / 227 (3.96%)	
occurrences causally related to treatment / all	0 / 1	1 / 9	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	0 / 230 (0.00%)	0 / 227 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea haemorrhagic			
subjects affected / exposed	0 / 230 (0.00%)	0 / 227 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterocolitis			
subjects affected / exposed	0 / 230 (0.00%)	0 / 227 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Gastritis			
subjects affected / exposed	0 / 230 (0.00%)	0 / 227 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhoids			
subjects affected / exposed	0 / 230 (0.00%)	0 / 227 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Melaena			
subjects affected / exposed	0 / 230 (0.00%)	0 / 227 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Proctitis ulcerative			
subjects affected / exposed	1 / 230 (0.43%)	0 / 227 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	0 / 230 (0.00%)	1 / 227 (0.44%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	0 / 230 (0.00%)	1 / 227 (0.44%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholelithiasis			
subjects affected / exposed	0 / 230 (0.00%)	1 / 227 (0.44%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Calculus urinary			
subjects affected / exposed	0 / 230 (0.00%)	0 / 227 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Nephrolithiasis			
subjects affected / exposed	0 / 230 (0.00%)	0 / 227 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urethral stenosis			
subjects affected / exposed	0 / 230 (0.00%)	1 / 227 (0.44%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 230 (0.00%)	0 / 227 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myalgia			
subjects affected / exposed	0 / 230 (0.00%)	0 / 227 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 230 (0.00%)	1 / 227 (0.44%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	0 / 230 (0.00%)	0 / 227 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium difficile infection			
subjects affected / exposed	1 / 230 (0.43%)	0 / 227 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Complicated appendicitis			
subjects affected / exposed	0 / 230 (0.00%)	2 / 227 (0.88%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

Gastroenteritis			
subjects affected / exposed	0 / 230 (0.00%)	0 / 227 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis norovirus			
subjects affected / exposed	1 / 230 (0.43%)	0 / 227 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestine infection			
subjects affected / exposed	0 / 230 (0.00%)	0 / 227 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Measles			
subjects affected / exposed	0 / 230 (0.00%)	1 / 227 (0.44%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nasopharyngitis			
subjects affected / exposed	0 / 230 (0.00%)	0 / 227 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia influenzal			
subjects affected / exposed	0 / 230 (0.00%)	0 / 227 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			
subjects affected / exposed	0 / 230 (0.00%)	0 / 227 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	0 / 230 (0.00%)	0 / 227 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vestibular neuronitis			

subjects affected / exposed	0 / 230 (0.00%)	0 / 227 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Yersinia infection			
subjects affected / exposed	0 / 230 (0.00%)	1 / 227 (0.44%)	
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	0 / 230 (0.00%)	0 / 227 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Cohort 1 (Induction Period): RPC1063 1mg	Cohort 1: Placebo	Cohort 2 (Induction Period): RPC1063 1mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	15 / 429 (3.50%)	13 / 216 (6.02%)	15 / 367 (4.09%)
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	15 / 429 (3.50%)	13 / 216 (6.02%)	15 / 367 (4.09%)
occurrences (all)	20	14	19

Non-serious adverse events	RPC01063 Maintenance Period	Placebo (Maintenance Period): Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 230 (0.87%)	4 / 227 (1.76%)	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 230 (0.87%)	4 / 227 (1.76%)	
occurrences (all)	2	5	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
07 December 2017	The number of investigators was updated to more accurately reflect the current number of investigators planned in this study. The estimated date of last patient completed was updated based on the current estimated enrollment rate. The proportion of patients in Cohort 1 and Cohort 2 have been adjusted to allow us to reinstate the original limit of ≤ 30% of patients who have received anti-TNF from RPC01-3101 protocol version 2.0, 2.1, 2.2, and 2.3. It is planned that the total sample size of the trial will remain unchanged. The original limit of ≤ 30% of patients who have received anti-TNF from RPC01-3101 protocol version 2.0, 2.1, 2.2, and 2.3 has been reinstated for Cohort 1. A limit of ≤ 50% has been established for Cohort 2. These limits have been established based on ongoing development programs in UC that have confirmed that patients with anti-TNF experience achieve limited clinical response. Study procedures have been clarified to allow for continuous enrollment of patients who have received anti-TNF therapy.
07 December 2017	A clarification was made to allow access to OCT images especially in case of suspicion of macular edema. Clarification was made to allow sites with qualified personnel to perform the pulmonary function test onsite under the supervision of a pulmonologist. A change was made to underscore that it is the choice of the patient to receive the VZV vaccination. A correction was made for patients who test positive for HBs antigen. While patients who test positive for HBs antigen will still be excluded, the presence of the HBs antibody alone is the result of vaccination so these patients will be eligible for the trial. A clarification was made in order to precisely define the timing of unblinding for Cohort 1 and the randomized component of the Maintenance Period. A statement was added to clarify that treatment group assignment during the Maintenance Period for patients who received placebo in Cohort 1 will be unblinded to the Sponsor during the Maintenance Period. Sections were added to clarify that analyses will be performed after the last patient has had their last visit in Cohort 1, Cohort 2 and the Maintenance Period, respectively. The abbreviation list has been updated based on changes in this amendment
29 May 2018	A clarification was made that Cohort 2 may need to be increased to ensure adequate powering of the Maintenance Period. The visit window for Visit Induction 3, Maintenance (M) 2, M 3, M 4, and M 5 was increased for operational efficiency. Added Safety Follow-Up section for consistency with other ongoing RPC1063 protocols. Revised instructions for elevated LFTs for consistency with other ongoing RPC1063 protocols. Added guidance for further liver function evaluation if a patient discontinues investigational drug due to elevated alanine aminotransferase (ALT) or aspartate aminotransferase (AST) > 5x ULN, or ALT or AST > 3x ULN and bilirubin > 2x ULN for additional clarification for the investigator. Changed "titration" to "dose escalation" throughout the protocol for consistency with other ongoing RPC1063 protocols. Added nomenclature and dose equivalency between RPC1063/ozanimod HCl (0.25 mg, 0.5 mg, and 1 mg) and ozanimod (0.23 mg, 0.46 mg, and 0.92 mg) for consistency across RPC1063 protocols. A change to the analysis method was made from the LOCF method to the NRI method Removed hemoglobin A1c from the chemistry panel because it is not needed for routine evaluation of patient safety. Minor editorial changes and changes for clarification were made.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported