Clinical trial results:
A Phase 2, multi-center, randomized, double-blind, placebo-controlled parallel-group study to evaluate the clinical efficacy and safety of induction therapy with RPC1063 in patients with moderately to severely active ulcerative colitis

Summary

EudraCT number	2012-003123-38
Trial protocol	BE HU PL SK BG GR NL
Global end of trial date	30 August 2019

Results information

Result version number	v1 (current)
This version publication date	13 September 2020
First version publication date	13 September 2020

Trial information

Trial identification

Sponsor protocol code	RPC01-202

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01647516
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Celgene International II Sàrl
Sponsor organisation address	Rue du Pré-Jorat 14, Couvet, Switzerland, 2108
Public contact	Clinical Trial Disclosure, Celgene International II Sàrl, 01 888-260-1599, ClinicalTrialDisclosure@Celgene.com
Scientific contact	Ernesto Oviedo-Orta, MD, PhD, MBA, Celgene International II Sàrl, 01 908-673-2861, Ernesto.Oviedo-Orta@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	30 August 2019
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	30 August 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study is to compare the efficacy of RPC1063 vs placebo for induction of clinical remission at Week 8 in patients with moderately to severely active ulcerative colitis (UC)

Protection of trial subjects:

Patient Confidentiality, Informed Consent and Archiving of Essential Documents

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	26 December 2012
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	6 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Belgium: 1
Country: Number of subjects enrolled	Bulgaria: 17
Country: Number of subjects enrolled	Hungary: 14
Country: Number of subjects enrolled	Greece: 2
Country: Number of subjects enrolled	Israel: 4
Country: Number of subjects enrolled	Korea, Republic of: 8
Country: Number of subjects enrolled	Netherlands: 3
Country: Number of subjects enrolled	New Zealand: 3
Country: Number of subjects enrolled	Poland: 30
Country: Number of subjects enrolled	Russian Federation: 44
Country: Number of subjects enrolled	Slovakia: 11
Country: Number of subjects enrolled	United States: 21
Country: Number of subjects enrolled	Ukraine: 39
Worldwide total number of subjects	197
EEA total number of subjects	78

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)	195
From 65 to 84 years	2
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at 57 sites from 13 countries located in Europe, North America, and the Asia-Pacific region.

Pre-assignment

Screening details:

Participants who received placebo, ozanimod 0.5 mg or ozanimod 1 mg capsules and completed the induction period and were non-responders at week 8 and those who completed the maintenance period or experienced a disease relapse, were given the option to enter the open label treatment period and received 1 mg ozanimod daily up to 6 years.

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, Monitor, Data analyst, Carer

Blinding implementation details:

Investigational medicinal product and placebo capsules were identical in physical appearance. The treatment each participant received was not disclosed to the Investigator, study center personnel, participant, sponsor and their representatives. The treatment codes were held according to an Interactive Voice Response System (IVRS).

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Participants received identically matching placebo capsules daily for 9 weeks during the induction period (weeks 0-9).

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:

Identically matching placebo capsules daily during the induction period (Weeks 0-9). Nine weeks total treatment.

Arm title	Ozanimod Hydrochloride 0.5mg

Arm description:

Participants received 0.5 mg capsules of ozanimod hydrochloride daily during the induction period weeks 0-9 (an initial 8-day dose escalation regimen in the induction period that consisted of 4 days of ozanimod HCl 0.25 mg (equivalent to ozanimod 0.23 mg), followed by 3 days of ozanimod HCl 0.5 mg, (equivalent to ozanimod 0.46 mg) followed by the assigned treatment level for at least 8 weeks.

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

Dosage and administration details:

Participants received 0.5 mg capsules of ozanimod hydrochloride daily during the induction period weeks

0-9 (an initial 8-day dose escalation regimen in the induction period that consisted of 4 days of ozanimod HCl 0.25 mg (equivalent to ozanimod 0.23 mg), followed by 3 days of ozanimod HCl 0.5 mg, (equivalent to ozanimod 0.46 mg) followed by the assigned treatment level for at least 8 weeks.

Arm title	Ozanimod Hydrochloride 1 mg

Arm description:

Participants received 1 mg capsules of ozanimod hydrochloride daily during the induction period weeks 0-9 (an initial 8-day dose escalation regimen in the induction period that consisted of 4 days of ozanimod HCl 0.25 mg (equivalent to ozanimod 0.23 mg), followed by 3 days of ozanimod HCl 0.5 mg, (equivalent to ozanimod 0.46 mg) followed by the assigned treatment level for at least 8 weeks.

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

Dosage and administration details:

Participants received 1 mg capsules of ozanimod hydrochloride daily during the induction period weeks 0-9 (an initial 8-day dose escalation regimen in the induction period that consisted of 4 days of ozanimod HCl 0.25 mg (equivalent to ozanimod 0.23 mg), followed by 3 days of ozanimod HCl 0.5 mg, (equivalent to ozanimod 0.46 mg) followed by the assigned treatment level for at least 8 weeks.

Number of subjects in period 1	Placebo	Ozanimod Hydrochloride 0.5mg	Ozanimod Hydrochloride 1 mg
Started	65	65	67
Received study drug	65	65	67
Completed	60	63	63
Not completed	5	2	4
Physician decision	2	-	-
Consent withdrawn by subject	1	-	3
Adverse event, non-fatal	1	2	-
Participant elected to stop dosing	-	-	1
Lack of efficacy	1	-	-

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, Monitor, Carer, Data analyst, Assessor

Blinding implementation details:

Investigational medicinal product and placebo capsules were identical in physical appearance. The treatment each participant received was not disclosed to the Investigator, study center personnel,

participant, sponsor and their representatives. The treatment codes were held according to an Interactive Voice Response System (IVRS).

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Participants received identically matching placebo capsules daily for 24 weeks during the maintenance period (weeks 9-32).

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:

Identically matching placebo capsules daily during the maintenance period (Weeks 9-32). Twenty-four weeks total treatment.

Arm title	Ozanimod Hydrochloride 0.5mg

Arm description:

Participants received 0.5 mg capsules of ozanimod hydrochloride daily for 24 weeks during the maintenance period (weeks 9-32).

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

Dosage and administration details:

Ozanimod hydrochloride 0.5mg capsules daily during the maintenance period (Weeks 9-32). Twenty-four weeks total treatment.

Arm title	Ozanimod Hydrochloride 1 mg

Arm description:

Participants received 1 mg capsules of ozanimod hydrochloride daily for 24 weeks during the maintenance period (weeks 9-32).

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

Dosage and administration details:

Ozanimod Hydrochloride 1 mg capsules daily during the maintenance period (Weeks 9-32). Twenty-four weeks total treatment.

Number of subjects in period 2[1]	Placebo	Ozanimod Hydrochloride 0.5mg	Ozanimod Hydrochloride 1 mg
Started	25	36	42
Received Study Drug	25	36	41
Completed	21	30	40
Not completed	4	6	2
Consent withdrawn by subject	-	1	1
Adverse event, non-fatal	2	1	-
Lack of efficacy	1	4	1
Noncompliance	1	-	-

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: Participants were considered responders in the maintenance period, which is a lower number than those completed in the induction period.

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Participants received identically matching placebo capsules daily for 9 weeks during the induction period (weeks 0-9).	
Reporting group title	Ozanimod Hydrochloride 0.5mg
Reporting group description:	
Participants received 0.5 mg capsules of ozanimod hydrochloride daily during the induction period weeks 0-9 (an initial 8-day dose escalation regimen in the induction period that consisted of 4 days of ozanimod HCl 0.25 mg (equivalent to ozanimod 0.23 mg), followed by 3 days of ozanimod HCl 0.5 mg, (equivalent to ozanimod 0.46 mg) followed by the assigned treatment level for at least 8 weeks.	
Reporting group title	Ozanimod Hydrochloride 1 mg
Reporting group description:	
Participants received 1 mg capsules of ozanimod hydrochloride daily during the induction period weeks 0-9 (an initial 8-day dose escalation regimen in the induction period that consisted of 4 days of ozanimod HCl 0.25 mg (equivalent to ozanimod 0.23 mg), followed by 3 days of ozanimod HCl 0.5 mg, (equivalent to ozanimod 0.46 mg) followed by the assigned treatment level for at least 8 weeks.	

Reporting group values	Placebo	Ozanimod Hydrochloride 0.5mg	Ozanimod Hydrochloride 1 mg
Number of subjects	65	65	67
Age Categorical Units: Subjects			
Adults (18-64 years)	64	64	67
From 65-84 years	1	1	0
Age Continuous Units: years			
arithmetic mean	41.9	38.8	41.8
standard deviation	± 12.30	± 12.06	± 11.01
Gender Categorical Units: Subjects			
Female	30	33	19
Male	35	32	48
Race Units: Subjects			
White	61	59	62
Black	2	1	1
Asian	2	3	3
American Indian or Alaska Native	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Other	0	1	1
Missing	0	1	0
Ethnicity Units: Subjects			
Hispanic or Latino	2	1	0
Not Hispanic or Latino	63	64	67

Mayo Score			
The Mayo Score is a composite index of four items (stool frequency, rectal bleeding, rectosigmoidoscopy findings, and physician's global assessment) with each item graded semi-quantitatively on a scale of 0 to 3 where 0 represents normal and higher score represents more severe disease status. The total Mayo Score is the sum of the four item scores, with a result ranging from 0 to 12 points. Higher scores represent more severe disease.			
Units: Units on a Scale			
arithmetic mean	8.6	8.3	8.5
standard deviation	± 1.51	± 1.45	± 1.61
Years Since Ulcerative Colitis Diagnosis			
Units: Years			
arithmetic mean	6.1	5.9	6.7
standard deviation	± 5.46	± 5.44	± 6.76

Reporting group values	Total		
Number of subjects	197		
Age Categorical			
Units: Subjects			
Adults (18-64 years)	195		
From 65-84 years	2		
Age Continuous			
Units: years			
arithmetic mean			
standard deviation	-		
Gender Categorical			
Units: Subjects			
Female	82		
Male	115		
Race			
Units: Subjects			
White	182		
Black	4		
Asian	8		
American Indian or Alaska Native	0		
Native Hawaiian or Other Pacific Islander	0		
Other	2		
Missing	1		
Ethnicity			
Units: Subjects			
Hispanic or Latino	3		
Not Hispanic or Latino	194		
Mayo Score			
The Mayo Score is a composite index of four items (stool frequency, rectal bleeding, rectosigmoidoscopy findings, and physician's global assessment) with each item graded semi-quantitatively on a scale of 0 to 3 where 0 represents normal and higher score represents more severe disease status. The total Mayo Score is the sum of the four item scores, with a result ranging from 0 to 12 points. Higher scores represent more severe disease.			
Units: Units on a Scale			
arithmetic mean			
standard deviation	-		
Years Since Ulcerative Colitis Diagnosis			
Units: Years			
arithmetic mean			

standard deviation	-		

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Participants received identically matching placebo capsules daily for 9 weeks during the induction period (weeks 0-9).	
Reporting group title	Ozanimod Hydrochloride 0.5mg
Reporting group description:	
Participants received 0.5 mg capsules of ozanimod hydrochloride daily during the induction period weeks 0-9 (an initial 8-day dose escalation regimen in the induction period that consisted of 4 days of ozanimod HCl 0.25 mg (equivalent to ozanimod 0.23 mg), followed by 3 days of ozanimod HCl 0.5 mg, (equivalent to ozanimod 0.46 mg) followed by the assigned treatment level for at least 8 weeks.	
Reporting group title	Ozanimod Hydrochloride 1 mg
Reporting group description:	
Participants received 1 mg capsules of ozanimod hydrochloride daily during the induction period weeks 0-9 (an initial 8-day dose escalation regimen in the induction period that consisted of 4 days of ozanimod HCl 0.25 mg (equivalent to ozanimod 0.23 mg), followed by 3 days of ozanimod HCl 0.5 mg, (equivalent to ozanimod 0.46 mg) followed by the assigned treatment level for at least 8 weeks.	
Reporting group title	Placebo
Reporting group description:	
Participants received identically matching placebo capsules daily for 24 weeks during the maintenance period (weeks 9-32).	
Reporting group title	Ozanimod Hydrochloride 0.5mg
Reporting group description:	
Participants received 0.5 mg capsules of ozanimod hydrochloride daily for 24 weeks during the maintenance period (weeks 9-32).	
Reporting group title	Ozanimod Hydrochloride 1 mg
Reporting group description:	
Participants received 1 mg capsules of ozanimod hydrochloride daily for 24 weeks during the maintenance period (weeks 9-32).	
Subject analysis set title	Placebo
Subject analysis set type	Safety analysis
Subject analysis set description:	
Participants who received identically matching placebo capsules during the maintenance period.	
Subject analysis set title	Ozanimod 0.5 mg
Subject analysis set type	Safety analysis
Subject analysis set description:	
Participants who received 0.5 mg capsules daily during the maintenance period.	
Subject analysis set title	Ozanimod 1 mg
Subject analysis set type	Safety analysis
Subject analysis set description:	
Participants who received 1 mg capsules daily during the maintenance period.	
Subject analysis set title	Open Label Treatment Period
Subject analysis set type	Safety analysis
Subject analysis set description:	
Participants who received placebo capsules, ozanimod 0.5 mg or ozanimod 1 mg capsules and completed the induction period and were non-responders at Week 8 and those who completed the maintenance period or experienced a disease relapse, were given the option to enter the open label treatment period (OLP) and received 1 mg ozanimod daily up to 6 years. Participants who had not shown clinical improvement 8 weeks after initiation of the OLP were discontinued from the study.	

Primary: Percentage of Participants Who Achieved Clinical Remission Based on the Central Read of the Mayo Score (MS), at Week 8

End point title	Percentage of Participants Who Achieved Clinical Remission Based on the Central Read of the Mayo Score (MS), at Week 8

End point description:

Clinical Remission was defined as: Mayo score of <2 points and with no individual subscore of > 1 point.

The Mayo Score is a composite index of four items (stool frequency, rectal bleeding, rectosigmoidoscopy findings, and physician's global assessment) with each item graded semi-quantitatively on a scale of 0 to 3 where 0 represents normal and higher score represents more severe disease status. The total Mayo Score is the sum of the four item scores, with a result ranging from 0 to 12 points. Higher scores represent more severe disease.
- Stool Frequency Subscore (SFS)
- Rectal bleeding Subscore (RBS)
- Endoscopy Subscore
- Physician's Global Assessment (PGA)

Clinical Remission was based on the 4-component Mayo definition.

The intent to treat (ITT) population consisted of all randomized participants who received at least one dose of study treatment, with treatment. Participants with missing Mayo scores were classified as non-responders.

End point type	Primary

End point timeframe:

Week 8

End point values	Placebo	Ozanimod Hydrochloride 0.5mg	Ozanimod Hydrochloride 1 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	65	65	67	
Units: Percentage of Participants				
number (not applicable)	6.2	13.8	16.4	

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v Ozanimod Hydrochloride 1 mg
Number of subjects included in analysis	132
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0482 [1]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	3.262
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.969
upper limit	10.984

Notes:

[1] - Stratified by prior anti-tumor necrosing factor (anti-TNF) therapy experience, (yes or no).

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v Ozanimod Hydrochloride 0.5mg
Number of subjects included in analysis	130
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1422 [2]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	2.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.722
upper limit	8.661

Notes:

[2] - Stratified by prior anti-TNF therapy experience, (yes or no).

Secondary: Percentage of Participants Who Achieved a Clinical Response in the Mayo Score (MS) at Week 8

End point title	Percentage of Participants Who Achieved a Clinical Response in the Mayo Score (MS) at Week 8

End point description:

Clinical response was defined as a reduction from baseline in Mayo score ≥3 points and ≥30%, and a decrease from baseline in the rectal bleeding subscore of ≥ 1 point or an absolute rectal bleeding subscore of ≤ 1 point. The Mayo Score is a composite index of four items (stool frequency, rectal bleeding, rectosigmoidoscopy findings, and physician's global assessment) with each item graded semi-quantitatively on a scale of 0 to 3 where 0 represents normal and higher score represents more severe disease status. The total Mayo Score is the sum of the four item scores, with a result ranging from 0 to 12 points. Higher scores represent more severe disease.
Clinical Respone was based on the 4-component Mayo definition.
The ITT population consisted of all randomized participants who received at least one dose of study treatment, with treatment assignment designated according to randomized treatment. Participants with missing Mayo score were considered non-responders. Non responder imputa

End point type	Secondary

End point timeframe:

Week 8

End point values	Placebo	Ozanimod Hydrochloride 0.5mg	Ozanimod Hydrochloride 1 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	65	65	67	
Units: Units on a Scale				
number (not applicable)	36.9	53.8	56.7	

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v Ozanimod Hydrochloride 1 mg
Number of subjects included in analysis	132
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0207 [3]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	2.158
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.093
upper limit	4.263

Notes:

[3] - Stratified by prior anti-TNF therapy experience, (yes or no).

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v Ozanimod Hydrochloride 0.5mg
Number of subjects included in analysis	130
Analysis specification	Pre-specified
Analysis type	superiority[4]
P-value	= 0.0648
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	1.947
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.961
upper limit	3.946

Notes:

[4] - Stratified by prior anti-TNF therapy experience, (yes or no).

Secondary: Change from Baseline in Mayo Score at Week 8

End point title	Change from Baseline in Mayo Score at Week 8

End point description:

The Mayo Score is a composite index of four items (stool frequency, rectal bleeding, rectosigmoidoscopy findings, and physician’s global assessment) with each item graded semi-quantitatively on a scale of 0 to 3 where 0 represents normal and higher score represents more severe disease status. The total Mayo Score is the sum of the four item scores, with a result ranging from 0 to 12 points. Higher scores represent more severe disease.

- Stool Frequency Subscore (SFS)
- Rectal bleeding Subscore (RBS)
- Endoscopy Subscore
- Physician’s Global Assessment (PGA)

The ITT population consisted of all randomized participants who received at least one dose of study treatment, with treatment assignment designated according to randomized treatment. Includes participants with available data.

End point type	Secondary

End point timeframe:
Baseline to Week 8

End point values	Placebo	Ozanimod Hydrochloride 0.5mg	Ozanimod Hydrochloride 1 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	62	64	65	
Units: Units on a Scale				
arithmetic mean (standard deviation)	2.0 (± 2.52)	-2.6 (± 2.92)	-3.4 (± 2.79)	

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v Ozanimod Hydrochloride 1 mg
Number of subjects included in analysis	127
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0042 [5]
Method	ANCOVA

Notes:
[5] - The analysis of covariance model, adjusting for baseline Mayo score and prior anti-TNF (yes or no).

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v Ozanimod Hydrochloride 0.5mg
Number of subjects included in analysis	126
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1415 [6]
Method	ANCOVA

Notes:
[6] - The analysis of covariance model, adjusting for baseline Mayo score and prior anti-TNF (yes or no)

Secondary: Percentage of Participants with Mucosal Healing at Week 8

End point title	Percentage of Participants with Mucosal Healing at Week 8

End point description:

Mucosal healing is defined as an endoscopy subscore ≤ 1 point. Endoscopy subscores were calculated based on central endoscopy reading.
The endoscopy scale:
0 = Normal or inactive disease
1 = Mild disease (erythema, decreased vascular pattern, mild friability)
2 = Moderate disease (marked erythema, lack of vascular pattern, friability, erosions)
3 = Severe disease (spontaneous bleeding, ulceration)

The ITT population consisted of all randomized participants who received at least one dose of study treatment, with treatment assignment designated according to randomized treatment. Non-responder imputation (NRI).

End point type	Secondary

End point timeframe:
Week 8

End point values	Placebo	Ozanimod Hydrochloride 0.5mg	Ozanimod Hydrochloride 1 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	65	65	67	
Units: Units on a Scale				
number (not applicable)	12.3	27.7	34.3	

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v Ozanimod Hydrochloride 1 mg
Number of subjects included in analysis	132
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0023 [7]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	3.861
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.572
upper limit	9.484

Notes:
[7] - Stratified by prior anti-TNF therapy experience, (yes or no).

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v Ozanimod Hydrochloride 0.5mg
Number of subjects included in analysis	130
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0348 [8]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	2.647
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.058
upper limit	6.621

Notes:

[8] - Stratified by prior anti-TNF therapy experience, (yes or no).

Secondary: Percentage of Participants Who Achieved Clinical Remission in the Mayo Score at Week 32

End point title	Percentage of Participants Who Achieved Clinical Remission in the Mayo Score at Week 32

End point description:

Clinical Remission was defined as: Mayo score of <2 points and with no individual subscore of > 1 point. The Mayo Score is a composite index of four items (stool frequency, rectal bleeding, rectosigmoidoscopy findings, and physician's global assessment) with each item graded semi-quantitatively on a scale of 0 to 3 where 0 represents normal and higher score represents more severe disease status. The total Mayo Score is the sum of the four item scores, with a result ranging from 0 to 12 points. Higher scores represent more severe disease. • Stool Frequency Subscore (SFS) • Rectal bleeding Subscore (RBS) • Endoscopy Subscore • Physician's Global Assessment (PGA)

The ITT population consisted of all randomized participants who received at least one dose of study treatment, with treatment assignment designated according to randomized treatment. Participants with missing Mayo score were considered non-responders. NRI.

End point type	Secondary

End point timeframe:

Week 32

End point values	Placebo	Ozanimod Hydrochloride 0.5mg	Ozanimod Hydrochloride 1 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	65	65	67	
Units: Percentage of Participants				
number (not applicable)	6.2	26.2	20.9	

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v Ozanimod Hydrochloride 1 mg
Number of subjects included in analysis	132
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0108 [9]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	4.332
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.323
upper limit	14.186

Notes:

[9] - Stratified by prior anti-TNF therapy experience, (yes or no).

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v Ozanimod Hydrochloride 0.5mg
Number of subjects included in analysis	130
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0021 [10]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	5.443
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.706
upper limit	17.365

Notes:

[10] - Stratified by prior anti-TNF therapy experience, (yes or no).

Secondary: Percentage of Participants Who Achieved a Clinical Response at Week 32

End point title	Percentage of Participants Who Achieved a Clinical Response at Week 32

End point description:

Clinical response was defined as a reduction from baseline in Mayo score ≥3 points and 30%, and a decrease from baseline in the rectal bleeding subscore of ≥ 1 point or an absolute rectal bleeding subscore of ≤ 1 point.

The Mayo Score is a composite index of four items (stool frequency, rectal bleeding, rectosigmoidoscopy findings, and physician's global assessment) with each item graded semi-quantitatively on a scale of 0 to 3 where 0 represents normal and higher score represents more severe disease status. The total Mayo Score is the sum of the four item scores, with a result ranging from 0 to 12 points. Higher scores represent more severe disease.

The ITT population = all randomized subjects who received at least one dose of study treatment, with treatment assignment designated according to randomized treatment. Subjects with missing Mayo score were considered non-responders. NRI.

End point type	Secondary

End point timeframe:

Week 32

End point values	Placebo	Ozanimod Hydrochloride 0.5mg	Ozanimod Hydrochloride 1 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	65	65	67	
Units: Percentage of Participants				
number (not applicable)	20.0	35.4	50.7	

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v Ozanimod Hydrochloride 1 mg
Number of subjects included in analysis	132
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0002 [11]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	4.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.871
upper limit	8.678

Notes:

[11] - Stratified by prior anti-TNF therapy experience, (yes or no).

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v Ozanimod Hydrochloride 1 mg
Number of subjects included in analysis	132
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0571 [12]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	2.154
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.974
upper limit	4.763

Notes:

[12] - Stratified by prior anti-TNF therapy experience, (yes or no).

Secondary: Percentage of Participants with Mucosal Healing at Week 32

End point title	Percentage of Participants with Mucosal Healing at Week 32

End point description:

Mucosal healing is defined as an endoscopy subscore ≤ 1 point. Endoscopy subscores were calculated based on central endoscopy reading.
The endoscopy scale:
0 = Normal or inactive disease
1 = Mild disease (erythema, decreased vascular pattern, mild friability)
2 = Moderate disease (marked erythema, lack of vascular pattern, friability, erosions)
3 = Severe disease (spontaneous bleeding, ulceration)

The ITT population consisted of all randomized participants who received at least one dose of study treatment, with treatment assignment designated according to randomized treatment. Non-responder imputation (NRI).

End point type	Secondary

End point timeframe:

Week 32

End point values	Placebo	Ozanimod Hydrochloride 0.5mg	Ozanimod Hydrochloride 1 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	65	65	67	
Units: Percentage of Participants				
number (not applicable)	12.3	32.3	32.8	

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v Ozanimod Hydrochloride 1 mg
Number of subjects included in analysis	132
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0046 [13]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	3.557
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.444
upper limit	8.762

Notes:

[13] - Stratified by prior anti-TNF therapy experience, (yes or no).

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v Ozanimod Hydrochloride 0.5mg
Number of subjects included in analysis	130
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0064 [14]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	3.428
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.384
upper limit	8.494

Notes:

[14] - Stratified by prior anti-TNF therapy experience, (yes or no).

Secondary: Number of Participants with Treatment Emergent Adverse Events During

the Induction Period

End point title	Number of Participants with Treatment Emergent Adverse Events During the Induction Period

End point description:

A TEAE was defined as any event with an onset date on or after first dose date or any ongoing event on the first dose date that worsens in severity after first dose date and until 30 days following the last dose of treatment with the study drug. earlier. A serious AE = any AE which results in death; is life-threatening; requires inpatient hospitalization or prolongation of existing hospitalization; results in persistent or significant disability/incapacity; is a congenital anomaly/birth defect; constitutes an important medical event. The severity of AEs was assessed by the investigator and based on the following scale: Mild = an AE usually transient in nature and generally not interfering with normal activities; Moderate = an AE that is sufficiently discomforting to interfere with normal activities; Severe = an AE that is incapacitating and prevents normal activities. Safety population = all participants who were enrolled and received at least 1 dose of study drug.

End point type	Secondary

End point timeframe:

From the first dose of investigational product (IP) up to 90 days after the last dose of IP or at follow-up visit; the mean total duration of IP exposure was 52.8 days, 56.1 days and 50.8 days respectively for 0.5 mg, 1 mg ozanimod and placebo.

End point values	Placebo	Ozanimod Hydrochloride 0.5mg	Ozanimod Hydrochloride 1 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	65	65	67	
Units: Participants				
number (not applicable)				
≥ 1 TEAE	21	24	17	
≥ 1 Moderate or Severe TEAE	7	12	6	
≥ 1 Severe TEAE	2	1	1	
≥ 1 Possibly, Probably or Definitely Related TEAE	2	5	5	
≥ 1 Serious SAE	4	1	2	
≥ 1 Possibly, Probably or Related Serious TEAE	0	0	0	
≥ 1 TEAE Leading to Withdrawal From Study	1	2	1	
Death	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Treatment Emergent Adverse Events During the Maintenance Period

End point title	Number of Participants with Treatment Emergent Adverse Events During the Maintenance Period

End point description:

A TEAE was defined as any event with an onset date on or after first dose date or any ongoing event on the first dose date that worsens in severity after first dose date and until 30 days following the last dose of treatment with the study drug. earlier. A serious AE = any AE which results in death; is life-threatening; requires inpatient hospitalization or prolongation of existing hospitalization; results in persistent or significant disability/incapacity; is a congenital anomaly/birth defect; constitutes an

important medical event. The severity of AEs was assessed by the investigator and based on the following scale: Mild = an AE usually transient in nature and generally not interfering with normal activities; Moderate = an AE that is sufficiently discomforting to interfere with normal activities; Severe = an AE that is incapacitating and prevents normal activities. Safety population included all participants who were enrolled and received at least 1 dose of investigational product

End point type	Secondary

End point timeframe:

From the first dose of IP up to 90 days after the last dose of IP or at follow-up visit; the mean total duration of IP exposure was 156.3 days, 171.1 days and 154.5 days respectively for 0.5 mg, 1 mg ozanimod and placebo.

End point values	Placebo	Ozanimod 0.5 mg	Ozanimod 1 mg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	25	36	42	
Units: Participants				
≥ 1 TEAE	8	4	11	
≥ 1 Moderate or Severe TEAE	4	1	5	
≥ 1 Severe TEAE	1	0	1	
≥ 1 Possibly, Probably or Definitely Related TEAE	0	0	2	
≥ 1 Serious TEAE	2	0	1	
≥ 1 Possibly, Probably or Related Serious TEAE	0	0	0	
≥ 1 TEAE Leading to Withdrawal From Study	3	0	0	
Death	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Treatment Emergent Adverse Events During the Open-Label Treatment Period (OLP)

End point title	Number of Participants with Treatment Emergent Adverse Events During the Open-Label Treatment Period (OLP)

End point description:

A TEAE was defined as any event with an onset date on or after first dose date or any ongoing event on the first dose date that worsens in severity after first dose date and until 30 days following the last dose of treatment with the study drug. earlier. A serious AE = any AE which results in death; is life-threatening; requires inpatient hospitalization or prolongation of existing hospitalization; results in persistent or significant disability/incapacity; is a congenital anomaly/birth defect; constitutes an important medical event. The severity of AEs was assessed by the investigator and based on the following scale: Mild = an AE usually transient in nature and generally not interfering with normal activities; Moderate = an AE that is sufficiently discomforting to interfere with normal activities; Severe = an AE that is incapacitating and prevents normal activities. Safety population included all participants who were enrolled and received at least 1 dose of investigational product

End point type	Secondary

End point timeframe:

From the first dose of IP until 90 days after the last dose of IP or at follow-up visit; the mean total duration of study drug exposure in the OLP was 2.42 years.

End point values	Open Label Treatment Period			
Subject group type	Subject analysis set			
Number of subjects analysed	170			
Units: Participants				
≥ 1 TEAE	101			
≥ 1 Moderate or Severe TEAE	63			
≥ 1 Severe TEAE	17			
≥ 1 Possible, Probable or Related TEAE	27			
≥ 1 Related TEAE	2			
≥ 1 Serious TEAE	27			
≥ 1 Related Serious TEAE	0			
≥ 1 Possible, Probable or Related Serious TEAE	4			
≥ 1 TEAE Leading to Discontinuation of IP	14			
≥ 1 TEAE Leading to Withdrawal from Study	13			
Death	1			
Death Possible, Probable or Related to IP	1			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From the first dose of IP up to 90 days after the last dose of IP or at follow-up visit; the mean total duration of IP exposure was 52.8 days, 56.1 days and 50.8 days respectively for 0.5 mg, 1 mg ozanimod and placebo during the induction period.

Adverse event reporting additional description:

The mean total duration of study drug exposure was 156.3 days, 171.1 days and 154.5 days respectively for 0.5 mg, 1 mg ozanimod and placebo during the maintenance period and 2.42 years during the open label treatment period,

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18.1

Reporting groups

Reporting group title	Induction Period: Placebo

Reporting group description:

Participants received identically matching placebo capsules daily for 9 weeks during the induction period (weeks 0 to 9)

Reporting group title	Induction Period: Ozanimod HCL 0.5 mg

Reporting group description:

Participants received 0.5 mg capsules of ozanimod hydrochloride daily during the induction period weeks 0-9 (an initial 8-day dose escalation regimen in the induction period that consisted of 4 days of ozanimod HCl 0.25 mg (equivalent to ozanimod 0.23 mg), followed by 3 days of ozanimod HCl 0.5 mg, (equivalent to ozanimod 0.46 mg) followed by the assigned treatment level for at least 8 weeks.

Reporting group title	Induction Period: Ozanimod HCL 1 mg

Reporting group description:

Participants received 1mg capsules of ozanimod hydrochloride daily during the induction period weeks 0-9 (an initial 8-day dose escalation regimen in the induction period that consisted of 4 days of ozanimod HCl 0.25 mg (equivalent to ozanimod 0.23 mg), followed by 3 days of ozanimod HCl 0.5 mg, (equivalent to ozanimod 0.46 mg) followed by the assigned treatment level for at least 8 weeks.

Reporting group title	Maintenance Period: Placebo

Reporting group description:

Participants originally assigned to placebo who completed the induction period and were responders at week 8 continued to receive placebo in the maintenance period. Participants received identically matching placebo capsules daily during the maintenance period (weeks 9-32).

Reporting group title	Maintenance Period: Ozanimod HCL 0.5 mg

Reporting group description:

Participants originally assigned to ozanimod 0.5 mg who completed the induction period and were responders at week 8 continued to receive ozanimod 0.5 mg daily in the maintenance period. Participants received 0.5 mg ozanimod capsules daily during the maintenance period (weeks 9 to 32).

Reporting group title	Maintenance Period: Ozanimod HCL 1 mg

Reporting group description:

Participants originally assigned to ozanimod 1 mg who completed the induction period and were responders at week 8 continued to receive ozanimod 0.5 mg daily in the maintenance period. Participants received 1 mg ozanimod capsules daily during the maintenance period (weeks 9 to 32).

Reporting group title	Open-Label Treatment Period (OLP): Placebo/Ozanimod

Reporting group description:

Participants who received placebo capsules and completed the induction period and were non-responders at Week 8 and those who completed the maintenance period or experienced a disease relapse, were given the option to enter the open label treatment period (OLP) and receive 1 mg ozanimod daily up to 6 years. Participants who had not shown clinical improvement 8 weeks after initiation of the OLP were discontinued from the study.

Reporting group title	OLP: Ozanimod 0.5 mg/Ozanimod 1 mg

Reporting group description:

Participants who received ozanimod 0.5 mg capsules and completed the induction period and were non-responders at Week 8 and who completed the maintenance period or experienced a disease relapse, were given the option to enter the OLP and receive 1 mg ozaninod capsules daily up to 6 years. Participants who had not shown clinical improvement 8 weeks after initiation of the OLP were discontinued from the study.

Reporting group title	OLP: Ozanimod 1mg/Ozanimod 1 mg

Reporting group description:

Participants who received 1 mg ozanimod capsules and completed the induction period and were non-responders at Week 8 and those who completed the maintenance period or experienced a disease relapse, were given the option to enter the open label treatment period (OLP) and continue to receive 1 mg ozaninod daily up to 6 years. Participants who had not shown clinical improvement 8 weeks after initiation of the OLP were discontinued from the study.

Serious adverse events	Induction Period: Placebo	Induction Period: Ozanimod HCL 0.5 mg	Induction Period: Ozanimod HCL 1 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 65 (6.15%)	1 / 65 (1.54%)	2 / 67 (2.99%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma			
subjects affected / exposed	0 / 65 (0.00%)	0 / 65 (0.00%)	0 / 67 (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
Basal cell carcinoma			
subjects affected / exposed	0 / 65 (0.00%)	0 / 65 (0.00%)	0 / 67 (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
Colon adenoma			
subjects affected / exposed	0 / 65 (0.00%)	0 / 65 (0.00%)	0 / 67 (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
Prostate cancer			
subjects affected / exposed	0 / 65 (0.00%)	0 / 65 (0.00%)	0 / 67 (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
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			

subjects affected / exposed	0 / 65 (0.00%)	0 / 65 (0.00%)	0 / 67 (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			
Hyperpyrexia			
subjects affected / exposed	0 / 65 (0.00%)	1 / 65 (1.54%)	0 / 67 (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
Respiratory, thoracic and mediastinal disorders			
Idiopathic pulmonary fibrosis			
subjects affected / exposed	0 / 65 (0.00%)	0 / 65 (0.00%)	0 / 67 (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
Interstitial lung disease			
subjects affected / exposed	0 / 65 (0.00%)	0 / 65 (0.00%)	0 / 67 (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
Pleurisy			
subjects affected / exposed	0 / 65 (0.00%)	0 / 65 (0.00%)	0 / 67 (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
Pulmonary bulla			
subjects affected / exposed	0 / 65 (0.00%)	0 / 65 (0.00%)	0 / 67 (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
Pulmonary microemboli			
subjects affected / exposed	0 / 65 (0.00%)	0 / 65 (0.00%)	0 / 67 (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
Psychiatric disorders			
Schizophrenia			

subjects affected / exposed	0 / 65 (0.00%)	0 / 65 (0.00%)	0 / 67 (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
Injury, poisoning and procedural complications			
Joint dislocation			
subjects affected / exposed	0 / 65 (0.00%)	0 / 65 (0.00%)	0 / 67 (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
Wrist fracture			
subjects affected / exposed	0 / 65 (0.00%)	0 / 65 (0.00%)	0 / 67 (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			
Acute coronary syndrome			
subjects affected / exposed	0 / 65 (0.00%)	0 / 65 (0.00%)	0 / 67 (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			
Ischaemic stroke			
subjects affected / exposed	0 / 65 (0.00%)	0 / 65 (0.00%)	0 / 67 (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	0 / 65 (0.00%)	0 / 65 (0.00%)	0 / 67 (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
Autoimmune haemolytic anaemia			
subjects affected / exposed	0 / 65 (0.00%)	0 / 65 (0.00%)	0 / 67 (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
Haemolytic anaemia			

subjects affected / exposed	0 / 65 (0.00%)	0 / 65 (0.00%)	0 / 67 (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
Hypochromic anaemia			
subjects affected / exposed	0 / 65 (0.00%)	0 / 65 (0.00%)	0 / 67 (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
Iron deficiency anaemia			
subjects affected / exposed	1 / 65 (1.54%)	0 / 65 (0.00%)	0 / 67 (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			
Ascites			
subjects affected / exposed	0 / 65 (0.00%)	0 / 65 (0.00%)	0 / 67 (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
Colitis			
subjects affected / exposed	0 / 65 (0.00%)	0 / 65 (0.00%)	0 / 67 (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
Colitis ulcerative			
subjects affected / exposed	2 / 65 (3.08%)	0 / 65 (0.00%)	2 / 67 (2.99%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Inguinal hernia			
subjects affected / exposed	0 / 65 (0.00%)	0 / 65 (0.00%)	0 / 67 (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
Intestinal obstruction			
subjects affected / exposed	0 / 65 (0.00%)	0 / 65 (0.00%)	0 / 67 (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
Umbilical hernia			

subjects affected / exposed	0 / 65 (0.00%)	0 / 65 (0.00%)	0 / 67 (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			
Hyperbilirubinaemia			
subjects affected / exposed	0 / 65 (0.00%)	0 / 65 (0.00%)	0 / 67 (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
Jaundice			
subjects affected / exposed	1 / 65 (1.54%)	0 / 65 (0.00%)	0 / 67 (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
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	0 / 65 (0.00%)	0 / 65 (0.00%)	0 / 67 (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			
Rheumatoid arthritis			
subjects affected / exposed	0 / 65 (0.00%)	0 / 65 (0.00%)	0 / 67 (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
Spinal column stenosis			
subjects affected / exposed	0 / 65 (0.00%)	0 / 65 (0.00%)	0 / 67 (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
Infections and infestations			
Erysipelas			
subjects affected / exposed	0 / 65 (0.00%)	0 / 65 (0.00%)	0 / 67 (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 viral			

subjects affected / exposed	0 / 65 (0.00%)	0 / 65 (0.00%)	0 / 67 (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
Herpes zoster			
subjects affected / exposed	0 / 65 (0.00%)	0 / 65 (0.00%)	0 / 67 (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
Pneumonia			
subjects affected / exposed	0 / 65 (0.00%)	0 / 65 (0.00%)	0 / 67 (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
Pneumonia pneumococcal			
subjects affected / exposed	0 / 65 (0.00%)	0 / 65 (0.00%)	0 / 67 (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 / 65 (0.00%)	0 / 65 (0.00%)	0 / 67 (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

Serious adverse events	Maintenance Period: Placebo	Maintenance Period: Ozanimod HCL 0.5 mg	Maintenance Period: Ozanimod HCL 1 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 25 (8.00%)	0 / 36 (0.00%)	1 / 42 (2.38%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma			
subjects affected / exposed	0 / 25 (0.00%)	0 / 36 (0.00%)	0 / 42 (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
Basal cell carcinoma			

subjects affected / exposed	0 / 25 (0.00%)	0 / 36 (0.00%)	0 / 42 (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
Colon adenoma			
subjects affected / exposed	0 / 25 (0.00%)	0 / 36 (0.00%)	1 / 42 (2.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostate cancer			
subjects affected / exposed	0 / 25 (0.00%)	0 / 36 (0.00%)	0 / 42 (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
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	0 / 25 (0.00%)	0 / 36 (0.00%)	0 / 42 (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			
Hyperpyrexia			
subjects affected / exposed	0 / 25 (0.00%)	0 / 36 (0.00%)	0 / 42 (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			
Idiopathic pulmonary fibrosis			
subjects affected / exposed	0 / 25 (0.00%)	0 / 36 (0.00%)	0 / 42 (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
Interstitial lung disease			
subjects affected / exposed	0 / 25 (0.00%)	0 / 36 (0.00%)	0 / 42 (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
Pleurisy			

subjects affected / exposed	0 / 25 (0.00%)	0 / 36 (0.00%)	0 / 42 (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
Pulmonary bulla			
subjects affected / exposed	0 / 25 (0.00%)	0 / 36 (0.00%)	0 / 42 (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
Pulmonary microemboli			
subjects affected / exposed	0 / 25 (0.00%)	0 / 36 (0.00%)	0 / 42 (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
Psychiatric disorders			
Schizophrenia			
subjects affected / exposed	0 / 25 (0.00%)	0 / 36 (0.00%)	0 / 42 (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
Injury, poisoning and procedural complications			
Joint dislocation			
subjects affected / exposed	0 / 25 (0.00%)	0 / 36 (0.00%)	0 / 42 (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
Wrist fracture			
subjects affected / exposed	0 / 25 (0.00%)	0 / 36 (0.00%)	0 / 42 (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			
Acute coronary syndrome			
subjects affected / exposed	0 / 25 (0.00%)	0 / 36 (0.00%)	0 / 42 (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			
Ischaemic stroke			

subjects affected / exposed	0 / 25 (0.00%)	0 / 36 (0.00%)	0 / 42 (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	0 / 25 (0.00%)	0 / 36 (0.00%)	0 / 42 (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
Autoimmune haemolytic anaemia			
subjects affected / exposed	1 / 25 (4.00%)	0 / 36 (0.00%)	0 / 42 (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
Haemolytic anaemia			
subjects affected / exposed	0 / 25 (0.00%)	0 / 36 (0.00%)	0 / 42 (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
Hypochromic anaemia			
subjects affected / exposed	0 / 25 (0.00%)	0 / 36 (0.00%)	0 / 42 (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
Iron deficiency anaemia			
subjects affected / exposed	0 / 25 (0.00%)	0 / 36 (0.00%)	0 / 42 (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
Gastrointestinal disorders			
Ascites			
subjects affected / exposed	0 / 25 (0.00%)	0 / 36 (0.00%)	0 / 42 (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
Colitis			
subjects affected / exposed	0 / 25 (0.00%)	0 / 36 (0.00%)	0 / 42 (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
Colitis ulcerative			

subjects affected / exposed	1 / 25 (4.00%)	0 / 36 (0.00%)	0 / 42 (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
Inguinal hernia			
subjects affected / exposed	0 / 25 (0.00%)	0 / 36 (0.00%)	0 / 42 (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
Intestinal obstruction			
subjects affected / exposed	0 / 25 (0.00%)	0 / 36 (0.00%)	0 / 42 (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
Umbilical hernia			
subjects affected / exposed	0 / 25 (0.00%)	0 / 36 (0.00%)	0 / 42 (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			
Hyperbilirubinaemia			
subjects affected / exposed	0 / 25 (0.00%)	0 / 36 (0.00%)	0 / 42 (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
Jaundice			
subjects affected / exposed	0 / 25 (0.00%)	0 / 36 (0.00%)	0 / 42 (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			
Nephrolithiasis			
subjects affected / exposed	0 / 25 (0.00%)	0 / 36 (0.00%)	0 / 42 (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			
Rheumatoid arthritis			
subjects affected / exposed	0 / 25 (0.00%)	0 / 36 (0.00%)	0 / 42 (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

Spinal column stenosis			
subjects affected / exposed	0 / 25 (0.00%)	0 / 36 (0.00%)	0 / 42 (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
Infections and infestations			
Erysipelas			
subjects affected / exposed	0 / 25 (0.00%)	0 / 36 (0.00%)	0 / 42 (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 viral			
subjects affected / exposed	0 / 25 (0.00%)	0 / 36 (0.00%)	0 / 42 (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
Herpes zoster			
subjects affected / exposed	1 / 25 (4.00%)	0 / 36 (0.00%)	0 / 42 (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			
subjects affected / exposed	0 / 25 (0.00%)	0 / 36 (0.00%)	0 / 42 (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
Pneumonia pneumococcal			
subjects affected / exposed	0 / 25 (0.00%)	0 / 36 (0.00%)	0 / 42 (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 / 25 (0.00%)	0 / 36 (0.00%)	0 / 42 (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

Serious adverse events	Open-Label Treatment Period (OLP): Placebo/Ozanimod	OLP: Ozanimod 0.5 mg/Ozanimod 1 mg	OLP: Ozanimod 1mg/Ozanimod 1 mg
Total subjects affected by serious adverse events			

subjects affected / exposed	5 / 55 (9.09%)	14 / 56 (25.00%)	11 / 59 (18.64%)
number of deaths (all causes)	0	1	0
number of deaths resulting from adverse events	0	1	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma			
subjects affected / exposed	0 / 55 (0.00%)	1 / 56 (1.79%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Basal cell carcinoma			
subjects affected / exposed	0 / 55 (0.00%)	1 / 56 (1.79%)	0 / 59 (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
Colon adenoma			
subjects affected / exposed	0 / 55 (0.00%)	0 / 56 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostate cancer			
subjects affected / exposed	0 / 55 (0.00%)	0 / 56 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	0 / 55 (0.00%)	0 / 56 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Hyperpyrexia			
subjects affected / exposed	0 / 55 (0.00%)	0 / 56 (0.00%)	0 / 59 (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			
Idiopathic pulmonary fibrosis			

subjects affected / exposed	0 / 55 (0.00%)	0 / 56 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Interstitial lung disease			
subjects affected / exposed	0 / 55 (0.00%)	0 / 56 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleurisy			
subjects affected / exposed	0 / 55 (0.00%)	1 / 56 (1.79%)	0 / 59 (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
Pulmonary bulla			
subjects affected / exposed	0 / 55 (0.00%)	0 / 56 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary microemboli			
subjects affected / exposed	0 / 55 (0.00%)	0 / 56 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Schizophrenia			
subjects affected / exposed	0 / 55 (0.00%)	1 / 56 (1.79%)	0 / 59 (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
Injury, poisoning and procedural complications			
Joint dislocation			
subjects affected / exposed	0 / 55 (0.00%)	0 / 56 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wrist fracture			
subjects affected / exposed	0 / 55 (0.00%)	1 / 56 (1.79%)	0 / 59 (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

Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	1 / 55 (1.82%)	0 / 56 (0.00%)	0 / 59 (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
Nervous system disorders			
Ischaemic stroke			
subjects affected / exposed	1 / 55 (1.82%)	1 / 56 (1.79%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 55 (1.82%)	1 / 56 (1.79%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Autoimmune haemolytic anaemia			
subjects affected / exposed	0 / 55 (0.00%)	1 / 56 (1.79%)	0 / 59 (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
Haemolytic anaemia			
subjects affected / exposed	0 / 55 (0.00%)	0 / 56 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypochromic anaemia			
subjects affected / exposed	0 / 55 (0.00%)	1 / 56 (1.79%)	0 / 59 (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
Iron deficiency anaemia			
subjects affected / exposed	0 / 55 (0.00%)	0 / 56 (0.00%)	0 / 59 (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
Gastrointestinal disorders			
Ascites			

subjects affected / exposed	0 / 55 (0.00%)	1 / 56 (1.79%)	0 / 59 (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
Colitis			
subjects affected / exposed	0 / 55 (0.00%)	0 / 56 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis ulcerative			
subjects affected / exposed	3 / 55 (5.45%)	1 / 56 (1.79%)	2 / 59 (3.39%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Inguinal hernia			
subjects affected / exposed	0 / 55 (0.00%)	1 / 56 (1.79%)	0 / 59 (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
Intestinal obstruction			
subjects affected / exposed	0 / 55 (0.00%)	1 / 56 (1.79%)	0 / 59 (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
Umbilical hernia			
subjects affected / exposed	0 / 55 (0.00%)	1 / 56 (1.79%)	0 / 59 (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
Hepatobiliary disorders			
Hyperbilirubinaemia			
subjects affected / exposed	0 / 55 (0.00%)	1 / 56 (1.79%)	0 / 59 (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
Jaundice			
subjects affected / exposed	0 / 55 (0.00%)	0 / 56 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			

Nephrolithiasis			
subjects affected / exposed	0 / 55 (0.00%)	1 / 56 (1.79%)	0 / 59 (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
Musculoskeletal and connective tissue disorders			
Rheumatoid arthritis			
subjects affected / exposed	1 / 55 (1.82%)	0 / 56 (0.00%)	0 / 59 (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
Spinal column stenosis			
subjects affected / exposed	0 / 55 (0.00%)	1 / 56 (1.79%)	0 / 59 (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
Infections and infestations			
Erysipelas			
subjects affected / exposed	0 / 55 (0.00%)	1 / 56 (1.79%)	0 / 59 (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
Gastroenteritis viral			
subjects affected / exposed	0 / 55 (0.00%)	1 / 56 (1.79%)	0 / 59 (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
Herpes zoster			
subjects affected / exposed	0 / 55 (0.00%)	0 / 56 (0.00%)	0 / 59 (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
Pneumonia			
subjects affected / exposed	0 / 55 (0.00%)	1 / 56 (1.79%)	0 / 59 (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
Pneumonia pneumococcal			
subjects affected / exposed	0 / 55 (0.00%)	1 / 56 (1.79%)	0 / 59 (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

Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 55 (0.00%)	0 / 56 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Induction Period: Placebo	Induction Period: Ozanimod HCL 0.5 mg	Induction Period: Ozanimod HCL 1 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	9 / 65 (13.85%)	8 / 65 (12.31%)	8 / 67 (11.94%)
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 65 (0.00%)	0 / 65 (0.00%)	2 / 67 (2.99%)
occurrences (all)	0	0	2
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 65 (0.00%)	0 / 65 (0.00%)	1 / 67 (1.49%)
occurrences (all)	0	0	1
Lymphocyte count decreased			
subjects affected / exposed	0 / 65 (0.00%)	0 / 65 (0.00%)	0 / 67 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 65 (0.00%)	1 / 65 (1.54%)	0 / 67 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
Headache			
subjects affected / exposed	3 / 65 (4.62%)	0 / 65 (0.00%)	2 / 67 (2.99%)
occurrences (all)	3	0	2
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	4 / 65 (6.15%)	4 / 65 (6.15%)	1 / 67 (1.49%)
occurrences (all)	4	4	1
Gastrointestinal disorders			
Colitis ulcerative			

subjects affected / exposed	1 / 65 (1.54%)	2 / 65 (3.08%)	0 / 67 (0.00%)
occurrences (all)	1	2	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 65 (1.54%)	1 / 65 (1.54%)	1 / 67 (1.49%)
occurrences (all)	1	1	1
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 65 (0.00%)	0 / 65 (0.00%)	1 / 67 (1.49%)
occurrences (all)	0	0	1
Nasopharyngitis			
subjects affected / exposed	0 / 65 (0.00%)	1 / 65 (1.54%)	0 / 67 (0.00%)
occurrences (all)	0	2	0
Respiratory tract infection viral			
subjects affected / exposed	0 / 65 (0.00%)	0 / 65 (0.00%)	0 / 67 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	2 / 65 (3.08%)	0 / 65 (0.00%)	1 / 67 (1.49%)
occurrences (all)	2	0	1

Non-serious adverse events	Maintenance Period: Placebo	Maintenance Period: Ozanimod HCL 0.5 mg	Maintenance Period: Ozanimod HCL 1 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 25 (12.00%)	2 / 36 (5.56%)	2 / 42 (4.76%)
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 25 (0.00%)	1 / 36 (2.78%)	1 / 42 (2.38%)
occurrences (all)	0	1	1
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 25 (0.00%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Lymphocyte count decreased			
subjects affected / exposed	0 / 25 (0.00%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			

Hypertension			
subjects affected / exposed	0 / 25 (0.00%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 25 (0.00%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 25 (0.00%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Colitis ulcerative			
subjects affected / exposed	1 / 25 (4.00%)	0 / 36 (0.00%)	1 / 42 (2.38%)
occurrences (all)	1	0	1
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 25 (0.00%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Bronchitis			
subjects affected / exposed	1 / 25 (4.00%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences (all)	1	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 25 (0.00%)	1 / 36 (2.78%)	0 / 42 (0.00%)
occurrences (all)	0	1	0
Respiratory tract infection viral			
subjects affected / exposed	0 / 25 (0.00%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	1 / 25 (4.00%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences (all)	1	0	0

Non-serious adverse events	Open-Label Treatment Period (OLP): Placebo/Ozanimod	OLP: Ozanimod 0.5 mg/Ozanimod 1 mg	OLP: Ozanimod 1mg/Ozanimod 1 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	19 / 55 (34.55%)	17 / 56 (30.36%)	22 / 59 (37.29%)

Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 55 (1.82%)	2 / 56 (3.57%)	3 / 59 (5.08%)
occurrences (all)	3	2	4
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 55 (1.82%)	3 / 56 (5.36%)	5 / 59 (8.47%)
occurrences (all)	1	3	7
Lymphocyte count decreased			
subjects affected / exposed	0 / 55 (0.00%)	3 / 56 (5.36%)	3 / 59 (5.08%)
occurrences (all)	0	3	3
Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 55 (3.64%)	1 / 56 (1.79%)	7 / 59 (11.86%)
occurrences (all)	2	1	8
Nervous system disorders			
Headache			
subjects affected / exposed	3 / 55 (5.45%)	1 / 56 (1.79%)	3 / 59 (5.08%)
occurrences (all)	3	1	3
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	4 / 55 (7.27%)	3 / 56 (5.36%)	0 / 59 (0.00%)
occurrences (all)	9	5	0
Gastrointestinal disorders			
Colitis ulcerative			
subjects affected / exposed	4 / 55 (7.27%)	0 / 56 (0.00%)	0 / 59 (0.00%)
occurrences (all)	5	0	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	2 / 55 (3.64%)	1 / 56 (1.79%)	4 / 59 (6.78%)
occurrences (all)	2	1	4
Infections and infestations			
Bronchitis			
subjects affected / exposed	3 / 55 (5.45%)	1 / 56 (1.79%)	0 / 59 (0.00%)
occurrences (all)	4	1	0
Nasopharyngitis			
subjects affected / exposed	1 / 55 (1.82%)	3 / 56 (5.36%)	3 / 59 (5.08%)
occurrences (all)	1	3	4

Respiratory tract infection viral subjects affected / exposed occurrences (all)	3 / 55 (5.45%) 3	1 / 56 (1.79%) 1	0 / 59 (0.00%) 0
Upper respiratory tract infection subjects affected / exposed occurrences (all)	3 / 55 (5.45%) 4	2 / 56 (3.57%) 2	5 / 59 (8.47%) 5

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
19 October 2012	• The limit on the proportion of patients that have previously received anti-TNF therapy anticipated to participate in the study has been increased from 35% to 50%. • The examination of the patient's skin for lesions has been incorporated into the PE by the Investigator. If a skin lesion is identified the subject will be referred to a Dermatologist. • PFT are no longer required at screening, Week 8 and 20 and will not be performed unless new pulmonary/respiratory signs and symptoms are noted. PFT will be done at End of Study/ET on all patients. • All patients with clinically relevant pulmonary signs and symptom will be excluded from the study, unless it is found that the subject's FEV1 and FVC were both > 70% of predicted value on pulmonary function testing during screening. • DLCO (diffusing capacity of the lung for carbon monoxide) has been removed from the PFT requirements. • OCT (Optical coherence tomography) will be required at Screening and at the End of Study/ET but an OCT at Week 8 has been removed. • Vedolizumab has been added to the list of medications that require a 4 month wash out. • Patients that were unresponsive to vedolizumab have been excluded from the study. • The protocol has been modified to more clarify windows allowed during dose titration. • The protocol has been modified to clarify the cardiac monitoring requirements and to clarify how the cardiac monitoring requirements will be modified once review of HR and Holter monitoring data from ongoing studies is complete and that review shows no notable HR or conduction abnormalities.
08 November 2012	• Increased the limit on the proportion of patients who had previously received anti-TNF therapy from 35% to 50% • Incorporated skin examinations into the physical examination by the Investigator with referrals to dermatologists as needed • Reduced the frequency of PFT and allowed for exceptions to DLCO testing • Excluded patients with clinically relevant pulmonary signs and symptoms unless the patient's FEV1 and FVC were both > 70% of predicted values at Screening • Reduced frequency of OCT assessment • Added vedolizumab to the list of medications requiring a 4-month washout and excluded patients who were unresponsive to vedolizumab • Added WBC alert criteria and the corresponding actions that should be taken regarding stopping and restarting study drug
05 August 2013	• Divided the Induction Period into a dose titration period lasting from 8 to 15 days and an assigned dose treatment period of 8 weeks. Changed the length of the induction period from 8 weeks to 9-10 weeks depending on the length of the titration period. • Allowed patients who complete the Maintenance Period or who relapse during the Maintenance Period to participate in the Open-Label Period • Extended the Open-Label Period until the last patient who enters the Open-Label Period completed 20 weeks in the Open-Label Period • Allowed patients to participate who had past history of stable cardiac conditions, chronic hepatitis A or hepatitis E infection, or current well-controlled type 2 diabetes • Excluded patients who had failed to respond to anti- integrin therapies • Added an interim analysis to be completed after 50% of patients completed Week 8
03 February 2014	• Increased the upper limit of the eligible age range from ≤ 65 years to ≤ 75 years • Increased the allowed concomitant daily dose of prednisone from ≤ 20 mg to ≤ 30 mg • Allowed patients who failed to respond to anti-integrin agents to participate in the trial • Allow patients receiving azathioprine, 6-MP, or methotrexate at Screening to continue these medications until randomization • Removed the interim analysis and defined the levels of significance for the final analyses • Removed substrates and weak inhibitors of CYP3A4 from the list of prohibited concomitant medications • Removed cardiac monitoring during dose escalation on Days 5 and 8 unless a patient had experienced cardiac safety issues on Day 1

23 December 2014	• Increased the duration of the Open-Label Period to up to 6 years, or approximately December 2019, or until marketing approval • Added endoscopies and Mayo score calculation at 48- week intervals for patients who continue in the Open- Label Period past Week 8

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported