



Clinical trial results:

Induction Study #1 - A Phase 3, Multicenter, Randomized, Double-Blind, Placebo-Controlled

Study of Oral Ozanimod as Induction Therapy for Moderately to Severely Active Crohn's Disease

Summary

EudraCT number	2017-004292-31
Trial protocol	LV CZ DE BG ES NO BE DK PL IE GB HR FR IT RO
Global end of trial date	01 October 2024

Results information

Result version number	v1 (current)
This version publication date	23 October 2025
First version publication date	23 October 2025

Trial information

Trial identification

Sponsor protocol code	RPC01-3201
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03440372
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, Global Submission Management, Clinical Trials, mg-gsm-ct@bms.com
Scientific contact	Bristol-Myers Squibb Study Director, Bristol-Myers Squibb, mg-gsm-ct@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	01 October 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	01 October 2024
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

Proportion of subjects with a CDAI score < 150 at Week 12

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 participants were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	27 February 2018
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	3 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 14
Country: Number of subjects enrolled	India: 22
Country: Number of subjects enrolled	Korea, Republic of: 4
Country: Number of subjects enrolled	Belarus: 2
Country: Number of subjects enrolled	Bosnia and Herzegovina: 1
Country: Number of subjects enrolled	Bulgaria: 8
Country: Number of subjects enrolled	Croatia: 7
Country: Number of subjects enrolled	Czechia: 38
Country: Number of subjects enrolled	Georgia: 2
Country: Number of subjects enrolled	Latvia: 3
Country: Number of subjects enrolled	Moldova, Republic of: 21
Country: Number of subjects enrolled	Poland: 73
Country: Number of subjects enrolled	Romania: 19
Country: Number of subjects enrolled	Russian Federation: 43
Country: Number of subjects enrolled	Serbia: 2
Country: Number of subjects enrolled	Ukraine: 116
Country: Number of subjects enrolled	Canada: 14
Country: Number of subjects enrolled	Mexico: 6
Country: Number of subjects enrolled	United States: 71

Country: Number of subjects enrolled	Argentina: 5
Country: Number of subjects enrolled	Chile: 11
Country: Number of subjects enrolled	Israel: 12
Country: Number of subjects enrolled	Saudi Arabia: 11
Country: Number of subjects enrolled	Türkiye: 5
Country: Number of subjects enrolled	Belgium: 9
Country: Number of subjects enrolled	France: 6
Country: Number of subjects enrolled	Germany: 31
Country: Number of subjects enrolled	Ireland: 7
Country: Number of subjects enrolled	Italy: 39
Country: Number of subjects enrolled	Spain: 7
Country: Number of subjects enrolled	Switzerland: 7
Country: Number of subjects enrolled	United Kingdom: 9
Worldwide total number of subjects	625
EEA total number of subjects	247

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)	593
From 65 to 84 years	32
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 625 participants were randomized and of these 623 received at least one dose of study treatment.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Treatment 1

Arm description:

Participants received ozanimod 0.92 mg

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

Dosage and administration details:

0.92 mg daily

Arm title	Treatment 2
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Arm description:

Participants received ozanimod matching placebo

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:

0.92 mg daily

Number of subjects in period 1	Treatment 1	Treatment 2
Started	417	208
Completed	416	207
Not completed	1	1
Not Completed	1	1

Period 2	
Period 2 title	Treatment
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Carer, Assessor
Arms	
Are arms mutually exclusive?	Yes
Arm title	Treatment 1
Arm description:	
Participants received ozanimod 0.92 mg	
Arm type	Experimental
Investigational medicinal product name	Ozanimod
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use
Dosage and administration details:	
0.92 mg daily	
Arm title	Treatment 2
Arm description:	
Participants received ozanimod matching placebo	
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:	
0.92 mg daily	

Number of subjects in period 2	Treatment 1	Treatment 2
Started	416	207
Completed	378	185
Not completed	38	22
Consent withdrawn by subject	12	8
Adverse event, non-fatal	16	8
Pregnancy	1	-
Other Reason	2	3
Study Terminated by Sponsor	2	1
Lost to follow-up	1	-

Lack of efficacy	4	2
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Baseline characteristics

Reporting groups

Reporting group title	Treatment 1
Reporting group description:	
Participants received ozanimod 0.92 mg	
Reporting group title	Treatment 2
Reporting group description:	
Participants received ozanimod matching placebo	

Reporting group values	Treatment 1	Treatment 2	Total
Number of subjects	417	208	625
Age Categorical			
Units: Participants			
<=18 years	0	0	0
Between 18 and 65 years	394	199	593
>=65 years	23	9	32
Sex: Female, Male			
Units: Participants			
Female	210	97	307
Male	207	111	318
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	0	1	1
Asian	21	9	30
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	2	4	6
White	378	188	566
More than one race	0	0	0
Unknown or Not Reported	16	6	22
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	20	14	34
Not Hispanic or Latino	391	190	581
Unknown or Not Reported	6	4	10

End points

End points reporting groups

Reporting group title	Treatment 1
Reporting group description:	
Participants received ozanimod 0.92 mg	
Reporting group title	Treatment 2
Reporting group description:	
Participants received ozanimod matching placebo	
Reporting group title	Treatment 1
Reporting group description:	
Participants received ozanimod 0.92 mg	
Reporting group title	Treatment 2
Reporting group description:	
Participants received ozanimod matching placebo	

Primary: Percent of Participants with a Crohn's Disease Activity Index (CDAI) Score < 150 at Week 12

End point title	Percent of Participants with a Crohn's Disease Activity Index (CDAI) Score < 150 at Week 12
End point description:	
Crohn's Disease Activity Index (CDAI) is a composite score used to measure the clinical activity of Crohn's disease. CDAI uses 8 variables: number of soft/liquid stools, severity of abdominal pain (0=none to 3=severe), general well-being (0=well to 4=terrible), presence of complications, need for antidiarrheal drugs, presence of abdominal mass, hematocrit, and change in body weight. Scores for stool number, abdominal pain, and well-being are summed over the 7 days before each visit. The other factors are also recorded and weighted to create a total CDAI score, which ranges from 0–600, with higher scores indicating worse disease (score 150–219 = mild, 220–450 = moderate, >450 = severe). This measure reports the percentage of participants whose CDAI score was below 150 at 12 weeks.	
End point type	Primary
End point timeframe:	
At Week 12	

End point values	Treatment 1	Treatment 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	416	207		
Units: Percentage of Participants				
number (not applicable)				
Responders	31.3	20.8		
Non-Responders	64.4	73.4		
Imputed Non-Responders	4.3	5.8		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Treatment 1 v Treatment 2
Number of subjects included in analysis	623
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0049
Method	Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	1.79
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.19
upper limit	2.7

Secondary: Percent of Participants with Average Daily Abdominal Pain Score ≤ 1 Point, and Average Daily Stool Frequency Score ≤ 3 Points with Abdominal Pain and Stool Frequency no Worse than Baseline at Week 12

End point title	Percent of Participants with Average Daily Abdominal Pain Score ≤ 1 Point, and Average Daily Stool Frequency Score ≤ 3 Points with Abdominal Pain and Stool Frequency no Worse than Baseline at Week 12
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End point description:

Abdominal pain (AP) and stool frequency (SF) clinical remission was defined as an average daily abdominal pain score ≤ 1 and average daily stool frequency ≤ 3 , with AP and SF no worse than baseline at Week 12. AP was graded on a scale from 0 (none) to 3 (severe), and SF was defined as the number of liquid or soft stools per day. This measure reports the percentage of participants who, by Week 12, had low abdominal pain (score ≤ 1) and three or fewer bowel movements per day, without worsening symptoms compared to when they started the study. Participants began using the diary at the first visit and continued throughout the study.

End point type	Secondary
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End point timeframe:

At Week 12

End point values	Treatment 1	Treatment 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	416	207		
Units: Percentage of Participants				
number (not applicable)				
Responders	30.5	21.7		
Non-Responders	66.3	72.5		
Imputed Non-Responders	3.1	5.8		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Treatment 1 v Treatment 2
Number of subjects included in analysis	623
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0179
Method	Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	1.63
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.09
upper limit	2.43

Secondary: Percent of Participants with a Simple Endoscopic Score for Crohn's Disease (SES-CD) Score Decrease from Baseline of $\geq 50\%$ at Week 12

End point title	Percent of Participants with a Simple Endoscopic Score for Crohn's Disease (SES-CD) Score Decrease from Baseline of $\geq 50\%$ at Week 12
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End point description:

The Simple Endoscopic Score for Crohn's Disease (SES-CD) is used to assess the degree of inflammation in patients with Crohn's disease. The SES-CD evaluates four components—size of ulcers, ulcerated surface, affected surface, and presence of narrowing—each scored from 0 (none) to 3 (severe). These components are assessed across five intestinal segments: ileum, right colon, transverse colon, left colon, and rectum. The total SES-CD score is the sum of the individual component scores across all segments, ranging from 0 to 12 per segment and 0 to 60 overall, with higher scores indicating greater inflammation. Baseline is defined as the last assessment prior to the first drug administration (based on the time of measurement, if available; otherwise, the last assessment prior to or on the date of first drug administration). This measure reports the percentage of participants whose SES-CD score improved by 50% or more from baseline to Week 12.

End point type	Secondary
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End point timeframe:

At Week 12

End point values	Treatment 1	Treatment 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	416	207		
Units: Percentage of Participants				
number (not applicable)				
Responders	22.1	18.4		
Non-Responders	71.6	77.3		
Imputed Non-Responders	6.3	4.3		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Treatment 1 v Treatment 2
Number of subjects included in analysis	623
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.272
Method	Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	1.27
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.83
upper limit	1.93

Secondary: Percent of Participants with Crohn's Disease Activity Index (CDAI) Reduction from Baseline of ≥ 100 Points or CDAI Score < 150 at Week 12

End point title	Percent of Participants with Crohn's Disease Activity Index (CDAI) Reduction from Baseline of ≥ 100 Points or CDAI Score < 150 at Week 12
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End point description:

The Crohn's Disease Activity Index (CDAI) is a composite score used to measure the clinical activity of Crohn's disease. CDAI is calculated using 8 variables: number of soft/liquid stools, severity of abdominal pain (0 [none] to 3 [severe]), general well-being (0 [well] to 4 [terrible]), presence of complications, use of antidiarrheal drugs, presence of an abdominal mass, hematocrit, and deviation in body weight. Scores for stool frequency, pain, and well-being are summed over the 7 days prior to each visit. The remaining variables are also weighted and included in the total CDAI score, which ranges from 0–600, with higher scores indicating worse disease activity (score 150–219 = mild, 220–450 = moderate, >450 = severe). This measure reports the percentage of participants whose CDAI score improved by at least 100 points, or was below 150, at 12 weeks.

End point type	Secondary
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End point timeframe:

At Week 12

End point values	Treatment 1	Treatment 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	416	207		
Units: Percentage of Participants				
number (not applicable)				
Responders	48.8	39.1		
Non-Responders	46.9	55.1		
Imputed Non-Responders	4.3	5.8		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Treatment 1 v Treatment 2
Number of subjects included in analysis	623
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0193
Method	Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	1.52
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.07
upper limit	2.15

Secondary: Percent of Participants with Crohn's Disease Activity Index (CDAI) Reduction from Baseline of ≥ 100 Points or CDAI Score < 150 and Simple Endoscopic Score for Crohn's Disease (SES-CD) Decrease from Baseline of $\geq 50\%$ at Week 12

End point title	Percent of Participants with Crohn's Disease Activity Index (CDAI) Reduction from Baseline of ≥ 100 Points or CDAI Score < 150 and Simple Endoscopic Score for Crohn's Disease (SES-CD) Decrease from Baseline of $\geq 50\%$ at Week 12
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End point description:

The Crohn's Disease Activity Index (CDAI) is a composite score used to measure clinical activity in Crohn's disease. CDAI is based on 8 variables: number of soft/liquid stools, severity of abdominal pain (0 [none] to 3 [severe]), general well-being (0 [well] to 4 [terrible]), presence of complications, use of antidiarrheal drugs, abdominal mass, hematocrit, and deviation in body weight. Scores for stool frequency, pain, and well-being are summed over 7 days prior to each visit. The total CDAI score ranges from 0–600, with higher scores indicating worse disease activity (score 150–219 = mild, 220–450 = moderate, >450 = severe). This measure reports the percentage of participants whose Crohn's disease improved at 12 weeks, defined as a CDAI decrease of at least 100 points or a score below 150, along with at least a 50% reduction in intestinal inflammation (SES-CD score).

End point type	Secondary
End point timeframe:	
At Week 12	

End point values	Treatment 1	Treatment 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	416	207		
Units: Percentage of Participants				
number (not applicable)				
Responders	16.6	13.5		
Non-Responders	78.6	84.1		
Imputed Non-Responders	4.8	2.4		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Treatment 1 v Treatment 2
Number of subjects included in analysis	623
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.3167
Method	Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	1.28
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.79
upper limit	2.05

Secondary: Percent of Participants with Crohn's Disease Activity Index (CDAI) Score < 150 at Week 12 and Simple Endoscopic Score for Crohn's Disease (SES-CD) Decrease from Baseline of ≥ 50% at Week 12

End point title	Percent of Participants with Crohn's Disease Activity Index (CDAI) Score < 150 at Week 12 and Simple Endoscopic Score for Crohn's Disease (SES-CD) Decrease from Baseline of ≥ 50% at Week 12
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End point description:

This endpoint measured the percentage of participants who achieved both clinical remission and significant endoscopic improvement at Week 12. Clinical remission was defined as a Crohn's Disease Activity Index (CDAI) score of less than 150 at Week 12. Endoscopic improvement was defined as a decrease of at least 50% from baseline in the Simple Endoscopic Score for Crohn's Disease (SES-CD) at Week 12. The CDAI was a composite score assessing disease activity based on symptoms and laboratory values, while the SES-CD evaluated endoscopic findings in the intestinal mucosa. Achieving both criteria indicated substantial improvement in both symptoms and intestinal inflammation.

End point type	Secondary
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End point timeframe:

At Week 12

End point values	Treatment 1	Treatment 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	416	207		
Units: Percent of Participants				
number (not applicable)				
Responders	16.6	13.5		
Non-Responders	78.6	84.1		
Imputed Non-Responders	4.8	2.4		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Treatment 1 v Treatment 2
Number of subjects included in analysis	623
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.3167
Method	Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	1.28
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.79
upper limit	2.05

Secondary: Percent of Participants with an Average Daily Abdominal Pain Score ≤ 1 Point, and Average Daily Stool Frequency Score ≤ 3 Points with Abdominal Pain and Stool Frequency no Worse than Baseline and an SES-CD ≤ 4 Points and Decrease ≥ 2 Points at Week 12

End point title	Percent of Participants with an Average Daily Abdominal Pain Score ≤ 1 Point, and Average Daily Stool Frequency Score ≤ 3 Points with Abdominal Pain and Stool Frequency no Worse than Baseline and an SES-CD ≤ 4 Points and Decrease ≥ 2 Points at Week 12
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End point description:

This measure reports the percentage of participants whose Crohn's disease symptoms and gut inflammation improved at 12 weeks. It includes those with mild or no belly pain (score ≤ 1), no more than three bowel movements per day (score ≤ 3), and no worsening from baseline. It also includes participants whose gut inflammation, measured by SES-CD, was low (score ≤ 4) and improved by at least 2 points. SES-CD assesses inflammation based on four components: size of ulcers, ulcerated surface, affected surface, and presence of narrowing, each scored from 0 (none) to 3 (severe) across five segments (ileum, right colon, transverse colon, left colon, rectum). The total SES-CD score ranges from 0–12 per segment and 0–60 overall, with higher scores indicating greater inflammation.

End point type	Secondary
End point timeframe:	
At Week 12	

End point values	Treatment 1	Treatment 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	416	207		
Units: Percentage of Participants				
number (not applicable)				
Responders	8.7	6.3		
Non-Responders	88.0	91.3		
Imputed Non-Responders	3.4	2.4		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Treatment 1 v Treatment 2
Number of subjects included in analysis	623
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.2978
Method	Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	1.42
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.73
upper limit	2.77

Secondary: Percent of Participants with an Average Daily Abdominal Pain Score ≤ 1 Point, and Average Daily Stool Frequency Score ≤ 3 Points with Abdominal Pain and Stool Frequency Score no Worse than Baseline and an SES-CD Decrease from Baseline of $\geq 50\%$ at Week 12

End point title	Percent of Participants with an Average Daily Abdominal Pain Score ≤ 1 Point, and Average Daily Stool Frequency Score ≤ 3 Points with Abdominal Pain and Stool Frequency Score no Worse than Baseline and an SES-CD Decrease from Baseline of $\geq 50\%$ at Week 12
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End point description:

This measure reports the percentage of participants whose Crohn's disease symptoms and gut inflammation improved at 12 weeks. It includes those with mild or no belly pain (score ≤ 1), no more than three bowel movements per day (score ≤ 3), and no worsening from baseline. It also includes participants whose gut inflammation, measured by SES-CD, improved by at least 50% from baseline. SES-CD assesses inflammation based on four components: size of ulcers, ulcerated surface, affected surface, and presence of narrowing, each scored from 0 (none) to 3 (severe) across five segments (ileum, right colon, transverse colon, left colon, rectum). The total SES-CD score ranges from 0–12 per segment and 0–60 overall, with higher scores indicating greater inflammation.

End point type	Secondary
End point timeframe:	
At Week 12	

End point values	Treatment 1	Treatment 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	416	207		
Units: Percentage of Participants				
number (not applicable)				
Responders	11.1	7.7		
Non-Responders	85.6	89.9		
Imputed Non-Responders	3.4	2.4		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Treatment 1 v Treatment 2
Number of subjects included in analysis	623
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.1895
Method	Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	1.49
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.82
upper limit	2.72

Secondary: Histologic Improvement Based on Differences between Ozanimod and Placebo in Histologic Disease Activity Scores (ie, Global Histologic Activity Score (GHAS) Changes) at Week 12

End point title	Histologic Improvement Based on Differences between Ozanimod and Placebo in Histologic Disease Activity Scores (ie, Global Histologic Activity Score (GHAS) Changes) at Week 12
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End point description:

This measure evaluated improvement in gut inflammation at 12 wks using Global Histologic Activity Score (GHAS). GHAS was assessed for each ileal & colonic segment (ileum, right colon, transverse colon, left colon-descending/sigmoid colon & rectum). Segment subscores were calculated by adding scores for epithelial damage/tissue changes(0–2), cellular infiltration for mononuclear & polymorphonuclear cells(0–2 each), presence of certain cells(0–3) & erosion, ulcers, granulomas(0 or 1). GHAS score within each segment ranged from 0–16 & across five segments ranged from 0–80. Higher scores indicated more inflammation. Responders with histologic remission was defined as GHAS score ≤ 8 (each segment) [meeting criteria: epithelial damage(0), architectural changes(0–2), mononuclear cell infiltration(0–2), polymorphonuclear cell infiltration(0), polymorphonuclear cells in epithelium(0), erosion/ulcers(0), granuloma(0–1) & affected biopsy specimens(0–3)] & ≤ 40 (across all segments).

End point type	Secondary
End point timeframe:	
At Week 12	

End point values	Treatment 1	Treatment 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	416	207		
Units: Percentage of Participants				
number (not applicable)				
Responders	14.9	9.2		
Non-Responders	78.4	85.5		
Imputed Non-Responders	6.7	5.3		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Treatment 1 v Treatment 2
Number of subjects included in analysis	623
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0452
Method	Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	1.73
Confidence interval	
level	95 %
sides	2-sided
lower limit	1
upper limit	2.97

Secondary: Percent of Participants with Crohn's Disease Activity Index (CDAI) Reduction from Baseline of ≥ 70 Points at Week 12

End point title	Percent of Participants with Crohn's Disease Activity Index (CDAI) Reduction from Baseline of ≥ 70 Points at Week 12
End point description:	
<p>This measure reports the percentage of participants whose Crohn's disease symptoms improved meaningfully after 12 weeks of treatment, defined as a decrease of at least 70 points in their Crohn's Disease Activity Index (CDAI) score from baseline. The CDAI is a composite score used to assess clinical activity in Crohn's disease, based on 8 variables: number of soft/liquid stools, severity of abdominal pain (0 [none] to 3 [severe]), general well-being (0 [well] to 4 [terrible]), presence of complications, use of antidiarrheal drugs, presence of an abdominal mass, hematocrit, and deviation in body weight. Scores for stool frequency, pain, and well-being are summed over 7 days prior to each visit. The total CDAI score ranges from 0–600, with higher scores indicating more severe disease (score 150–219 = mild, 220–450 = moderate, >450 = severe).</p>	
End point type	Secondary
End point timeframe:	
At Week 12	

End point values	Treatment 1	Treatment 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	416	207		
Units: Percentage of Participants				
number (not applicable)				
Responders	55.3	45.4		
Non-Responders	40.4	48.8		
Imputed Non-Responders	4.3	5.8		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Treatment 1 v Treatment 2
Number of subjects included in analysis	623
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0173
Method	Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	1.52
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.08
upper limit	2.14

Secondary: Percent of Participants with Absence of Ulcers ≥ 0.5 cm with No Segment with Any Ulcerated Surface $\geq 10\%$ at Week 12

End point title	Percent of Participants with Absence of Ulcers ≥ 0.5 cm with No Segment with Any Ulcerated Surface $\geq 10\%$ at Week 12
End point description:	This measure shows the percentage of participants have no longer any large ulcers (bigger than 0.5 cm) in their gut and in any section of the gut, less than 10% of the surface has ulcers at 12 weeks. This helps to understand how well the treatment is healing the gut and reducing ulceration.
End point type	Secondary
End point timeframe:	
At Week 12	

End point values	Treatment 1	Treatment 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	416	207		
Units: Percentage of Participants				
number (not applicable)				
Responders	26.9	20.3		

Non-Responders	66.8	75.4		
Imputed Non-Responders	6.3	4.3		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Treatment 1 v Treatment 2
Number of subjects included in analysis	623
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.067
Method	Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	1.46
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.97
upper limit	2.2

Secondary: Percent of Participants with a Crohn's Disease Endoscopic Index of Severity (CDEIS) Decrease from Baseline of $\geq 50\%$ at Week 12

End point title	Percent of Participants with a Crohn's Disease Endoscopic Index of Severity (CDEIS) Decrease from Baseline of $\geq 50\%$ at Week 12
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End point description:

CDEIS is an index used to determine Crohn's disease severity by endoscopic exam of the ileum and colon. The intestine is divided into 5 segments: rectum, sigmoid/left colon, transverse colon, right colon, and ileum. In each segment, four variables are assessed: deep ulceration, superficial ulceration, percentage of ulcerated surface, and percentage of surface affected by Crohn's disease, using 10-cm visual analogue scales. The presence of ulcerated and nonulcerated stenosis is also evaluated across the entire intestine. These factors are weighted and summed for a total score from 0–44, with higher scores indicating more severe disease. This measure reports the percentage of participants whose CDEIS score improved by at least 50% at 12 weeks, based on endoscopic exam.

End point type	Secondary
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End point timeframe:

At Week 12

End point values	Treatment 1	Treatment 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	416	207		
Units: Percentage of Participants				
number (not applicable)				
Responders	25.5	19.3		
Non-Responders	68.3	76.3		

Imputed Non-Responders	6.3	4.3		
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Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Treatment 1 v Treatment 2
Number of subjects included in analysis	623
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0835
Method	Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	1.43
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.95
upper limit	2.16

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Participants were assessed for Serious Adverse Events (SAEs) and Other Adverse Events (AEs) were assessed from first dose of study medication until study completion (assessed up to approximately 79 months 5 days).

Adverse event reporting additional description:

Serious Adverse Events and Other (Not Including Serious) Adverse Events represents all participants that received at least 1 dose of study medication.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	27.0
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Reporting groups

Reporting group title	Treatment 2
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Reporting group description:

Participants received ozanimod matching placebo

Reporting group title	Treatment 1
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Reporting group description:

Participants received ozanimod 0.92 mg

Serious adverse events	Treatment 2	Treatment 1	
Total subjects affected by serious adverse events			
subjects affected / exposed	10 / 207 (4.83%)	27 / 416 (6.49%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Investigations			
Heart rate irregular			
subjects affected / exposed	1 / 207 (0.48%)	0 / 416 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma of colon			
subjects affected / exposed	0 / 207 (0.00%)	1 / 416 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma			

subjects affected / exposed	0 / 207 (0.00%)	1 / 416 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Concussion			
subjects affected / exposed	0 / 207 (0.00%)	1 / 416 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Craniofacial fracture			
subjects affected / exposed	0 / 207 (0.00%)	1 / 416 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Incision site haemorrhage			
subjects affected / exposed	1 / 207 (0.48%)	0 / 416 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin laceration			
subjects affected / exposed	1 / 207 (0.48%)	0 / 416 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Cardiac arrest			
subjects affected / exposed	0 / 207 (0.00%)	1 / 416 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Depressed level of consciousness			
subjects affected / exposed	0 / 207 (0.00%)	1 / 416 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epilepsy			
subjects affected / exposed	0 / 207 (0.00%)	1 / 416 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 207 (0.00%)	1 / 416 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Iron deficiency anaemia			
subjects affected / exposed	0 / 207 (0.00%)	1 / 416 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Gastritis			
subjects affected / exposed	0 / 207 (0.00%)	1 / 416 (0.24%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal obstruction			
subjects affected / exposed	0 / 207 (0.00%)	1 / 416 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumoperitoneum			
subjects affected / exposed	0 / 207 (0.00%)	1 / 416 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subileus			
subjects affected / exposed	1 / 207 (0.48%)	0 / 416 (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 / 207 (0.00%)	1 / 416 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Crohn's disease			
subjects affected / exposed	4 / 207 (1.93%)	10 / 416 (2.40%)	
occurrences causally related to treatment / all	0 / 5	2 / 11	
deaths causally related to treatment / all	0 / 0	0 / 0	

Anal fistula			
subjects affected / exposed	0 / 207 (0.00%)	1 / 416 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain			
subjects affected / exposed	0 / 207 (0.00%)	1 / 416 (0.24%)	
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			
Arthritis			
subjects affected / exposed	1 / 207 (0.48%)	0 / 416 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Abdominal abscess			
subjects affected / exposed	1 / 207 (0.48%)	0 / 416 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal abscess			
subjects affected / exposed	0 / 207 (0.00%)	2 / 416 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium difficile colitis			
subjects affected / exposed	0 / 207 (0.00%)	1 / 416 (0.24%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia aspiration			
subjects affected / exposed	1 / 207 (0.48%)	0 / 416 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			
subjects affected / exposed	0 / 207 (0.00%)	1 / 416 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Respiratory tract infection			
subjects affected / exposed	0 / 207 (0.00%)	1 / 416 (0.24%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Malnutrition			
subjects affected / exposed	1 / 207 (0.48%)	0 / 416 (0.00%)	
occurrences causally related to treatment / all	0 / 1	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	Treatment 2	Treatment 1	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	22 / 207 (10.63%)	22 / 416 (5.29%)	
Gastrointestinal disorders			
Crohn's disease			
subjects affected / exposed	11 / 207 (5.31%)	9 / 416 (2.16%)	
occurrences (all)	12	9	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	11 / 207 (5.31%)	13 / 416 (3.13%)	
occurrences (all)	11	13	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
26 September 2017	Protocol Version 1
19 December 2017	Protocol Version 02 (<ul style="list-style-type: none">• A general statement was made to note that additional detailed statistical information can be found in the study Statistical Analysis Plan. Therefore, details were removed from Section 9 (Statistical Considerations).• Abbreviations lists in footnotes were updated.• The list of references has been updated based on changes in this amendment.• Minor typographical corrections have been made.))
18 June 2018	Protocol Amendment 03 (<ul style="list-style-type: none">• A 75-day (± 10 days) Safety Follow-up Visit was added throughout the document and to the Table of Events to ensure adequate collection of adverse events that could be associated with investigational product. The timing of the visit is based on the estimated time needed to clear the major active metabolite of ozanimod (RPC1063, which is 5 half-lives of CC112273).• The term "patient" was changed to "subject" throughout the document in order to maintain consistency throughout the protocol.• The terms "investigational drug" and "study drug" were changed to "investigational product" throughout the document to comply with regulatory guidances and maintain consistency throughout the protocol• The term "disease remission" was changed to "clinical remission" throughout the document in order to maintain consistency with the rest of the protocol• Abbreviations lists in footnotes were updated.• The list of references has been updated based on changes in this amendment.• Minor typographical corrections have been made.• Minor editorial changes and changes for clarification were made.))
10 June 2019	Protocol Amendment 04 (<ul style="list-style-type: none">• Revisions to reflect the addition of adolescent subjects• Change to safety follow up from 75 days to 90-day (± 10 days) Safety Follow-up Visit to ensure adequate collection of adverse events that could be associated with investigational drug. The timing of the visit is based on the estimated time needed to clear the major active metabolites of RPC1063 in the vast majority of patients (ie, 5 half-lives of CC112273 and CC1084037 and accounting for variation of half-life duration in a human population).• Extended the requirements for contraception in females after treatment discontinuation from the 75-day Safety Follow-up Visit to the 90-day Safety Follow-up Visit.• Minor editorial changes to enhance clarity of the protocol, and update study personnel names.))

27 August 2020	<p>Protocol Amendment 05 (• Adjustment of Sample Size</p> <ul style="list-style-type: none"> • Refinement of Per-Protocol Population • Update Summary of Clinical Studies in Inflammatory Bowel Disease (IBD) • Update of Exploratory, Endoscopic Remission Endpoint • Exclusion Criterion for Subjects with Cardiovascular Conditions • Addition of Exclusion Criteria and Testing for SARS-CoV-2 Subjects • Pharmacodynamic (PD) Biomarker Blood and Stool Sampling to Occur at Baseline • First Dose Monitoring Will Be Required Only in Subjects Identified as at Risk for Cardiac Events • Optical Coherence Tests and Pulmonary Function Tests Will Only Be Required in Subjects Identified as At Risk • Instructions for Missed Doses • Prohibited Medication Clarifications • Inclusion of Progressive Multifocal Leukoencephalopathy (PML) and Posterior Reversible Encephalopathy Syndrome (PRES) as Adverse Events of Special Interest and Study Discontinuation Criteria • Update to Liver Function Testing and Discontinuation Criteria • Removal of Pregnant Partner • Minor administrative changes to enhance clarity of the protocol and update study personnel names.)
14 June 2021	<p>Protocol Amendment 06 (• Removal of Adolescent Subjects</p> <ul style="list-style-type: none"> • Update Summary of Clinical Studies in Inflammatory Bowel Disease (IBD) • Addition of SARS-CoV-2 Guidance • Modification of Cardiac Exclusion Criteria • Pulmonary Function Tests for all Subjects • Revision of Ocular Testing Requirements • Modification of First Dose Monitoring Requirements • Biomarker Clarifications • Product Quality Complaint Notification Update • Minor editorial changes were made to enhance clarity of the protocol, as well as an update to sponsor address, abbreviations, and references.)

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported