



Clinical trial results:

Induction Study #2 - 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	2017-004293-33
Trial protocol	HU SK LT DE FR SI AT BG GR ES SE NL PL PT FI
Global end of trial date	21 November 2023

Results information

Result version number	v1 (current)
This version publication date	27 November 2024
First version publication date	27 November 2024

Trial information

Trial identification

Sponsor protocol code	RPC01-3202
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03440385
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Bristol-Myers Squibb
Sponsor organisation address	Chaussée de la Hulpe 185, Brussels, Belgium,
Public contact	EU Study Start-Up Unit, Bristol-Myers Squibb International Corporation, clinical.trials@bms.com
Scientific contact	EU Study Start-Up Unit, Bristol-Myers Squibb International Corporation, Clinical.Trials@bms.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	18 March 2024
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	21 November 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This is a study to explore the effect of oral ozanimod as an induction treatment for participants with moderately to severely active Crohn's Disease.

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	07 March 2018
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Canada: 9
Country: Number of subjects enrolled	United States: 71
Country: Number of subjects enrolled	Bulgaria: 12
Country: Number of subjects enrolled	Georgia: 54
Country: Number of subjects enrolled	Hungary: 21
Country: Number of subjects enrolled	Lithuania: 1
Country: Number of subjects enrolled	Poland: 57
Country: Number of subjects enrolled	Russian Federation: 71
Country: Number of subjects enrolled	Serbia: 21
Country: Number of subjects enrolled	Slovakia: 17
Country: Number of subjects enrolled	Slovenia: 2
Country: Number of subjects enrolled	Ukraine: 84
Country: Number of subjects enrolled	Austria: 3
Country: Number of subjects enrolled	France: 13
Country: Number of subjects enrolled	Germany: 34
Country: Number of subjects enrolled	Greece: 1
Country: Number of subjects enrolled	Netherlands: 15
Country: Number of subjects enrolled	Portugal: 5
Country: Number of subjects enrolled	Spain: 3
Country: Number of subjects enrolled	Australia: 17

Country: Number of subjects enrolled	China: 64
Country: Number of subjects enrolled	Korea, Republic of: 3
Country: Number of subjects enrolled	Taiwan: 7
Country: Number of subjects enrolled	Colombia: 7
Country: Number of subjects enrolled	Israel: 12
Country: Number of subjects enrolled	South Africa: 2
Worldwide total number of subjects	606
EEA total number of subjects	184

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)	571
From 65 to 84 years	35
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Participants were enrolled in 26 countries.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
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Arm title	Ozanimod
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Arm description:

Participants with moderate to severe acute Crohn's disease were administered Ozanimod capsule orally. Participants were administered 0.23 milligram (mg) of Ozanimod capsule (daily) from Day 1 to Day 4 followed by 0.46 mg of Ozanimod (2 capsules of 0.23 mg daily) from Day 5 to Day 7 followed by 0.92 mg of Ozanimod capsule (daily) from Day 8 to Week 12.

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 capsule

Arm title	Placebo
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Arm description:

Participants with moderate to severely active Crohn's disease were orally administered Placebo (daily) from Day 1 to Week 12.

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:

Administered as capsule

Number of subjects in period 1	Ozanimod	Placebo
Started	403	203
Completed	360	183
Not completed	43	20
Consent withdrawn by subject	12	6
Site Closed	1	-
Adverse event, non-fatal	15	11
Other Reason	4	1
Lost to follow-up	2	-
Lack of efficacy	9	2

Baseline characteristics

Reporting groups

Reporting group title	Ozanimod
Reporting group description:	
Participants with moderate to severe acute Crohn's disease were administered Ozanimod capsule orally. Participants were administered 0.23 milligram (mg) of Ozanimod capsule (daily) from Day 1 to Day 4 followed by 0.46 mg of Ozanimod (2 capsules of 0.23 mg daily) from Day 5 to Day 7 followed by 0.92 mg of Ozanimod capsule (daily) from Day 8 to Week 12.	
Reporting group title	Placebo
Reporting group description:	
Participants with moderate to severely active Crohn's disease were orally administered Placebo (daily) from Day 1 to Week 12.	

Reporting group values	Ozanimod	Placebo	Total
Number of subjects	403	203	606
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	378	193	571
From 65-84 years	25	10	35
85 years and over	0	0	0
Age Continuous			
Units: years			
arithmetic mean	39.8	37.7	
standard deviation	± 13.69	± 13.79	-
Sex: Female, Male			
Units: Participants			
Female	182	90	272
Male	221	113	334
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	13	12	25
Not Hispanic or Latino	378	188	566
Unknown or Not Reported	12	3	15
Race/Ethnicity, Customized			
Units: Subjects			
WHITE	329	166	495
BLACK OR AFRICAN AMERICAN	7	1	8
AMERICAN INDIAN OR ALASKA NATIVE	1	0	1
ASIAN	47	29	76
NATIVE HAWAIIAN OR OTHER PACIFIC ISLANDER	1	0	1

OTHER	8	4	12
NOT REPORTED	10	3	13

End points

End points reporting groups

Reporting group title	Ozanimod
Reporting group description: Participants with moderate to severe acute Crohn's disease were administered Ozanimod capsule orally. Participants were administered 0.23 milligram (mg) of Ozanimod capsule (daily) from Day 1 to Day 4 followed by 0.46 mg of Ozanimod (2 capsules of 0.23 mg daily) from Day 5 to Day 7 followed by 0.92 mg of Ozanimod capsule (daily) from Day 8 to Week 12.	
Reporting group title	Placebo
Reporting group description: Participants with moderate to severely active Crohn's disease were orally administered Placebo (daily) from Day 1 to Week 12.	

Primary: Percentage of Participants with Crohn's Disease Activity Index (CDAI) Score < 150

End point title	Percentage of Participants with Crohn's Disease Activity Index (CDAI) Score < 150
End point description: The CDAI is a composite score that is used to measure the clinical activity of Crohn's disease (CD). The CDAI uses a questionnaire with 8 disease activity variables: number of soft/liquid stools, severity of abdominal pain, general well-being, presence of complications, need for antidiarrheal drugs, presence of an abdominal mass, hematocrit, and deviation in body weight. The sub scores of number of soft/liquid stool, severity of abdominal pain (0 [none] to 3 [Severe]), general well-being (0 [well] to 4 [terrible] were summed over the 7 days prior to each visit. Additionally, the remaining predictors were also noted and weighted to create the total CDAI score which ranged from 0-600 with a higher score indicating a worse outcome.	
End point type	Primary
End point timeframe: Week 12	

End point values	Ozanimod	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	403	203		
Units: percentage of participants				
number (not applicable)	29.8	30.5		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Ozanimod v Placebo

Number of subjects included in analysis	606
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.8125
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	0.96
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.66
upper limit	1.39

Secondary: Percentage of Participants with Abdominal Pain and Stool Frequency Clinical Remission

End point title	Percentage of Participants with Abdominal Pain and Stool Frequency Clinical Remission
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End point description:

Abdominal pain and stool frequency clinical remission was defined as average daily abdominal pain score ≤ 1 point, and average daily stool frequency ≤ 3 times with abdominal pain and stool frequency no worse than baseline at Week 12. Participants entered the responses in diaries daily. The 7 days entries prior to Week 12 visit were considered for calculating average abdominal pain score and stool frequency. The abdominal pain was graded on severity of 0 (none) to 3 (severe) scale and stool frequency was defined number of liquid or soft stools per day. Baseline was defined as the last assessment prior to the start time of the first drug administration if time of measurement is available else the last assessment prior to or on the date of the first drug administration.

End point type	Secondary
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End point timeframe:

Week 12

End point values	Ozanimod	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	403	203		
Units: percentage of participants				
number (not applicable)	29.0	26.6		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Ozanimod v Placebo

Number of subjects included in analysis	606
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.54
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	1.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.77
upper limit	1.66

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

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

The SES-CD assessed the degree of inflammation. The SES-CD assesses the following 4 components: size of ulcers, ulcerated surface, affected surface, and presence of narrowing. Each of these components was scored on a scale of 0 (none/unaffected) to 3 (worst). In the SES-CD, each of these 4 components are assessed in the five segments: ileum, right colon, transverse colon, left colon, and rectum. The SES-CD was the sum of the individual scores of each of the components across the five segments. The range of SES-CD scores was 0 - 12 for each segment, and 0 - 60 for the overall SES-CD score, with larger scores indicating greater degree of inflammation. Baseline was defined as the last assessment prior to the start time of the first drug administration if time of measurement is available else the last assessment prior to or on the date of the first drug administration.

End point type	Secondary
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End point timeframe:

Week 12

End point values	Ozanimod	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	403	203		
Units: percentage of participants				
number (not applicable)	25.6	21.2		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Ozanimod v Placebo

Number of subjects included in analysis	606
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.2411
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	1.28
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.85
upper limit	1.95

Secondary: Percentage of Participants with Reduction from Baseline in the Crohn's Disease Activity Index (CDAI) score of ≥ 100 points or a total CDAI score < 150

End point title	Percentage of Participants with Reduction from Baseline in the Crohn's Disease Activity Index (CDAI) score of ≥ 100 points or a total CDAI score < 150
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End point description:

The CDAI is a composite score that is used to measure the clinical activity of Crohn's disease (CD). The CDAI uses a questionnaire with 8 disease activity variables: number of soft/liquid stools, severity of abdominal pain, general well-being, presence of complications, need for antidiarrheal drugs, presence of an abdominal mass, hematocrit, and deviation in body weight. The sub scores of number of soft/liquid stool, severity of abdominal pain (0 [none] to 3 [Severe]), general well-being (0 [well] to 4 [terrible] were summed over the 7 days prior to each visit. Additionally, the remaining predictors were also noted and weighted to create the total CDAI score which ranged from 0-600 with a higher score indicating a worse outcome. Baseline was defined as the last assessment prior to the start time of the first drug administration if time of measurement is available else the last assessment prior to or on the date of the first drug administration.

End point type	Secondary
End point timeframe:	
Week 12	

End point values	Ozanimod	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	403	203		
Units: percentage of participants				
number (not applicable)	46.2	47.3		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Ozanimod v Placebo

Number of subjects included in analysis	606
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.7469
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	0.94
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.67
upper limit	1.34

Secondary: Percentage of Participants with Crohn's Disease Activity Index (CDAI) Score Reduction from Baseline of ≥ 100 points or CDAI score < 150 and SES-CD Decrease from Baseline of $\geq 50\%$

End point title	Percentage of Participants with Crohn's Disease Activity Index (CDAI) Score Reduction from Baseline of ≥ 100 points or CDAI score < 150 and SES-CD Decrease from Baseline of $\geq 50\%$
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End point description:

CDAI include 8 components number of soft/liquid stools, severity of abdominal pain, wellbeing, complications, need antidiarrheal drugs, abdominal mass, hematocrit, deviation in body wt. Subscores of numbers of soft/liquid stool, severity of abdominal pain (0 [none] to 3 [Severe]), general well-being (0 [well] to 4 [terrible] were summed over the 7 days prior to visit. The others weighted to create the total CDAI score ranging 0-600 with higher score indicating worse outcome. The SES-CD has 4 components size of ulcers, ulcerated surface, affected surface, presence of narrowing. Each component was scored on scale of 0 (none) to 3 (worst). In SES-CD, each of 4 components are assessed in the five segments: ileum, right, transverse, left colon, and rectum. The SES-CD was the sum of the individual scores of each of the components across the five segments. The range of SES-CD scores was 0 - 12 for each segment, and 0 - 60 for overall, with larger scores show greater degree of inflammation.

End point type	Secondary
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End point timeframe:

Week 12

End point values	Ozanimod	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	403	203		
Units: percentage of participants				
number (not applicable)	16.9	14.3		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Ozanimod v Placebo

Number of subjects included in analysis	606
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.4255
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	1.22
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.75
upper limit	1.97

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

End point title	Percentage of Participants with Crohn's Disease Activity Index (CDAI) Score < 150 and Simple Endoscopic Score for Crohn's Disease (SES-CD) Score Decrease from Baseline of ≥ 50%
End point description:	CDAI include 8 components number of soft/liquid stools, severity of abdominal pain, wellbeing, complications, need antidiarrheal drugs, abdominal mass, hematocrit, deviation in body wt. Subscores of numbers of soft/liquid stool, severity of abdominal pain (0 [none] to 3 [Severe]), general well-being (0 [well] to 4 [terrible] were summed over the 7 days prior to visit. The others weighted to create the total CDAI score ranging 0-600 with higher score indicating worse outcome. The SES-CD has 4 components size of ulcers, ulcerated surface, affected surface, presence of narrowing. Each component was scored on scale of 0 (none) to 3 (worst). In SES-CD, each of 4 components are assessed in the five segments: ileum, right, transverse, left colon, and rectum. The SES-CD was the sum of the individual scores of each of the components across the five segments. The range of SES-CD scores was 0 - 12 for each segment, and 0 - 60 for overall, with larger scores show greater degree of inflammation.
End point type	Secondary
End point timeframe:	
Week 12	

End point values	Ozanimod	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	403	203		
Units: percentage of participants				
number (not applicable)	11.7	11.3		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Ozanimod v Placebo

Number of subjects included in analysis	606
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.9313
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	1.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.6
upper limit	1.76

Secondary: Percentage of Participants with Abdominal Pain and Stool Frequency Clinical Remission and a Simple Endoscopic Score for Crohn's Disease (SES-CD) Score ≤ 4 Points and Decrease ≥ 2 Points

End point title	Percentage of Participants with Abdominal Pain and Stool Frequency Clinical Remission and a Simple Endoscopic Score for Crohn's Disease (SES-CD) Score ≤ 4 Points and Decrease ≥ 2 Points
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End point description:

Abdominal pain (AP) and stool frequency (SF) clinical remission was defined as average daily abdominal pain score ≤ 1 point, and average daily stool frequency ≤ 3 times with AP and SF no worse than baseline at Week 12. Participants entered responses in diaries daily. The 7 days entries prior to visit were considered for calculating average AP score and SF. The AP was graded on severity of 0 (none) to 3 (severe) scale and SF was defined number of liquid or soft stools per day. The SES-CD has 4 components size of ulcers, ulcerated surface, affected surface, presence of narrowing. Each component was scored on scale of 0 (none) to 3 (worst). In SES-CD, each of 4 components are assessed in the five segments: ileum, right, transverse, left colon, and rectum. The SES-CD was the sum of the individual scores of each of the components across the five segments. The range of SES-CD scores was 0 - 12 for each segment, and 0 - 60 for overall, with larger scores show greater degree of inflammation.

End point type	Secondary
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End point timeframe:

Week 12

End point values	Ozanimod	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	403	203		
Units: percentage of participants				
number (not applicable)	10.4	8.4		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Ozanimod v Placebo

Number of subjects included in analysis	606
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.4339
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	1.27
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.7
upper limit	2.31

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

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

CDEIS is an index for determining the severity of Crohn's disease with endoscopic localization to ileum and colon. The CDEIS divides the intestine into 5 segments: rectum, sigmoid and left colon, transverse colon, right colon, and ileum. Four variables are assessed in each segment: the presence of deep ulceration, the presence of superficial ulceration, the percentage of ulcerated surface, and the percentage of surface affected by CD, indicated on 10-cm visual analogue scales. In addition, the presence of ulcerated stenosis and the presence of nonulcerated stenosis are also assessed over the entire intestine. These factors are weighted and summed to calculate the total score ranging from 0- 44, with higher scores indicating more severe disease.

End point type	Secondary
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End point timeframe:

Week 12

End point values	Ozanimod	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	403	203		
Units: percentage of participants				
number (not applicable)	27.5	21.7		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Ozanimod v Placebo

Number of subjects included in analysis	606
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.1187
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	1.39
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.92
upper limit	2.11

Secondary: Percentage of Participants with CDAI Reduction from Baseline of ≥ 70 points

End point title	Percentage of Participants with CDAI Reduction from Baseline of ≥ 70 points
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End point description:

The CDAI is a composite score that is used to measure the clinical activity of Crohn's disease (CD). The CDAI uses a questionnaire with 8 disease activity variables: number of soft/liquid stools, severity of abdominal pain, general well-being, presence of complications, need for antidiarrheal drugs, presence of an abdominal mass, hematocrit, and deviation in body weight. The sub scores of number of soft/liquid stool, severity of abdominal pain (0 [none] to 3 [Severe]), general well-being (0 [well] to 4 [terrible] were summed over the 7 days prior to each visit. Additionally, the remaining predictors were also noted and weighted to create the total CDAI score which ranged from 0-600 with a higher score indicating a worse outcome. Baseline was defined as the last assessment prior to the start time of the first drug administration if time of measurement is available else the last assessment prior to or on the date of the first drug administration.

End point type	Secondary
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End point timeframe:

Week 12

End point values	Ozanimod	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	403	203		
Units: percentage of participants				
number (not applicable)	52.9	51.7		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Ozanimod v Placebo

Number of subjects included in analysis	606
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.82
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	1.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.74
upper limit	1.47

Secondary: Percentage of Participants with Absence of Ulcers ≥ 0.5 cm with no Segment with any Ulcerated Surface $\geq 10\%$

End point title	Percentage of Participants with Absence of Ulcers ≥ 0.5 cm with no Segment with any Ulcerated Surface $\geq 10\%$
End point description:	
The ulcerated surface were assessed via endoscopy.	
End point type	Secondary
End point timeframe:	
Week 12	

End point values	Ozanimod	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	403	203		
Units: percentage of participants				
number (not applicable)	25.3	24.1		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Ozanimod v Placebo
Number of subjects included in analysis	606
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.6906
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	1.06

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.71
upper limit	1.59

Secondary: Percentage of Participants with Abdominal Pain (AP) and Stool Frequency (SF) Clinical Remission and an Endoscopic (50%) Response

End point title	Percentage of Participants with Abdominal Pain (AP) and Stool Frequency (SF) Clinical Remission and an Endoscopic (50%) Response
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End point description:

AP and SF clinical remission is average daily abdominal pain score ≤ 1 point, and average daily stool frequency ≤ 3 times with AP and SF no worse than baseline at Week 12. Participants entered responses in diaries daily. The 7 days entries prior to visit were considered for calculating average AP score and SF. AP was graded on severity of 0 (none) to 3 (severe) scale and SF was defined number of liquid or soft stools per day. SES-CD has 4 components size of ulcers, ulcerated surface, affected surface, presence of narrowing. Each component was scored on scale of 0 (none) to 3 (worst). Endoscopic Response is defined as $\geq 50\%$ decrease from baseline in SES-CD. In SES-CD, each of 4 components are assessed in five segments: ileum, right, transverse, left colon, and rectum. The SES-CD was sum of individual scores of each of components across five segments. Range of SES-CD scores was 0 - 12 for each segment, and 0 - 60 for overall, with larger scores show greater degree of inflammation.

End point type	Secondary
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End point timeframe:

Week 12

End point values	Ozanimod	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	403	203		
Units: percentage of participants				
number (not applicable)	11.7	9.4		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Ozanimod v Placebo
Number of subjects included in analysis	606
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.403
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	1.28

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.72
upper limit	2.26

Secondary: Percentage of Participants with Global Histologic Activity Score (GHAS) Remission

End point title	Percentage of Participants with Global Histologic Activity Score (GHAS) Remission
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End point description:

GHAS assesses the inflammation and mucosal damage. GHAS has 8 components Epithelial damage, Architectural changes, Infiltration of mononuclear cells in the lamina propria, Infiltration of polymorphonuclear cells in the lamina propria, Polymorphonuclear cells in epithelium, Presence of erosion and/or ulcers, Presence of granuloma and number of biopsy specimens affected. Each of these components was scored on a scale of 0 (none/unaffected) to 2 (worst). Each of these 8 components are assessed in the five segments: ileum, right colon, transverse colon, left colon, and rectum. Within each segment, the GHAS score has a range of 0 – 16, and the total GHAS score has a range of 0 – 80. Higher numbers correspond to more inflammation and more mucosal damage. Baseline was defined as the last assessment prior to the start time of the first drug administration if time of measurement is available else the last assessment prior to or on the date of the first drug administration.

End point type	Secondary
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End point timeframe:

Week 12

End point values	Ozanimod	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	403	203		
Units: percentage of participants				
number (not applicable)	13.6	10.8		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Ozanimod v Placebo
Number of subjects included in analysis	606
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.333
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	1.3

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.77
upper limit	2.2

Secondary: Percentage of Participants with Robarts Histologic Index (RHI) Mucosal Healing at Week 12

End point title	Percentage of Participants with Robarts Histologic Index (RHI) Mucosal Healing at Week 12
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End point description:

RHI mucosal healing was defined as RHI remission combined with SES-CD ≤ 4 points and a SES-CD decrease from baseline ≥ 2 points with no SES-CD sub-score >1 point. RHI Remission is defined as no active inflammation in any measured segment. The SES-CD assesses the following 4 components: size of ulcers, ulcerated surface, affected surface, and presence of narrowing. Each of these components was scored on a scale of 0 (none/unaffected) to 3 (worst). In the SES-CD, each of these 4 components are assessed in the five segments: ileum, right colon, transverse colon, left colon, and rectum. The SES-CD was the sum of the individual scores of each of the components across the five segments. The range of SES-CD scores was 0 - 12 for each segment, and 0 - 60 for the overall SES-CD score, with larger scores indicating greater degree of inflammation.

End point type	Secondary
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End point timeframe:

Week 12

End point values	Ozanimod	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	403	203		
Units: percentage of participants				
number (not applicable)	4.0	4.9		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Ozanimod v Placebo
Number of subjects included in analysis	606
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.563 ^[1]
Method	Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	0.79
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.35
upper limit	1.78

Notes:

[1] - Odds ratio, and p-value are obtained using the CMH test stratified by corticosteroid use at baseline (yes or no), and prior biologic use (yes or no).

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All cause mortality, non serious adverse events and serious adverse events were collected from the first dose and up to approximately 31 weeks.

Adverse event reporting additional description:

Treated population include all the participants who were treated with at least one dose of study drug. 1 participant earlier randomized or pre-assigned to Placebo arm in error received Ozanimod

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	26.1
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Reporting groups

Reporting group title	Placebo
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Reporting group description:

Participants with moderate to severely active Crohn's disease were orally administered Placebo (daily) from Day 1 to Week 12.

Reporting group title	Ozanimod 0.92 mg
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Reporting group description:

Participants with moderate to severe acute Crohn's disease were administered Ozanimod capsule orally. Participants were administered 0.23 milligram (mg) of Ozanimod capsule (daily) from Day 1 to Day 4 followed by 0.46 mg of Ozanimod (2 capsules of 0.23 mg daily) from Day 5 to Day 7 followed by 0.92 mg of Ozanimod capsule (daily) from Day 8 to Week 12.

Serious adverse events	Placebo	Ozanimod 0.92 mg	
Total subjects affected by serious adverse events			
subjects affected / exposed	11 / 202 (5.45%)	24 / 404 (5.94%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Femur fracture			
subjects affected / exposed	0 / 202 (0.00%)	1 / 404 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Incision site haematoma			
subjects affected / exposed	1 / 202 (0.50%)	0 / 404 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative ileus			

subjects affected / exposed	0 / 202 (0.00%)	1 / 404 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Pericarditis			
subjects affected / exposed	1 / 202 (0.50%)	0 / 404 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Syncope			
subjects affected / exposed	0 / 202 (0.00%)	1 / 404 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vertebrobasilar insufficiency			
subjects affected / exposed	0 / 202 (0.00%)	1 / 404 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 202 (0.00%)	1 / 404 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Retinal vein occlusion			
subjects affected / exposed	0 / 202 (0.00%)	1 / 404 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Crohn's disease			
subjects affected / exposed	6 / 202 (2.97%)	10 / 404 (2.48%)	
occurrences causally related to treatment / all	1 / 6	2 / 10	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colonic fistula			

subjects affected / exposed	1 / 202 (0.50%)	0 / 404 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain			
subjects affected / exposed	0 / 202 (0.00%)	2 / 404 (0.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal obstruction			
subjects affected / exposed	0 / 202 (0.00%)	4 / 404 (0.99%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Proctitis			
subjects affected / exposed	1 / 202 (0.50%)	0 / 404 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis			
subjects affected / exposed	0 / 202 (0.00%)	1 / 404 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal obstruction			
subjects affected / exposed	0 / 202 (0.00%)	1 / 404 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fistula of small intestine			
subjects affected / exposed	0 / 202 (0.00%)	1 / 404 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 202 (0.00%)	1 / 404 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			

Rash papular			
subjects affected / exposed	1 / 202 (0.50%)	0 / 404 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Arthritis enteropathic			
subjects affected / exposed	0 / 202 (0.00%)	1 / 404 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Abdominal wall abscess			
subjects affected / exposed	1 / 202 (0.50%)	0 / 404 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19			
subjects affected / exposed	0 / 202 (0.00%)	1 / 404 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	1 / 202 (0.50%)	0 / 404 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Electrolyte imbalance			
subjects affected / exposed	0 / 202 (0.00%)	1 / 404 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypokalaemia			
subjects affected / exposed	0 / 202 (0.00%)	1 / 404 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malnutrition			

subjects affected / exposed	0 / 202 (0.00%)	1 / 404 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Placebo	Ozanimod 0.92 mg	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	11 / 202 (5.45%)	15 / 404 (3.71%)	
Gastrointestinal disorders			
Crohn's disease			
subjects affected / exposed	11 / 202 (5.45%)	15 / 404 (3.71%)	
occurrences (all)	13	18	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
19 December 2017	The CDEIS is being introduced as an additional secondary endpoint because it is an established endoscopic measure. A change has been made to provide further guidance to investigators on the management of subjects with symptomatic bradycardia, including a reference to local guidelines.
18 June 2018	Exploratory endpoints updated
10 June 2019	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.
03 September 2020	Adjustment of Sample Size, Refinement of Per-Protocol Population, Update Summary of Clinical Studies in Inflammatory Bowel Disease (IBD), Exploratory, Endoscopic Remission Endpoint, and Exclusion criteria was updated
14 January 2021	Removal of Adolescent Subjects

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported