Clinical trial results:
A Phase 2, Randomized, Double-Blind, Placebo-Controlled, Parallel Group, Multi-Center Study to Investigate the Safety and Efficacy of APD334 in Patients with Moderately to Severely Active Ulcerative Colitis

Summary

EudraCT number	2015-001942-28
Trial protocol	CZ GB ES DE LV HU LT FR PL BG BE AT
Global end of trial date	14 February 2018

Results information

Result version number	v1 (current)
This version publication date	16 December 2018
First version publication date	16 December 2018

Trial information

Trial identification

Sponsor protocol code	APD334-003

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02447302
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Arena Pharmaceuticals, Inc.
Sponsor organisation address	6154 Nancy Ridge Drive, San Diego, United States, CA 92121
Public contact	Chris Cabell, Arena Pharmaceuticals, Inc., ct.gov@arenapharm.com
Scientific contact	Chris Cabell, Arena Pharmaceuticals, Inc., ct.gov@arenapharm.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 July 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	14 February 2018
Global end of trial reached?	Yes
Global end of trial date	14 February 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine the effect of treatment with APD334 in inducing clinical remission at 12 weeks.

Protection of trial subjects:

Compliance was assessed using subject data recorded in the drug accountability form of the electronic Case Report Forms (eCRFs). On each day, a subject had to take his or her assigned study drug. The compliance rate for each subject was computed as 100% × (actual number of capsules taken over the study period) / (designated total number of capsules that should have been taken over the study period).
There are prohibited medications and medications considered with regard to concomitant procedures.

Background therapy: -

Evidence for comparator:

For all analyses, one model was fitted for the individual treatment comparisons etrasimod 2 mg versus placebo, etrasimod 1 mg versus placebo, and etrasimod 2 mg versus etrasimod 1 mg with the treatment term containing the 3 groups (etrasimod 1 mg, etrasimod 2 mg, and placebo), and the second model was fitted for the pooled treatment comparison (etrasimod 1 mg and etrasimod 2 mg versus placebo) with the treatment term containing 2 treatment groups (pooled 2 mg etrasimod and 1 mg, and placebo).

Actual start date of recruitment	01 July 2015
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	Poland: 24
Country: Number of subjects enrolled	Romania: 1
Country: Number of subjects enrolled	Spain: 5
Country: Number of subjects enrolled	United Kingdom: 2
Country: Number of subjects enrolled	Austria: 1
Country: Number of subjects enrolled	Belgium: 3
Country: Number of subjects enrolled	Bulgaria: 6
Country: Number of subjects enrolled	Germany: 11
Country: Number of subjects enrolled	Hungary: 10
Country: Number of subjects enrolled	Latvia: 2
Country: Number of subjects enrolled	Lithuania: 1
Country: Number of subjects enrolled	Canada: 5
Country: Number of subjects enrolled	Korea, Republic of: 3
Country: Number of subjects enrolled	Russian Federation: 23

Country: Number of subjects enrolled	Ukraine: 24
Country: Number of subjects enrolled	United States: 35
Worldwide total number of subjects	156
EEA total number of subjects	66

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)	150
From 65 to 84 years	6
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study included a screening period (up to 28 days), a double-blind induction treatment period (12 weeks), and a possible follow-up visit (2 weeks after the last study visit). The target population consisted of male or female subjects aged between 18 and 80 years (inclusive), with moderately to severely active Ulcerative Colitis.

Pre-assignment

Screening details:

During the screening period (Days −28 to −1), subjects were evaluated for study entry based on the inclusion and exclusion criteria. Screening procedures to evaluate subject eligibility for the study were to be conducted within 28 days prior to study drug administration on Day 1.

Period 1

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

Blinding implementation details:

All study personnel directly related to this study (investigators, study site personnel, monitors, and CRO and Sponsor personnel), with the exception of the clinical supply staff, safety staff, and the unblinded statistician supporting the DSMB, were blinded to the identity of study drug. Randomization codes were generated by a CRO statistician not directly involved with the study.

Arms

Are arms mutually exclusive?	Yes
Arm title	Etrasimod 1 mg

Arm description:

Etrasimod 1 mg was administered orally once daily (QD) for 12 weeks, administered with approximately 240 mL (8 ounces) of water. The study drug was to be taken on an empty stomach after an overnight fast of approximately 8 hours.

Arm type	Experimental
Investigational medicinal product name	Etrasimod 1 mg
Investigational medicinal product code	-
Other name	APD334, 1 mg
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

1 × 1 mg etrasimod capsule orally QD for 12 weeks

Arm title	Etrasimod 2 mg

Arm description:

Etrasimod 2 mg was administered orally once daily (QD) for 12 weeks, administered with approximately 240 mL (8 ounces) of water. The study drug was to be taken on an empty stomach after an overnight fast of approximately 8 hours.

Arm type	Experimental
Investigational medicinal product name	Etrasimod 2 mg
Investigational medicinal product code	-
Other name	APD334, 2 mg
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

1 × 2 mg etrasimod capsule orally QD for 12 weeks

Arm title	Placebo

Arm description:

Placebo was administered orally once daily (QD) for 12 weeks, administered with approximately 240 mL (8 ounces) of water. Placebo was to be taken on an empty stomach after an overnight fast of approximately 8 hours.

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

Dosage and administration details:

1 × matching etrasimod capsule orally QD for 12 weeks

Number of subjects in period 1	Etrasimod 1 mg	Etrasimod 2 mg	Placebo
Started	52	50	54
Completed	47	46	48
Not completed	5	4	6
Physician decision	1	-	-
Consent withdrawn by subject	-	1	5
Adverse event, non-fatal	4	3	-
Sponsor Decision	-	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Etrasimod 1 mg
Reporting group description:	
Etrasimod 1 mg was administered orally once daily (QD) for 12 weeks, administered with approximately 240 mL (8 ounces) of water. The study drug was to be taken on an empty stomach after an overnight fast of approximately 8 hours.	
Reporting group title	Etrasimod 2 mg
Reporting group description:	
Etrasimod 2 mg was administered orally once daily (QD) for 12 weeks, administered with approximately 240 mL (8 ounces) of water. The study drug was to be taken on an empty stomach after an overnight fast of approximately 8 hours.	
Reporting group title	Placebo
Reporting group description:	
Placebo was administered orally once daily (QD) for 12 weeks, administered with approximately 240 mL (8 ounces) of water. Placebo was to be taken on an empty stomach after an overnight fast of approximately 8 hours.	

Reporting group values	Etrasimod 1 mg	Etrasimod 2 mg	Placebo
Number of subjects	52	50	54
Age categorical Units: Subjects			
Adults (18-64 years)	52	49	49
From 65-84 years	0	1	5
Age continuous Units: years			
median	44.0	38.5	46.0
full range (min-max)	21 to 64	21 to 67	20 to 73
Gender categorical Units: Subjects			
Female	22	23	22
Male	30	27	32

Reporting group values	Total		
Number of subjects	156		
Age categorical Units: Subjects			
Adults (18-64 years)	150		
From 65-84 years	6		
Age continuous Units: years			
median			
full range (min-max)	-		
Gender categorical Units: Subjects			
Female	67		
Male	89		

Subject analysis sets

Subject analysis set title	Induction Treatment Period
Subject analysis set type	Intention-to-treat

Subject analysis set description:

The 12-week double-blind induction treatment period started at Week 0 (Day 1) immediately after randomly assigning subjects to a treatment group and ended at Week 12. Eligible subjects were randomly assigned in a 1:1:1 ratio to 1 of the 3 treatment groups: etrasimod 1 mg, etrasimod 2 mg, or placebo. Randomization was stratified by presence or absence of current oral corticosteroid usage and prior exposure to tumor necrosis factor alpha (TNFα) antagonists. The study drugs were administered orally once daily (QD) for 12 weeks. All doses were administered with approximately 240 mL (8 ounces) of water. The study drugs were to be taken on an empty stomach after an overnight fast of approximately 8 hours. After the first study drug administration (Week 0 [Day 1]), subjects were to return to the study site for 5 evaluation visits (Weeks 1, 2, 4, 8, and 12) during the double-blind treatment period.

Reporting group values	Induction Treatment Period		
Number of subjects	156		
Age categorical Units: Subjects			
Adults (18-64 years)	150		
From 65-84 years	6		
Age continuous Units: years			
median	42.0		
full range (min-max)	20 to 73		
Gender categorical Units: Subjects			
Female	67		
Male	89		

End points

End points reporting groups

Reporting group title	Etrasimod 1 mg

Reporting group description:

Etrasimod 1 mg was administered orally once daily (QD) for 12 weeks, administered with approximately 240 mL (8 ounces) of water. The study drug was to be taken on an empty stomach after an overnight fast of approximately 8 hours.

Reporting group title	Etrasimod 2 mg

Reporting group description:

Etrasimod 2 mg was administered orally once daily (QD) for 12 weeks, administered with approximately 240 mL (8 ounces) of water. The study drug was to be taken on an empty stomach after an overnight fast of approximately 8 hours.

Reporting group title	Placebo

Reporting group description:

Placebo was administered orally once daily (QD) for 12 weeks, administered with approximately 240 mL (8 ounces) of water. Placebo was to be taken on an empty stomach after an overnight fast of approximately 8 hours.

Subject analysis set title	Induction Treatment Period
Subject analysis set type	Intention-to-treat

Subject analysis set description:

The 12-week double-blind induction treatment period started at Week 0 (Day 1) immediately after randomly assigning subjects to a treatment group and ended at Week 12. Eligible subjects were randomly assigned in a 1:1:1 ratio to 1 of the 3 treatment groups: etrasimod 1 mg, etrasimod 2 mg, or placebo. Randomization was stratified by presence or absence of current oral corticosteroid usage and prior exposure to tumor necrosis factor alpha (TNFα) antagonists. The study drugs were administered orally once daily (QD) for 12 weeks. All doses were administered with approximately 240 mL (8 ounces) of water. The study drugs were to be taken on an empty stomach after an overnight fast of approximately 8 hours. After the first study drug administration (Week 0 [Day 1]), subjects were to return to the study site for 5 evaluation visits (Weeks 1, 2, 4, 8, and 12) during the double-blind treatment period.

Primary: Adapted Mayo Score (MCS) at Week 12

End point title	Adapted Mayo Score (MCS) at Week 12

End point description:

Using the multiple imputation method to handle missing data, change from baseline in the adapted MCS at Week 12 was analyzed using ANCOVA on each multiply imputed dataset for the ITT population.

End point type	Primary

End point timeframe:

The primary efficacy endpoint was the change from baseline in the adapted MCS (stool frequency, rectal bleeding, and findings on endoscopy) at Week 12.

End point values	Etrasimod 1 mg	Etrasimod 2 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	52	50	54	
Units: mean				
least squares mean (confidence interval 90%)	-1.94 (-2.45 to -1.42)	-2.49 (-3.01 to -1.98)	-1.50 (-2.00 to -1.01)	

Statistical analyses

Statistical analysis title	ITT Statistical Analysis Plan

Statistical analysis description:

The primary efficacy endpoint was analyzed using an analysis of covariance (ANCOVA) model with terms of treatment, current oral corticosteroid use, prior exposure to TNFα antagonists, and baseline value as covariates. Least-squares (LS) mean by treatment group and its 90% confidence interval (CI), and LS mean difference between treatment group and its 90% CI were reported. Same method was applied to analyze change from baseline at Week 12 for score-based endpoints.

Comparison groups	Etrasimod 1 mg v Etrasimod 2 mg v Placebo
Number of subjects included in analysis	156
Analysis specification	Pre-specified
Analysis type	superiority[1]
P-value	= 0.0091
Method	ANCOVA
Parameter estimate	Mean diff. in 2mg etrasimod vs pbo =-.99
Confidence interval	
level	90 %
sides	1-sided
lower limit	-1.68
upper limit	-0.3
Variability estimate	Standard error of the mean
Dispersion value	0.42

Notes:

[1] - The proportion of subjects who achieved endoscopic improvement was analyzed individually using the Cochran-Mantel-Haenszel (CMH) test adjusted for the stratification factors of presence or absence of current oral corticosteroid therapy at baseline and previous exposure to TNFα antagonists, to compare the difference of proportions between treatment groups.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events (AEs) were able to be reported by the subject at any time for the duration of the study. All AEs were monitored up to 30 days after the study drug administration.

Adverse event reporting additional description:

The Investigator assessed the severity of each Treatment-Emergent Adverse Event (TEAE) using CTCAE criteria v4.03. Most TEAEs were mild (grade 1) or moderate (grade 2) in severity. An independent Data Safety Monitoring Board (DSMB) was established to review safety data from this study.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.1

Reporting groups

Reporting group title	Etrasimod 1 mg

Reporting group description:

Etrasimod 1 mg was administered orally once daily (QD) for 12 weeks, administered with approximately 240 mL (8 ounces) of water. The study drug was to be taken on an empty stomach after an overnight fast of approximately 8 hours.

Reporting group title	Etrasimod 2 mg

Reporting group description:

Etrasimod 2 mg was administered orally once daily (QD) for 12 weeks, administered with approximately 240 mL (8 ounces) of water. The study drug was to be taken on an empty stomach after an overnight fast of approximately 8 hours.

Reporting group title	Placebo

Reporting group description:

Placebo was administered orally once daily (QD) for 12 weeks, administered with approximately 240 mL (8 ounces) of water. Placebo was to be taken on an empty stomach after an overnight fast of approximately 8 hours.

Serious adverse events	Etrasimod 1 mg	Etrasimod 2 mg	Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 52 (5.77%)	0 / 50 (0.00%)	6 / 54 (11.11%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 52 (0.00%)	0 / 50 (0.00%)	1 / 54 (1.85%)
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	2 / 52 (3.85%)	0 / 50 (0.00%)	3 / 54 (5.56%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Duodenal ulcer perforation			
subjects affected / exposed	0 / 52 (0.00%)	0 / 50 (0.00%)	1 / 54 (1.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Jaundice			
subjects affected / exposed	0 / 52 (0.00%)	0 / 50 (0.00%)	1 / 54 (1.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Hydronephrosis			
subjects affected / exposed	0 / 52 (0.00%)	0 / 50 (0.00%)	1 / 54 (1.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Anal abscess			
subjects affected / exposed	1 / 52 (1.92%)	0 / 50 (0.00%)	0 / 54 (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

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

Non-serious adverse events	Etrasimod 1 mg	Etrasimod 2 mg	Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	29 / 52 (55.77%)	28 / 50 (56.00%)	24 / 54 (44.44%)
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 52 (0.00%)	3 / 50 (6.00%)	1 / 54 (1.85%)
occurrences (all)	0	3	2
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 52 (3.85%)	3 / 50 (6.00%)	2 / 54 (3.70%)
occurrences (all)	3	3	3
Gastrointestinal disorders			
Colitis ulcerative			

subjects affected / exposed	3 / 52 (5.77%)	2 / 50 (4.00%)	1 / 54 (1.85%)
occurrences (all)	3	2	1
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	2 / 52 (3.85%)	1 / 50 (2.00%)	4 / 54 (7.41%)
occurrences (all)	2	2	4
Upper respiratory tract infection			
subjects affected / exposed	4 / 52 (7.69%)	2 / 50 (4.00%)	2 / 54 (3.70%)
occurrences (all)	4	2	2

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
01 May 2015	The first amendment to the protocol, dated 01 May 2015, included the following important changes: • The term partial MCS was changed to 3-component MCS throughout the protocol. • Use of Inflammatory Bowel Disease Questionnaire and corresponding exploratory objective, endpoint, and analysis were added. • Definition of an intolerable AE was added. • A clarification was made to specify that the stool sample collected during the study was used for the analysis of both the fecal calprotectin assay and for culture, ova, and parasite evaluation and C difficile assay. • Requirement for a chest X-ray to be taken at the Week 12 visit was removed for subjects not continuing into the extension study. • Clarified that study medication should be taken after an overnight fast (~8 hours) and food should be avoided for ~1 hour after dosing. • Inclusion criterion pertaining to corticosteroid usage was updated to remove the references pertaining to the allowance of corticosteroid tapering in the study, with the requirement of stable dosage regimen throughout the study duration for corticosteroid usage. • The requirement of capping the number of subjects with prior exposure to TNFα antagonists for randomization into the study was added. • Information about blinding requirements for analysis of total lymphocyte and white blood cell (WBC) counts to be followed during the study was added. • The ECG assessment information was updated to clarify that the ECGs were to be read and interpreted by both the study physician and centrally. • Reference to "continuous telemetry" in the protocol was corrected to "Holter monitoring." • The laboratory parameters were updated to add and remove certain evaluation parameters from the assessments. • "Pharmacodynamic" assessments in the study were replaced with "hematologic" assessments. • Subgroup analyses parameters for fecal calprotectin and CRP were defined.

17 June 2015	The second amendment to the protocol, dated 17 Jun 2015, included the following important changes: • Analysis time points to the efficacy parameters of rectal bleeding, stool frequency, fecal calprotectin, CRP reduction, and 2-component Mayo Score were added. • The following exploratory endpoints were added: (1) change from baseline in Mayo endoscopic subscore at Week 12; (2) change from baseline in Mayo PGA at Week 12; (3) change from baseline in 2-component Mayo score at Weeks 1, 2, 4, 8, and 12; and (4) change from baseline in lymphocyte counts at Weeks 1, 2, 4, 8, 12, and 14. • A secondary method for the primary efficacy analysis was added, which included a logistic regression analysis with terms of treatment, presence or absence of current oral corticosteroid therapy at baseline, previous exposure to TNFα antagonists, and the interaction between 2 stratification factors (if appropriate). • Requirement of clinical laboratory tests to be performed at screening and Week 12 under fasting conditions was removed. • Inclusion criterion related to colonoscopy for subjects with history of extensive pancolitis or left-sided colitis was clarified. • Exclusion criterion pertaining to the serology requirements was updated to exclude subjects without documented varicella zoster virus (VZV) IgG antibody status. • Addition of 3 exclusion criteria: (1) use of moderate to strong inhibitors of CYP2C9; (2) history of severe renal impairment; and (3) history of severe hepatic impairment. • Dosage instructions for study drug administration were clarified to instruct subjects not to take their study drug dose at home on days with scheduled study visits in order to complete predose study procedures and to remain fasted as instructed on the days of scheduled visits prior to dosing. • Moderate to strong inhibitors of CYP2C9 were added to the excluded (i.e., prohibited) medications list.
30 June 2015	The third amendment to the protocol, dated 30 Jun 2015, included the following important changes: • An exclusion criterion of “previous treatment with 2 or more biologic agents” was added. • Vedolizumab was added to the list of medications that were to be excluded within 60 days prior to randomization. • Consideration for a repeat flexible proctosigmoidoscopy was added.
21 September 2015	The fourth amendment to the protocol, dated 21 Sep 2015, included the following important changes: • Information on retinal photos to be taken at each ophthalmoscopy was added. Requirement of Week 12 ophthalmoscopy applicable only to subjects who did not enter the extension study was removed. • Inclusion criterion about the permitted use of corticosteroids prior to study entry was updated. • Exclusion criteria related to history or evidence of adenomatous colonic polyps and colonic mucosal dysplasia were updated.

10 October 2016	The fifth amendment to the protocol, dated 10 Oct 2016, included the following important changes: • Subject entry requirement for participation in the extension Study APD334-005 was updated to include only responders and not both responders and nonresponders. • Blood sample collection at 8 hours postdose for PK assessments was removed. • Added possibility to prolong time window for screening to 35 days. Extended window for specified procedures (proctosigmoidoscopy) to 10 days. Removed all other visit and procedure windows. • The duration within which certain screening procedures were to be completed prior to randomization was updated from 7 to 10 days. • Assessment timings and requirements for heart rate, blood pressure, and ECG measurements were updated. • Exclusion criterion related to use of biologic agents prior to study entry was updated, with subjects who received previous treatment with more than 3 biologics were not to be enrolled. • Additional monitoring considerations for changes in heart rate and ECG parameters were added. • Recipient of notification of SAE was changed from the Sponsor to PPD (contract research organization [CRO]). • Information on extending the screening period window to 35 days and clarification on rescreening procedures was added. • Information about the 2-component May score to be calculated at Weeks 1, 2, 4, and 8 was added. • Added specification that APD334-003 study will remain blinded until completion of the APD334-005 study. • Clarified that clinical laboratory tests and CBC tests should be performed prior to dosing.
27 March 2017	The sixth amendment to the protocol, dated 27 Mar 2017, included the following important changes: • The primary objective was updated to determine the effect of treatment with etrasimod in improving 3-component MCS (score ranging from 0 to 9, including stool frequency, rectal bleeding, and findings on endoscopy) at Week 12. • The following secondary objectives were added: (1) to determine the effect of treatment with etrasimod on a combination of clinical remission and clinical response reflected by a composite endpoint at 12 weeks; and (2) to determine the effect of treatment with etrasimod in inducing clinical remission at 12 weeks. • The following exploratory objectives were added: (1) to determine the effect of etrasimod treatment on total MCS at 12 weeks; and (2) to determine dose response effect of etrasimod on 3-component MCS, combination of clinical remission and clinical response reflected by a composite endpoint, clinical remission, clinical response, and endoscopic improvement, at 12 weeks. • The primary, secondary, and exploratory efficacy endpoints were updated based on the changes made to the study objectives. • The study design information was updated to designate this study as a proof of concept study. • Subject entry requirement for participation in the extension Study APD334-005 was updated to include both responders and nonresponders. • Inclusion criterion about integrin antagonists was updated to include subjects in the study who had discontinued prior treatment with vedolizumab despite clinical benefit. • The exclusion criterion of "a history of primary nonresponse to a treatment regimen of vedolizumab per the current labeling and/or institutional standard of care. • Sample size language was changed to up to 240, with the added statement that the Sponsor can stop enrollment for any reason prior to that. • Sponsor considerations for conducting interim analysis were added. • Added section that outlined reasons to terminate the study.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

None reported

Notes: