# Clinical trial results:
# A Randomized, Double-Blind, Placebo-Controlled Phase 4 Study to Evaluate the Efficacy and Safety of Entyvio (Vedolizumab IV) in the Treatment of Chronic Pouchitis (EARNEST)

## Summary

| | |
|---|---|
| EudraCT number | 2015-003472-78 |
| Trial protocol | DE GB BE ES NL IT |
| Global end of trial date | 02 February 2021 |

### Results information

| | |
|---|---|
| Result version number | v2 (current) |
| This version publication date | 18 February 2022 |
| First version publication date | 25 June 2021 |
| Version creation reason | |

## Trial information

### Trial identification

| | |
|---|---|
| Sponsor protocol code | Vedolizumab-4004 |

### Additional study identifiers

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02790138 |
| WHO universal trial number (UTN) | U1111-1171-0918 |

Notes:

### Sponsors

| | |
|---|---|
| Sponsor organisation name | Takeda |
| Sponsor organisation address | 95 Hayden Avenue, Lexington, MA, United States, 02421 |
| Public contact | Takeda, Study Director, +1 877-825-3327, TrialDisclosures@takeda.com |
| Scientific contact | Takeda, Study Director, +1 877-825-3327, TrialDisclosures@takeda.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 | 02 February 2021 |
| Is this the analysis of the primary completion data? | No |

| | |
|---|---|
| Global end of trial reached? | Yes |
| Global end of trial date | 02 February 2021 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

The purpose of this study is to compare the efficacy of vedolizumab intravenous (IV) and placebo in terms of the percentage of participants with chronic or recurrent pouchitis achieving clinically relevant remission.

Protection of trial subjects:

All study participants were required to read and sign an Informed Consent Form.

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 12 October 2016 |
| Long term follow-up planned | Yes |
| Long term follow-up rationale | Safety |
| Long term follow-up duration | 6 Months |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

## Population of trial subjects

### Subjects enrolled per country

| | |
|---|---|
| Country: Number of subjects enrolled | Canada: 16 |
| Country: Number of subjects enrolled | United States: 23 |
| Country: Number of subjects enrolled | Belgium: 7 |
| Country: Number of subjects enrolled | France: 7 |
| Country: Number of subjects enrolled | Germany: 3 |
| Country: Number of subjects enrolled | Italy: 20 |
| Country: Number of subjects enrolled | Netherlands: 10 |
| Country: Number of subjects enrolled | Spain: 1 |
| Country: Number of subjects enrolled | United Kingdom: 15 |
| Worldwide total number of subjects | 102 |
| EEA total number of subjects | 48 |

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) | 97 |
| From 65 to 84 years | 5 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details:

Participants took part in the study at 31 investigative sites in Canada, United States, Belgium, France, Germany, Italy, Netherlands, Spain, and United Kingdom from 12 October 2016 to 2 February 2021.

### Pre-assignment

Screening details:

Participants with a diagnosis of chronic or recurrent pouchitis were enrolled in a 1:1 ratio to receive placebo IV or vedolizumab IV 300 mg.

### 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 | Investigator, Carer, Subject, Assessor |

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | Placebo IV |

Arm description:

Vedolizumab placebo-matching IV infusion, once at Day 1, Weeks 2, 6, 14, 22, and 30 along with ciprofloxacin 500 mg, tablet, orally twice daily up to Week 4.

| | |
|---|---|
| Arm type | Placebo |
| Investigational medicinal product name | Ciprofloxacin |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Ciprofloxacin tablets

| | |
|---|---|
| Investigational medicinal product name | Vedolizumab Placebo-matching |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Vedolizumab placebo-matching IV infusion

| | |
|---|---|
| **Arm title** | Vedolizumab IV 300 mg |

Arm description:

Vedolizumab 300 mg, IV infusion, once at Day 1, Weeks 2, 6, 14, 22, and 30 along with ciprofloxacin 500 mg, tablet, orally twice daily up to Week 4.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Vedolizumab |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Vedolizumab IV infusion

| | |
|---|---|
| Investigational medicinal product name | Ciprofloxacin |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Ciprofloxacin tablets

| **Number of subjects in period 1** | Placebo IV | Vedolizumab IV 300 mg |
|---|---|---|
| Started | 51 | 51 |
| Completed | 30 | 32 |
| Not completed | 21 | 19 |
| Adverse event, non-fatal | 5 | 2 |
| Voluntary Withdrawal | 8 | 9 |
| Significant Protocol Deviation | - | 1 |
| Lost to follow-up | 1 | - |
| Reason not Specified | 1 | - |
| Lack of efficacy | 6 | 7 |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | Placebo IV |
| Reporting group description: | |
| Vedolizumab placebo-matching IV infusion, once at Day 1, Weeks 2, 6, 14, 22, and 30 along with ciprofloxacin 500 mg, tablet, orally twice daily up to Week 4. | |
| Reporting group title | Vedolizumab IV 300 mg |
| Reporting group description: | |
| Vedolizumab 300 mg, IV infusion, once at Day 1, Weeks 2, 6, 14, 22, and 30 along with ciprofloxacin 500 mg, tablet, orally twice daily up to Week 4. | |

| Reporting group values | Placebo IV | Vedolizumab IV 300 mg | Total |
|---|---|---|---|
| Number of subjects | 51 | 51 | 102 |
| Age categorical<br>Units: Subjects | | | |
| Age continuous<br>Units: years | | | |
| arithmetic mean | 42.9 | 40.8 | |
| standard deviation | ± 13.48 | ± 11.32 | - |
| Gender categorical<br>Units: Subjects | | | |
| Female | 13 | 19 | 32 |
| Male | 38 | 32 | 70 |
| Race (NIH/OMB)<br>Units: Subjects | | | |
| American Indian or Alaska Native | 0 | 0 | 0 |
| Asian | 6 | 3 | 9 |
| Native Hawaiian or Other Pacific Islander | 0 | 0 | 0 |
| Black or African American | 1 | 1 | 2 |
| White | 42 | 44 | 86 |
| More than one race | 0 | 1 | 1 |
| Unknown or Not Reported | 2 | 2 | 4 |
| Ethnicity (NIH/OMB)<br>Units: Subjects | | | |
| Hispanic or Latino | 0 | 0 | 0 |
| Not Hispanic or Latino | 11 | 12 | 23 |
| Unknown or Not Reported | 40 | 39 | 79 |
| Region of Enrollment<br>Units: Subjects | | | |
| Canada | 7 | 9 | 16 |
| United States | 11 | 12 | 23 |
| Belgium | 6 | 1 | 7 |
| France | 2 | 5 | 7 |
| Germany | 1 | 2 | 3 |
| Italy | 10 | 10 | 20 |
| Netherlands | 6 | 4 | 10 |

| | | | |
|---|---|---|---|
| Spain | 1 | 0 | 1 |
| United Kingdom | 7 | 8 | 15 |

| | | | |
|---|---|---|---|
| Height | | | |
| Units: cm | | | |
| arithmetic mean | 175.3 | 172.4 | |
| standard deviation | ± 9.10 | ± 10.79 | - |
| Weight | | | |
| Units: kg | | | |
| arithmetic mean | 79.60 | 72.13 | |
| standard deviation | ± 19.115 | ± 17.588 | - |
| Body Mass Index (BMI) | | | |
| BMI = weight (kg)/[height (m)^2 | | | |
| Units: kg/m^2 | | | |
| arithmetic mean | 25.74 | 24.13 | |
| standard deviation | ± 5.125 | ± 4.891 | - |

## End points

### End points reporting groups

| | |
|---|---|
| Reporting group title | Placebo IV |
| Reporting group description: | |
| Vedolizumab placebo-matching IV infusion, once at Day 1, Weeks 2, 6, 14, 22, and 30 along with ciprofloxacin 500 mg, tablet, orally twice daily up to Week 4. | |
| Reporting group title | Vedolizumab IV 300 mg |
| Reporting group description: | |
| Vedolizumab 300 mg, IV infusion, once at Day 1, Weeks 2, 6, 14, 22, and 30 along with ciprofloxacin 500 mg, tablet, orally twice daily up to Week 4. | |

### Primary: Percentage of Participants with Chronic or Recurrent Pouchitis Achieving Clinically Relevant Remission at Week 14

| | |
|---|---|
| End point title | Percentage of Participants with Chronic or Recurrent Pouchitis Achieving Clinically Relevant Remission at Week 14 |
| End point description: | |
| Clinically relevant remission is defined as modified Pouchitis Disease Activity Index (mPDAI) score <5 and a reduction of mPDAI score by ≥2 points from Baseline. The 12-point mPDAI score is calculated from two 6-point subscales: 1) Clinical Symptoms: Stool Frequency (0=usual to postoperative stool frequency to 2=three or more stools/day>postoperative usual); Rectal bleeding (0=None or rare to 1=Present daily); Fecal urgency or abdominal cramps (0=None to 2=Usual), Fever [temperature >37.8 degrees C] (0=Absent and 1=Present) for a clinical symptoms subscore of 0 (best) to 6 (worse); 2) Endoscopic Inflammation Findings: Edema, Granularity, Friability, Loss of vascular pattern, Mucous exudates and Ulcerations. Each item is scored on a scale of 0=not present to 1=present summed up to an endoscopic subscore ranging from 0 (best) to 6 (worst). Full Analysis Set (FAS) included all randomised participants who received at least 1 dose of study medication, as randomised. | |
| End point type | Primary |
| End point timeframe: | |
| Week 14 | |

| End point values | Placebo IV | Vedolizumab IV 300 mg | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 51 | 51 | | |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | 9.8 (3.3 to 21.4) | 31.4 (19.1 to 45.9) | | |

### Statistical analyses

| | |
|---|---|
| **Statistical analysis title** | Statistical Analysis 1 |
| Comparison groups | Placebo IV v Vedolizumab IV 300 mg |

| | |
|---|---|
| Number of subjects included in analysis | 102 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.013 [1] |
| Method | Fisher’s Exact Test |
| Parameter estimate | Percentage Difference |
| Point estimate | 21.6 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 4.9 |
| upper limit | 37.5 |

Notes:

[1] - The significance level was 0.05.

## Secondary: Percentage of Participants With Chronic or Recurrent Pouchitis Achieving Clinically Relevant Remission at Week 34

| | |
|---|---|
| End point title | Percentage of Participants With Chronic or Recurrent Pouchitis Achieving Clinically Relevant Remission at Week 34 |

End point description:

Clinically relevant remission is defined as mPDAI score <5 and a reduction of mPDAI score by ≥2 points from Baseline. The 12-point mPDAI score is calculated from two 6-point scales: 1) Clinical Symptoms: Stool Frequency (0=usual to postoperative stool frequency to 2=3 or more stools/day>postoperative usual); Rectal bleeding (0=None or rare to 1=Present daily); Fecal urgency or abdominal cramps (0=None to 2=Usual), Fever [temperature >37.8 degrees C] (0=Absent and 1=Present) for a clinical symptoms subscore of 0 (best) to 6 (worse); 2) Endoscopic Inflammation Findings: Edema, Granularity, Friability, Loss of vascular pattern, Mucous exudates and Ulcerations. Each item is scored on a scale of 0=not present to 1=present summed up to an endoscopic subscore ranging from 0 (best) to 6 (worst). FAS included all randomised participants who received at least 1 dose of study medication, as randomised.

| | |
|---|---|
| End point type | Secondary |

End point timeframe:

Week 34

| **End point values** | Placebo IV | Vedolizumab IV 300 mg | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 51 | 51 | | |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | 17.6 (8.4 to 30.9) | 35.3 (22.4 to 49.9) | | |

### Statistical analyses

| **Statistical analysis title** | Statistical Analysis 1 |
|---|---|
| Comparison groups | Placebo IV v Vedolizumab IV 300 mg |

| | |
|---|---|
| Number of subjects included in analysis | 102 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.043 [2] |
| Method | Chi-squared Test |
| Parameter estimate | Percentage Difference |
| Point estimate | 17.6 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.3 |
| upper limit | 35.1 |

Notes:

[2] - No multiplicity adjustment for inferential testing for secondary endpoints was pre-planned, p-values from these tests are presented as nominal p-values. The significance level was 0.05.

## Secondary: Percentage of Participants Achieving PDAI Remission at Weeks 14 and 34

| | |
|---|---|
| End point title | Percentage of Participants Achieving PDAI Remission at Weeks 14 and 34 |

End point description:

Pouchitis Disease Activity Index(PDAI)remission:defined as PDAI score<7and a reduction of PDAI score by≥3points from Baseline.18-point PDAI score[0(best)-18(worse)]:calculated from three 6-point domain scales with possible subscore of 0(best)-6(worse):1) Clinical Symptoms:Stool Frequency(0=usual to postoperative stool frequency to 2=3 or more stools/day>postoperative usual);Rectal bleeding(0=None/rare,1=Present daily);Fecal urgency or abdominal cramps(0=None to 2=Usual),Fever[temperature>37.8 degrees C](0=Absent,1=Present);2) Endoscopic Inflammation:Edema,Granularity,Friability,Loss of vascular pattern,Mucous exudates,Ulcerations.Each item scored on 0=not present-1=present scale,summed to endoscopic subscore 0(best)-6(worst);3) Acute Histologic Inflammation:Polymorphic nuclear leukocyte infiltration(0=None to 3=Severe plus crypt abscess),Ulceration per low power field [mean](0=0% to 3= >50%).FAS:all randomised participants with≥1dose of study medication,as randomised.

| | |
|---|---|
| End point type | Secondary |

End point timeframe:

Weeks 14 and 34

| **End point values** | Placebo IV | Vedolizumab IV 300 mg | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 51 | 51 | | |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | | | | |
| Week 14 | 9.8 (3.3 to 21.4) | 35.3 (22.4 to 49.9) | | |
| Week 34 | 17.6 (8.4 to 30.9) | 37.3 (24.1 to 51.9) | | |

## Statistical analyses

| | |
|---|---|
| **Statistical analysis title** | Statistical Analysis 1 |

| | |
|---|---|
| Statistical analysis description: | |
| Week 14 | |
| Comparison groups | Placebo IV v Vedolizumab IV 300 mg |
| Number of subjects included in analysis | 102 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.004 [3] |
| Method | Fisher's Exact Test |
| Parameter estimate | Percentage Difference |
| Point estimate | 25.5 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 8 |
| upper limit | 41.4 |

Notes:

[3] - No multiplicity adjustment for inferential testing for secondary endpoints was pre-planned, p-values from these tests are presented as nominal p-values. The significance level was 0.05.

| **Statistical analysis title** | Statistical Analysis 2 |
|---|---|
| Statistical analysis description: | |
| Week 34 | |
| Comparison groups | Placebo IV v Vedolizumab IV 300 mg |
| Number of subjects included in analysis | 102 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.027 [4] |
| Method | Chi-squared Test |
| Parameter estimate | Percentage Difference |
| Point estimate | 19.6 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.9 |
| upper limit | 37 |

Notes:

[4] - No multiplicity adjustment for inferential testing for secondary endpoints was pre-planned, p-values from these tests are presented as nominal p-values. The significance level was 0.05.

## Secondary: Time to PDAI Remission

| End point title | Time to PDAI Remission |
|---|---|

End point description:

Time to remission is defined as time from Baseline to PDAI remission. PDAI remission is defined as PDAI score<7 and reduction of PDAI score by>=3 points, calculated form three domain scales: 1) Clinical symptoms: stool frequency (0=usual to postoperative stool frequency to 2=3 or more stools/day>postoperative usual; rectal bleeding (0=None/rare,1=Present daily); fecal urgency or abdominal cramps(0=None to 2=Usual); fever[temperature>37.8 degrees celsius; 2) Endoscopic Inflammation: Edema,Granularity,Friability,Loss of vascular pattern,Mucous exudates,ulcerations (0=Absent,1=Present),summed to endoscopic subscore 0(best)-6(worst); 3) Acute Histologic Inflammation:Polymorphic nuclear leukocyte infiltration(0=None to 3=Severe plus crypt abscess),Ulceration/low power field [mean](0=0% to 3=>50%). The total score ranges from 0-18 (0=best; 18 (worse). FAS population, Number analyzed are the number of participants with data evaluable for analyses.99999=Median, Lower and upper limit of CI.

| End point type | Secondary |
|---|---|

End point timeframe:

Baseline up to Week 34

| End point values | Placebo IV | Vedolizumab IV 300 mg | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 51 | 50 | | |
| Units: days | | | | |
| median (confidence interval 95%) | 99999 (99999 to 99999) | 239.0 (101.0 to 99999) | | |

### Statistical analyses

| Statistical analysis title | Statistical Analysis 1 |
|---|---|
| Comparison groups | Placebo IV v Vedolizumab IV 300 mg |
| Number of subjects included in analysis | 101 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[5] |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 3.95 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.7 |
| upper limit | 9.4 |

Notes:

[5] - Hazard ratio for achieving PDAI remission.

## Secondary: Percentage of Participants Achieving a Partial mPDAI Response at Weeks 14 and 34

| End point title | Percentage of Participants Achieving a Partial mPDAI Response at Weeks 14 and 34 |
|---|---|

End point description:

Partial mPDAI response is defined as a reduction in mPDAI score by ≥2 points from Baseline. The 12-point mPDAI score is calculated from two 6-point scales: 1) Clinical Symptoms: Stool Frequency (0=usual to postoperative stool frequency to 2=3 or more stools/day>postoperative usual); Rectal bleeding (0=None or rare to 1=Present daily); Fecal urgency or abdominal cramps (0=None to 2=Usual), Fever [temperature >37.8 degrees C] (0=Absent and 1=Present) for a clinical symptoms subscore of 0 (best) to 6 (worse); 2) Endoscopic Inflammation Findings: Edema, Granularity, Friability, Loss of vascular pattern, Mucous exudates and Ulcerations. Each item is scored on a scale of 0=not present to 1=present summed up to an endoscopic subscore ranging from 0 (best) to 6 (worst). Last observation carried forward (LOCF) method was used for analyses. FAS included all randomised participants who received at least 1 dose of study medication, as randomised.

| End point type | Secondary |
|---|---|

End point timeframe:

Weeks 14 and 34

| End point values | Placebo IV | Vedolizumab IV 300 mg | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 51 | 51 | | |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | | | | |
| Week 14 | 33.3 (20.8 to 47.9) | 62.7 (48.1 to 75.9) | | |
| Week 34 | 29.4 (17.5 to 43.8) | 51.0 (36.6 to 65.2) | | |

## Statistical analyses

| Statistical analysis title | Statistical Analysis 1 |
|---|---|
| Statistical analysis description: Week 14 | |
| Comparison groups | Placebo IV v Vedolizumab IV 300 mg |
| Number of subjects included in analysis | 102 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.003 [6] |
| Method | Chi-squared Test |
| Parameter estimate | Percentage Difference |
| Point estimate | 29.4 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 8 |
| upper limit | 47.6 |

Notes:

[6] - No multiplicity adjustment for inferential testing for secondary endpoints was pre-planned, p-values from these tests are presented as nominal p-values. The significance level was 0.05.

| Statistical analysis title | Statistical Analysis 2 |
|---|---|
| Statistical analysis description: Week 34 | |
| Comparison groups | Placebo IV v Vedolizumab IV 300 mg |
| Number of subjects included in analysis | 102 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.026 [7] |
| Method | Chi-squared Test |
| Parameter estimate | Percentage Difference |
| Point estimate | 21.6 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.9 |
| upper limit | 39.8 |

Notes:

[7] - No multiplicity adjustment for inferential testing for secondary endpoints was pre-planned, p-values from these tests are presented as nominal p-values. The significance level was 0.05.

## Secondary: Change From Baseline in PDAI Endoscopic Inflammation Subscore at Weeks 14 and 34

| End point title | Change From Baseline in PDAI Endoscopic Inflammation Subscore at Weeks 14 and 34 |
|---|---|

End point description:

The PDAI Endoscopic Inflammation subscore is a sum of scores from findings for Edema, Granularity, Friability, Loss of vascular pattern, Mucous exudates, and Ulcerations, each scored on 0=not present to 1=present scale summed up to a subscore ranging from 0 (best) to 6 (worse) where higher scores indicate more severe disease. A negative change from Baseline indicates improvement. LOCF method was used for analyses. FAS included all randomised participants who received at least 1 dose of study medication, as randomised.

| End point type | Secondary |
|---|---|

End point timeframe:

Baseline up to Weeks 14 and 34

| **End point values** | Placebo IV | Vedolizumab IV 300 mg | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 51 | 51 | | |
| Units: score on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline | 4.5 (± 1.36) | 4.6 (± 1.15) | | |
| Change from Baseline at Week 14 | -0.2 (± 1.36) | -1.1 (± 1.59) | | |
| Change from Baseline at Week 34 | -0.6 (± 1.86) | -1.2 (± 1.87) | | |

### Statistical analyses

| **Statistical analysis title** | Statistical Analysis 1 |
|---|---|

Statistical analysis description:

Change from Baseline at Week 14

| Comparison groups | Placebo IV v Vedolizumab IV 300 mg |
|---|---|
| Number of subjects included in analysis | 102 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[8] |
| P-value | = 0.002 [9] |
| Method | Wilcoxon (Mann-Whitney) |
| Parameter estimate | Odds Estimator |
| Point estimate | 2.02 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.11 |
| upper limit | 2.93 |

Notes:

[8] - P-value is from Wilcoxon Rank-sum Test comparing change from Baseline to relevant visits. Wilcoxon-Mann-Whitney odds estimator,95% CI are presented.
[9] - No multiplicity adjustment for inferential testing for secondary endpoints was pre-planned, p-values from these tests are presented as nominal p-values. The significance level was 0.05.

| **Statistical analysis title** | Statistical Analysis 2 |
|---|---|
| Statistical analysis description: | |
| Change from Baseline at Week 34 | |
| Comparison groups | Placebo IV v Vedolizumab IV 300 mg |
| Number of subjects included in analysis | 102 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[10] |
| P-value | = 0.02 [11] |
| Method | Wilcoxon (Mann-Whitney) |
| Parameter estimate | Odds Estimator |
| Point estimate | 1.71 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.92 |
| upper limit | 2.49 |

Notes:

[10] - P-value is from Wilcoxon Rank-sum Test comparing change from Baseline to relevant visits. Wilcoxon-Mann-Whitney odds estimator,95% CI are presented.
[11] - No multiplicity adjustment for inferential testing for secondary endpoints was pre-planned, p-values from these tests are presented as nominal p-values. The significance level was 0.05.

## Secondary: Change From Baseline in PDAI Acute Histologic Inflammation Subscore at Weeks 14 and 34

| End point title | Change From Baseline in PDAI Acute Histologic Inflammation Subscore at Weeks 14 and 34 |
|---|---|

End point description:

The PDAI Acute Histologic Inflammation subscore is a sum score from findings for Polymorphic nuclear leukocyte infiltration (0=None to 3=Severe plus crypt abscess), and Ulceration per low power field [mean] (0=0% to 3= >50%) summed up to a subscore ranging from 0 (best) to 6 (worse) where higher scores indicate more severe disease. A negative change from Baseline indicates improvement. LOCF method was used for analyses. FAS included all randomised participants who received at least 1 dose of study medication, as randomised. Overall number analysed are the number of participants with data evaluable for analyses.

| End point type | Secondary |
|---|---|

End point timeframe:

Baseline up to Weeks 14 and 34

| **End point values** | Placebo IV | Vedolizumab IV 300 mg | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 51 | 50 | | |
| Units: score on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline | 2.6 (± 1.39) | 2.5 (± 1.42) | | |
| Change from Baseline at Week 14 | -0.1 (± 1.33) | -0.4 (± 1.98) | | |
| Change from Baseline at Week 34 | -0.2 (± 1.52) | -0.2 (± 2.03) | | |

## Statistical analyses

| Statistical analysis title | Statistical Analysis 1 |
|---|---|
| Statistical analysis description: | |
| Change from Baseline at Week 14 | |
| Comparison groups | Placebo IV v Vedolizumab IV 300 mg |
| Number of subjects included in analysis | 101 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[12] |
| P-value | = 0.191 [13] |
| Method | Wilcoxon (Mann-Whitney) |
| Parameter estimate | Odds Estimator |
| Point estimate | 1.34 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.74 |
| upper limit | 1.94 |

Notes:

[12] - P-value is from Wilcoxon Rank-sum Test comparing change from Baseline to relevant visits. Wilcoxon-Mann-Whitney odds estimator,95% CI are presented.
[13] - No multiplicity adjustment for inferential testing for secondary endpoints was pre-planned, p-values from these tests are presented as nominal p-values. The significance level was 0.05.

| Statistical analysis title | Statistical Analysis 2 |
|---|---|
| Statistical analysis description: | |
| Change from Baseline at Week 34 | |
| Comparison groups | Placebo IV v Vedolizumab IV 300 mg |
| Number of subjects included in analysis | 101 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[14] |
| P-value | = 0.766 [15] |
| Method | Wilcoxon (Mann-Whitney) |
| Parameter estimate | Odds Estimator |
| Point estimate | 1.07 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.6 |
| upper limit | 1.54 |

Notes:

[14] - P-value is from Wilcoxon Rank-sum Test comparing change from Baseline to relevant visits. Wilcoxon-Mann-Whitney odds estimator,95% CI are presented.
[15] - No multiplicity adjustment for inferential testing for secondary endpoints was pre-planned, p-values from these tests are presented as nominal p-values. The significance level was 0.05.

## Secondary: Change From Baseline in Total PDAI Score at Weeks 14 and 34

| End point title | Change From Baseline in Total PDAI Score at Weeks 14 and 34 |
|---|---|

End point description:

18-point PDAI score:calculated from three 6-point domain scales,possible subscore of 0(best)-18(worse):1)Clinical Symptoms:Stool Frequency(0=usual to postoperative stool frequency to 2=3 or more stools/day>postoperative usual);Rectal bleeding(0=None/rare,1=Present daily);Fecal urgency or abdominal cramps(0=None-2=Usual),Fever [temperature>37.8degrees C](0=Absent,1=Present);2)Endoscopic Inflammation:Edema,Granularity,Friability,Loss of vascular pattern,Mucous exudates,Ulcerations.Each item is scored on 0=not present-1=present scale, summed to endoscopic subscore 0(best)-6(worst);3)Acute Histologic Inflammation:Polymorphic nuclear leukocyte infiltration(0=None-3=Severe plus crypt abscess),Ulceration per low power field[mean](0=0%-3= >50%).Sub-scores combined to total score of 1(best)-18(worse).Negative change from Baseline=improvement. LOCF used.FAS:all randomised participants with ≥1 dose of study medication,as randomised. Subjects analysed:subjects with data evaluable for analyses.

| End point type | Secondary |
|---|---|

End point timeframe:

Baseline up to Weeks 14 and 34

| **End point values** | Placebo IV | Vedolizumab IV 300 mg | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 51 | 50 | | |
| Units: score on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline | 10.5 (± 2.48) | 10.5 (± 2.20) | | |
| Change from Baseline at Week 14 | -1.34 (± 2.68) | -2.7 (± 3.86) | | |
| Change from Baseline at Week 34 | -1.6 (± 3.41) | -2.9 (± 3.93) | | |

## Statistical analyses

| **Statistical analysis title** | Statistical Analysis 1 |
|---|---|

Statistical analysis description:

Change from Baseline at Week 14

| Comparison groups | Placebo IV v Vedolizumab IV 300 mg |
|---|---|
| Number of subjects included in analysis | 101 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[16] |
| P-value | = 0.055 [17] |
| Method | Wilcoxon (Mann-Whitney) |
| Parameter estimate | Odds Estimator |
| Point estimate | 1.57 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.83 |
| upper limit | 2.31 |

Notes:

[16] - P-value is from Wilcoxon Rank-sum Test comparing change from Baseline to relevant visits. Wilcoxon-Mann-Whitney odds estimator,95% CI are presented.

[17] - No multiplicity adjustment for inferential testing for secondary endpoints was pre-planned, p-

values from these tests are presented as nominal p-values. The significance level was 0.05.

| **Statistical analysis title** | Statistical Analysis 2 |
|---|---|
| Statistical analysis description: | |
| Change from Baseline at Week 34 | |
| Comparison groups | Placebo IV v Vedolizumab IV 300 mg |
| Number of subjects included in analysis | 101 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[18] |
| P-value | = 0.095 [19] |
| Method | Wilcoxon (Mann-Whitney) |
| Parameter estimate | Odds Estimator |
| Point estimate | 1.48 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.79 |
| upper limit | 2.16 |

Notes:

[18] - P-value is from Wilcoxon Rank-sum Test comparing change from Baseline to relevant visits. Wilcoxon-Mann-Whitney odds estimator,95% CI are presented.
[19] - No multiplicity adjustment for inferential testing for secondary endpoints was pre-planned, p-values from these tests are presented as nominal p-values. The significance level was 0.05.

## Secondary: Change From Baseline in Inflammatory Bowel Disease Questionnaire (IBDQ) Total Score at Weeks 14, 22, and 34

| End point title | Change From Baseline in Inflammatory Bowel Disease Questionnaire (IBDQ) Total Score at Weeks 14, 22, and 34 |
|---|---|

End point description:

The IBDQ is an instrument used to assess quality of life in adult participants with inflammatory bowel disease (IBD). It includes 32 questions on 4 domains of Health-Related Quality-of-Life (HRQOL): Bowel Systems (10 items), Emotional Function (12 items), Social Function (5 items), and Systemic Function (5 items). Participants are asked to recall symptoms and quality of life from the last 2 weeks and rate each item on a 7-point Likert scale (1=worst to 7=best). A total IBDQ score is calculated by summing the scores from each domain; the total IBDQ score ranges from 32 to 224, with lower scores reflecting worse HRQOL. A negative change from Baseline indicates worsening. LOCF method was used for analyses. FAS included all randomised participants who received at least 1 dose of study medication, as randomised. Overall number analysed are the number of participants with data evaluable for analyses.

| End point type | Secondary |
|---|---|

End point timeframe:

Baseline up to Weeks 14, 22, and 34

| **End point values** | Placebo IV | Vedolizumab IV 300 mg | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 50 | 51 | | |
| Units: score on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline | 131.5 (± 30.78) | 137.9 (± 33.53) | | |
| Change from Baseline at Week 14 | 14.6 (± 26.67) | 18.3 (± 29.20) | | |
| Change from Baseline at Week 22 | 16.0 (± 29.12) | 21.3 (± 31.28) | | |

| | | | | |
|---|---|---|---|---|
| Change from Baseline at Week 34 | 10.4 (± 25.98) | 24.4 (± 34.21) | | |

## Statistical analyses

| **Statistical analysis title** | Statistical Analysis 1 |
|---|---|
| Statistical analysis description: | |
| Change from Baseline at Week 14 | |
| Comparison groups | Placebo IV v Vedolizumab IV 300 mg |
| Number of subjects included in analysis | 101 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[20] |
| P-value | = 0.575 [21] |
| Method | Wilcoxon (Mann-Whitney) |
| Parameter estimate | Odds Estimator |
| Point estimate | 1.14 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.61 |
| upper limit | 1.67 |

Notes:

[20] - P-value is from Wilcoxon Rank-sum Test comparing change from Baseline to relevant visits. Wilcoxon-Mann-Whitney odds estimator,95% CI are presented.
[21] - No multiplicity adjustment for inferential testing for secondary endpoints was pre-planned, p-values from these tests are presented as nominal p-values. The significance level was 0.05.

| **Statistical analysis title** | Statistical Analysis 3 |
|---|---|
| Statistical analysis description: | |
| Change from Baseline at Week 34 | |
| Comparison groups | Placebo IV v Vedolizumab IV 300 mg |
| Number of subjects included in analysis | 101 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[22] |
| P-value | = 0.047 [23] |
| Method | Wilcoxon (Mann-Whitney) |
| Parameter estimate | Odds Estimator |
| Point estimate | 1.6 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.85 |
| upper limit | 2.34 |

Notes:

[22] - P-value is from Wilcoxon Rank-sum Test comparing change from Baseline to relevant visits. Wilcoxon-Mann-Whitney odds estimator,95% CI are presented.
[23] - No multiplicity adjustment for inferential testing for secondary endpoints was pre-planned, p-values from these tests are presented as nominal p-values. The significance level was 0.05.

| **Statistical analysis title** | Statistical Analysis 2 |
|---|---|

| | |
|---|---|
| Statistical analysis description: | |
| Change from Baseline at Week 22 | |
| Comparison groups | Placebo IV v Vedolizumab IV 300 mg |
| Number of subjects included in analysis | 101 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[24] |
| P-value | = 0.403 [25] |
| Method | Wilcoxon (Mann-Whitney) |
| Parameter estimate | Odds Estimator |
| Point estimate | 1.21 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.65 |
| upper limit | 1.78 |

Notes:

[24] - P-value is from Wilcoxon Rank-sum Test comparing change from Baseline to relevant visits. Wilcoxon-Mann-Whitney odds estimator,95% CI are presented.
[25] - No multiplicity adjustment for inferential testing for secondary endpoints was pre-planned, p-values from these tests are presented as nominal p-values. The significance level was 0.05.

## Secondary: Change From Baseline in Cleveland Global Quality of Life (CGQL) at Weeks 14, 22, and 34

| | |
|---|---|
| End point title | Change From Baseline in Cleveland Global Quality of Life (CGQL) at Weeks 14, 22, and 34 |

End point description:

The CGQL (Fazio score) is a quality-of-life indicator specifically for participants with ileal pouch-anal anastomosis. Participants rate 3 items (current quality of life, current quality of health, and current energy level), each on a scale of 0 to 10 (0=worst; 10=best). The scores are added, and the final CGQL utility score is obtained by dividing this result by 30. The total score ranges from 0 (worst) to 1 (best) where lower scores indicate less quality of life. A negative change from Baseline indicates worsening. LOCF method was used for analyses. FAS included all randomised participants who received at least 1 dose of study medication, as randomised. Overall number analysed are the number of participants with data evaluable for analyses.

| | |
|---|---|
| End point type | Secondary |

End point timeframe:

Baseline up to Weeks 14, 22, and 34

| **End point values** | Placebo IV | Vedolizumab IV 300 mg | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 49 | 50 | | |
| Units: score on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline | 0.522 (± 0.1953) | 0.556 (± 0.1626) | | |
| Change from Baseline at Week 14 | 0.051 (± 0.1518) | 0.088 (± 0.1715) | | |
| Change from Baseline at Week 22 | 0.073 (± 0.1491) | 0.093 (± 0.1648) | | |
| Change from Baseline at Week 34 | 0.056 (± 0.1544) | 0.083 (± 0.1831) | | |

## Statistical analyses

| **Statistical analysis title** | Statistical Analysis 2 |
|---|---|
| Statistical analysis description: | |
| Change from Baseline at Week 22 | |
| Comparison groups | Placebo IV v Vedolizumab IV 300 mg |
| Number of subjects included in analysis | 99 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[26] |
| P-value | = 0.542 [27] |
| Method | Wilcoxon (Mann-Whitney) |
| Parameter estimate | Odds Estimator |
| Point estimate | 1.15 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.62 |
| upper limit | 1.69 |

Notes:

[26] - P-value is from Wilcoxon Rank-sum Test comparing change from Baseline to relevant visits. Wilcoxon-Mann-Whitney odds estimator,95% CI are presented.
[27] - No multiplicity adjustment for inferential testing for secondary endpoints was pre-planned, p-values from these tests are presented as nominal p-values. The significance level was 0.05.

| **Statistical analysis title** | Statistical Analysis 1 |
|---|---|
| Statistical analysis description: | |
| Change from Baseline at Week 14 | |
| Comparison groups | Placebo IV v Vedolizumab IV 300 mg |
| Number of subjects included in analysis | 99 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[28] |
| P-value | = 0.119 [29] |
| Method | Wilcoxon (Mann-Whitney) |
| Parameter estimate | Odds Estimator |
| Point estimate | 1.44 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.77 |
| upper limit | 2.12 |

Notes:

[28] - P-value is from Wilcoxon Rank-sum Test comparing change from Baseline to relevant visits. Wilcoxon-Mann-Whitney odds estimator,95% CI are presented.
[29] - No multiplicity adjustment for inferential testing for secondary endpoints was pre-planned, p-values from these tests are presented as nominal p-values. The significance level was 0.05.

| **Statistical analysis title** | Statistical Analysis 3 |
|---|---|

| Statistical analysis description: | |
|---|---|
| Change from Baseline at Week 34 | |
| Comparison groups | Placebo IV v Vedolizumab IV 300 mg |
| Number of subjects included in analysis | 99 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[30] |
| P-value | = 0.404 [31] |
| Method | Wilcoxon (Mann-Whitney) |
| Parameter estimate | Odds Estimator |
| Point estimate | 1.22 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.65 |
| upper limit | 1.78 |

Notes:

[30] - P-value is from Wilcoxon Rank-sum Test comparing change from Baseline to relevant visits. Wilcoxon-Mann-Whitney odds estimator,95% CI are presented.
[31] - No multiplicity adjustment for inferential testing for secondary endpoints was pre-planned, p-values from these tests are presented as nominal p-values. The significance level was 0.05.

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

From first dose of study drug up to 18 weeks after last dose (Up to 50 weeks)

Adverse event reporting additional description:

At each visit the investigator had to document any occurrence of adverse events and abnormal laboratory findings. Any event spontaneously reported by the participant or observed by the investigator was recorded, irrespective of the relation to study treatment.

| | |
|---|---|
| Assessment type | Systematic |

### Dictionary used

| | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 23.0 |

### Reporting groups

| | |
|---|---|
| Reporting group title | Vedolizumab IV 300 mg |

Reporting group description:

Vedolizumab 300 mg, IV infusion, once at Day 1, Weeks 2, 6, 14, 22, and 30 along with ciprofloxacin 500 mg, tablet, orally twice daily up to Week 4.

| | |
|---|---|
| Reporting group title | Placebo IV |

Reporting group description:

Vedolizumab placebo-matching intravenous (IV) infusion, once at Day 1, Weeks 2, 6, 14, 22, and 30 along with ciprofloxacin 500 mg, tablet, orally twice daily up to Week 4.

| Serious adverse events | Vedolizumab IV 300 mg | Placebo IV | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 3 / 51 (5.88%) | 4 / 51 (7.84%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Basal cell carcinoma | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 51 (1.96%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 51 (1.96%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pouchitis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 2 / 51 (3.92%) | 1 / 51 (1.96%) | |
| occurrences causally related to treatment / all | 0 / 2 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Intestinal obstruction | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 51 (1.96%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Gastroenteritis | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 51 (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** | Vedolizumab IV 300 mg | Placebo IV | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 42 / 51 (82.35%) | 35 / 51 (68.63%) | |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 10 / 51 (19.61%) | 3 / 51 (5.88%) | |
| occurrences (all) | 11 | 4 | |
| Gastrointestinal disorders | | | |
| Pouchitis | | | |
| subjects affected / exposed | 23 / 51 (45.10%) | 20 / 51 (39.22%) | |
| occurrences (all) | 31 | 24 | |
| Nausea | | | |
| subjects affected / exposed | 5 / 51 (9.80%) | 5 / 51 (9.80%) | |
| occurrences (all) | 5 | 6 | |
| Abdominal pain | | | |
| subjects affected / exposed | 4 / 51 (7.84%) | 2 / 51 (3.92%) | |
| occurrences (all) | 5 | 2 | |
| Frequent bowel movements | | | |
| subjects affected / exposed | 4 / 51 (7.84%) | 2 / 51 (3.92%) | |
| occurrences (all) | 5 | 2 | |

| | | | |
|---|---|---|---|
| Respiratory, thoracic and mediastinal disorders | | | |
| Dyspnoea | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 3 / 51 (5.88%) | |
| occurrences (all) | 0 | 4 | |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 7 / 51 (13.73%) | 9 / 51 (17.65%) | |
| occurrences (all) | 7 | 11 | |
| Back pain | | | |
| subjects affected / exposed | 2 / 51 (3.92%) | 5 / 51 (9.80%) | |
| occurrences (all) | 2 | 5 | |
| Infections and infestations | | | |
| Gastroenteritis | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 3 / 51 (5.88%) | |
| occurrences (all) | 1 | 3 | |
| Influenza | | | |
| subjects affected / exposed | 4 / 51 (7.84%) | 1 / 51 (1.96%) | |
| occurrences (all) | 4 | 1 | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 6 / 51 (11.76%) | 6 / 51 (11.76%) | |
| occurrences (all) | 9 | 9 | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 5 / 51 (9.80%) | 1 / 51 (1.96%) | |
| occurrences (all) | 5 | 1 | |

## More information

## Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 20 October 2016 | The primary purpose of this amendment was to make following changes:<br>- Updated the protocol to clarify the exclusion criteria, excluded medications, and proper post-study care.<br>- Chest X-ray added to exclusion criterion for latent tuberculosis (TB).<br>- Text modified for participants receiving investigational nonbiologic therapy or an approved nonbiologic in an investigational protocol to extend the exclusion period.<br>- Modified exclusion criterion for participants with a history of tendon rupture to include tendon disease related to quinolone treatment.<br>- New exclusion criterion added for participants with glucose-6-phosphate dehydrogenase (G6PD) deficiency.<br>- Added disopyramide, probenecid, and omeprazole to list of excluded medications.<br>- Deleted methotrexate from list of permitted immunomodulators.<br>- Added text regarding post-study care for participants upon completion of the study or early withdrawal. |
| 21 April 2017 | The primary purpose of this amendment was to make following changes:<br>- Changed primary endpoint from Pouchitis Disease Activity Index (PDAI) score to modified Pouchitis Disease Activity Index (mPDAI) score.<br>- Reduced number of biopsy samples.<br>- Added minimum endoscopic subscore of 2 and specified definitions of chronic and recurrent pouchitis for study inclusion.<br>- Adjusted sample size calculation and decreased the total sample size from 200 to 110 participants.<br>- Added a futility analysis after 25 patients per arm reach Week 14.<br>- Added exclusion criteria.<br>- Added collection of stool sample for Clostridium (C) difficile testing to the Screening visit.<br>- Changed the maximum dose of oral corticosteroids from 30 to 20 mg/day and removed the recommended tapering schedule.<br>- Removed some of the exclusion criteria.<br>- Added a section on the Steering Committee.<br>- Added an investigator responsibility per updated International Conference on Harmonisation guideline.<br>- Updated indications for vedolizumab in the background information.<br>- Updated background information on the basis of the current Investigator’s Brochure.<br>- Updated the approximate total blood volume from 65 to 75 mL.<br>- Added a section on participant rescreening.<br>- Changed wording in the safety section from severity to intensity.<br>- Added frequency to the list of pretreatment event and AE reporting.<br>- Corrected an item in the PDAI and mPDAI to fecal urgency or abdominal cramps as per the original tool.<br>- Modified the criteria for discontinuation or withdrawal to add monitoring for leukopenia and lymphopenia and to clarify other criteria.<br>- Added clarifications to the Schedule of Study Procedures table. |

Notes:

## Interruptions (globally)

Were there any global interruptions to the trial? No

## Limitations and caveats

None reported