# Clinical trial results:
# A Phase 3 Randomized, Double-Blind, Placebo-Controlled Study to Evaluate the Efficacy and Safety of Vedolizumab Subcutaneous as Maintenance Therapy in Subjects With Moderately to Severely Active Crohn's Disease Who Achieved Clinical Response Following Open-Label Vedolizumab Intravenous Therapy

## Summary

| | |
|---|---|
| EudraCT number | 2015-000481-58 |
| Trial protocol | SK CZ NL BG GB DE BE SE DK LT HU ES IT |
| Global end of trial date | 06 August 2019 |

**Results information**

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 23 May 2020 |
| First version publication date | 23 May 2020 |

## Trial information

**Trial identification**

| | |
|---|---|
| Sponsor protocol code | MLN0002SC-3031 |

**Additional study identifiers**

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02611817 |
| WHO universal trial number (UTN) | U1111-1168-0845 |

Notes:

**Sponsors**

| | |
|---|---|
| Sponsor organisation name | Takeda |
| Sponsor organisation address | 40 Landsdowne Street, Cambridge, MA, United States, 02139 |
| Public contact | Medical Director, Clinical Science, Takeda, +1 877-825-3327, trialdisclosure@takeda.com |
| Scientific contact | Medical Director, Clinical Science, Takeda, +1 877-825-3327, trialdisclosure@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 | 06 August 2019 |
| Is this the analysis of the primary completion data? | No |

| | |
|---|---|
| Global end of trial reached? | Yes |
| Global end of trial date | 06 August 2019 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

The purpose of this study is to assess the effect of vedolizumab subcutaneous (SC) as maintenance treatment in subjects with moderately to severely active Crohn's disease (CD) who achieved clinical response following administration of vedolizumab intravenous (IV) induction therapy.

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 04 January 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? | Yes |

Notes:

## Population of trial subjects

### Subjects enrolled per country

| | |
|---|---|
| Country: Number of subjects enrolled | Australia: 13 |
| Country: Number of subjects enrolled | South Africa: 5 |
| Country: Number of subjects enrolled | Czech Republic: 32 |
| Country: Number of subjects enrolled | Hungary: 24 |
| Country: Number of subjects enrolled | Poland: 122 |
| Country: Number of subjects enrolled | Romania: 15 |
| Country: Number of subjects enrolled | Serbia: 14 |
| Country: Number of subjects enrolled | Slovakia: 10 |
| Country: Number of subjects enrolled | Japan: 21 |
| Country: Number of subjects enrolled | Korea, Republic of: 18 |
| Country: Number of subjects enrolled | Bosnia and Herzegovina: 1 |
| Country: Number of subjects enrolled | Bulgaria: 2 |
| Country: Number of subjects enrolled | Estonia: 2 |
| Country: Number of subjects enrolled | Israel: 33 |
| Country: Number of subjects enrolled | Russian Federation: 49 |
| Country: Number of subjects enrolled | Turkey: 6 |
| Country: Number of subjects enrolled | Ukraine: 38 |
| Country: Number of subjects enrolled | Canada: 37 |
| Country: Number of subjects enrolled | United States: 133 |

| | |
|---|---|
| Country: Number of subjects enrolled | Brazil: 10 |
| Country: Number of subjects enrolled | Mexico: 1 |
| Country: Number of subjects enrolled | Belgium: 9 |
| Country: Number of subjects enrolled | Denmark: 4 |
| Country: Number of subjects enrolled | Germany: 10 |
| Country: Number of subjects enrolled | Italy: 15 |
| Country: Number of subjects enrolled | Lithuania: 5 |
| Country: Number of subjects enrolled | Netherlands: 5 |
| Country: Number of subjects enrolled | Spain: 1 |
| Country: Number of subjects enrolled | Sweden: 2 |
| Country: Number of subjects enrolled | United Kingdom: 7 |
| Worldwide total number of subjects | 644 |
| EEA total number of subjects | 265 |

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) | 621 |
| From 65 to 84 years | 23 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details:

Subjects with moderate to severe CD took part in the study at 169 investigative sites in North America, South America, Western/Northern Europe, Central Europe, Eastern Europe, East Asia, and Africa/Australia from 04 Jan 2016 to 06 Aug 2019.

### Pre-assignment

Screening details:

Subjects were enrolled in open-label (OL) induction phase to receive vedolizumab IV. Subjects with CR at Week 6 were randomized into double-blind maintenance phase to receive vedolizumab subcutaneous/placebo, and who did not achieve CR at Week 6 received 3rd infusion of OL vedolizumab IV and completed Week 14 visit.

### Period 1

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

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | Open-label Induction Phase: Vedolizumab 300 mg IV |

Arm description:

Vedolizumab 300 milligram (mg), infusion, intravenously, once at Weeks 0, 2 in the open-label induction phase. Subjects who did not achieve clinical response at Week 6 received third infusion of vedolizumab 300 mg IV on Week 6.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Vedolizumab 300 mg IV |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Vedolizumab 300 mg, infusion, intravenously, once at Weeks 0, 2 in the open-label induction phase. Subjects who did not achieve clinical response at Week 6 received third infusion of vedolizumab 300 mg IV on Week 6.

| | |
|---|---|
| **Arm title** | Maintenance Phase: Induction IV + Placebo |

Arm description:

Vedolizumab placebo-matching injection, subcutaneously, once every 2 weeks from Week 6 up to Week 50. Subjects who received vedolizumab 300 mg IV infusion in open-label induction phase and achieved clinical response at Week 6 were randomized to receive placebo in maintenance phase.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Vedolizumab placebo-matching injection, subcutaneously, once every 2 weeks from Week 6 up to Week 50. Subjects who received vedolizumab 300 mg IV infusion in open-label induction phase and achieved clinical response at Week 6 were randomized to receive placebo in maintenance phase.

| | |
|---|---|
| **Arm title** | Maintenance Phase: Induction IV + Vedolizumab 108 mg SC |

Arm description:

Vedolizumab 108 mg, injection, subcutaneously, once every 2 weeks from Week 6 up to Week 50. Subjects who received vedolizumab 300 mg IV infusion in open-label induction phase and achieved clinical response at Week 6 were randomized to receive vedolizumab injection subcutaneously in maintenance phase.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Vedolizumab 108 mg SC |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Vedolizumab 108 mg, injection, subcutaneously, once every 2 weeks from Week 6 up to Week 50. Subjects who received vedolizumab 300 mg IV infusion in open-label induction phase and achieved clinical response at Week 6 were randomized to receive vedolizumab injection subcutaneously in maintenance phase.

| **Number of subjects in period 1** | Open-label Induction Phase: Vedolizumab 300 mg IV | Maintenance Phase: Induction IV + Placebo | Maintenance Phase: Induction IV + Vedolizumab 108 mg SC |
|---|---|---|---|
| Started | 235 | 134 | 275 |
| Completed | 235 | 72 | 168 |
| Not completed | 0 | 62 | 107 |
| Consent withdrawn by subject | - | 5 | 14 |
| Adverse event, non-fatal | - | 12 | 11 |
| Other | - | 1 | 2 |
| Pregnancy | - | - | 1 |
| Randomized but not Treated | - | 1 | - |
| Lost to follow-up | - | - | 1 |
| Lack of efficacy | - | 43 | 78 |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | Open-label Induction Phase: Vedolizumab 300 mg IV |
| Reporting group description: | |
| Vedolizumab 300 milligram (mg), infusion, intravenously, once at Weeks 0, 2 in the open-label induction phase. Subjects who did not achieve clinical response at Week 6 received third infusion of vedolizumab 300 mg IV on Week 6. | |
| Reporting group title | Maintenance Phase: Induction IV + Placebo |
| Reporting group description: | |
| Vedolizumab placebo-matching injection, subcutaneously, once every 2 weeks from Week 6 up to Week 50. Subjects who received vedolizumab 300 mg IV infusion in open-label induction phase and achieved clinical response at Week 6 were randomized to receive placebo in maintenance phase. | |
| Reporting group title | Maintenance Phase: Induction IV + Vedolizumab 108 mg SC |
| Reporting group description: | |
| Vedolizumab 108 mg, injection, subcutaneously, once every 2 weeks from Week 6 up to Week 50. Subjects who received vedolizumab 300 mg IV infusion in open-label induction phase and achieved clinical response at Week 6 were randomized to receive vedolizumab injection subcutaneously in maintenance phase. | |

| **Reporting group values** | Open-label Induction Phase: Vedolizumab 300 mg IV | Maintenance Phase: Induction IV + Placebo | Maintenance Phase: Induction IV + Vedolizumab 108 mg SC |
|---|---|---|---|
| Number of subjects | 235 | 134 | 275 |
| Age categorical<br>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) | 228 | 131 | 262 |
| From 65-84 years | 7 | 3 | 13 |
| 85 years and over | 0 | 0 | 0 |
| Age Continuous<br>Units: years | | | |
| arithmetic mean | 37.4 | 36.1 | 38.2 |
| standard deviation | ± 12.79 | ± 12.93 | ± 13.85 |
| Sex: Female, Male<br>Units: participants | | | |
| Female | 119 | 68 | 118 |
| Male | 116 | 66 | 157 |
| Ethnicity (NIH/OMB)<br>Units: Subjects | | | |
| Hispanic or Latino | 0 | 1 | 2 |
| Not Hispanic or Latino | 50 | 20 | 60 |
| Unknown or Not Reported | 185 | 113 | 213 |
| Race (NIH/OMB)<br>Units: Subjects | | | |

| | | | |
|---|---|---|---|
| American Indian or Alaska Native | 0 | 2 | 0 |
| Asian | 23 | 6 | 17 |
| Native Hawaiian or Other Pacific Islander | 2 | 1 | 0 |
| Black or African American | 3 | 1 | 7 |
| White | 207 | 124 | 250 |
| More than one race | 0 | 0 | 1 |
| Unknown or Not Reported | 0 | 0 | 0 |
| Smoking Classification | | | |
| Units: Subjects | | | |
| Never smoked | 140 | 85 | 148 |
| Current smoker | 49 | 26 | 54 |
| Ex-smoker | 46 | 23 | 73 |
| Weight | | | |
| Units: kilogram (kg) | | | |
| arithmetic mean | 69.94 | 69.79 | 74.08 |
| standard deviation | ± 18.403 | ± 18.103 | ± 18.994 |
| Body Mass Index | | | |
| Units: kilogram per square meter (kg/m^2) | | | |
| arithmetic mean | 24.20 | 23.93 | 25.06 |
| standard deviation | ± 6.073 | ± 5.541 | ± 5.915 |

| **Reporting group values** | Total | | |
|---|---|---|---|
| Number of subjects | 644 | | |
| Age categorical | | | |
| Units: Subjects | | | |
| In utero | 0 | | |
| Preterm newborn infants (gestational age < 37 wks) | 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) | 621 | | |
| From 65-84 years | 23 | | |
| 85 years and over | 0 | | |
| Age Continuous | | | |
| Units: years | | | |
| arithmetic mean | | | |
| standard deviation | - | | |
| Sex: Female, Male | | | |
| Units: participants | | | |
| Female | 305 | | |
| Male | 339 | | |
| Ethnicity (NIH/OMB) | | | |
| Units: Subjects | | | |
| Hispanic or Latino | 3 | | |
| Not Hispanic or Latino | 130 | | |
| Unknown or Not Reported | 511 | | |
| Race (NIH/OMB) | | | |
| Units: Subjects | | | |

| | | | |
|---|---|---|---|
| American Indian or Alaska Native | 2 | | |
| Asian | 46 | | |
| Native Hawaiian or Other Pacific Islander | 3 | | |
| Black or African American | 11 | | |
| White | 581 | | |
| More than one race | 1 | | |
| Unknown or Not Reported | 0 | | |
| Smoking Classification | | | |
| Units: Subjects | | | |
| Never smoked | 373 | | |
| Current smoker | 129 | | |
| Ex-smoker | 142 | | |
| Weight | | | |
| Units: kilogram (kg) | | | |
| arithmetic mean | | | |
| standard deviation | - | | |
| Body Mass Index | | | |
| Units: kilogram per square meter (kg/m^2) | | | |
| arithmetic mean | | | |
| standard deviation | - | | |

## End points

### End points reporting groups

| | |
|---|---|
| Reporting group title | Open-label Induction Phase: Vedolizumab 300 mg IV |

Reporting group description:

Vedolizumab 300 milligram (mg), infusion, intravenously, once at Weeks 0, 2 in the open-label induction phase. Subjects who did not achieve clinical response at Week 6 received third infusion of vedolizumab 300 mg IV on Week 6.

| | |
|---|---|
| Reporting group title | Maintenance Phase: Induction IV + Placebo |

Reporting group description:

Vedolizumab placebo-matching injection, subcutaneously, once every 2 weeks from Week 6 up to Week 50. Subjects who received vedolizumab 300 mg IV infusion in open-label induction phase and achieved clinical response at Week 6 were randomized to receive placebo in maintenance phase.

| | |
|---|---|
| Reporting group title | Maintenance Phase: Induction IV + Vedolizumab 108 mg SC |

Reporting group description:

Vedolizumab 108 mg, injection, subcutaneously, once every 2 weeks from Week 6 up to Week 50. Subjects who received vedolizumab 300 mg IV infusion in open-label induction phase and achieved clinical response at Week 6 were randomized to receive vedolizumab injection subcutaneously in maintenance phase.

| | |
|---|---|
| Subject analysis set title | Maintenance Phase: Induction IV + Placebo |
| Subject analysis set type | Full analysis |

Subject analysis set description:

Vedolizumab placebo-matching injection, subcutaneously, once every 2 weeks from Week 6 up to Week 50. Subjects who received vedolizumab 300 mg IV infusion in open-label induction phase and achieved clinical response at Week 6 were randomized to receive placebo in maintenance phase.

| | |
|---|---|
| Subject analysis set title | Maintenance Phase: Induction IV + Vedolizumab 108 mg SC |
| Subject analysis set type | Full analysis |

Subject analysis set description:

Vedolizumab 108 mg, injection, subcutaneously, once every 2 weeks from Week 6 up to Week 50. Subjects who received vedolizumab 300 mg IV infusion in open-label induction phase and achieved clinical response at Week 6 were randomized to receive vedolizumab injection subcutaneously in maintenance phase.

### Primary: Percentage of Subjects Achieving Clinical Remission at Week 52

| | |
|---|---|
| End point title | Percentage of Subjects Achieving Clinical Remission at Week |

End point description:

Clinical remission:Crohn's Disease Activity Index (CDAI) score less than or equal to(<=)150 at Week52.CDAI is a multi-item instrument which measures severity of active Crohn's Disease monitored over 7 days includes subject reported symptoms,physician-assessed signs/laboratory markers. CDAI score is equal to (=) sum of weighted scores for subjective items (number of liquid/soft stools,degree of abdominal pain,general well-being); objective items (use of anti-diarrhoeal medication, abdominal mass, haematocrit, presence of extraintestinal manifestations, body weight). CDAI scores range approx. from 0 to 600, higher scores indicating greater disease activity. Full analysis set(FAS):All randomized subjects who received at least 1 dose of study SC drug (placebo/VDZ).Subjects who only received induction IV therapy and not randomized into the maintenance phase were not included in FAS.Subjects in this set were analyzed according to treatment they were randomized to receive.

| | |
|---|---|
| End point type | Primary |

End point timeframe:

Week 52

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Descriptive data was planned to be analyzed for the reported arms.

| End point values | Maintenance Phase: Induction IV + Placebo | Maintenance Phase: Induction IV + Vedolizumab 108 mg SC | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 134 | 275 | | |
| Units: percentage of subjects | | | | |
| number (confidence interval 95%) | 34.3 (26.3 to 43.0) | 48.0 (42.0 to 54.1) | | |

## Statistical analyses

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

Statistical analysis description:

P-value was calculated by Cochran-Mantel-Haenszel (CMH) test stratified by electronic data capture (EDC) stratum according to concomitant use of corticosteroids, clinical remission status at Week 6, and previous TNF-alpha antagonist failure/exposed or concomitant immunomodulator use.

| | |
|---|---|
| Comparison groups | Maintenance Phase: Induction IV + Placebo v Maintenance Phase: Induction IV + Vedolizumab 108 mg SC |
| Number of subjects included in analysis | 409 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.008 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Clopper-Pearson method |
| Point estimate | 13.7 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 3.8 |
| upper limit | 23.7 |

## Secondary: Percentage of Subjects Achieving Enhanced Clinical Response at Week 52

| End point title | Percentage of Subjects Achieving Enhanced Clinical Response at Week 52[2] |
|---|---|

End point description:

Enhanced clinical response: A decrease from Baseline of greater than or equal to(>=)100 points in the CDAI score at Week 52.CDAI is a multi-item instrument which measures severity of active CD monitored over 7 days includes subject reported symptoms, physician-assessed signs, and laboratory markers.CDAI score = Sum of weighted scores for subjective items (number of liquid/soft stools, degree of abdominal pain, general well-being); and objective items (use of anti-diarrhoeal medication, abdominal mass, haematocrit, presence of extraintestinal manifestations, body weight). CDAI scores range approx from 0 to 600, higher scores indicating greater disease activity. FAS included all randomized subjects who received at least 1 dose of study SC drug (placebo/VDZ). Subjects who only received induction IV therapy and not randomized into the maintenance phase were not included in FAS. Subjects in this set were analyzed according to the treatment they were randomized to receive.

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

End point timeframe:

Week 52

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Descriptive data was planned to be analyzed for the reported arms.

| **End point values** | Maintenance Phase: Induction IV + Placebo | Maintenance Phase: Induction IV + Vedolizumab 108 mg SC | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 134 | 275 | | |
| Units: percentage of subjects | | | | |
| number (confidence interval 95%) | 44.8 (36.2 to 53.6) | 52.0 (45.9 to 58.0) | | |

### Statistical analyses

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

Statistical analysis description:

P-value was calculated by CMH test stratified by EDC stratum according to concomitant use of corticosteroids, clinical remission status at Week 6, and previous TNF-alpha antagonist failure/exposed or concomitant immunomodulator use.

| Comparison groups | Maintenance Phase: Induction IV + Placebo v Maintenance Phase: Induction IV + Vedolizumab 108 mg SC |
|---|---|
| Number of subjects included in analysis | 409 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.167 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Clopper-Pearson method |
| Point estimate | 7.3 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -3 |
| upper limit | 17.5 |

## Secondary: Percentage of Subjects Achieving Corticosteroid-free Remission at Week 52

| End point title | Percentage of Subjects Achieving Corticosteroid-free Remission at Week 52[3] |
|---|---|

End point description:

Corticosteroid-free remission is defined as subjects using oral corticosteroids at Baseline (Week 0) who have discontinued oral corticosteroids and are in clinical remission at Week 52. Clinical remission is defined as a CDAI score <=150 at Week 52. CDAI score = Sum of weighted scores for subjective items (number of liquid/soft stools, degree of abdominal pain, general well-being); and objective items (use of anti-diarrhoeal medication, abdominal mass, haematocrit, presence of extraintestinal manifestations, body weight). CDAI scores range approximately from 0 to 600, higher scores indicating greater disease activity. Subjects from FAS, who used concomitant oral corticosteroid at Baseline. FAS had all subjects who received at least 1 dose of SC drug. Subjects who only received induction IV therapy and were not randomized into maintenance phase were not included in FAS. Subjects were analyzed according to

randomized treatment assignment.

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

End point timeframe:

Week 52

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Descriptive data was planned to be analyzed for the reported arms.

| **End point values** | Maintenance Phase: Induction IV + Placebo | Maintenance Phase: Induction IV + Vedolizumab 108 mg SC | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 44 | 95 | | |
| Units: percentage of subjects | | | | |
| number (confidence interval 95%) | 18.2 (8.2 to 32.7) | 45.3 (35.0 to 55.8) | | |

## Statistical analyses

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

Statistical analysis description:

P-value was calculated by CMH test stratified by EDC stratum according to concomitant use of corticosteroids, clinical remission status at Week 6, and previous TNF-alpha antagonist failure/exposed or concomitant immunomodulator use.

| Comparison groups | Maintenance Phase: Induction IV + Placebo v Maintenance Phase: Induction IV + Vedolizumab 108 mg SC |
|---|---|
| Number of subjects included in analysis | 139 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.002 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Clopper-Pearson method |
| Point estimate | 27.1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 11.9 |
| upper limit | 42.3 |

## Secondary: Percentage of TNF-alpha Antagonist Naive Subjects Achieving Clinical Remission at Week 52

| End point title | Percentage of TNF-alpha Antagonist Naive Subjects Achieving Clinical Remission at Week 52[4] |
|---|---|

End point description:

Clinical remission is defined as CDAI score <=150 at Week 52. CDAI score = Sum of weighted scores for subjective items (number of liquid/soft stools, degree of abdominal pain, general well-being); and objective items (use of anti-diarrhoeal medication, abdominal mass, haematocrit, presence of extraintestinal manifestation, body weight). CDAI scores range approximately from 0 to 600, higher

scores indicating greater disease activity. Subjects from FAS, who were TNF-alpha antagonist naïve and had clinical remission. FAS had all subjects who received at least 1 dose of SC drug. Subjects who only received induction IV therapy and were not randomized in maintenance phase were not included in FAS. Subjects were analyzed according to randomized treatment assignment.

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

End point timeframe:

Week 52

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Descriptive data was planned to be analyzed for the reported arms.

| **End point values** | Maintenance Phase: Induction IV + Placebo | Maintenance Phase: Induction IV + Vedolizumab 108 mg SC | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 63 | 107 | | |
| Units: percentage of subjects | | | | |
| number (confidence interval 95%) | 42.9 (30.5 to 56.0) | 48.6 (38.8 to 58.5) | | |

## Statistical analyses

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

Statistical analysis description:

P-value was calculated by CMH test stratified by EDC stratum according to concomitant use of corticosteroids, clinical remission status at Week 6, and previous TNF-alpha antagonist failure/exposed or concomitant immunomodulator use.

| Comparison groups | Maintenance Phase: Induction IV + Placebo v Maintenance Phase: Induction IV + Vedolizumab 108 mg SC |
|---|---|
| Number of subjects included in analysis | 170 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.591 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Clopper-Pearson method |
| Point estimate | 4.3 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -11.6 |
| upper limit | 20.3 |

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Treatment-emergent adverse events are adverse events that started after the first dose of study drug up to 18 weeks after the last dose of study drug (up to Week 68)

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 subject or observed by the investigator was recorded, irrespective of the relation to study treatment.

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

### Dictionary used

| | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 22.0 |

### Reporting groups

| | |
|---|---|
| Reporting group title | Induction Phase Only: Vedolizumab 300 mg IV |

Reporting group description:

Vedolizumab 300 mg, infusion, intravenously, once at Weeks 0, 2 in the open-label induction phase. Subjects who did not achieve clinical response at Week 6 received third infusion of vedolizumab 300 mg IV on Week 6.

| | |
|---|---|
| Reporting group title | Maintenance Phase: Induction IV + Vedolizumab 108 mg SC |

Reporting group description:

Vedolizumab 108 mg, injection, subcutaneously, once every 2 weeks from Week 6 up to Week 50. Subjects who received vedolizumab 300 mg IV infusion in open-label induction phase and achieved clinical response at Week 6 were randomized to receive vedolizumab injection subcutaneously in maintenance phase.

| | |
|---|---|
| Reporting group title | Maintenance Phase: Induction IV + Placebo |

Reporting group description:

Vedolizumab placebo-matching injection, subcutaneously, once every 2 weeks from Week 6 up to Week 50. Subjects who received vedolizumab 300 mg IV infusion in open-label induction phase and achieved clinical response at Week 6 were randomized to receive placebo in maintenance phase.

| **Serious adverse events** | Induction Phase Only: Vedolizumab 300 mg IV | Maintenance Phase: Induction IV + Vedolizumab 108 mg SC | Maintenance Phase: Induction IV + Placebo |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 39 / 235 (16.60%) | 23 / 275 (8.36%) | 14 / 134 (10.45%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Intraductal papilloma of breast | | | |
| subjects affected / exposed | 0 / 235 (0.00%) | 1 / 275 (0.36%) | 0 / 134 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General disorders and administration site conditions | | | |

| | | | |
|---|---|---|---|
| General physical health deterioration | | | |
| subjects affected / exposed | 0 / 235 (0.00%) | 1 / 275 (0.36%) | 0 / 134 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Immune system disorders | | | |
| Anaphylactic reaction | | | |
| subjects affected / exposed | 1 / 235 (0.43%) | 0 / 275 (0.00%) | 0 / 134 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Psychiatric disorders | | | |
| Alcoholism | | | |
| subjects affected / exposed | 0 / 235 (0.00%) | 1 / 275 (0.36%) | 0 / 134 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Suicidal ideation | | | |
| subjects affected / exposed | 0 / 235 (0.00%) | 1 / 275 (0.36%) | 0 / 134 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Investigations | | | |
| White blood cell count increased | | | |
| subjects affected / exposed | 0 / 235 (0.00%) | 1 / 275 (0.36%) | 0 / 134 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Injury, poisoning and procedural complications | | | |
| Gastrointestinal anastomotic complication | | | |
| subjects affected / exposed | 1 / 235 (0.43%) | 0 / 275 (0.00%) | 0 / 134 (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 |
| Incisional hernia | | | |
| subjects affected / exposed | 0 / 235 (0.00%) | 1 / 275 (0.36%) | 0 / 134 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal anastomotic stenosis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 235 (0.00%) | 1 / 275 (0.36%) | 0 / 134 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infusion related reaction | | | |
| subjects affected / exposed | 1 / 235 (0.43%) | 0 / 275 (0.00%) | 0 / 134 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac disorders | | | |
| Angina pectoris | | | |
| subjects affected / exposed | 0 / 235 (0.00%) | 1 / 275 (0.36%) | 0 / 134 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Atrial fibrillation | | | |
| subjects affected / exposed | 0 / 235 (0.00%) | 2 / 275 (0.73%) | 0 / 134 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| Haemorrhagic stroke | | | |
| subjects affected / exposed | 0 / 235 (0.00%) | 1 / 275 (0.36%) | 0 / 134 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Intraventricular haemorrhage | | | |
| subjects affected / exposed | 0 / 235 (0.00%) | 0 / 275 (0.00%) | 1 / 134 (0.75%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hemiparesis | | | |
| subjects affected / exposed | 1 / 235 (0.43%) | 0 / 275 (0.00%) | 0 / 134 (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 |
| Hemiplegia | | | |
| subjects affected / exposed | 1 / 235 (0.43%) | 0 / 275 (0.00%) | 0 / 134 (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 |
| Blood and lymphatic system disorders | | | |

| | | | |
|---|---|---|---|
| Anaemias | | | |
| subjects affected / exposed | 1 / 235 (0.43%) | 1 / 275 (0.36%) | 1 / 134 (0.75%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Leukocytosis | | | |
| subjects affected / exposed | 0 / 235 (0.00%) | 0 / 275 (0.00%) | 1 / 134 (0.75%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Febrile neutropenia | | | |
| subjects affected / exposed | 1 / 235 (0.43%) | 0 / 275 (0.00%) | 0 / 134 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| Pancreatitis | | | |
| subjects affected / exposed | 0 / 235 (0.00%) | 0 / 275 (0.00%) | 1 / 134 (0.75%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Crohn's disease | | | |
| subjects affected / exposed | 14 / 235 (5.96%) | 6 / 275 (2.18%) | 5 / 134 (3.73%) |
| occurrences causally related to treatment / all | 3 / 14 | 1 / 7 | 0 / 7 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Small intestinal obstruction | | | |
| subjects affected / exposed | 1 / 235 (0.43%) | 1 / 275 (0.36%) | 2 / 134 (1.49%) |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 1 | 1 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ileal stenosis | | | |
| subjects affected / exposed | 0 / 235 (0.00%) | 1 / 275 (0.36%) | 0 / 134 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Anal fistula | | | |
| subjects affected / exposed | 1 / 235 (0.43%) | 1 / 275 (0.36%) | 1 / 134 (0.75%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Enterovesical fistula | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 235 (0.00%) | 0 / 275 (0.00%) | 1 / 134 (0.75%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Intestinal obstruction | | | |
| subjects affected / exposed | 1 / 235 (0.43%) | 2 / 275 (0.73%) | 0 / 134 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Subileus | | | |
| subjects affected / exposed | 1 / 235 (0.43%) | 1 / 275 (0.36%) | 0 / 134 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Abdominal pain | | | |
| subjects affected / exposed | 2 / 235 (0.85%) | 0 / 275 (0.00%) | 0 / 134 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Enterocutaneous fistula | | | |
| subjects affected / exposed | 1 / 235 (0.43%) | 0 / 275 (0.00%) | 0 / 134 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Jejunal perforation | | | |
| subjects affected / exposed | 1 / 235 (0.43%) | 0 / 275 (0.00%) | 0 / 134 (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 |
| Large intestinal ulcer | | | |
| subjects affected / exposed | 1 / 235 (0.43%) | 0 / 275 (0.00%) | 0 / 134 (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 |
| Large intestine perforation | | | |
| subjects affected / exposed | 1 / 235 (0.43%) | 0 / 275 (0.00%) | 0 / 134 (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 |
| Nausea | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 235 (0.43%) | 0 / 275 (0.00%) | 0 / 134 (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 |
| Vomiting | | | |
| subjects affected / exposed | 1 / 235 (0.43%) | 0 / 275 (0.00%) | 0 / 134 (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 |
| Hepatobiliary disorders | | | |
| Hepatitis cholestatic | | | |
| subjects affected / exposed | 1 / 235 (0.43%) | 0 / 275 (0.00%) | 0 / 134 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal and urinary disorders | | | |
| Ureterolithiasis | | | |
| subjects affected / exposed | 1 / 235 (0.43%) | 0 / 275 (0.00%) | 0 / 134 (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 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 0 / 235 (0.00%) | 1 / 275 (0.36%) | 0 / 134 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Anal abscess | | | |
| subjects affected / exposed | 2 / 235 (0.85%) | 1 / 275 (0.36%) | 1 / 134 (0.75%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Abdominal wall abscess | | | |
| subjects affected / exposed | 1 / 235 (0.43%) | 0 / 275 (0.00%) | 1 / 134 (0.75%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Abscess intestinal | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 235 (0.00%) | 1 / 275 (0.36%) | 0 / 134 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Appendicitis | | | |
| subjects affected / exposed | 0 / 235 (0.00%) | 0 / 275 (0.00%) | 1 / 134 (0.75%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastroenteritis | | | |
| subjects affected / exposed | 1 / 235 (0.43%) | 0 / 275 (0.00%) | 1 / 134 (0.75%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Rectal abscess | | | |
| subjects affected / exposed | 0 / 235 (0.00%) | 1 / 275 (0.36%) | 0 / 134 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dengue fever | | | |
| subjects affected / exposed | 0 / 235 (0.00%) | 0 / 275 (0.00%) | 1 / 134 (0.75%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bronchitis | | | |
| subjects affected / exposed | 0 / 235 (0.00%) | 0 / 275 (0.00%) | 1 / 134 (0.75%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia | | | |
| subjects affected / exposed | 1 / 235 (0.43%) | 1 / 275 (0.36%) | 0 / 134 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Abdominal abscess | | | |
| subjects affected / exposed | 4 / 235 (1.70%) | 0 / 275 (0.00%) | 0 / 134 (0.00%) |
| occurrences causally related to treatment / all | 0 / 6 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cellulitis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 235 (0.43%) | 0 / 275 (0.00%) | 0 / 134 (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 |
| Colonic abscess | | | |
| subjects affected / exposed | 1 / 235 (0.43%) | 0 / 275 (0.00%) | 0 / 134 (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 |
| Perirectal abscess | | | |
| subjects affected / exposed | 1 / 235 (0.43%) | 0 / 275 (0.00%) | 0 / 134 (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 |
| Metabolism and nutrition disorders | | | |
| Weight gain poor | | | |
| subjects affected / exposed | 0 / 235 (0.00%) | 0 / 275 (0.00%) | 1 / 134 (0.75%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

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

| **Non-serious adverse events** | Induction Phase Only: Vedolizumab 300 mg IV | Maintenance Phase: Induction IV + Vedolizumab 108 mg SC | Maintenance Phase: Induction IV + Placebo |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 40 / 235 (17.02%) | 102 / 275 (37.09%) | 54 / 134 (40.30%) |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 10 / 235 (4.26%) | 15 / 275 (5.45%) | 5 / 134 (3.73%) |
| occurrences (all) | 10 | 19 | 9 |
| Gastrointestinal disorders | | | |
| Crohn's disease | | | |
| subjects affected / exposed | 7 / 235 (2.98%) | 36 / 275 (13.09%) | 23 / 134 (17.16%) |
| occurrences (all) | 7 | 36 | 25 |
| Abdominal pain | | | |
| subjects affected / exposed | 9 / 235 (3.83%) | 21 / 275 (7.64%) | 11 / 134 (8.21%) |
| occurrences (all) | 11 | 25 | 14 |
| Nausea | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 9 / 235 (3.83%) | 11 / 275 (4.00%) | 7 / 134 (5.22%) |
| occurrences (all) | 10 | 14 | 7 |
| Vomiting | | | |
| subjects affected / exposed | 4 / 235 (1.70%) | 6 / 275 (2.18%) | 7 / 134 (5.22%) |
| occurrences (all) | 5 | 7 | 8 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 8 / 235 (3.40%) | 17 / 275 (6.18%) | 9 / 134 (6.72%) |
| occurrences (all) | 8 | 21 | 10 |
| Infections and infestations | | | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 7 / 235 (2.98%) | 25 / 275 (9.09%) | 6 / 134 (4.48%) |
| occurrences (all) | 8 | 26 | 8 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 2 / 235 (0.85%) | 17 / 275 (6.18%) | 5 / 134 (3.73%) |
| occurrences (all) | 2 | 23 | 6 |

## More information

## Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 12 October 2015 | The primary purpose of this amendment was to update the protocol regarding inclusion of additional exploratory objectives and endpoints to gather alternative clinical data. |
| 10 February 2016 | The primary purpose of this amendment was to update the protocol regarding inclusion of a benefit-risk assessment. |
| 12 May 2016 | The primary purpose of this amendment was to update the protocol to include additional information for clarification. |
| 28 July 2016 | The primary purpose of this amendment was to clarify the inclusion/exclusion criteria and to provide additional information regarding the voluntary ileocolonoscopies. |
| 28 September 2016 | The primary purpose of this amendment was to extend the visit window for Week 6a from 3 days to 5 days to adjust for clinical practice in Japan. |
| 24 August 2017 | The primary purpose of this amendment was to include a pre-Week 14 visit and to clarify the Week 14 procedures for subjects who enroll or do not enroll into the OLE study (SC-3030). |

Notes:

## Interruptions (globally)

Were there any global interruptions to the trial? No

## Limitations and caveats

None reported