



## Clinical trial results:

### An Open-Label Phase 3b Study to Assess Mucosal Healing in Subjects With Moderately to Severely Active Crohn's Disease Treated With Vedolizumab IV

#### Summary

|                          |                  |
|--------------------------|------------------|
| EudraCT number           | 2014-003509-13   |
| Trial protocol           | HU CZ PL BE IT   |
| Global end of trial date | 21 February 2018 |

#### Results information

|                                |                 |
|--------------------------------|-----------------|
| Result version number          | v1 (current)    |
| This version publication date  | 04 October 2019 |
| First version publication date | 04 October 2019 |

#### Trial information

##### Trial identification

|                       |              |
|-----------------------|--------------|
| Sponsor protocol code | MLN0002-3028 |
|-----------------------|--------------|

##### Additional study identifiers

|                                    |                 |
|------------------------------------|-----------------|
| ISRCTN number                      | -               |
| ClinicalTrials.gov id (NCT number) | NCT02425111     |
| WHO universal trial number (UTN)   | U1111-1159-5806 |

Notes:

#### Sponsors

|                              |   |
|------------------------------|---|
| Sponsor organisation name    | Takeda  |
| Sponsor organisation address | 40 Landsdowne Street, Cambridge, MA, United States, 02139               |
| Public contact               | Medical Director, Takeda, +1 8778253327, clinicaltrialregistry@tpna.com |
| Scientific contact           | Medical Director, Takeda, +1 8778253327, clinicaltrialregistry@tpna.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                       | 21 February 2018 |
| Is this the analysis of the primary completion data? | No               |
| Global end of trial reached?                         | Yes              |
| Global end of trial date                             | 21 February 2018 |
| Was the trial ended prematurely?                     | No               |

Notes:

## General information about the trial

Main objective of the trial:

The purpose of this study is to evaluate endoscopic remission at Week 26 as assessed by ileocolonoscopy.

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                          | 30 March 2015 |
| 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 | Belgium: 8         |
| Country: Number of subjects enrolled | Canada: 14         |
| Country: Number of subjects enrolled | Czech Republic: 14 |
| Country: Number of subjects enrolled | France: 2          |
| Country: Number of subjects enrolled | Hungary: 14        |
| Country: Number of subjects enrolled | Italy: 9           |
| Country: Number of subjects enrolled | Poland: 7          |
| Country: Number of subjects enrolled | United States: 33  |
| Worldwide total number of subjects   | 101                |
| EEA total number of subjects         | 54                 |

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          | 0 |

|                           |    |
|---------------------------|----|
| months)                   |    |
| Children (2-11 years)     | 0  |
| Adolescents (12-17 years) | 0  |
| Adults (18-64 years)      | 96 |
| From 65 to 84 years       | 5  |
| 85 years and over         | 0  |

## Subject disposition

### Recruitment

Recruitment details:

Participants took part in the study at 42 investigative sites in Belgium, Canada, Czech Republic, France, Hungary, Italy, Poland and the United States from 30 March 2015 to 21 February 2018.

### Pre-assignment

Screening details:

Participants with a diagnosis of Crohn's Disease were enrolled to receive vedolizumab IV.

### Period 1

|                              |                             |
|------------------------------|-----------------------------|
| Period 1 title               | Part A: Treatment Period    |
| Is this the baseline period? | Yes                         |
| Allocation method            | Non-randomised - controlled |
| Blinding used                | Not blinded                 |

### Arms

|                  |                    |
|------------------|--------------------|
| <b>Arm title</b> | Vedolizumab 300 mg |
|------------------|--------------------|

Arm description:

Part A: Vedolizumab 300 mg, intravenously (IV), once on Day 1 and Weeks 2, 6, 14 and 22, followed by Part B: Vedolizumab 300 mg, intravenously (IV), once at Weeks 30, 38, and 46.

|  |                                    |
|--|------------------------------------|
| Arm type                               | Experimental                       |
| Investigational medicinal product name | Vedolizumab                        |
| Investigational medicinal product code |                                    |
| Other name                             |                                    |
| Pharmaceutical forms                   | Blood fraction modifier, Injection |
| Routes of administration               | Intravenous use                    |

Dosage and administration details:

Vedolizumab 300 mg IV injection

| Number of subjects in period 1       | Vedolizumab 300 mg |
|--------------------------------------|--------------------|
| Started                              | 101                |
| Completed                            | 74                 |
| Not completed                        | 27                 |
| Pretreatment Event/Adverse Event (s) | 5                  |
| Voluntary Withdrawal                 | 4                  |
| Lost to follow-up                    | 2                  |
| Lack of efficacy                     | 16                 |

**Period 2**

|                              |                                    |
|------------------------------|------------------------------------|
| Period 2 title               | Part B: Treatment Extension Period |
| Is this the baseline period? | No                                 |
| Allocation method            | Non-randomised - controlled        |
| Blinding used                | Not blinded                        |

**Arms**

|                  |                    |
|------------------|--------------------|
| <b>Arm title</b> | Vedolizumab 300 mg |
|------------------|--------------------|

Arm description:

Part A: Vedolizumab 300 mg, intravenously (IV), once on Day 1 and Weeks 2, 6, 14 and 22, followed by Part B: Vedolizumab 300 mg, intravenously (IV), once at Weeks 30, 38, and 46.

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

Dosage and administration details:

Vedolizumab 300 mg IV injection

|   |                    |
|---|--------------------|
| <b>Number of subjects in period 2<sup>[1]</sup></b> | Vedolizumab 300 mg |
| Started   | 56                 |
| Completed   | 46                 |
| Not completed                                       | 10                 |
| Pretreatment Event/Adverse Event (s)                | 3                  |
| Lack of efficacy                                    | 7                  |

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: A total of 56 participants were consented under Amendment 4 and were thus eligible for Part B.

## Baseline characteristics

### Reporting groups

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

Reporting group description:

Part A: Vedolizumab 300 mg, intravenously (IV), once on Day 1 and Weeks 2, 6, 14 and 22, followed by  
Part B: Vedolizumab 300 mg, intravenously (IV), once at Weeks 30, 38, and 46.

| Reporting group values                             | Vedolizumab 300 mg | Total |  |
|--|--------------------|-------|--|
| Number of subjects                                 | 101                | 101   |  |
| Age categorical                                    |                    |       |  |
| Units: Subjects                                    |                    |       |  |
| Adults (18-64 years)                               | 96                 | 96    |  |
| From 65-84 years                                   | 5                  | 5     |  |
| Age Continuous                                     |                    |       |  |
| Units: years                                       |                    |       |  |
| arithmetic mean                                    | 38.0               |       |  |
| standard deviation                                 | ± 14.00            | -     |  |
| Sex: Female, Male                                  |                    |       |  |
| Units: Subjects                                    |                    |       |  |
| Female   | 49                 | 49    |  |
| Male   | 52                 | 52    |  |
| Race/Ethnicity, Customized                         |                    |       |  |
| Ethnicity was collected only in the United States. |                    |       |  |
| Units: Subjects                                    |                    |       |  |
| Hispanic or Latino                                 | 1                  | 1     |  |
| Non-Hispanic and Latino                            | 32                 | 32    |  |
| Not Collected                                      | 68                 | 68    |  |
| Race/Ethnicity, Customized                         |                    |       |  |
| Units: Subjects                                    |                    |       |  |
| Asian  | 2                  | 2     |  |
| Black or African American                          | 1                  | 1     |  |
| White  | 98                 | 98    |  |
| Smoking Classification                             |                    |       |  |
| Units: Subjects                                    |                    |       |  |
| Participant has never smoked                       | 46                 | 46    |  |
| Participant is a current smoker                    | 33                 | 33    |  |
| Participant is an ex-smoker                        | 22                 | 22    |  |
| Female Reproductive Status                         |                    |       |  |
| Units: Subjects                                    |                    |       |  |
| Postmenopausal                                     | 6                  | 6     |  |
| Surgically Sterile                                 | 9                  | 9     |  |
| Female of Childbearing Potential                   | 34                 | 34    |  |
| N/A (Participant is a Male)                        | 52                 | 52    |  |
| Region of Enrollment                               |                    |       |  |
| Units: Subjects                                    |                    |       |  |
| Belgium  | 8                  | 8     |  |
| Canada   | 14                 | 14    |  |
| Czech Republic                                     | 14                 | 14    |  |

|  |              |    |  |
|--|--------------|----|--|
| France   | 2            | 2  |  |
| Hungary  | 14           | 14 |  |
| Italy  | 9            | 9  |  |
| Poland   | 7            | 7  |  |
| United States  | 33           | 33 |  |
| Number of Participants with Endoscopic Remission   |              |    |  |
| Endoscopic remission is defined as a simple endoscopic score for Crohn's Disease (SES-CD) score of $\leq 4$ . FAS included all enrolled participants who received at least 1 dose of study drug. |              |    |  |
| Units: Subjects  |              |    |  |
| Endoscopic Remission - Yes   | 3            | 3  |  |
| Endoscopic Remission - No  | 98           | 98 |  |
| Height   |              |    |  |
| Units: cm  |              |    |  |
| arithmetic mean  | 172.5        |    |  |
| standard deviation   | $\pm 9.81$   | -  |  |
| Weight   |              |    |  |
| Units: kg  |              |    |  |
| arithmetic mean  | 73.94        |    |  |
| standard deviation   | $\pm 18.807$ | -  |  |
| Body Mass Index (BMI)  |              |    |  |
| Body Mass Index = weight (kg)/[height (m) <sup>2</sup> ]   |              |    |  |
| Units: kg/m <sup>2</sup>   |              |    |  |
| arithmetic mean  | 24.71        |    |  |
| standard deviation   | $\pm 5.370$  | -  |  |

## End points

### End points reporting groups

|  |                    |
|--|--------------------|
| Reporting group title  | Vedolizumab 300 mg |
| Reporting group description:   |                    |
| Part A: Vedolizumab 300 mg, intravenously (IV), once on Day 1 and Weeks 2, 6, 14 and 22, followed by Part B: Vedolizumab 300 mg, intravenously (IV), once at Weeks 30, 38, and 46. |                    |
| Reporting group title  | Vedolizumab 300 mg |
| Reporting group description:   |                    |
| Part A: Vedolizumab 300 mg, intravenously (IV), once on Day 1 and Weeks 2, 6, 14 and 22, followed by Part B: Vedolizumab 300 mg, intravenously (IV), once at Weeks 30, 38, and 46. |                    |

### Primary: Part A: Percentage of Participants Achieving Endoscopic Remission at Week 26

|   |   |
|---|---|
| End point title   | Part A: Percentage of Participants Achieving Endoscopic Remission at Week 26 <sup>[1]</sup> |
| End point description:  |   |
| Endoscopic remission is defined as a simple endoscopic score for Crohn's Disease (SES-CD) score of $\leq 4$ . The SES-CD evaluates 4 endoscopic variables (ulcer size, proportion of the surface area that is ulcerated, proportion of the surface area affected, and stenosis in 5 segments evaluated during ileocolonoscopy (ileum, right colon, transverse colon, left colon, and rectum). The score for each endoscopic variable is the sum of values obtained for each segment. The SES-CD total is the sum of the 4 endoscopic variable scores from 0 to 56, where higher scores indicate more severe disease. FAS included all enrolled participants who received at least 1 dose of study drug. |   |
| End point type  | Primary   |
| End point timeframe:  |   |
| Week 26   |   |

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Statistical analyses were not planned for this endpoint.

|                                   |                    |  |  |  |
|-----------------------------------|--------------------|--|--|--|
| <b>End point values</b>           | Vedolizumab 300 mg |  |  |  |
| Subject group type                | Reporting group    |  |  |  |
| Number of subjects analysed       | 101                |  |  |  |
| Units: percentage of participants |                    |  |  |  |
| number (confidence interval 95%)  | 11.9 (6.3 to 19.8) |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Part A: Percentage of Participants Achieving Complete Mucosal Healing at Week 26

|  |  |
|--|--|
| End point title  | Part A: Percentage of Participants Achieving Complete Mucosal Healing at Week 26 |
| End point description:   |  |
| Complete mucosal healing is defined as absence of ulceration. FAS included all enrolled participants who |  |



received at least 1 dose of study drug.

|                      |           |
|----------------------|-----------|
| End point type       | Secondary |
| End point timeframe: |           |
| Week 26              |           |

|                                   |                       |  |  |  |
|-----------------------------------|-----------------------|--|--|--|
| <b>End point values</b>           | Vedolizumab<br>300 mg |  |  |  |
| Subject group type                | Reporting group       |  |  |  |
| Number of subjects analysed       | 101                   |  |  |  |
| Units: percentage of participants |                       |  |  |  |
| number (confidence interval 95%)  | 14.9 (8.6 to<br>23.3) |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Part B: Percentage of Participants Achieving Complete Mucosal Healing at Week 52

|                 |  |
|-----------------|--|
| End point title | Part B: Percentage of Participants Achieving Complete Mucosal Healing at Week 52 |
|-----------------|--|

End point description:

Complete mucosal healing is defined as absence of ulceration. FAS-Extension is the subset of participants in the FAS who were able to be consented for Part B, based on the timing of Amendment 4. FAS included all enrolled participants who received at least 1 dose of study drug.

|                      |           |
|----------------------|-----------|
| End point type       | Secondary |
| End point timeframe: |           |
| Week 52              |           |

|                                   |                       |  |  |  |
|-----------------------------------|-----------------------|--|--|--|
| <b>End point values</b>           | Vedolizumab<br>300 mg |  |  |  |
| Subject group type                | Reporting group       |  |  |  |
| Number of subjects analysed       | 56                    |  |  |  |
| Units: percentage of participants |                       |  |  |  |
| number (confidence interval 95%)  | 17.9 (8.9 to<br>30.4) |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Part A: Percentage of Participants Achieving Endoscopic Remission at Week 14

|                 |   |
|-----------------|---|
| End point title | Part A: Percentage of Participants Achieving Endoscopic |
|-----------------|---|

## End point description:

Endoscopic remission is defined as a SES-CD score of  $\leq 4$ . The SES-CD evaluates 4 endoscopic variables (ulcer size, proportion of the surface area that is ulcerated, proportion of the surface area affected, and stenosis in 5 segments evaluated during ileocolonoscopy (ileum, right colon, transverse colon, left colon, and rectum). The score for each endoscopic variable is the sum of values obtained for each segment. The SES-CD total is the sum of the 4 endoscopic variable scores from 0 to 56, where higher scores indicate more severe disease. FAS included all enrolled participants who received at least 1 dose of study drug.

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

End point timeframe:

Week 14

| End point values                  | Vedolizumab<br>300 mg  |  |  |  |
|-----------------------------------|------------------------|--|--|--|
| Subject group type                | Reporting group        |  |  |  |
| Number of subjects analysed       | 101                    |  |  |  |
| Units: percentage of participants |                        |  |  |  |
| number (confidence interval 95%)  | 16.8 (10.1 to<br>25.6) |  |  |  |

## Statistical analyses

No statistical analyses for this end point

**Secondary: Part B: Percentage of Participants Achieving Endoscopic Remission at Week 52**

|                 |  |
|-----------------|--|
| End point title | Part B: Percentage of Participants Achieving Endoscopic Remission at Week 52 |
|-----------------|--|

## End point description:

Endoscopic remission is defined as a SES-CD score of  $\leq 4$ . The SES-CD evaluates 4 endoscopic variables (ulcer size, proportion of the surface area that is ulcerated, proportion of the surface area affected, and stenosis in 5 segments evaluated during ileocolonoscopy (ileum, right colon, transverse colon, left colon, and rectum). The score for each endoscopic variable is the sum of values obtained for each segment. The SES-CD total is the sum of the 4 endoscopic variable scores from 0 to 56, where higher scores indicate more severe disease. FAS-Extension is the subset of participants in the FAS who were able to be consented for Part B, based on the timing of Amendment 4. FAS included all enrolled participants who received at least 1 dose of study drug.

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

End point timeframe:

Week 52

|                                   |                       |  |  |  |
|-----------------------------------|-----------------------|--|--|--|
| <b>End point values</b>           | Vedolizumab<br>300 mg |  |  |  |
| Subject group type                | Reporting group       |  |  |  |
| Number of subjects analysed       | 56                    |  |  |  |
| Units: percentage of participants |                       |  |  |  |
| number (confidence interval 95%)  | 17.9 (8.9 to<br>30.4) |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Part A: Percentage of Participants with Endoscopic Response at Week 14

|                 |  |
|-----------------|--|
| End point title | Part A: Percentage of Participants with Endoscopic Response at Week 14 |
|-----------------|--|

End point description:

Endoscopic response is defined as a reduction in SES-CD from Baseline by  $\geq 50\%$ . The SES-CD evaluates 4 endoscopic variables (ulcer size, proportion of the surface area that is ulcerated, proportion of the surface area affected, and stenosis in 5 segments evaluated during ileocolonoscopy (ileum, right colon, transverse colon, left colon, and rectum). The score for each endoscopic variable is the sum of values obtained for each segment. The SES-CD total is the sum of the 4 endoscopic variable scores from 0 to 56, where higher scores indicate more severe disease. FAS included all enrolled participants who received at least 1 dose of study drug.

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

End point timeframe:

Baseline and Week 14

|                                   |                        |  |  |  |
|-----------------------------------|------------------------|--|--|--|
| <b>End point values</b>           | Vedolizumab<br>300 mg  |  |  |  |
| Subject group type                | Reporting group        |  |  |  |
| Number of subjects analysed       | 101                    |  |  |  |
| Units: percentage of participants |                        |  |  |  |
| number (confidence interval 95%)  | 33.7 (24.6 to<br>43.8) |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Part A: Percentage of Participants with Endoscopic Response at Week 26

|                 |  |
|-----------------|--|
| End point title | Part A: Percentage of Participants with Endoscopic Response at Week 26 |
|-----------------|--|

End point description:

Endoscopic response is defined as a reduction in SES-CD from Baseline by  $\geq 50\%$ . The SES-CD evaluates 4 endoscopic variables (ulcer size, proportion of the surface area that is ulcerated, proportion of the surface area affected, and stenosis in 5 segments evaluated during ileocolonoscopy (ileum, right colon, transverse colon, left colon, and rectum). The score for each endoscopic variable is the sum of values obtained for each segment. The SES-CD total is the sum of the 4 endoscopic variable scores from 0 to 56, where higher scores indicate more severe disease. FAS included all enrolled participants who

received at least 1 dose of study drug.

|                      |           |
|----------------------|-----------|
| End point type       | Secondary |
| End point timeframe: |           |
| Baseline and Week 26 |           |

|                                   |                        |  |  |  |
|-----------------------------------|------------------------|--|--|--|
| <b>End point values</b>           | Vedolizumab<br>300 mg  |  |  |  |
| Subject group type                | Reporting group        |  |  |  |
| Number of subjects analysed       | 101                    |  |  |  |
| Units: percentage of participants |                        |  |  |  |
| number (confidence interval 95%)  | 24.8 (16.7 to<br>34.3) |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Part B: Percentage of Participants with Endoscopic Response at Week 52

|                 |  |
|-----------------|--|
| End point title | Part B: Percentage of Participants with Endoscopic Response at Week 52 |
|-----------------|--|

End point description:

Endoscopic response is defined as a reduction in SES-CD from Baseline by  $\geq 50\%$ . The SES-CD evaluates 4 endoscopic variables (ulcer size, proportion of the surface area that is ulcerated, proportion of the surface area affected, and stenosis in 5 segments evaluated during ileocolonoscopy (ileum, right colon, transverse colon, left colon, and rectum). The score for each endoscopic variable is the sum of values obtained for each segment. The SES-CD total is the sum of the 4 endoscopic variable scores from 0 to 56, where higher scores indicate more severe disease. FAS-Extension is the subset of participants in the FAS who were able to be consented for Part B, based on the timing of Amendment 4. FAS included all enrolled participants who received at least 1 dose of study drug.

|                      |           |
|----------------------|-----------|
| End point type       | Secondary |
| End point timeframe: |           |
| Baseline and Week 52 |           |

|                                   |                        |  |  |  |
|-----------------------------------|------------------------|--|--|--|
| <b>End point values</b>           | Vedolizumab<br>300 mg  |  |  |  |
| Subject group type                | Reporting group        |  |  |  |
| Number of subjects analysed       | 56                     |  |  |  |
| Units: percentage of participants |                        |  |  |  |
| number (confidence interval 95%)  | 53.6 (39.7 to<br>67.0) |  |  |  |

### Statistical analyses

No statistical analyses for this end point

**Secondary: Part A: Percentage of Participants Achieving Clinical Response at Week 10**

|                 |   |
|-----------------|---|
| End point title | Part A: Percentage of Participants Achieving Clinical Response at Week 10 |
|-----------------|---|

End point description:

Clinical response is defined as Crohn's Disease Activity Index (CDAI) decrease from Baseline of  $\geq 100$  points. CDAI is a scoring system for the assessment of Crohn's Disease Activity, index values of 150 and below are associated with quiescent disease; values above that indicate active disease and values above 450 are seen with extremely severe disease. FAS included all enrolled participants who received at least 1 dose of study drug.

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

End point timeframe:

Baseline and Week 10

|                                   |                        |  |  |  |
|-----------------------------------|------------------------|--|--|--|
| <b>End point values</b>           | Vedolizumab<br>300 mg  |  |  |  |
| Subject group type                | Reporting group        |  |  |  |
| Number of subjects analysed       | 101                    |  |  |  |
| Units: percentage of participants |                        |  |  |  |
| number (confidence interval 95%)  | 54.5 (44.2 to<br>64.4) |  |  |  |

**Statistical analyses**

No statistical analyses for this end point

**Secondary: Part A: Percentage of Participants Achieving Clinical Response at Week 26**

|                 |   |
|-----------------|---|
| End point title | Part A: Percentage of Participants Achieving Clinical Response at Week 26 |
|-----------------|---|

End point description:

Clinical response is defined as CDAI decrease from Baseline of  $\geq 100$  points. CDAI is a scoring system for the assessment of Crohn's Disease Activity, index values of 150 and below are associated with quiescent disease; values above that indicate active disease and values above 450 are seen with extremely severe disease. FAS included all enrolled participants who received at least 1 dose of study drug.

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

End point timeframe:

Baseline and Week 26

|                                   |                        |  |  |  |
|-----------------------------------|------------------------|--|--|--|
| <b>End point values</b>           | Vedolizumab<br>300 mg  |  |  |  |
| Subject group type                | Reporting group        |  |  |  |
| Number of subjects analysed       | 101                    |  |  |  |
| Units: percentage of participants |                        |  |  |  |
| number (confidence interval 95%)  | 60.4 (50.2 to<br>70.0) |  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Part B: Percentage of Participants Achieving Clinical Response at Week 52

|                 |   |
|-----------------|---|
| End point title | Part B: Percentage of Participants Achieving Clinical Response at Week 52 |
|-----------------|---|

End point description:

Clinical response is defined as CDAI decrease from Baseline of  $\geq 100$  points. CDAI is a scoring system for the assessment of Crohn's Disease Activity, index values of 150 and below are associated with quiescent disease; values above that indicate active disease and values above 450 are seen with extremely severe disease. FAS-Extension is the subset of participants in the FAS who were able to be consented for Part B, based on the timing of Amendment 4. FAS included all enrolled participants who received at least 1 dose of study drug.

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

End point timeframe:

Baseline and Week 52

|                                   |                        |  |  |  |
|-----------------------------------|------------------------|--|--|--|
| <b>End point values</b>           | Vedolizumab<br>300 mg  |  |  |  |
| Subject group type                | Reporting group        |  |  |  |
| Number of subjects analysed       | 56                     |  |  |  |
| Units: percentage of participants |                        |  |  |  |
| number (confidence interval 95%)  | 58.9 (45.0 to<br>71.9) |  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Part A: Percentage of Participants Achieving Clinical Remission at Week 10

|                 |  |
|-----------------|--|
| End point title | Part A: Percentage of Participants Achieving Clinical Remission at Week 10 |
|-----------------|--|

End point description:

Clinical remission is defined as CDAI score of  $\leq 150$  points. CDAI is a scoring system for the assessment of Crohn's Disease Activity, index values of 150 and below are associated with quiescent disease; values above that indicate active disease and values above 450 are seen with extremely severe disease. FAS included all enrolled participants who received at least 1 dose of study drug.

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

End point timeframe:

Week 10

|                                   |                        |  |  |  |
|-----------------------------------|------------------------|--|--|--|
| <b>End point values</b>           | Vedolizumab<br>300 mg  |  |  |  |
| Subject group type                | Reporting group        |  |  |  |
| Number of subjects analysed       | 101                    |  |  |  |
| Units: percentage of participants |                        |  |  |  |
| number (confidence interval 95%)  | 35.6 (26.4 to<br>45.8) |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Part A: Percentage of Participants Achieving Clinical Remission at Week 26

|                 |  |
|-----------------|--|
| End point title | Part A: Percentage of Participants Achieving Clinical Remission at Week 26 |
|-----------------|--|

End point description:

Clinical remission is defined as CDAI score of  $\leq 150$  points. CDAI is a scoring system for the assessment of Crohn's Disease Activity, index values of 150 and below are associated with quiescent disease; values above that indicate active disease and values above 450 are seen with extremely severe disease. FAS included all enrolled participants who received at least 1 dose of study drug.

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

End point timeframe:

Week 26

|                                   |                        |  |  |  |
|-----------------------------------|------------------------|--|--|--|
| <b>End point values</b>           | Vedolizumab<br>300 mg  |  |  |  |
| Subject group type                | Reporting group        |  |  |  |
| Number of subjects analysed       | 101                    |  |  |  |
| Units: percentage of participants |                        |  |  |  |
| number (confidence interval 95%)  | 41.6 (31.9 to<br>51.8) |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Part B: Percentage of Participants Achieving Clinical Remission at Week 52

|                 |  |
|-----------------|--|
| End point title | Part B: Percentage of Participants Achieving Clinical Remission at Week 52 |
|-----------------|--|

End point description:

Clinical remission is defined as CDAI score of  $\leq 150$  points. CDAI is a scoring system for the assessment

of Crohn's Disease Activity, index values of 150 and below are associated with quiescent disease; values above that indicate active disease and values above 450 are seen with extremely severe disease. PPS (Per Protocol Set)-Extension is the subset of participants in the PPS who continue into Part B. PPS is a subset of the FAS and consists of all participants who do not deviate the terms of the protocol in a way that would impact the study outcome significantly.

|                      |           |
|----------------------|-----------|
| End point type       | Secondary |
| End point timeframe: |           |
| Week 52              |           |

|                                   |                        |  |  |  |
|-----------------------------------|------------------------|--|--|--|
| <b>End point values</b>           | Vedolizumab<br>300 mg  |  |  |  |
| Subject group type                | Reporting group        |  |  |  |
| Number of subjects analysed       | 56                     |  |  |  |
| Units: percentage of participants |                        |  |  |  |
| number (confidence interval 95%)  | 50.0 (36.3 to<br>63.7) |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Part B: Percentage of Participants with Durable Clinical Remission

|                 |  |
|-----------------|--|
| End point title | Part B: Percentage of Participants with Durable Clinical Remission |
|-----------------|--|

End point description:

Durable clinical remission is defined as clinical remission at both Week 26 and Week 52. Clinical remission is defined as CDAI score of  $\leq 150$  points. CDAI is a scoring system for the assessment of Crohn's Disease Activity, index values of 150 and below are associated with quiescent disease; values above that indicate active disease and values above 450 are seen with extremely severe disease. The percentage of participants assessed at Week 52 who had clinical remission at Week 26 of Part A and also had clinical remission at Week 52 is reported. FAS-Extension is the subset of participants in the FAS who were able to be consented for Part B, based on the timing of Amendment 4. FAS included all enrolled participants who received at least 1 dose of study drug. Participants with missing durable clinical remission status are considered as No durable clinical remission.

|                      |           |
|----------------------|-----------|
| End point type       | Secondary |
| End point timeframe: |           |
| Weeks 26 and 52      |           |

|                                   |                        |  |  |  |
|-----------------------------------|------------------------|--|--|--|
| <b>End point values</b>           | Vedolizumab<br>300 mg  |  |  |  |
| Subject group type                | Reporting group        |  |  |  |
| Number of subjects analysed       | 56                     |  |  |  |
| Units: percentage of participants |                        |  |  |  |
| number (confidence interval 95%)  | 37.5 (24.9 to<br>51.5) |  |  |  |



## Statistical analyses

---

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

First dose of study drug and up to the last dose or early termination plus 18-week follow-up if applicable  
(Up to 44 Weeks for Part A Treatment and Up to 70 Weeks for Part B Extension)

Adverse event reporting additional description:

At each visit adverse events (AEs) and abnormal laboratory findings reported by participant or observed by the investigator were recorded, irrespective of relation to study treatment. Due to the design of the study, the most common ( $\geq 3\%$ ) non-serious AEs were determined separately for each period of the study, Part A and Part B.

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

### Dictionary used

|                    |        |
|--------------------|--------|
| Dictionary name    | MedDRA |
| Dictionary version | 20.0   |

### Reporting groups

|                       |                           |
|-----------------------|---------------------------|
| Reporting group title | Vedolizumab 300 mg Part B |
|-----------------------|---------------------------|

Reporting group description:

Following Part A, Part B: Vedolizumab 300 mg, intravenously (IV), once at Weeks 30, 38, and 46.

|                       |                           |
|-----------------------|---------------------------|
| Reporting group title | Vedolizumab 300 mg Part A |
|-----------------------|---------------------------|

Reporting group description:

Part A: Vedolizumab 300 mg, intravenously (IV), once on Day 1 and Weeks 2, 6, 14 and 22.

| Serious adverse events  | Vedolizumab 300 mg Part B | Vedolizumab 300 mg Part A |  |
|---|---------------------------|---------------------------|--|
| Total subjects affected by serious adverse events                   |                           |                           |  |
| subjects affected / exposed   | 6 / 56 (10.71%)           | 12 / 101 (11.88%)         |  |
| 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   | 1 / 56 (1.79%)            | 0 / 101 (0.00%)           |  |
| occurrences causally related to treatment / all                     | 0 / 1                     | 0 / 0                     |  |
| deaths causally related to treatment / all                          | 0 / 0                     | 0 / 0                     |  |
| Injury, poisoning and procedural complications                      |                           |                           |  |
| Postoperative ileus   |                           |                           |  |
| subjects affected / exposed   | 1 / 56 (1.79%)            | 0 / 101 (0.00%)           |  |
| occurrences causally related to treatment / all                     | 0 / 1                     | 0 / 0                     |  |
| deaths causally related to treatment / all                          | 0 / 0                     | 0 / 0                     |  |
| Vascular disorders  |                           |                           |  |
| Aortic aneurysm   |                           |                           |  |

|  |                |                 |  |
|--|----------------|-----------------|--|
| subjects affected / exposed                          | 0 / 56 (0.00%) | 1 / 101 (0.99%) |  |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 1           |  |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0           |  |
| Cardiac disorders                                    |                |                 |  |
| Coronary artery disease                              |                |                 |  |
| subjects affected / exposed                          | 1 / 56 (1.79%) | 0 / 101 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 2          | 0 / 0           |  |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0           |  |
| Pregnancy, puerperium and perinatal conditions       |                |                 |  |
| Abortion spontaneous                                 |                |                 |  |
| subjects affected / exposed                          | 1 / 56 (1.79%) | 0 / 101 (0.00%) |  |
| occurrences causally related to treatment / all      | 1 / 1          | 0 / 0           |  |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0           |  |
| General disorders and administration site conditions |                |                 |  |
| Asthenia   |                |                 |  |
| subjects affected / exposed                          | 0 / 56 (0.00%) | 1 / 101 (0.99%) |  |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 1           |  |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0           |  |
| Gastrointestinal disorders                           |                |                 |  |
| Crohn's disease                                      |                |                 |  |
| subjects affected / exposed                          | 1 / 56 (1.79%) | 6 / 101 (5.94%) |  |
| occurrences causally related to treatment / all      | 0 / 1          | 0 / 6           |  |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0           |  |
| Anal fistula   |                |                 |  |
| subjects affected / exposed                          | 0 / 56 (0.00%) | 1 / 101 (0.99%) |  |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 1           |  |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0           |  |
| Subileus   |                |                 |  |
| subjects affected / exposed                          | 1 / 56 (1.79%) | 0 / 101 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 2          | 0 / 0           |  |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0           |  |
| Renal and urinary disorders                          |                |                 |  |
| Acute kidney injury                                  |                |                 |  |

|   |                |                 |  |
|---|----------------|-----------------|--|
| subjects affected / exposed                     | 0 / 56 (0.00%) | 1 / 101 (0.99%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |
| <b>Infections and infestations</b>              |                |                 |  |
| Abdominal abscess                               |                |                 |  |
| subjects affected / exposed                     | 0 / 56 (0.00%) | 1 / 101 (0.99%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 3           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |
| Gastroenteritis                                 |                |                 |  |
| subjects affected / exposed                     | 0 / 56 (0.00%) | 1 / 101 (0.99%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |
| Osteomyelitis                                   |                |                 |  |
| subjects affected / exposed                     | 0 / 56 (0.00%) | 1 / 101 (0.99%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |
| Pneumonia                                       |                |                 |  |
| subjects affected / exposed                     | 0 / 56 (0.00%) | 1 / 101 (0.99%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |
| Infected bite                                   |                |                 |  |
| subjects affected / exposed                     | 1 / 56 (1.79%) | 0 / 101 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |
| Urinary tract infection                         |                |                 |  |
| subjects affected / exposed                     | 1 / 56 (1.79%) | 0 / 101 (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: 3 %

| <b>Non-serious adverse events</b>                     | Vedolizumab 300 mg Part B | Vedolizumab 300 mg Part A |  |
|---|---------------------------|---------------------------|--|
| Total subjects affected by non-serious adverse events |                           |                           |  |
| subjects affected / exposed                           | 17 / 56 (30.36%)          | 40 / 101 (39.60%)         |  |
| Nervous system disorders                              |                           |                           |  |
| Headache  |                           |                           |  |
| subjects affected / exposed                           | 2 / 56 (3.57%)            | 5 / 101 (4.95%)           |  |
| occurrences (all)                                     | 3                         | 8                         |  |
| Sciatica  |                           |                           |  |
| subjects affected / exposed                           | 0 / 56 (0.00%)            | 3 / 101 (2.97%)           |  |
| occurrences (all)                                     | 0                         | 3                         |  |
| Paraesthesia  |                           |                           |  |
| subjects affected / exposed                           | 2 / 56 (3.57%)            | 0 / 101 (0.00%)           |  |
| occurrences (all)                                     | 2                         | 0                         |  |
| General disorders and administration site conditions  |                           |                           |  |
| Asthenia  |                           |                           |  |
| subjects affected / exposed                           | 0 / 56 (0.00%)            | 4 / 101 (3.96%)           |  |
| occurrences (all)                                     | 0                         | 4                         |  |
| Pyrexia   |                           |                           |  |
| subjects affected / exposed                           | 0 / 56 (0.00%)            | 4 / 101 (3.96%)           |  |
| occurrences (all)                                     | 0                         | 5                         |  |
| Gastrointestinal disorders                            |                           |                           |  |
| Crohn's disease                                       |                           |                           |  |
| subjects affected / exposed                           | 5 / 56 (8.93%)            | 12 / 101 (11.88%)         |  |
| occurrences (all)                                     | 5                         | 12                        |  |
| Abdominal pain  |                           |                           |  |
| subjects affected / exposed                           | 3 / 56 (5.36%)            | 5 / 101 (4.95%)           |  |
| occurrences (all)                                     | 5                         | 5                         |  |
| Nausea  |                           |                           |  |
| subjects affected / exposed                           | 0 / 56 (0.00%)            | 5 / 101 (4.95%)           |  |
| occurrences (all)                                     | 0                         | 6                         |  |
| Vomiting  |                           |                           |  |
| subjects affected / exposed                           | 0 / 56 (0.00%)            | 4 / 101 (3.96%)           |  |
| occurrences (all)                                     | 0                         | 4                         |  |
| Anal fistula  |                           |                           |  |
| subjects affected / exposed                           | 2 / 56 (3.57%)            | 0 / 101 (0.00%)           |  |
| occurrences (all)                                     | 2                         | 0                         |  |

|   |   |  |  |
|---|---|--|--|
| Respiratory, thoracic and mediastinal disorders<br>Cough<br>subjects affected / exposed<br>occurrences (all)  | 0 / 56 (0.00%)<br>0   | 3 / 101 (2.97%)<br>3   |  |
| Musculoskeletal and connective tissue disorders<br>Arthralgia<br>subjects affected / exposed<br>occurrences (all)   | 0 / 56 (0.00%)<br>0   | 4 / 101 (3.96%)<br>4   |  |
| Infections and infestations<br>Viral upper respiratory tract infection<br>subjects affected / exposed<br>occurrences (all)<br><br>Bronchitis<br>subjects affected / exposed<br>occurrences (all)<br><br>Influenza<br>subjects affected / exposed<br>occurrences (all)<br><br>Sinusitis<br>subjects affected / exposed<br>occurrences (all)<br><br>Upper respiratory tract infection<br>subjects affected / exposed<br>occurrences (all) | 3 / 56 (5.36%)<br>3<br><br>0 / 56 (0.00%)<br>0<br><br>0 / 56 (0.00%)<br>0<br><br>0 / 56 (0.00%)<br>0<br><br>2 / 56 (3.57%)<br>2 | 6 / 101 (5.94%)<br>7<br><br>3 / 101 (2.97%)<br>3<br><br>3 / 101 (2.97%)<br>3<br><br>3 / 101 (2.97%)<br>3<br><br>0 / 101 (0.00%)<br>0 |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date            | Amendment   |
|-----------------|---|
| 23 January 2015 | Amendment No. 1: The duration of the long term follow up (LTFU) safety questionnaire has been reduced from 24 months from the last dose of study drug to 6 months from the last dose of study drug. Clarification on the collection and reporting of SAEs was added.  |
| 28 April 2016   | Amendment No. 4: Updated the protocol on the duration of the treatment period from 26 weeks to 52 weeks. The study design was split into two parts, Part A for treatment up to 26 weeks and Part B for treatment from 26 weeks to 52 weeks. Updated the protocol regarding the required duration of observation following infusion and to include an overall risk/benefit assessment. |

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported