



## Clinical trial results:

**A Phase 2, multi-center, randomized, double-blind, placebo-controlled parallel-group study to evaluate the clinical efficacy and safety of induction therapy with RPC1063 in patients with moderately to severely active ulcerative colitis**

### Summary

|                          |                      |
|--------------------------|----------------------|
| EudraCT number           | 2012-003123-38       |
| Trial protocol           | BE HU PL SK BG GR NL |
| Global end of trial date | 30 August 2019       |

### Results information

|                                |                   |
|--------------------------------|-------------------|
| Result version number          | v1 (current)      |
| This version publication date  | 13 September 2020 |
| First version publication date | 13 September 2020 |

### Trial information

#### Trial identification

|                       |           |
|-----------------------|-----------|
| Sponsor protocol code | RPC01-202 |
|-----------------------|-----------|

#### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT01647516 |
| WHO universal trial number (UTN)   | -           |

Notes:

### Sponsors

|                              |  |
|------------------------------|--|
| Sponsor organisation name    | Celgene International II Sàrl  |
| Sponsor organisation address | Rue du Pré-Jorat 14, Couvet, Switzerland, 2108   |
| Public contact               | Clinical Trial Disclosure, Celgene International II Sàrl, 01 888-260-1599, ClinicalTrialDisclosure@Celgene.com |
| Scientific contact           | Ernesto Oviedo-Orta, MD, PhD, MBA, Celgene International II Sàrl, 01 908-673-2861, Ernesto.Oviedo-Orta@BMS.com |

Notes:

### Paediatric regulatory details

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

Notes:

## Results analysis stage

|  |                |
|--|----------------|
| Analysis stage                                       | Final          |
| Date of interim/final analysis                       | 30 August 2019 |
| Is this the analysis of the primary completion data? | No             |
| Global end of trial reached?                         | Yes            |
| Global end of trial date                             | 30 August 2019 |
| Was the trial ended prematurely?                     | No             |

Notes:

## General information about the trial

Main objective of the trial:

The primary objective of the study is to compare the efficacy of RPC1063 vs placebo for induction of clinical remission at Week 8 in patients with moderately to severely active ulcerative colitis (UC)

Protection of trial subjects:

Patient Confidentiality, Informed Consent and Archiving of Essential Documents

Background therapy: -

Evidence for comparator: -

|   |                  |
|---|------------------|
| Actual start date of recruitment                          | 26 December 2012 |
| Long term follow-up planned                               | Yes              |
| Long term follow-up rationale                             | Safety           |
| Long term follow-up duration                              | 6 Years          |
| Independent data monitoring committee (IDMC) involvement? | Yes              |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |                        |
|--------------------------------------|------------------------|
| Country: Number of subjects enrolled | Belgium: 1             |
| Country: Number of subjects enrolled | Bulgaria: 17           |
| Country: Number of subjects enrolled | Hungary: 14            |
| Country: Number of subjects enrolled | Greece: 2              |
| Country: Number of subjects enrolled | Israel: 4              |
| Country: Number of subjects enrolled | Korea, Republic of: 8  |
| Country: Number of subjects enrolled | Netherlands: 3         |
| Country: Number of subjects enrolled | New Zealand: 3         |
| Country: Number of subjects enrolled | Poland: 30             |
| Country: Number of subjects enrolled | Russian Federation: 44 |
| Country: Number of subjects enrolled | Slovakia: 11           |
| Country: Number of subjects enrolled | United States: 21      |
| Country: Number of subjects enrolled | Ukraine: 39            |
| Worldwide total number of subjects   | 197                    |
| EEA total number of subjects         | 78                     |

Notes:

| <b>Subjects enrolled per age group</b>    |     |
|---|-----|
| 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)                      | 195 |
| From 65 to 84 years                       | 2   |
| 85 years and over                         | 0   |

## Subject disposition

### Recruitment

Recruitment details:

Participants were enrolled at 57 sites from 13 countries located in Europe, North America, and the Asia-Pacific region.

### Pre-assignment

Screening details:

Participants who received placebo, ozanimod 0.5 mg or ozanimod 1 mg capsules and completed the induction period and were non-responders at week 8 and those who completed the maintenance period or experienced a disease relapse, were given the option to enter the open label treatment period and received 1 mg ozanimod daily up to 6 years.

### Period 1

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

Blinding implementation details:

Investigational medicinal product and placebo capsules were identical in physical appearance. The treatment each participant received was not disclosed to the Investigator, study center personnel, participant, sponsor and their representatives. The treatment codes were held according to an Interactive Voice Response System (IVRS).

### Arms

|                              |         |
|------------------------------|---------|
| Are arms mutually exclusive? | Yes     |
| <b>Arm title</b>             | Placebo |

Arm description:

Participants received identically matching placebo capsules daily for 9 weeks during the induction period (weeks 0-9).

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

Dosage and administration details:

Identically matching placebo capsules daily during the induction period (Weeks 0-9). Nine weeks total treatment.

|                  |                              |
|------------------|------------------------------|
| <b>Arm title</b> | Ozanimod Hydrochloride 0.5mg |
|------------------|------------------------------|

Arm description:

Participants received 0.5 mg capsules of ozanimod hydrochloride daily during the induction period weeks 0-9 (an initial 8-day dose escalation regimen in the induction period that consisted of 4 days of ozanimod HCl 0.25 mg (equivalent to ozanimod 0.23 mg), followed by 3 days of ozanimod HCl 0.5 mg, (equivalent to ozanimod 0.46 mg) followed by the assigned treatment level for at least 8 weeks.

|  |              |
|--|--------------|
| Arm type                               | Experimental |
| Investigational medicinal product name | RPC1063      |
| Investigational medicinal product code |              |
| Other name                             | Zeposia      |
| Pharmaceutical forms                   | Capsule      |
| Routes of administration               | Oral use     |

Dosage and administration details:

Participants received 0.5 mg capsules of ozanimod hydrochloride daily during the induction period weeks

0-9 (an initial 8-day dose escalation regimen in the induction period that consisted of 4 days of ozanimod HCl 0.25 mg (equivalent to ozanimod 0.23 mg), followed by 3 days of ozanimod HCl 0.5 mg, (equivalent to ozanimod 0.46 mg) followed by the assigned treatment level for at least 8 weeks.

|   |                             |
|---|-----------------------------|
| <b>Arm title</b>  | Ozanimod Hydrochloride 1 mg |
| Arm description:<br>Participants received 1 mg capsules of ozanimod hydrochloride daily during the induction period weeks 0-9 (an initial 8-day dose escalation regimen in the induction period that consisted of 4 days of ozanimod HCl 0.25 mg (equivalent to ozanimod 0.23 mg), followed by 3 days of ozanimod HCl 0.5 mg, (equivalent to ozanimod 0.46 mg) followed by the assigned treatment level for at least 8 weeks. |                             |
| Arm type  | Experimental                |
| Investigational medicinal product name  | RPC1063                     |
| Investigational medicinal product code  |                             |
| Other name  | Zeposia                     |
| Pharmaceutical forms  | Capsule                     |
| Routes of administration  | Oral use                    |

**Dosage and administration details:**

Participants received 1 mg capsules of ozanimod hydrochloride daily during the induction period weeks 0-9 (an initial 8-day dose escalation regimen in the induction period that consisted of 4 days of ozanimod HCl 0.25 mg (equivalent to ozanimod 0.23 mg), followed by 3 days of ozanimod HCl 0.5 mg, (equivalent to ozanimod 0.46 mg) followed by the assigned treatment level for at least 8 weeks.

| <b>Number of subjects in period 1</b> | Placebo | Ozanimod Hydrochloride 0.5mg | Ozanimod Hydrochloride 1 mg |
|---------------------------------------|---------|------------------------------|-----------------------------|
| Started                               | 65      | 65                           | 67                          |
| Received study drug                   | 65      | 65                           | 67                          |
| Completed                             | 60      | 63                           | 63                          |
| Not completed                         | 5       | 2                            | 4                           |
| Physician decision                    | 2       | -                            | -                           |
| Consent withdrawn by subject          | 1       | -                            | 3                           |
| Adverse event, non-fatal              | 1       | 2                            | -                           |
| Participant elected to stop dosing    | -       | -                            | 1                           |
| Lack of efficacy                      | 1       | -                            | -                           |

**Period 2**

|                              |   |
|------------------------------|---|
| Period 2 title               | Maintenance Period  |
| Is this the baseline period? | No  |
| Allocation method            | Randomised - controlled                                       |
| Blinding used                | Double blind  |
| Roles blinded                | Subject, Investigator, Monitor, Data analyst, Carer, Assessor |

**Blinding implementation details:**

Investigational medicinal product and placebo capsules were identical in physical appearance. The treatment each participant received was not disclosed to the Investigator, study center personnel,

participant, sponsor and their representatives. The treatment codes were held according to an Interactive Voice Response System (IVRS).

## Arms

|                              |         |
|------------------------------|---------|
| Are arms mutually exclusive? | Yes     |
| <b>Arm title</b>             | Placebo |

### Arm description:

Participants received identically matching placebo capsules daily for 24 weeks during the maintenance period (weeks 9-32).

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

### Dosage and administration details:

Identically matching placebo capsules daily during the maintenance period (Weeks 9-32). Twenty-four weeks total treatment.

|                  |                              |
|------------------|------------------------------|
| <b>Arm title</b> | Ozanimod Hydrochloride 0.5mg |
|------------------|------------------------------|

### Arm description:

Participants received 0.5 mg capsules of ozanimod hydrochloride daily for 24 weeks during the maintenance period (weeks 9-32).

|  |              |
|--|--------------|
| Arm type                               | Experimental |
| Investigational medicinal product name | RPC1063      |
| Investigational medicinal product code |              |
| Other name                             | Zeposia      |
| Pharmaceutical forms                   | Capsule      |
| Routes of administration               | Oral use     |

### Dosage and administration details:

Ozanimod hydrochloride 0.5mg capsules daily during the maintenance period (Weeks 9-32). Twenty-four weeks total treatment.

|                  |                             |
|------------------|-----------------------------|
| <b>Arm title</b> | Ozanimod Hydrochloride 1 mg |
|------------------|-----------------------------|

### Arm description:

Participants received 1 mg capsules of ozanimod hydrochloride daily for 24 weeks during the maintenance period (weeks 9-32).

|  |              |
|--|--------------|
| Arm type                               | Experimental |
| Investigational medicinal product name | RPC1063      |
| Investigational medicinal product code |              |
| Other name                             | Zeposia      |
| Pharmaceutical forms                   | Capsule      |
| Routes of administration               | Oral use     |

### Dosage and administration details:

Ozanimod Hydrochloride 1 mg capsules daily during the maintenance period (Weeks 9-32). Twenty-four weeks total treatment.

| Number of subjects in period<br>2 <sup>[1]</sup> | Placebo | Ozanimod<br>Hydrochloride 0.5mg | Ozanimod<br>Hydrochloride 1 mg |
|--|---------|---------------------------------|--------------------------------|
|  |         |                                 |                                |
| Started  | 25      | 36                              | 42                             |
| Received Study Drug                              | 25      | 36                              | 41                             |
| Completed  | 21      | 30                              | 40                             |
| Not completed                                    | 4       | 6                               | 2                              |
| Consent withdrawn by subject                     | -       | 1                               | 1                              |
| Adverse event, non-fatal                         | 2       | 1                               | -                              |
| Lack of efficacy                                 | 1       | 4                               | 1                              |
| Noncompliance                                    | 1       | -                               | -                              |

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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: Participants were considered responders in the maintenance period, which is a lower number than those completed in the induction period.

## Baseline characteristics

### Reporting groups

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

Reporting group description:

Participants received identically matching placebo capsules daily for 9 weeks during the induction period (weeks 0-9).

|                       |                              |
|-----------------------|------------------------------|
| Reporting group title | Ozanimod Hydrochloride 0.5mg |
|-----------------------|------------------------------|

Reporting group description:

Participants received 0.5 mg capsules of ozanimod hydrochloride daily during the induction period weeks 0-9 (an initial 8-day dose escalation regimen in the induction period that consisted of 4 days of ozanimod HCl 0.25 mg (equivalent to ozanimod 0.23 mg), followed by 3 days of ozanimod HCl 0.5 mg, (equivalent to ozanimod 0.46 mg) followed by the assigned treatment level for at least 8 weeks.

|                       |                             |
|-----------------------|-----------------------------|
| Reporting group title | Ozanimod Hydrochloride 1 mg |
|-----------------------|-----------------------------|

Reporting group description:

Participants received 1 mg capsules of ozanimod hydrochloride daily during the induction period weeks 0-9 (an initial 8-day dose escalation regimen in the induction period that consisted of 4 days of ozanimod HCl 0.25 mg (equivalent to ozanimod 0.23 mg), followed by 3 days of ozanimod HCl 0.5 mg, (equivalent to ozanimod 0.46 mg) followed by the assigned treatment level for at least 8 weeks.

| Reporting group values                    | Placebo | Ozanimod Hydrochloride 0.5mg | Ozanimod Hydrochloride 1 mg |
|---|---------|------------------------------|-----------------------------|
| Number of subjects                        | 65      | 65                           | 67                          |
| Age Categorical<br>Units: Subjects        |         |                              |                             |
| Adults (18-64 years)                      | 64      | 64                           | 67                          |
| From 65-84 years                          | 1       | 1                            | 0                           |
| Age Continuous<br>Units: years            |         |                              |                             |
| arithmetic mean                           | 41.9    | 38.8                         | 41.8                        |
| standard deviation                        | ± 12.30 | ± 12.06                      | ± 11.01                     |
| Gender Categorical<br>Units: Subjects     |         |                              |                             |
| Female                                    | 30      | 33                           | 19                          |
| Male                                      | 35      | 32                           | 48                          |
| Race<br>Units: Subjects                   |         |                              |                             |
| White                                     | 61      | 59                           | 62                          |
| Black                                     | 2       | 1                            | 1                           |
| Asian                                     | 2       | 3                            | 3                           |
| American Indian or Alaska Native          | 0       | 0                            | 0                           |
| Native Hawaiian or Other Pacific Islander | 0       | 0                            | 0                           |
| Other                                     | 0       | 1                            | 1                           |
| Missing                                   | 0       | 1                            | 0                           |
| Ethnicity<br>Units: Subjects              |         |                              |                             |
| Hispanic or Latino                        | 2       | 1                            | 0                           |
| Not Hispanic or Latino                    | 63      | 64                           | 67                          |



|  |        |        |        |
|--|--------|--------|--------|
| Mayo Score   |        |        |        |
| The Mayo Score is a composite index of four items (stool frequency, rectal bleeding, rectosigmoidoscopy findings, and physician's global assessment) with each item graded semi-quantitatively on a scale of 0 to 3 where 0 represents normal and higher score represents more severe disease status. The total Mayo Score is the sum of the four item scores, with a result ranging from 0 to 12 points. Higher scores represent more severe disease. |        |        |        |
| Units: Units on a Scale  |        |        |        |
| arithmetic mean  | 8.6    | 8.3    | 8.5    |
| standard deviation   | ± 1.51 | ± 1.45 | ± 1.61 |
| Years Since Ulcerative Colitis Diagnosis   |        |        |        |
| Units: Years   |        |        |        |
| arithmetic mean  | 6.1    | 5.9    | 6.7    |
| standard deviation   | ± 5.46 | ± 5.44 | ± 6.76 |

|  |       |  |  |
|--|-------|--|--|
| <b>Reporting group values</b>  | Total |  |  |
| Number of subjects   | 197   |  |  |
| Age Categorical  |       |  |  |
| Units: Subjects  |       |  |  |
| Adults (18-64 years)   | 195   |  |  |
| From 65-84 years   | 2     |  |  |
| Age Continuous   |       |  |  |
| Units: years   |       |  |  |
| arithmetic mean  |       |  |  |
| standard deviation   | -     |  |  |
| Gender Categorical   |       |  |  |
| Units: Subjects  |       |  |  |
| Female   | 82    |  |  |
| Male   | 115   |  |  |
| Race   |       |  |  |
| Units: Subjects  |       |  |  |
| White  | 182   |  |  |
| Black  | 4     |  |  |
| Asian  | 8     |  |  |
| American Indian or Alaska Native   | 0     |  |  |
| Native Hawaiian or Other Pacific Islander  | 0     |  |  |
| Other  | 2     |  |  |
| Missing  | 1     |  |  |
| Ethnicity  |       |  |  |
| Units: Subjects  |       |  |  |
| Hispanic or Latino   | 3     |  |  |
| Not Hispanic or Latino   | 194   |  |  |
| Mayo Score   |       |  |  |
| The Mayo Score is a composite index of four items (stool frequency, rectal bleeding, rectosigmoidoscopy findings, and physician's global assessment) with each item graded semi-quantitatively on a scale of 0 to 3 where 0 represents normal and higher score represents more severe disease status. The total Mayo Score is the sum of the four item scores, with a result ranging from 0 to 12 points. Higher scores represent more severe disease. |       |  |  |
| Units: Units on a Scale  |       |  |  |
| arithmetic mean  |       |  |  |
| standard deviation   | -     |  |  |
| Years Since Ulcerative Colitis Diagnosis   |       |  |  |
| Units: Years   |       |  |  |
| arithmetic mean  |       |  |  |

|                    |   |  |  |
|--------------------|---|--|--|
| standard deviation | - |  |  |
|--------------------|---|--|--|

|  |
|--|
|  |
|--|

## End points

### End points reporting groups

|   |                              |
|---|------------------------------|
| Reporting group title   | Placebo                      |
| Reporting group description:<br>Participants received identically matching placebo capsules daily for 9 weeks during the induction period (weeks 0-9).  |                              |
| Reporting group title   | Ozanimod Hydrochloride 0.5mg |
| Reporting group description:<br>Participants received 0.5 mg capsules of ozanimod hydrochloride daily during the induction period weeks 0-9 (an initial 8-day dose escalation regimen in the induction period that consisted of 4 days of ozanimod HCl 0.25 mg (equivalent to ozanimod 0.23 mg), followed by 3 days of ozanimod HCl 0.5 mg, (equivalent to ozanimod 0.46 mg) followed by the assigned treatment level for at least 8 weeks.   |                              |
| Reporting group title   | Ozanimod Hydrochloride 1 mg  |
| Reporting group description:<br>Participants received 1 mg capsules of ozanimod hydrochloride daily during the induction period weeks 0-9 (an initial 8-day dose escalation regimen in the induction period that consisted of 4 days of ozanimod HCl 0.25 mg (equivalent to ozanimod 0.23 mg), followed by 3 days of ozanimod HCl 0.5 mg, (equivalent to ozanimod 0.46 mg) followed by the assigned treatment level for at least 8 weeks.   |                              |
| Reporting group title   | Placebo                      |
| Reporting group description:<br>Participants received identically matching placebo capsules daily for 24 weeks during the maintenance period (weeks 9-32).  |                              |
| Reporting group title   | Ozanimod Hydrochloride 0.5mg |
| Reporting group description:<br>Participants received 0.5 mg capsules of ozanimod hydrochloride daily for 24 weeks during the maintenance period (weeks 9-32).  |                              |
| Reporting group title   | Ozanimod Hydrochloride 1 mg  |
| Reporting group description:<br>Participants received 1 mg capsules of ozanimod hydrochloride daily for 24 weeks during the maintenance period (weeks 9-32).  |                              |
| Subject analysis set title  | Placebo                      |
| Subject analysis set type   | Safety analysis              |
| Subject analysis set description:<br>Participants who received identically matching placebo capsules during the maintenance period.   |                              |
| Subject analysis set title  | Ozanimod 0.5 mg              |
| Subject analysis set type   | Safety analysis              |
| Subject analysis set description:<br>Participants who received 0.5 mg capsules daily during the maintenance period.   |                              |
| Subject analysis set title  | Ozanimod 1 mg                |
| Subject analysis set type   | Safety analysis              |
| Subject analysis set description:<br>Participants who received 1 mg capsules daily during the maintenance period.   |                              |
| Subject analysis set title  | Open Label Treatment Period  |
| Subject analysis set type   | Safety analysis              |
| Subject analysis set description:<br>Participants who received placebo capsules, ozanimod 0.5 mg or ozanimod 1 mg capsules and completed the induction period and were non-responders at Week 8 and those who completed the maintenance period or experienced a disease relapse, were given the option to enter the open label treatment period (OLP) and received 1 mg ozanimod daily up to 6 years. Participants who had not shown clinical improvement 8 weeks after initiation of the OLP were discontinued from the study. |                              |

## Primary: Percentage of Participants Who Achieved Clinical Remission Based on the Central Read of the Mayo Score (MS), at Week 8

|                 |  |
|-----------------|--|
| End point title | Percentage of Participants Who Achieved Clinical Remission Based on the Central Read of the Mayo Score (MS), at Week 8 |
|-----------------|--|

End point description:

Clinical Remission was defined as: Mayo score of <2 points and with no individual subscore of > 1 point.

The Mayo Score is a composite index of four items (stool frequency, rectal bleeding, rectosigmoidoscopy findings, and physician's global assessment) with each item graded semi-quantitatively on a scale of 0 to 3 where 0 represents normal and higher score represents more severe disease status. The total Mayo Score is the sum of the four item scores, with a result ranging from 0 to 12 points. Higher scores represent more severe disease.

- Stool Frequency Subscore (SFS)
- Rectal bleeding Subscore (RBS)
- Endoscopy Subscore
- Physician's Global Assessment (PGA)

Clinical Remission was based on the 4-component Mayo definition.

The intent to treat (ITT) population consisted of all randomized participants who received at least one dose of study treatment, with treatment. Participants with missing Mayo scores were classified as non-responders.

|                      |         |
|----------------------|---------|
| End point type       | Primary |
| End point timeframe: | Week 8  |

| End point values                  | Placebo         | Ozanimod Hydrochloride 0.5mg | Ozanimod Hydrochloride 1 mg |  |
|-----------------------------------|-----------------|------------------------------|-----------------------------|--|
| Subject group type                | Reporting group | Reporting group              | Reporting group             |  |
| Number of subjects analysed       | 65              | 65                           | 67                          |  |
| Units: Percentage of Participants |                 |                              |                             |  |
| number (not applicable)           | 6.2             | 13.8                         | 16.4                        |  |

## Statistical analyses

|   |                                       |
|---|---------------------------------------|
| Statistical analysis title              | Statistical Analysis 1                |
| Comparison groups                       | Placebo v Ozanimod Hydrochloride 1 mg |
| Number of subjects included in analysis | 132                                   |
| Analysis specification                  | Pre-specified                         |
| Analysis type                           | superiority                           |
| P-value                                 | = 0.0482 <sup>[1]</sup>               |
| Method                                  | Cochran-Mantel-Haenszel               |
| Parameter estimate                      | Odds ratio (OR)                       |
| Point estimate                          | 3.262                                 |
| Confidence interval                     |                                       |
| level                                   | 95 %                                  |
| sides                                   | 2-sided                               |
| lower limit                             | 0.969                                 |
| upper limit                             | 10.984                                |

Notes:

[1] - Stratified by prior anti-tumor necrosing factor (anti-TNF) therapy experience, (yes or no).

|   |  |
|---|--|
| <b>Statistical analysis title</b>       | Statistical Analysis 2                 |
| Comparison groups                       | Placebo v Ozanimod Hydrochloride 0.5mg |
| Number of subjects included in analysis | 130                                    |
| Analysis specification                  | Pre-specified                          |
| Analysis type                           | superiority                            |
| P-value                                 | = 0.1422 [2]                           |
| Method                                  | Cochran-Mantel-Haenszel                |
| Parameter estimate                      | Odds ratio (OR)                        |
| Point estimate                          | 2.5                                    |
| Confidence interval                     |  |
| level                                   | 95 %                                   |
| sides                                   | 2-sided                                |
| lower limit                             | 0.722                                  |
| upper limit                             | 8.661                                  |

Notes:

[2] - Stratified by prior anti-TNF therapy experience, (yes or no).

### Secondary: Percentage of Participants Who Achieved a Clinical Response in the Mayo Score (MS) at Week 8

|                 |  |
|-----------------|--|
| End point title | Percentage of Participants Who Achieved a Clinical Response in the Mayo Score (MS) at Week 8 |
|-----------------|--|

End point description:

Clinical response was defined as a reduction from baseline in Mayo score  $\geq 3$  points and  $\geq 30\%$ , and a decrease from baseline in the rectal bleeding subscore of  $\geq 1$  point or an absolute rectal bleeding subscore of  $\leq 1$  point. The Mayo Score is a composite index of four items (stool frequency, rectal bleeding, rectosigmoidoscopy findings, and physician's global assessment) with each item graded semi-quantitatively on a scale of 0 to 3 where 0 represents normal and higher score represents more severe disease status. The total Mayo Score is the sum of the four item scores, with a result ranging from 0 to 12 points. Higher scores represent more severe disease.

Clinical Response was based on the 4-component Mayo definition.

The ITT population consisted of all randomized participants who received at least one dose of study treatment, with treatment assignment designated according to randomized treatment. Participants with missing Mayo score were considered non-responders. Non responder imputa

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

End point timeframe:

Week 8

| End point values            | Placebo         | Ozanimod Hydrochloride 0.5mg | Ozanimod Hydrochloride 1 mg |  |
|-----------------------------|-----------------|------------------------------|-----------------------------|--|
| Subject group type          | Reporting group | Reporting group              | Reporting group             |  |
| Number of subjects analysed | 65              | 65                           | 67                          |  |
| Units: Units on a Scale     |                 |                              |                             |  |
| number (not applicable)     | 36.9            | 53.8                         | 56.7                        |  |

## Statistical analyses

|   |                                       |
|---|---------------------------------------|
| <b>Statistical analysis title</b>       | Statistical Analysis 1                |
| Comparison groups                       | Placebo v Ozanimod Hydrochloride 1 mg |
| Number of subjects included in analysis | 132                                   |
| Analysis specification                  | Pre-specified                         |
| Analysis type                           | superiority                           |
| P-value                                 | = 0.0207 <sup>[3]</sup>               |
| Method                                  | Cochran-Mantel-Haenszel               |
| Parameter estimate                      | Odds ratio (OR)                       |
| Point estimate                          | 2.158                                 |
| Confidence interval                     |                                       |
| level                                   | 95 %                                  |
| sides                                   | 2-sided                               |
| lower limit                             | 1.093                                 |
| upper limit                             | 4.263                                 |

Notes:

[3] - Stratified by prior anti-TNF therapy experience, (yes or no).

|   |  |
|---|--|
| <b>Statistical analysis title</b>       | Statistical Analysis 2                 |
| Comparison groups                       | Placebo v Ozanimod Hydrochloride 0.5mg |
| Number of subjects included in analysis | 130                                    |
| Analysis specification                  | Pre-specified                          |
| Analysis type                           | superiority <sup>[4]</sup>             |
| P-value                                 | = 0.0648                               |
| Method                                  | Cochran-Mantel-Haenszel                |
| Parameter estimate                      | Odds ratio (OR)                        |
| Point estimate                          | 1.947                                  |
| Confidence interval                     |  |
| level                                   | 95 %                                   |
| sides                                   | 2-sided                                |
| lower limit                             | 0.961                                  |
| upper limit                             | 3.946                                  |

Notes:

[4] - Stratified by prior anti-TNF therapy experience, (yes or no).

## Secondary: Change from Baseline in Mayo Score at Week 8

|   |  |
|---|--|
| End point title   | Change from Baseline in Mayo Score at Week 8 |
| End point description:  |  |
| <p>The Mayo Score is a composite index of four items (stool frequency, rectal bleeding, rectosigmoidoscopy findings, and physician's global assessment) with each item graded semi-quantitatively on a scale of 0 to 3 where 0 represents normal and higher score represents more severe disease status. The total Mayo Score is the sum of the four item scores, with a result ranging from 0 to 12 points. Higher scores represent more severe disease.</p> <ul style="list-style-type: none"><li>• Stool Frequency Subscore (SFS)</li><li>• Rectal bleeding Subscore (RBS)</li><li>• Endoscopy Subscore</li><li>• Physician's Global Assessment (PGA)</li></ul> <p>The ITT population consisted of all randomized participants who received at least one dose of study treatment, with treatment assignment designated according to randomized treatment. Includes participants with available data.</p> |  |
| End point type  | Secondary                                    |

End point timeframe:

Baseline to Week 8

| End point values                     | Placebo         | Ozanimod Hydrochloride 0.5mg | Ozanimod Hydrochloride 1 mg |  |
|--------------------------------------|-----------------|------------------------------|-----------------------------|--|
| Subject group type                   | Reporting group | Reporting group              | Reporting group             |  |
| Number of subjects analysed          | 62              | 64                           | 65                          |  |
| Units: Units on a Scale              |                 |                              |                             |  |
| arithmetic mean (standard deviation) | 2.0 (± 2.52)    | -2.6 (± 2.92)                | -3.4 (± 2.79)               |  |

### Statistical analyses

|   |                                       |
|---|---------------------------------------|
| Statistical analysis title              | Statistical Analysis 1                |
| Comparison groups                       | Placebo v Ozanimod Hydrochloride 1 mg |
| Number of subjects included in analysis | 127                                   |
| Analysis specification                  | Pre-specified                         |
| Analysis type                           | superiority                           |
| P-value                                 | = 0.0042 <sup>[5]</sup>               |
| Method                                  | ANCOVA                                |

Notes:

[5] - The analysis of covariance model, adjusting for baseline Mayo score and prior anti-TNF (yes or no).

|   |  |
|---|--|
| Statistical analysis title              | Statistical Analysis 2                 |
| Comparison groups                       | Placebo v Ozanimod Hydrochloride 0.5mg |
| Number of subjects included in analysis | 126                                    |
| Analysis specification                  | Pre-specified                          |
| Analysis type                           | superiority                            |
| P-value                                 | = 0.1415 <sup>[6]</sup>                |
| Method                                  | ANCOVA                                 |

Notes:

[6] - The analysis of covariance model, adjusting for baseline Mayo score and prior anti-TNF (yes or no)

### Secondary: Percentage of Participants with Mucosal Healing at Week 8

|                 |   |
|-----------------|---|
| End point title | Percentage of Participants with Mucosal Healing at Week 8 |
|-----------------|---|

End point description:

Mucosal healing is defined as an endoscopy subscore  $\leq 1$  point. Endoscopy subscores were calculated based on central endoscopy reading.

The endoscopy scale:

0 = Normal or inactive disease

1 = Mild disease (erythema, decreased vascular pattern, mild friability)

2 = Moderate disease (marked erythema, lack of vascular pattern, friability, erosions)

3 = Severe disease (spontaneous bleeding, ulceration)

The ITT population consisted of all randomized participants who received at least one dose of study treatment, with treatment assignment designated according to randomized treatment. Non-responder imputation (NRI).

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

End point timeframe:

Week 8

| End point values            | Placebo         | Ozanimod Hydrochloride 0.5mg | Ozanimod Hydrochloride 1 mg |  |
|-----------------------------|-----------------|------------------------------|-----------------------------|--|
| Subject group type          | Reporting group | Reporting group              | Reporting group             |  |
| Number of subjects analysed | 65              | 65                           | 67                          |  |
| Units: Units on a Scale     |                 |                              |                             |  |
| number (not applicable)     | 12.3            | 27.7                         | 34.3                        |  |

### Statistical analyses

|   |                                       |
|---|---------------------------------------|
| <b>Statistical analysis title</b>       | Statistical Analysis 1                |
| Comparison groups                       | Placebo v Ozanimod Hydrochloride 1 mg |
| Number of subjects included in analysis | 132                                   |
| Analysis specification                  | Pre-specified                         |
| Analysis type                           | superiority                           |
| P-value                                 | = 0.0023 <sup>[7]</sup>               |
| Method                                  | Cochran-Mantel-Haenszel               |
| Parameter estimate                      | Odds ratio (OR)                       |
| Point estimate                          | 3.861                                 |
| Confidence interval                     |                                       |
| level                                   | 95 %                                  |
| sides                                   | 2-sided                               |
| lower limit                             | 1.572                                 |
| upper limit                             | 9.484                                 |

Notes:

[7] - Stratified by prior anti-TNF therapy experience, (yes or no).

|   |  |
|---|--|
| <b>Statistical analysis title</b>       | Statistical Analysis 2                 |
| Comparison groups                       | Placebo v Ozanimod Hydrochloride 0.5mg |
| Number of subjects included in analysis | 130                                    |
| Analysis specification                  | Pre-specified                          |
| Analysis type                           | superiority                            |
| P-value                                 | = 0.0348 <sup>[8]</sup>                |
| Method                                  | Cochran-Mantel-Haenszel                |
| Parameter estimate                      | Odds ratio (OR)                        |
| Point estimate                          | 2.647                                  |
| Confidence interval                     |  |
| level                                   | 95 %                                   |
| sides                                   | 2-sided                                |
| lower limit                             | 1.058                                  |
| upper limit                             | 6.621                                  |



Notes:

[8] - Stratified by prior anti-TNF therapy experience, (yes or no).

## Secondary: Percentage of Participants Who Achieved Clinical Remission in the Mayo Score at Week 32

|                 |   |
|-----------------|---|
| End point title | Percentage of Participants Who Achieved Clinical Remission in the Mayo Score at Week 32 |
|-----------------|---|

End point description:

Clinical Remission was defined as: Mayo score of <2 points and with no individual subscore of > 1 point. The Mayo Score is a composite index of four items (stool frequency, rectal bleeding, rectosigmoidoscopy findings, and physician's global assessment) with each item graded semi-quantitatively on a scale of 0 to 3 where 0 represents normal and higher score represents more severe disease status. The total Mayo Score is the sum of the four item scores, with a result ranging from 0 to 12 points. Higher scores represent more severe disease. • Stool Frequency Subscore (SFS) • Rectal bleeding Subscore (RBS) • Endoscopy Subscore • Physician's Global Assessment (PGA)

The ITT population consisted of all randomized participants who received at least one dose of study treatment, with treatment assignment designated according to randomized treatment. Participants with missing Mayo score were considered non-responders. NRI.

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

End point timeframe:

Week 32

| End point values                  | Placebo         | Ozanimod Hydrochloride 0.5mg | Ozanimod Hydrochloride 1 mg |  |
|-----------------------------------|-----------------|------------------------------|-----------------------------|--|
| Subject group type                | Reporting group | Reporting group              | Reporting group             |  |
| Number of subjects analysed       | 65              | 65                           | 67                          |  |
| Units: Percentage of Participants |                 |                              |                             |  |
| number (not applicable)           | 6.2             | 26.2                         | 20.9                        |  |

## Statistical analyses

|   |                                       |
|---|---------------------------------------|
| Statistical analysis title              | Statistical Analysis 1                |
| Comparison groups                       | Placebo v Ozanimod Hydrochloride 1 mg |
| Number of subjects included in analysis | 132                                   |
| Analysis specification                  | Pre-specified                         |
| Analysis type                           | superiority                           |
| P-value                                 | = 0.0108 <sup>[9]</sup>               |
| Method                                  | Cochran-Mantel-Haenszel               |
| Parameter estimate                      | Odds ratio (OR)                       |
| Point estimate                          | 4.332                                 |
| Confidence interval                     |                                       |
| level                                   | 95 %                                  |
| sides                                   | 2-sided                               |
| lower limit                             | 1.323                                 |
| upper limit                             | 14.186                                |

Notes:

[9] - Stratified by prior anti-TNF therapy experience, (yes or no).

|   |  |
|---|--|
| <b>Statistical analysis title</b>       | Statistical Analysis 2                 |
| Comparison groups                       | Placebo v Ozanimod Hydrochloride 0.5mg |
| Number of subjects included in analysis | 130                                    |
| Analysis specification                  | Pre-specified                          |
| Analysis type                           | superiority                            |
| P-value                                 | = 0.0021 <sup>[10]</sup>               |
| Method                                  | Cochran-Mantel-Haenszel                |
| Parameter estimate                      | Odds ratio (OR)                        |
| Point estimate                          | 5.443                                  |
| Confidence interval                     |  |
| level                                   | 95 %                                   |
| sides                                   | 2-sided                                |
| lower limit                             | 1.706                                  |
| upper limit                             | 17.365                                 |

Notes:

[10] - Stratified by prior anti-TNF therapy experience, (yes or no).

## Secondary: Percentage of Participants Who Achieved a Clinical Response at Week 32

|                 |  |
|-----------------|--|
| End point title | Percentage of Participants Who Achieved a Clinical Response at Week 32 |
|-----------------|--|

End point description:

Clinical response was defined as a reduction from baseline in Mayo score  $\geq 3$  points and 30%, and a decrease from baseline in the rectal bleeding subscore of  $\geq 1$  point or an absolute rectal bleeding subscore of  $\leq 1$  point.

The Mayo Score is a composite index of four items (stool frequency, rectal bleeding, rectosigmoidoscopy findings, and physician's global assessment) with each item graded semi-quantitatively on a scale of 0 to 3 where 0 represents normal and higher score represents more severe disease status. The total Mayo Score is the sum of the four item scores, with a result ranging from 0 to 12 points. Higher scores represent more severe disease.

The ITT population = all randomized subjects who received at least one dose of study treatment, with treatment assignment designated according to randomized treatment. Subjects with missing Mayo score were considered non-responders. NRI.

|                      |           |
|----------------------|-----------|
| End point type       | Secondary |
| End point timeframe: |           |
| Week 32              |           |

| End point values                  | Placebo         | Ozanimod Hydrochloride 0.5mg | Ozanimod Hydrochloride 1 mg |  |
|-----------------------------------|-----------------|------------------------------|-----------------------------|--|
| Subject group type                | Reporting group | Reporting group              | Reporting group             |  |
| Number of subjects analysed       | 65              | 65                           | 67                          |  |
| Units: Percentage of Participants |                 |                              |                             |  |
| number (not applicable)           | 20.0            | 35.4                         | 50.7                        |  |

## Statistical analyses

|   |                                       |
|---|---------------------------------------|
| <b>Statistical analysis title</b>       | Statistical Analysis 1                |
| Comparison groups                       | Placebo v Ozanimod Hydrochloride 1 mg |
| Number of subjects included in analysis | 132                                   |
| Analysis specification                  | Pre-specified                         |
| Analysis type                           | superiority                           |
| P-value                                 | = 0.0002 <sup>[11]</sup>              |
| Method                                  | Cochran-Mantel-Haenszel               |
| Parameter estimate                      | Odds ratio (OR)                       |
| Point estimate                          | 4.03                                  |
| Confidence interval                     |                                       |
| level                                   | 95 %                                  |
| sides                                   | 2-sided                               |
| lower limit                             | 1.871                                 |
| upper limit                             | 8.678                                 |

Notes:

[11] - Stratified by prior anti-TNF therapy experience, (yes or no).

|   |                                       |
|---|---------------------------------------|
| <b>Statistical analysis title</b>       | Statistical Analysis 2                |
| Comparison groups                       | Placebo v Ozanimod Hydrochloride 1 mg |
| Number of subjects included in analysis | 132                                   |
| Analysis specification                  | Pre-specified                         |
| Analysis type                           | superiority                           |
| P-value                                 | = 0.0571 <sup>[12]</sup>              |
| Method                                  | Cochran-Mantel-Haenszel               |
| Parameter estimate                      | Odds ratio (OR)                       |
| Point estimate                          | 2.154                                 |
| Confidence interval                     |                                       |
| level                                   | 95 %                                  |
| sides                                   | 2-sided                               |
| lower limit                             | 0.974                                 |
| upper limit                             | 4.763                                 |

Notes:

[12] - Stratified by prior anti-TNF therapy experience, (yes or no).

## Secondary: Percentage of Participants with Mucosal Healing at Week 32

|  |  |
|--|--|
| End point title  | Percentage of Participants with Mucosal Healing at Week 32 |
| End point description:   |  |
| Mucosal healing is defined as an endoscopy subscore $\leq 1$ point. Endoscopy subscores were calculated based on central endoscopy reading.  |  |
| The endoscopy scale:   |  |
| 0 = Normal or inactive disease   |  |
| 1 = Mild disease (erythema, decreased vascular pattern, mild friability)   |  |
| 2 = Moderate disease (marked erythema, lack of vascular pattern, friability, erosions)   |  |
| 3 = Severe disease (spontaneous bleeding, ulceration)  |  |
| The ITT population consisted of all randomized participants who received at least one dose of study treatment, with treatment assignment designated according to randomized treatment. Non-responder imputation (NRI). |  |
| End point type   | Secondary  |
| End point timeframe:   |  |
| Week 32  |  |

| <b>End point values</b>           | Placebo         | Ozanimod Hydrochloride 0.5mg | Ozanimod Hydrochloride 1 mg |  |
|-----------------------------------|-----------------|------------------------------|-----------------------------|--|
| Subject group type                | Reporting group | Reporting group              | Reporting group             |  |
| Number of subjects analysed       | 65              | 65                           | 67                          |  |
| Units: Percentage of Participants |                 |                              |                             |  |
| number (not applicable)           | 12.3            | 32.3                         | 32.8                        |  |

## Statistical analyses

|   |                                       |
|---|---------------------------------------|
| <b>Statistical analysis title</b>       | Statistical Analysis 1                |
| Comparison groups                       | Placebo v Ozanimod Hydrochloride 1 mg |
| Number of subjects included in analysis | 132                                   |
| Analysis specification                  | Pre-specified                         |
| Analysis type                           | superiority                           |
| P-value                                 | = 0.0046 <sup>[13]</sup>              |
| Method                                  | Cochran-Mantel-Haenszel               |
| Parameter estimate                      | Odds ratio (OR)                       |
| Point estimate                          | 3.557                                 |
| Confidence interval                     |                                       |
| level                                   | 95 %                                  |
| sides                                   | 2-sided                               |
| lower limit                             | 1.444                                 |
| upper limit                             | 8.762                                 |

Notes:

[13] - Stratified by prior anti-TNF therapy experience, (yes or no).

|   |  |
|---|--|
| <b>Statistical analysis title</b>       | Statistical Analysis 2                 |
| Comparison groups                       | Placebo v Ozanimod Hydrochloride 0.5mg |
| Number of subjects included in analysis | 130                                    |
| Analysis specification                  | Pre-specified                          |
| Analysis type                           | superiority                            |
| P-value                                 | = 0.0064 <sup>[14]</sup>               |
| Method                                  | Cochran-Mantel-Haenszel                |
| Parameter estimate                      | Odds ratio (OR)                        |
| Point estimate                          | 3.428                                  |
| Confidence interval                     |  |
| level                                   | 95 %                                   |
| sides                                   | 2-sided                                |
| lower limit                             | 1.384                                  |
| upper limit                             | 8.494                                  |

Notes:

[14] - Stratified by prior anti-TNF therapy experience, (yes or no).

## Secondary: Number of Participants with Treatment Emergent Adverse Events During

## the Induction Period

|                 |   |
|-----------------|---|
| End point title | Number of Participants with Treatment Emergent Adverse Events During the Induction Period |
|-----------------|---|

### End point description:

A TEAE was defined as any event with an onset date on or after first dose date or any ongoing event on the first dose date that worsens in severity after first dose date and until 30 days following the last dose of treatment with the study drug. earlier. A serious AE = any AE which results in death; is life-threatening; requires inpatient hospitalization or prolongation of existing hospitalization; results in persistent or significant disability/incapacity; is a congenital anomaly/birth defect; constitutes an important medical event. The severity of AEs was assessed by the investigator and based on the following scale: Mild = an AE usually transient in nature and generally not interfering with normal activities; Moderate = an AE that is sufficiently discomforting to interfere with normal activities; Severe = an AE that is incapacitating and prevents normal activities. Safety population = all participants who were enrolled and received at least 1 dose of study drug.

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

### End point timeframe:

From the first dose of investigational product (IP) up to 90 days after the last dose of IP or at follow-up visit; the mean total duration of IP exposure was 52.8 days, 56.1 days and 50.8 days respectively for 0.5 mg, 1 mg ozanimod and placebo.

| End point values                                  | Placebo         | Ozanimod Hydrochloride 0.5mg | Ozanimod Hydrochloride 1 mg |  |
|---|-----------------|------------------------------|-----------------------------|--|
| Subject group type                                | Reporting group | Reporting group              | Reporting group             |  |
| Number of subjects analysed                       | 65              | 65                           | 67                          |  |
| Units: Participants                               |                 |                              |                             |  |
| number (not applicable)                           |                 |                              |                             |  |
| ≥ 1 TEAE  | 21              | 24                           | 17                          |  |
| ≥ 1 Moderate or Severe TEAE                       | 7               | 12                           | 6                           |  |
| ≥ 1 Severe TEAE                                   | 2               | 1                            | 1                           |  |
| ≥ 1 Possibly, Probably or Definitely Related TEAE | 2               | 5                            | 5                           |  |
| ≥ 1 Serious SAE                                   | 4               | 1                            | 2                           |  |
| ≥ 1 Possibly, Probably or Related Serious TEAE    | 0               | 0                            | 0                           |  |
| ≥ 1 TEAE Leading to Withdrawal From Study         | 1               | 2                            | 1                           |  |
| Death   | 0               | 0                            | 0                           |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Participants with Treatment Emergent Adverse Events During the Maintenance Period

|                 |   |
|-----------------|---|
| End point title | Number of Participants with Treatment Emergent Adverse Events During the Maintenance Period |
|-----------------|---|

### End point description:

A TEAE was defined as any event with an onset date on or after first dose date or any ongoing event on the first dose date that worsens in severity after first dose date and until 30 days following the last dose of treatment with the study drug. earlier. A serious AE = any AE which results in death; is life-threatening; requires inpatient hospitalization or prolongation of existing hospitalization; results in persistent or significant disability/incapacity; is a congenital anomaly/birth defect; constitutes an

important medical event. The severity of AEs was assessed by the investigator and based on the following scale: Mild = an AE usually transient in nature and generally not interfering with normal activities; Moderate = an AE that is sufficiently discomforting to interfere with normal activities; Severe = an AE that is incapacitating and prevents normal activities. Safety population included all participants who were enrolled and received at least 1 dose of investigational product

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

End point timeframe:

From the first dose of IP up to 90 days after the last dose of IP or at follow-up visit; the mean total duration of IP exposure was 156.3 days, 171.1 days and 154.5 days respectively for 0.5 mg, 1 mg ozanimod and placebo.

| End point values                                  | Placebo              | Ozanimod 0.5 mg      | Ozanimod 1 mg        |  |
|---|----------------------|----------------------|----------------------|--|
| Subject group type                                | Subject analysis set | Subject analysis set | Subject analysis set |  |
| Number of subjects analysed                       | 25                   | 36                   | 42                   |  |
| Units: Participants                               |                      |                      |                      |  |
| ≥ 1 TEAE  | 8                    | 4                    | 11                   |  |
| ≥ 1 Moderate or Severe TEAE                       | 4                    | 1                    | 5                    |  |
| ≥ 1 Severe TEAE                                   | 1                    | 0                    | 1                    |  |
| ≥ 1 Possibly, Probably or Definitely Related TEAE | 0                    | 0                    | 2                    |  |
| ≥ 1 Serious TEAE                                  | 2                    | 0                    | 1                    |  |
| ≥ 1 Possibly, Probably or Related Serious TEAE    | 0                    | 0                    | 0                    |  |
| ≥ 1 TEAE Leading to Withdrawal From Study         | 3                    | 0                    | 0                    |  |
| Death   | 0                    | 0                    | 0                    |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Participants with Treatment Emergent Adverse Events During the Open-Label Treatment Period (OLP)

|                 |  |
|-----------------|--|
| End point title | Number of Participants with Treatment Emergent Adverse Events During the Open-Label Treatment Period (OLP) |
|-----------------|--|

End point description:

A TEAE was defined as any event with an onset date on or after first dose date or any ongoing event on the first dose date that worsens in severity after first dose date and until 30 days following the last dose of treatment with the study drug. earlier. A serious AE = any AE which results in death; is life-threatening; requires inpatient hospitalization or prolongation of existing hospitalization; results in persistent or significant disability/incapacity; is a congenital anomaly/birth defect; constitutes an important medical event. The severity of AEs was assessed by the investigator and based on the following scale: Mild = an AE usually transient in nature and generally not interfering with normal activities; Moderate = an AE that is sufficiently discomforting to interfere with normal activities; Severe = an AE that is incapacitating and prevents normal activities. Safety population included all participants who were enrolled and received at least 1 dose of investigational product

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

End point timeframe:

From the first dose of IP until 90 days after the last dose of IP or at follow-up visit; the mean total duration of study drug exposure in the OLP was 2.42 years.

| <b>End point values</b>                           | Open Label<br>Treatment<br>Period |  |  |  |
|---|-----------------------------------|--|--|--|
| Subject group type                                | Subject analysis set              |  |  |  |
| Number of subjects analysed                       | 170                               |  |  |  |
| Units: Participants                               |                                   |  |  |  |
| ≥ 1 TEAE  | 101                               |  |  |  |
| ≥ 1 Moderate or Severe TEAE                       | 63                                |  |  |  |
| ≥ 1 Severe TEAE                                   | 17                                |  |  |  |
| ≥ 1 Possible, Probable or Related TEAE            | 27                                |  |  |  |
| ≥ 1 Related TEAE                                  | 2                                 |  |  |  |
| ≥ 1 Serious TEAE                                  | 27                                |  |  |  |
| ≥ 1 Related Serious TEAE                          | 0                                 |  |  |  |
| ≥ 1 Possible, Probable or Related<br>Serious TEAE | 4                                 |  |  |  |
| ≥ 1 TEAE Leading to Discontinuation of<br>IP      | 14                                |  |  |  |
| ≥ 1 TEAE Leading to Withdrawal from<br>Study      | 13                                |  |  |  |
| Death   | 1                                 |  |  |  |
| Death Possible, Probable or Related to<br>IP      | 1                                 |  |  |  |

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

From the first dose of IP up to 90 days after the last dose of IP or at follow-up visit; the mean total duration of IP exposure was 52.8 days, 56.1 days and 50.8 days respectively for 0.5 mg, 1 mg ozanimod and placebo during the induction period.

Adverse event reporting additional description:

The mean total duration of study drug exposure was 156.3 days, 171.1 days and 154.5 days respectively for 0.5 mg, 1 mg ozanimod and placebo during the maintenance period and 2.42 years during the open label treatment period,

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

### Dictionary used

|                 |        |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

|                    |      |
|--------------------|------|
| Dictionary version | 18.1 |
|--------------------|------|

### Reporting groups

|                       |                           |
|-----------------------|---------------------------|
| Reporting group title | Induction Period: Placebo |
|-----------------------|---------------------------|

Reporting group description:

Participants received identically matching placebo capsules daily for 9 weeks during the induction period (weeks 0 to 9)

|                       |                                       |
|-----------------------|---------------------------------------|
| Reporting group title | Induction Period: Ozanimod HCL 0.5 mg |
|-----------------------|---------------------------------------|

Reporting group description:

Participants received 0.5 mg capsules of ozanimod hydrochloride daily during the induction period weeks 0-9 (an initial 8-day dose escalation regimen in the induction period that consisted of 4 days of ozanimod HCL 0.25 mg (equivalent to ozanimod 0.23 mg), followed by 3 days of ozanimod HCL 0.5 mg, (equivalent to ozanimod 0.46 mg) followed by the assigned treatment level for at least 8 weeks.

|                       |                                     |
|-----------------------|-------------------------------------|
| Reporting group title | Induction Period: Ozanimod HCL 1 mg |
|-----------------------|-------------------------------------|

Reporting group description:

Participants received 1mg capsules of ozanimod hydrochloride daily during the induction period weeks 0-9 (an initial 8-day dose escalation regimen in the induction period that consisted of 4 days of ozanimod HCL 0.25 mg (equivalent to ozanimod 0.23 mg), followed by 3 days of ozanimod HCL 0.5 mg, (equivalent to ozanimod 0.46 mg) followed by the assigned treatment level for at least 8 weeks.

|                       |                             |
|-----------------------|-----------------------------|
| Reporting group title | Maintenance Period: Placebo |
|-----------------------|-----------------------------|

Reporting group description:

Participants originally assigned to placebo who completed the induction period and were responders at week 8 continued to receive placebo in the maintenance period. Participants received identically matching placebo capsules daily during the maintenance period (weeks 9-32).

|                       |   |
|-----------------------|---|
| Reporting group title | Maintenance Period: Ozanimod HCL 0.5 mg |
|-----------------------|---|

Reporting group description:

Participants originally assigned to ozanimod 0.5 mg who completed the induction period and were responders at week 8 continued to receive ozanimod 0.5 mg daily in the maintenance period. Participants received 0.5 mg ozanimod capsules daily during the maintenance period (weeks 9 to 32).

|                       |                                       |
|-----------------------|---------------------------------------|
| Reporting group title | Maintenance Period: Ozanimod HCL 1 mg |
|-----------------------|---------------------------------------|

Reporting group description:

Participants originally assigned to ozanimod 1 mg who completed the induction period and were responders at week 8 continued to receive ozanimod 0.5 mg daily in the maintenance period. Participants received 1 mg ozanimod capsules daily during the maintenance period (weeks 9 to 32).

|                       |   |
|-----------------------|---|
| Reporting group title | Open-Label Treatment Period (OLP): Placebo/Ozanimod |
|-----------------------|---|

Reporting group description:

Participants who received placebo capsules and completed the induction period and were non-responders at Week 8 and those who completed the maintenance period or experienced a disease relapse, were given the option to enter the open label treatment period (OLP) and receive 1 mg ozanimod daily up to 6 years. Participants who had not shown clinical improvement 8 weeks after initiation of the OLP were discontinued from the study.

|                       |                                    |
|-----------------------|------------------------------------|
| Reporting group title | OLP: Ozanimod 0.5 mg/Ozanimod 1 mg |
|-----------------------|------------------------------------|



Reporting group description:

Participants who received ozanimod 0.5 mg capsules and completed the induction period and were non-responders at Week 8 and who completed the maintenance period or experienced a disease relapse, were given the option to enter the OLP and receive 1 mg ozanimod capsules daily up to 6 years. Participants who had not shown clinical improvement 8 weeks after initiation of the OLP were discontinued from the study.

|                       |                                 |
|-----------------------|---------------------------------|
| Reporting group title | OLP: Ozanimod 1mg/Ozanimod 1 mg |
|-----------------------|---------------------------------|

Reporting group description:

Participants who received 1 mg ozanimod capsules and completed the induction period and were non-responders at Week 8 and those who completed the maintenance period or experienced a disease relapse, were given the option to enter the open label treatment period (OLP) and continue to receive 1 mg ozanimod daily up to 6 years. Participants who had not shown clinical improvement 8 weeks after initiation of the OLP were discontinued from the study.

| <b>Serious adverse events</b>                                       | Induction Period:<br>Placebo | Induction Period:<br>Ozanimod HCL 0.5<br>mg | Induction Period:<br>Ozanimod HCL 1 mg |
|---|------------------------------|---|--|
| Total subjects affected by serious adverse events                   |                              |   |  |
| subjects affected / exposed   | 4 / 65 (6.15%)               | 1 / 65 (1.54%)                              | 2 / 67 (2.99%)                         |
| number of deaths (all causes)                                       | 0                            | 0   | 0                                      |
| number of deaths resulting from adverse events                      | 0                            | 0   | 0                                      |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                              |   |  |
| Adenocarcinoma  |                              |   |  |
| subjects affected / exposed   | 0 / 65 (0.00%)               | 0 / 65 (0.00%)                              | 0 / 67 (0.00%)                         |
| occurrences causally related to treatment / all                     | 0 / 0                        | 0 / 0                                       | 0 / 0                                  |
| deaths causally related to treatment / all                          | 0 / 0                        | 0 / 0                                       | 0 / 0                                  |
| Basal cell carcinoma  |                              |   |  |
| subjects affected / exposed   | 0 / 65 (0.00%)               | 0 / 65 (0.00%)                              | 0 / 67 (0.00%)                         |
| occurrences causally related to treatment / all                     | 0 / 0                        | 0 / 0                                       | 0 / 0                                  |
| deaths causally related to treatment / all                          | 0 / 0                        | 0 / 0                                       | 0 / 0                                  |
| Colon adenoma   |                              |   |  |
| subjects affected / exposed   | 0 / 65 (0.00%)               | 0 / 65 (0.00%)                              | 0 / 67 (0.00%)                         |
| occurrences causally related to treatment / all                     | 0 / 0                        | 0 / 0                                       | 0 / 0                                  |
| deaths causally related to treatment / all                          | 0 / 0                        | 0 / 0                                       | 0 / 0                                  |
| Prostate cancer   |                              |   |  |
| subjects affected / exposed   | 0 / 65 (0.00%)               | 0 / 65 (0.00%)                              | 0 / 67 (0.00%)                         |
| occurrences causally related to treatment / all                     | 0 / 0                        | 0 / 0                                       | 0 / 0                                  |
| deaths causally related to treatment / all                          | 0 / 0                        | 0 / 0                                       | 0 / 0                                  |
| Pregnancy, puerperium and perinatal conditions                      |                              |   |  |
| Abortion spontaneous  |                              |   |  |

|  |                |                |                |
|--|----------------|----------------|----------------|
| subjects affected / exposed                          | 0 / 65 (0.00%) | 0 / 65 (0.00%) | 0 / 67 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| General disorders and administration site conditions |                |                |                |
| Hyperpyrexia   |                |                |                |
| subjects affected / exposed                          | 0 / 65 (0.00%) | 1 / 65 (1.54%) | 0 / 67 (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          |
| Respiratory, thoracic and mediastinal disorders      |                |                |                |
| Idiopathic pulmonary fibrosis                        |                |                |                |
| subjects affected / exposed                          | 0 / 65 (0.00%) | 0 / 65 (0.00%) | 0 / 67 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| Interstitial lung disease                            |                |                |                |
| subjects affected / exposed                          | 0 / 65 (0.00%) | 0 / 65 (0.00%) | 0 / 67 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| Pleurisy   |                |                |                |
| subjects affected / exposed                          | 0 / 65 (0.00%) | 0 / 65 (0.00%) | 0 / 67 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| Pulmonary bulla                                      |                |                |                |
| subjects affected / exposed                          | 0 / 65 (0.00%) | 0 / 65 (0.00%) | 0 / 67 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| Pulmonary microemboli                                |                |                |                |
| subjects affected / exposed                          | 0 / 65 (0.00%) | 0 / 65 (0.00%) | 0 / 67 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| Psychiatric disorders                                |                |                |                |
| Schizophrenia  |                |                |                |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 65 (0.00%) | 0 / 65 (0.00%) | 0 / 67 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Injury, poisoning and procedural complications  |                |                |                |
| Joint dislocation                               |                |                |                |
| subjects affected / exposed                     | 0 / 65 (0.00%) | 0 / 65 (0.00%) | 0 / 67 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Wrist fracture                                  |                |                |                |
| subjects affected / exposed                     | 0 / 65 (0.00%) | 0 / 65 (0.00%) | 0 / 67 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Cardiac disorders                               |                |                |                |
| Acute coronary syndrome                         |                |                |                |
| subjects affected / exposed                     | 0 / 65 (0.00%) | 0 / 65 (0.00%) | 0 / 67 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Nervous system disorders                        |                |                |                |
| Ischaemic stroke                                |                |                |                |
| subjects affected / exposed                     | 0 / 65 (0.00%) | 0 / 65 (0.00%) | 0 / 67 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Blood and lymphatic system disorders            |                |                |                |
| Anaemia   |                |                |                |
| subjects affected / exposed                     | 0 / 65 (0.00%) | 0 / 65 (0.00%) | 0 / 67 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Autoimmune haemolytic anaemia                   |                |                |                |
| subjects affected / exposed                     | 0 / 65 (0.00%) | 0 / 65 (0.00%) | 0 / 67 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Haemolytic anaemia                              |                |                |                |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 65 (0.00%) | 0 / 65 (0.00%) | 0 / 67 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Hypochromic anaemia                             |                |                |                |
| subjects affected / exposed                     | 0 / 65 (0.00%) | 0 / 65 (0.00%) | 0 / 67 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Iron deficiency anaemia                         |                |                |                |
| subjects affected / exposed                     | 1 / 65 (1.54%) | 0 / 65 (0.00%) | 0 / 67 (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                      |                |                |                |
| Ascites   |                |                |                |
| subjects affected / exposed                     | 0 / 65 (0.00%) | 0 / 65 (0.00%) | 0 / 67 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Colitis   |                |                |                |
| subjects affected / exposed                     | 0 / 65 (0.00%) | 0 / 65 (0.00%) | 0 / 67 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Colitis ulcerative                              |                |                |                |
| subjects affected / exposed                     | 2 / 65 (3.08%) | 0 / 65 (0.00%) | 2 / 67 (2.99%) |
| occurrences causally related to treatment / all | 0 / 2          | 0 / 0          | 0 / 2          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Inguinal hernia                                 |                |                |                |
| subjects affected / exposed                     | 0 / 65 (0.00%) | 0 / 65 (0.00%) | 0 / 67 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Intestinal obstruction                          |                |                |                |
| subjects affected / exposed                     | 0 / 65 (0.00%) | 0 / 65 (0.00%) | 0 / 67 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Umbilical hernia                                |                |                |                |

|  |                |                |                |
|--|----------------|----------------|----------------|
| subjects affected / exposed                            | 0 / 65 (0.00%) | 0 / 65 (0.00%) | 0 / 67 (0.00%) |
| occurrences causally related to treatment / all        | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all             | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>Hepatobiliary disorders</b>                         |                |                |                |
| Hyperbilirubinaemia                                    |                |                |                |
| subjects affected / exposed                            | 0 / 65 (0.00%) | 0 / 65 (0.00%) | 0 / 67 (0.00%) |
| occurrences causally related to treatment / all        | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all             | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>Jaundice</b>  |                |                |                |
| subjects affected / exposed                            | 1 / 65 (1.54%) | 0 / 65 (0.00%) | 0 / 67 (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          |
| <b>Renal and urinary disorders</b>                     |                |                |                |
| Nephrolithiasis  |                |                |                |
| subjects affected / exposed                            | 0 / 65 (0.00%) | 0 / 65 (0.00%) | 0 / 67 (0.00%) |
| occurrences causally related to treatment / all        | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all             | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>Musculoskeletal and connective tissue disorders</b> |                |                |                |
| Rheumatoid arthritis                                   |                |                |                |
| subjects affected / exposed                            | 0 / 65 (0.00%) | 0 / 65 (0.00%) | 0 / 67 (0.00%) |
| occurrences causally related to treatment / all        | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all             | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>Spinal column stenosis</b>                          |                |                |                |
| subjects affected / exposed                            | 0 / 65 (0.00%) | 0 / 65 (0.00%) | 0 / 67 (0.00%) |
| occurrences causally related to treatment / all        | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all             | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>Infections and infestations</b>                     |                |                |                |
| Erysipelas   |                |                |                |
| subjects affected / exposed                            | 0 / 65 (0.00%) | 0 / 65 (0.00%) | 0 / 67 (0.00%) |
| occurrences causally related to treatment / all        | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all             | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>Gastroenteritis viral</b>                           |                |                |                |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 65 (0.00%) | 0 / 65 (0.00%) | 0 / 67 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Herpes zoster                                   |                |                |                |
| subjects affected / exposed                     | 0 / 65 (0.00%) | 0 / 65 (0.00%) | 0 / 67 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Pneumonia                                       |                |                |                |
| subjects affected / exposed                     | 0 / 65 (0.00%) | 0 / 65 (0.00%) | 0 / 67 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Pneumonia pneumococcal                          |                |                |                |
| subjects affected / exposed                     | 0 / 65 (0.00%) | 0 / 65 (0.00%) | 0 / 67 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Metabolism and nutrition disorders              |                |                |                |
| Dehydration                                     |                |                |                |
| subjects affected / exposed                     | 0 / 65 (0.00%) | 0 / 65 (0.00%) | 0 / 67 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |

| <b>Serious adverse events</b>                                       | Maintenance Period:<br>Placebo | Maintenance Period:<br>Ozanimod HCL 0.5<br>mg | Maintenance Period:<br>Ozanimod HCL 1 mg |
|---|--------------------------------|---|--|
| Total subjects affected by serious adverse events                   |                                |   |  |
| subjects affected / exposed   | 2 / 25 (8.00%)                 | 0 / 36 (0.00%)                                | 1 / 42 (2.38%)                           |
| number of deaths (all causes)                                       | 0                              | 0   | 0  |
| number of deaths resulting from adverse events                      | 0                              | 0   | 0  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                                |   |  |
| Adenocarcinoma  |                                |   |  |
| subjects affected / exposed   | 0 / 25 (0.00%)                 | 0 / 36 (0.00%)                                | 0 / 42 (0.00%)                           |
| occurrences causally related to treatment / all                     | 0 / 0                          | 0 / 0   | 0 / 0                                    |
| deaths causally related to treatment / all                          | 0 / 0                          | 0 / 0   | 0 / 0                                    |
| Basal cell carcinoma  |                                |   |  |

|  |                |                |                |
|--|----------------|----------------|----------------|
| subjects affected / exposed                          | 0 / 25 (0.00%) | 0 / 36 (0.00%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| Colon adenoma  |                |                |                |
| subjects affected / exposed                          | 0 / 25 (0.00%) | 0 / 36 (0.00%) | 1 / 42 (2.38%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| Prostate cancer                                      |                |                |                |
| subjects affected / exposed                          | 0 / 25 (0.00%) | 0 / 36 (0.00%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| Pregnancy, puerperium and perinatal conditions       |                |                |                |
| Abortion spontaneous                                 |                |                |                |
| subjects affected / exposed                          | 0 / 25 (0.00%) | 0 / 36 (0.00%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| General disorders and administration site conditions |                |                |                |
| Hyperpyrexia   |                |                |                |
| subjects affected / exposed                          | 0 / 25 (0.00%) | 0 / 36 (0.00%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| Respiratory, thoracic and mediastinal disorders      |                |                |                |
| Idiopathic pulmonary fibrosis                        |                |                |                |
| subjects affected / exposed                          | 0 / 25 (0.00%) | 0 / 36 (0.00%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| Interstitial lung disease                            |                |                |                |
| subjects affected / exposed                          | 0 / 25 (0.00%) | 0 / 36 (0.00%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| Pleurisy   |                |                |                |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 25 (0.00%) | 0 / 36 (0.00%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Pulmonary bulla                                 |                |                |                |
| subjects affected / exposed                     | 0 / 25 (0.00%) | 0 / 36 (0.00%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Pulmonary microemboli                           |                |                |                |
| subjects affected / exposed                     | 0 / 25 (0.00%) | 0 / 36 (0.00%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Psychiatric disorders                           |                |                |                |
| Schizophrenia                                   |                |                |                |
| subjects affected / exposed                     | 0 / 25 (0.00%) | 0 / 36 (0.00%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Injury, poisoning and procedural complications  |                |                |                |
| Joint dislocation                               |                |                |                |
| subjects affected / exposed                     | 0 / 25 (0.00%) | 0 / 36 (0.00%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Wrist fracture                                  |                |                |                |
| subjects affected / exposed                     | 0 / 25 (0.00%) | 0 / 36 (0.00%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Cardiac disorders                               |                |                |                |
| Acute coronary syndrome                         |                |                |                |
| subjects affected / exposed                     | 0 / 25 (0.00%) | 0 / 36 (0.00%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Nervous system disorders                        |                |                |                |
| Ischaemic stroke                                |                |                |                |



|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 25 (0.00%) | 0 / 36 (0.00%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>Blood and lymphatic system disorders</b>     |                |                |                |
| Anaemia   |                |                |                |
| subjects affected / exposed                     | 0 / 25 (0.00%) | 0 / 36 (0.00%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Autoimmune haemolytic anaemia                   |                |                |                |
| subjects affected / exposed                     | 1 / 25 (4.00%) | 0 / 36 (0.00%) | 0 / 42 (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          |
| Haemolytic anaemia                              |                |                |                |
| subjects affected / exposed                     | 0 / 25 (0.00%) | 0 / 36 (0.00%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Hypochromic anaemia                             |                |                |                |
| subjects affected / exposed                     | 0 / 25 (0.00%) | 0 / 36 (0.00%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Iron deficiency anaemia                         |                |                |                |
| subjects affected / exposed                     | 0 / 25 (0.00%) | 0 / 36 (0.00%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>Gastrointestinal disorders</b>               |                |                |                |
| Ascites   |                |                |                |
| subjects affected / exposed                     | 0 / 25 (0.00%) | 0 / 36 (0.00%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Colitis   |                |                |                |
| subjects affected / exposed                     | 0 / 25 (0.00%) | 0 / 36 (0.00%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Colitis ulcerative                              |                |                |                |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 1 / 25 (4.00%) | 0 / 36 (0.00%) | 0 / 42 (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          |
| Inguinal hernia                                 |                |                |                |
| subjects affected / exposed                     | 0 / 25 (0.00%) | 0 / 36 (0.00%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Intestinal obstruction                          |                |                |                |
| subjects affected / exposed                     | 0 / 25 (0.00%) | 0 / 36 (0.00%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Umbilical hernia                                |                |                |                |
| subjects affected / exposed                     | 0 / 25 (0.00%) | 0 / 36 (0.00%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Hepatobiliary disorders                         |                |                |                |
| Hyperbilirubinaemia                             |                |                |                |
| subjects affected / exposed                     | 0 / 25 (0.00%) | 0 / 36 (0.00%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Jaundice  |                |                |                |
| subjects affected / exposed                     | 0 / 25 (0.00%) | 0 / 36 (0.00%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Renal and urinary disorders                     |                |                |                |
| Nephrolithiasis                                 |                |                |                |
| subjects affected / exposed                     | 0 / 25 (0.00%) | 0 / 36 (0.00%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Musculoskeletal and connective tissue disorders |                |                |                |
| Rheumatoid arthritis                            |                |                |                |
| subjects affected / exposed                     | 0 / 25 (0.00%) | 0 / 36 (0.00%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |

|   |  |                                       |                                       |
|---|--|---------------------------------------|---------------------------------------|
| Spinal column stenosis                            |  |                                       |                                       |
| subjects affected / exposed                       | 0 / 25 (0.00%)   | 0 / 36 (0.00%)                        | 0 / 42 (0.00%)                        |
| occurrences causally related to treatment / all   | 0 / 0  | 0 / 0                                 | 0 / 0                                 |
| deaths causally related to treatment / all        | 0 / 0  | 0 / 0                                 | 0 / 0                                 |
| Infections and infestations                       |  |                                       |                                       |
| Erysipelas  |  |                                       |                                       |
| subjects affected / exposed                       | 0 / 25 (0.00%)   | 0 / 36 (0.00%)                        | 0 / 42 (0.00%)                        |
| occurrences causally related to treatment / all   | 0 / 0  | 0 / 0                                 | 0 / 0                                 |
| deaths causally related to treatment / all        | 0 / 0  | 0 / 0                                 | 0 / 0                                 |
| Gastroenteritis viral                             |  |                                       |                                       |
| subjects affected / exposed                       | 0 / 25 (0.00%)   | 0 / 36 (0.00%)                        | 0 / 42 (0.00%)                        |
| occurrences causally related to treatment / all   | 0 / 0  | 0 / 0                                 | 0 / 0                                 |
| deaths causally related to treatment / all        | 0 / 0  | 0 / 0                                 | 0 / 0                                 |
| Herpes zoster                                     |  |                                       |                                       |
| subjects affected / exposed                       | 1 / 25 (4.00%)   | 0 / 36 (0.00%)                        | 0 / 42 (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                                 |
| Pneumonia   |  |                                       |                                       |
| subjects affected / exposed                       | 0 / 25 (0.00%)   | 0 / 36 (0.00%)                        | 0 / 42 (0.00%)                        |
| occurrences causally related to treatment / all   | 0 / 0  | 0 / 0                                 | 0 / 0                                 |
| deaths causally related to treatment / all        | 0 / 0  | 0 / 0                                 | 0 / 0                                 |
| Pneumonia pneumococcal                            |  |                                       |                                       |
| subjects affected / exposed                       | 0 / 25 (0.00%)   | 0 / 36 (0.00%)                        | 0 / 42 (0.00%)                        |
| occurrences causally related to treatment / all   | 0 / 0  | 0 / 0                                 | 0 / 0                                 |
| deaths causally related to treatment / all        | 0 / 0  | 0 / 0                                 | 0 / 0                                 |
| Metabolism and nutrition disorders                |  |                                       |                                       |
| Dehydration                                       |  |                                       |                                       |
| subjects affected / exposed                       | 0 / 25 (0.00%)   | 0 / 36 (0.00%)                        | 0 / 42 (0.00%)                        |
| occurrences causally related to treatment / all   | 0 / 0  | 0 / 0                                 | 0 / 0                                 |
| deaths causally related to treatment / all        | 0 / 0  | 0 / 0                                 | 0 / 0                                 |
| Serious adverse events                            |  |                                       |                                       |
|   | Open-Label<br>Treatment Period<br>(OLP):<br>Placebo/Ozanimod | OLP: Ozanimod 0.5<br>mg/Ozanimod 1 mg | OLP: Ozanimod<br>1mg/Ozanimod 1<br>mg |
| Total subjects affected by serious adverse events |  |                                       |                                       |

|   |                |                  |                  |
|---|----------------|------------------|------------------|
| subjects affected / exposed   | 5 / 55 (9.09%) | 14 / 56 (25.00%) | 11 / 59 (18.64%) |
| number of deaths (all causes)                                       | 0              | 1                | 0                |
| number of deaths resulting from adverse events                      | 0              | 1                | 0                |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                |                  |                  |
| Adenocarcinoma  |                |                  |                  |
| subjects affected / exposed   | 0 / 55 (0.00%) | 1 / 56 (1.79%)   | 0 / 59 (0.00%)   |
| occurrences causally related to treatment / all                     | 0 / 0          | 1 / 1            | 0 / 0            |
| deaths causally related to treatment / all                          | 0 / 0          | 1 / 1            | 0 / 0            |
| Basal cell carcinoma  |                |                  |                  |
| subjects affected / exposed   | 0 / 55 (0.00%) | 1 / 56 (1.79%)   | 0 / 59 (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            |
| Colon adenoma   |                |                  |                  |
| subjects affected / exposed   | 0 / 55 (0.00%) | 0 / 56 (0.00%)   | 1 / 59 (1.69%)   |
| occurrences causally related to treatment / all                     | 0 / 0          | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all                          | 0 / 0          | 0 / 0            | 0 / 0            |
| Prostate cancer   |                |                  |                  |
| subjects affected / exposed   | 0 / 55 (0.00%) | 0 / 56 (0.00%)   | 1 / 59 (1.69%)   |
| occurrences causally related to treatment / all                     | 0 / 0          | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all                          | 0 / 0          | 0 / 0            | 0 / 0            |
| Pregnancy, puerperium and perinatal conditions                      |                |                  |                  |
| Abortion spontaneous  |                |                  |                  |
| subjects affected / exposed   | 0 / 55 (0.00%) | 0 / 56 (0.00%)   | 1 / 59 (1.69%)   |
| occurrences causally related to treatment / all                     | 0 / 0          | 0 / 0            | 1 / 1            |
| deaths causally related to treatment / all                          | 0 / 0          | 0 / 0            | 0 / 0            |
| General disorders and administration site conditions                |                |                  |                  |
| Hyperpyrexia  |                |                  |                  |
| subjects affected / exposed   | 0 / 55 (0.00%) | 0 / 56 (0.00%)   | 0 / 59 (0.00%)   |
| occurrences causally related to treatment / all                     | 0 / 0          | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all                          | 0 / 0          | 0 / 0            | 0 / 0            |
| Respiratory, thoracic and mediastinal disorders                     |                |                  |                  |
| Idiopathic pulmonary fibrosis                                       |                |                  |                  |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 55 (0.00%) | 0 / 56 (0.00%) | 1 / 59 (1.69%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Interstitial lung disease                       |                |                |                |
| subjects affected / exposed                     | 0 / 55 (0.00%) | 0 / 56 (0.00%) | 1 / 59 (1.69%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 3          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Pleurisy  |                |                |                |
| subjects affected / exposed                     | 0 / 55 (0.00%) | 1 / 56 (1.79%) | 0 / 59 (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          |
| Pulmonary bulla                                 |                |                |                |
| subjects affected / exposed                     | 0 / 55 (0.00%) | 0 / 56 (0.00%) | 1 / 59 (1.69%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 2          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Pulmonary microemboli                           |                |                |                |
| subjects affected / exposed                     | 0 / 55 (0.00%) | 0 / 56 (0.00%) | 1 / 59 (1.69%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Psychiatric disorders                           |                |                |                |
| Schizophrenia                                   |                |                |                |
| subjects affected / exposed                     | 0 / 55 (0.00%) | 1 / 56 (1.79%) | 0 / 59 (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  |                |                |                |
| Joint dislocation                               |                |                |                |
| subjects affected / exposed                     | 0 / 55 (0.00%) | 0 / 56 (0.00%) | 1 / 59 (1.69%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Wrist fracture                                  |                |                |                |
| subjects affected / exposed                     | 0 / 55 (0.00%) | 1 / 56 (1.79%) | 0 / 59 (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          |

|   |                |                |                |
|---|----------------|----------------|----------------|
| Cardiac disorders                               |                |                |                |
| Acute coronary syndrome                         |                |                |                |
| subjects affected / exposed                     | 1 / 55 (1.82%) | 0 / 56 (0.00%) | 0 / 59 (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          |
| Nervous system disorders                        |                |                |                |
| Ischaemic stroke                                |                |                |                |
| subjects affected / exposed                     | 1 / 55 (1.82%) | 1 / 56 (1.79%) | 0 / 59 (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          |
| Blood and lymphatic system disorders            |                |                |                |
| Anaemia   |                |                |                |
| subjects affected / exposed                     | 1 / 55 (1.82%) | 1 / 56 (1.79%) | 0 / 59 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 1          | 0 / 0          |
| Autoimmune haemolytic anaemia                   |                |                |                |
| subjects affected / exposed                     | 0 / 55 (0.00%) | 1 / 56 (1.79%) | 0 / 59 (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          |
| Haemolytic anaemia                              |                |                |                |
| subjects affected / exposed                     | 0 / 55 (0.00%) | 0 / 56 (0.00%) | 1 / 59 (1.69%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Hypochromic anaemia                             |                |                |                |
| subjects affected / exposed                     | 0 / 55 (0.00%) | 1 / 56 (1.79%) | 0 / 59 (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          |
| Iron deficiency anaemia                         |                |                |                |
| subjects affected / exposed                     | 0 / 55 (0.00%) | 0 / 56 (0.00%) | 0 / 59 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Gastrointestinal disorders                      |                |                |                |
| Ascites   |                |                |                |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 55 (0.00%) | 1 / 56 (1.79%) | 0 / 59 (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          |
| Colitis   |                |                |                |
| subjects affected / exposed                     | 0 / 55 (0.00%) | 0 / 56 (0.00%) | 1 / 59 (1.69%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Colitis ulcerative                              |                |                |                |
| subjects affected / exposed                     | 3 / 55 (5.45%) | 1 / 56 (1.79%) | 2 / 59 (3.39%) |
| occurrences causally related to treatment / all | 0 / 3          | 0 / 1          | 0 / 2          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Inguinal hernia                                 |                |                |                |
| subjects affected / exposed                     | 0 / 55 (0.00%) | 1 / 56 (1.79%) | 0 / 59 (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          |
| Intestinal obstruction                          |                |                |                |
| subjects affected / exposed                     | 0 / 55 (0.00%) | 1 / 56 (1.79%) | 0 / 59 (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          |
| Umbilical hernia                                |                |                |                |
| subjects affected / exposed                     | 0 / 55 (0.00%) | 1 / 56 (1.79%) | 0 / 59 (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          |
| Hepatobiliary disorders                         |                |                |                |
| Hyperbilirubinaemia                             |                |                |                |
| subjects affected / exposed                     | 0 / 55 (0.00%) | 1 / 56 (1.79%) | 0 / 59 (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          |
| Jaundice  |                |                |                |
| subjects affected / exposed                     | 0 / 55 (0.00%) | 0 / 56 (0.00%) | 1 / 59 (1.69%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Renal and urinary disorders                     |                |                |                |

|   |                |                |                |
|---|----------------|----------------|----------------|
| Nephrolithiasis                                 |                |                |                |
| subjects affected / exposed                     | 0 / 55 (0.00%) | 1 / 56 (1.79%) | 0 / 59 (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          |
| Musculoskeletal and connective tissue disorders |                |                |                |
| Rheumatoid arthritis                            |                |                |                |
| subjects affected / exposed                     | 1 / 55 (1.82%) | 0 / 56 (0.00%) | 0 / 59 (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          |
| Spinal column stenosis                          |                |                |                |
| subjects affected / exposed                     | 0 / 55 (0.00%) | 1 / 56 (1.79%) | 0 / 59 (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                     |                |                |                |
| Erysipelas                                      |                |                |                |
| subjects affected / exposed                     | 0 / 55 (0.00%) | 1 / 56 (1.79%) | 0 / 59 (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          |
| Gastroenteritis viral                           |                |                |                |
| subjects affected / exposed                     | 0 / 55 (0.00%) | 1 / 56 (1.79%) | 0 / 59 (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          |
| Herpes zoster                                   |                |                |                |
| subjects affected / exposed                     | 0 / 55 (0.00%) | 0 / 56 (0.00%) | 0 / 59 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Pneumonia                                       |                |                |                |
| subjects affected / exposed                     | 0 / 55 (0.00%) | 1 / 56 (1.79%) | 0 / 59 (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          |
| Pneumonia pneumococcal                          |                |                |                |
| subjects affected / exposed                     | 0 / 55 (0.00%) | 1 / 56 (1.79%) | 0 / 59 (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          |



|   |                |                |                |
|---|----------------|----------------|----------------|
| Metabolism and nutrition disorders              |                |                |                |
| Dehydration                                     |                |                |                |
| subjects affected / exposed                     | 0 / 55 (0.00%) | 0 / 56 (0.00%) | 1 / 59 (1.69%) |
| 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 %

| <b>Non-serious adverse events</b>                     | Induction Period:<br>Placebo | Induction Period:<br>Ozanimod HCL 0.5<br>mg | Induction Period:<br>Ozanimod HCL 1 mg |
|---|------------------------------|---|--|
| Total subjects affected by non-serious adverse events |                              |   |  |
| subjects affected / exposed                           | 9 / 65 (13.85%)              | 8 / 65 (12.31%)                             | 8 / 67 (11.94%)                        |
| Investigations  |                              |   |  |
| Alanine aminotransferase increased                    |                              |   |  |
| subjects affected / exposed                           | 0 / 65 (0.00%)               | 0 / 65 (0.00%)                              | 2 / 67 (2.99%)                         |
| occurrences (all)                                     | 0                            | 0   | 2                                      |
| Gamma-glutamyltransferase increased                   |                              |   |  |
| subjects affected / exposed                           | 0 / 65 (0.00%)               | 0 / 65 (0.00%)                              | 1 / 67 (1.49%)                         |
| occurrences (all)                                     | 0                            | 0   | 1                                      |
| Lymphocyte count decreased                            |                              |   |  |
| subjects affected / exposed                           | 0 / 65 (0.00%)               | 0 / 65 (0.00%)                              | 0 / 67 (0.00%)                         |
| occurrences (all)                                     | 0                            | 0   | 0                                      |
| Vascular disorders                                    |                              |   |  |
| Hypertension  |                              |   |  |
| subjects affected / exposed                           | 0 / 65 (0.00%)               | 1 / 65 (1.54%)                              | 0 / 67 (0.00%)                         |
| occurrences (all)                                     | 0                            | 1   | 0                                      |
| Nervous system disorders                              |                              |   |  |
| Headache  |                              |   |  |
| subjects affected / exposed                           | 3 / 65 (4.62%)               | 0 / 65 (0.00%)                              | 2 / 67 (2.99%)                         |
| occurrences (all)                                     | 3                            | 0   | 2                                      |
| Blood and lymphatic system disorders                  |                              |   |  |
| Anaemia   |                              |   |  |
| subjects affected / exposed                           | 4 / 65 (6.15%)               | 4 / 65 (6.15%)                              | 1 / 67 (1.49%)                         |
| occurrences (all)                                     | 4                            | 4   | 1                                      |
| Gastrointestinal disorders                            |                              |   |  |
| Colitis ulcerative                                    |                              |   |  |

|  |                     |                     |                     |
|--|---------------------|---------------------|---------------------|
| subjects affected / exposed<br>occurrences (all)   | 1 / 65 (1.54%)<br>1 | 2 / 65 (3.08%)<br>2 | 0 / 67 (0.00%)<br>0 |
| Musculoskeletal and connective tissue disorders<br>Back pain<br>subjects affected / exposed<br>occurrences (all) | 1 / 65 (1.54%)<br>1 | 1 / 65 (1.54%)<br>1 | 1 / 67 (1.49%)<br>1 |
| Infections and infestations<br>Bronchitis<br>subjects affected / exposed<br>occurrences (all)                    | 0 / 65 (0.00%)<br>0 | 0 / 65 (0.00%)<br>0 | 1 / 67 (1.49%)<br>1 |
| Nasopharyngitis<br>subjects affected / exposed<br>occurrences (all)  | 0 / 65 (0.00%)<br>0 | 1 / 65 (1.54%)<br>2 | 0 / 67 (0.00%)<br>0 |
| Respiratory tract infection viral<br>subjects affected / exposed<br>occurrences (all)                            | 0 / 65 (0.00%)<br>0 | 0 / 65 (0.00%)<br>0 | 0 / 67 (0.00%)<br>0 |
| Upper respiratory tract infection<br>subjects affected / exposed<br>occurrences (all)                            | 2 / 65 (3.08%)<br>2 | 0 / 65 (0.00%)<br>0 | 1 / 67 (1.49%)<br>1 |

| <b>Non-serious adverse events</b>  | Maintenance Period:<br>Placebo | Maintenance Period:<br>Ozanimod HCL 0.5<br>mg | Maintenance Period:<br>Ozanimod HCL 1 mg |
|--|--------------------------------|---|--|
| Total subjects affected by non-serious<br>adverse events<br>subjects affected / exposed                  | 3 / 25 (12.00%)                | 2 / 36 (5.56%)                                | 2 / 42 (4.76%)                           |
| Investigations<br>Alanine aminotransferase increased<br>subjects affected / exposed<br>occurrences (all) | 0 / 25 (0.00%)<br>0            | 1 / 36 (2.78%)<br>1                           | 1 / 42 (2.38%)<br>1                      |
| Gamma-glutamyltransferase<br>increased<br>subjects affected / exposed<br>occurrences (all)               | 0 / 25 (0.00%)<br>0            | 0 / 36 (0.00%)<br>0                           | 0 / 42 (0.00%)<br>0                      |
| Lymphocyte count decreased<br>subjects affected / exposed<br>occurrences (all)                           | 0 / 25 (0.00%)<br>0            | 0 / 36 (0.00%)<br>0                           | 0 / 42 (0.00%)<br>0                      |
| Vascular disorders   |                                |   |  |

|  |  |  |   |
|--|--|--|---|
| Hypertension<br>subjects affected / exposed<br>occurrences (all)   | 0 / 25 (0.00%)<br>0  | 0 / 36 (0.00%)<br>0  | 0 / 42 (0.00%)<br>0   |
| Nervous system disorders<br>Headache<br>subjects affected / exposed<br>occurrences (all)   | 0 / 25 (0.00%)<br>0  | 0 / 36 (0.00%)<br>0  | 0 / 42 (0.00%)<br>0   |
| Blood and lymphatic system disorders<br>Anaemia<br>subjects affected / exposed<br>occurrences (all)  | 0 / 25 (0.00%)<br>0  | 0 / 36 (0.00%)<br>0  | 0 / 42 (0.00%)<br>0   |
| Gastrointestinal disorders<br>Colitis ulcerative<br>subjects affected / exposed<br>occurrences (all)   | 1 / 25 (4.00%)<br>1  | 0 / 36 (0.00%)<br>0  | 1 / 42 (2.38%)<br>1   |
| Musculoskeletal and connective tissue disorders<br>Back pain<br>subjects affected / exposed<br>occurrences (all)   | 0 / 25 (0.00%)<br>0  | 0 / 36 (0.00%)<br>0  | 0 / 42 (0.00%)<br>0   |
| Infections and infestations<br>Bronchitis<br>subjects affected / exposed<br>occurrences (all)<br><br>Nasopharyngitis<br>subjects affected / exposed<br>occurrences (all)<br><br>Respiratory tract infection viral<br>subjects affected / exposed<br>occurrences (all)<br><br>Upper respiratory tract infection<br>subjects affected / exposed<br>occurrences (all) | 1 / 25 (4.00%)<br>1<br><br>0 / 25 (0.00%)<br>0<br><br>0 / 25 (0.00%)<br>0<br><br>1 / 25 (4.00%)<br>1 | 0 / 36 (0.00%)<br>0<br><br>1 / 36 (2.78%)<br>1<br><br>0 / 36 (0.00%)<br>0<br><br>0 / 36 (0.00%)<br>0 | 0 / 42 (0.00%)<br>0<br><br>0 / 42 (0.00%)<br>0<br><br>0 / 42 (0.00%)<br>0 |

|   |  |                                       |                                       |
|---|--|---------------------------------------|---------------------------------------|
| <b>Non-serious adverse events</b>   | Open-Label<br>Treatment Period<br>(OLP):<br>Placebo/Ozanimod | OLP: Ozanimod 0.5<br>mg/Ozanimod 1 mg | OLP: Ozanimod<br>1mg/Ozanimod 1<br>mg |
| Total subjects affected by non-serious<br>adverse events<br>subjects affected / exposed | 19 / 55 (34.55%)   | 17 / 56 (30.36%)                      | 22 / 59 (37.29%)                      |

|   |                |                |                 |
|---|----------------|----------------|-----------------|
| Investigations                                  |                |                |                 |
| Alanine aminotransferase increased              |                |                |                 |
| subjects affected / exposed                     | 1 / 55 (1.82%) | 2 / 56 (3.57%) | 3 / 59 (5.08%)  |
| occurrences (all)                               | 3              | 2              | 4               |
| Gamma-glutamyltransferase increased             |                |                |                 |
| subjects affected / exposed                     | 1 / 55 (1.82%) | 3 / 56 (5.36%) | 5 / 59 (8.47%)  |
| occurrences (all)                               | 1              | 3              | 7               |
| Lymphocyte count decreased                      |                |                |                 |
| subjects affected / exposed                     | 0 / 55 (0.00%) | 3 / 56 (5.36%) | 3 / 59 (5.08%)  |
| occurrences (all)                               | 0              | 3              | 3               |
| Vascular disorders                              |                |                |                 |
| Hypertension                                    |                |                |                 |
| subjects affected / exposed                     | 2 / 55 (3.64%) | 1 / 56 (1.79%) | 7 / 59 (11.86%) |
| occurrences (all)                               | 2              | 1              | 8               |
| Nervous system disorders                        |                |                |                 |
| Headache  |                |                |                 |
| subjects affected / exposed                     | 3 / 55 (5.45%) | 1 / 56 (1.79%) | 3 / 59 (5.08%)  |
| occurrences (all)                               | 3              | 1              | 3               |
| Blood and lymphatic system disorders            |                |                |                 |
| Anaemia   |                |                |                 |
| subjects affected / exposed                     | 4 / 55 (7.27%) | 3 / 56 (5.36%) | 0 / 59 (0.00%)  |
| occurrences (all)                               | 9              | 5              | 0               |
| Gastrointestinal disorders                      |                |                |                 |
| Colitis ulcerative                              |                |                |                 |
| subjects affected / exposed                     | 4 / 55 (7.27%) | 0 / 56 (0.00%) | 0 / 59 (0.00%)  |
| occurrences (all)                               | 5              | 0              | 0               |
| Musculoskeletal and connective tissue disorders |                |                |                 |
| Back pain                                       |                |                |                 |
| subjects affected / exposed                     | 2 / 55 (3.64%) | 1 / 56 (1.79%) | 4 / 59 (6.78%)  |
| occurrences (all)                               | 2              | 1              | 4               |
| Infections and infestations                     |                |                |                 |
| Bronchitis                                      |                |                |                 |
| subjects affected / exposed                     | 3 / 55 (5.45%) | 1 / 56 (1.79%) | 0 / 59 (0.00%)  |
| occurrences (all)                               | 4              | 1              | 0               |
| Nasopharyngitis                                 |                |                |                 |
| subjects affected / exposed                     | 1 / 55 (1.82%) | 3 / 56 (5.36%) | 3 / 59 (5.08%)  |
| occurrences (all)                               | 1              | 3              | 4               |

|   |                     |                     |                     |
|---|---------------------|---------------------|---------------------|
| Respiratory tract infection viral<br>subjects affected / exposed<br>occurrences (all) | 3 / 55 (5.45%)<br>3 | 1 / 56 (1.79%)<br>1 | 0 / 59 (0.00%)<br>0 |
| Upper respiratory tract infection<br>subjects affected / exposed<br>occurrences (all) | 3 / 55 (5.45%)<br>4 | 2 / 56 (3.57%)<br>2 | 5 / 59 (8.47%)<br>5 |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date             | Amendment   |
|------------------|---|
| 19 October 2012  | <ul style="list-style-type: none"><li>• The limit on the proportion of patients that have previously received anti-TNF therapy anticipated to participate in the study has been increased from 35% to 50%.</li><li>• The examination of the patient's skin for lesions has been incorporated into the PE by the Investigator. If a skin lesion is identified the subject will be referred to a Dermatologist.</li><li>• PFT are no longer required at screening, Week 8 and 20 and will not be performed unless new pulmonary/respiratory signs and symptoms are noted. PFT will be done at End of Study/ET on all patients.</li><li>• All patients with clinically relevant pulmonary signs and symptom will be excluded from the study, unless it is found that the subject's FEV1 and FVC were both &gt; 70% of predicted value on pulmonary function testing during screening.</li><li>• DLCO (diffusing capacity of the lung for carbon monoxide) has been removed from the PFT requirements.</li><li>• OCT (Optical coherence tomography) will be required at Screening and at the End of Study/ET but an OCT at Week 8 has been removed.</li><li>• Vedolizumab has been added to the list of medications that require a 4 month wash out.</li><li>• Patients that were unresponsive to vedolizumab have been excluded from the study.</li><li>• The protocol has been modified to more clarify windows allowed during dose titration.</li><li>• The protocol has been modified to clarify the cardiac monitoring requirements and to clarify how the cardiac monitoring requirements will be modified once review of HR and Holter monitoring data from ongoing studies is complete and that review shows no notable HR or conduction abnormalities.</li></ul> |
| 08 November 2012 | <ul style="list-style-type: none"><li>• Increased the limit on the proportion of patients who had previously received anti-TNF therapy from 35% to 50%</li><li>• Incorporated skin examinations into the physical examination by the Investigator with referrals to dermatologists as needed</li><li>• Reduced the frequency of PFT and allowed for exceptions to DLCO testing</li><li>• Excluded patients with clinically relevant pulmonary signs and symptoms unless the patient's FEV1 and FVC were both &gt; 70% of predicted values at Screening</li><li>• Reduced frequency of OCT assessment</li><li>• Added vedolizumab to the list of medications requiring a 4-month washout and excluded patients who were unresponsive to vedolizumab</li><li>• Added WBC alert criteria and the corresponding actions that should be taken regarding stopping and restarting study drug</li></ul>   |
| 05 August 2013   | <ul style="list-style-type: none"><li>• Divided the Induction Period into a dose titration period lasting from 8 to 15 days and an assigned dose treatment period of 8 weeks. Changed the length of the induction period from 8 weeks to 9-10 weeks depending on the length of the titration period.</li><li>• Allowed patients who complete the Maintenance Period or who relapse during the Maintenance Period to participate in the Open-Label Period</li><li>• Extended the Open-Label Period until the last patient who enters the Open-Label Period completed 20 weeks in the Open-Label Period</li><li>• Allowed patients to participate who had past history of stable cardiac conditions, chronic hepatitis A or hepatitis E infection, or current well-controlled type 2 diabetes</li><li>• Excluded patients who had failed to respond to anti- integrin therapies</li><li>• Added an interim analysis to be completed after 50% of patients completed Week 8</li></ul>  |
| 03 February 2014 | <ul style="list-style-type: none"><li>• Increased the upper limit of the eligible age range from ≤ 65 years to ≤ 75 years</li><li>• Increased the allowed concomitant daily dose of prednisone from ≤ 20 mg to ≤ 30 mg</li><li>• Allowed patients who failed to respond to anti-integrin agents to participate in the trial</li><li>• Allow patients receiving azathioprine, 6-MP, or methotrexate at Screening to continue these medications until randomization</li><li>• Removed the interim analysis and defined the levels of significance for the final analyses</li><li>• Removed substrates and weak inhibitors of CYP3A4 from the list of prohibited concomitant medications</li><li>• Removed cardiac monitoring during dose escalation on Days 5 and 8 unless a patient had experienced cardiac safety issues on Day 1</li></ul>   |

|                  |   |
|------------------|---|
| 23 December 2014 | <ul style="list-style-type: none"> <li>• Increased the duration of the Open-Label Period to up to 6 years, or approximately December 2019, or until marketing approval</li> <li>• Added endoscopies and Mayo score calculation at 48- week intervals for patients who continue in the Open- Label Period past Week 8</li> </ul> |
|------------------|---|

Notes:

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## **Interruptions (globally)**

Were there any global interruptions to the trial? No

## **Limitations and caveats**

None reported