



Clinical trial results:

A Randomized, Double Blind, Multiple Dose Placebo Controlled Study to Evaluate the Safety, Tolerability, and Efficacy of AMG 181 in Subjects with Moderate to Severe Ulcerative Colitis

Summary

| | |
|--------------------------|--|
| EudraCT number | 2011-005251-13 |
| Trial protocol | GR DE DK GB CZ BE HU NL AT IT PL EE LV |
| Global end of trial date | 10 April 2018 |

Results information

| | |
|--------------------------------|---------------|
| Result version number | v1 (current) |
| This version publication date | 24 April 2019 |
| First version publication date | 24 April 2019 |

Trial information

Trial identification

| | |
|-----------------------|----------|
| Sponsor protocol code | 20110166 |
|-----------------------|----------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01694485 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Amgen Inc. |
| Sponsor organisation address | One Amgen Center Drive, Thousand Oaks, CA, United States, 91320 |
| Public contact | IHQ Medical Info-Clinical Trials, Amgen (EUROPE) GmbH, MedInfoInternational@amgen.com |
| Scientific contact | IHQ Medical Info-Clinical Trials, Amgen (EUROPE) GmbH, MedInfoInternational@amgen.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 | 10 April 2018 |
| Is this the analysis of the primary completion data? | No |

| | |
|----------------------------------|---------------|
| Global end of trial reached? | Yes |
| Global end of trial date | 10 April 2018 |
| Was the trial ended prematurely? | Yes |

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is to evaluate the effect of abrilumab on induction of remission in adults with moderate to severe ulcerative colitis after 8 weeks of treatment as assessed by a total Mayo Score ≤ 2 points, with no individual subscore > 1 point.

Protection of trial subjects:

This study was conducted in accordance with International Council for Harmonisation (ICH) Good Clinical Practice (GCP) and other applicable countries regulations/guidelines. The Independent Ethics Committees (IECs) or Institutional Review Boards (IRBs) involved at each center in this study reviewed and approved the study Protocol and the Informed Consent Form (ICF) before recruitment of subjects into the study and shipment of investigational product. Subjects provided their written informed consent at will, after adequate explanation of the aims, methods, anticipated benefits, and potential hazards of the study and before any protocol-specific screening procedures were conducted or any investigational product was administered.

Background therapy: -

Evidence for comparator: -

| | |
|---|------------------|
| Actual start date of recruitment | 16 November 2012 |
| Long term follow-up planned | Yes |
| Long term follow-up rationale | Safety |
| Long term follow-up duration | 24 Months |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|--------------------|
| Country: Number of subjects enrolled | Canada: 25 |
| Country: Number of subjects enrolled | United States: 17 |
| Country: Number of subjects enrolled | Australia: 18 |
| Country: Number of subjects enrolled | Austria: 2 |
| Country: Number of subjects enrolled | Belgium: 28 |
| Country: Number of subjects enrolled | Czech Republic: 16 |
| Country: Number of subjects enrolled | Denmark: 14 |
| Country: Number of subjects enrolled | Estonia: 4 |
| Country: Number of subjects enrolled | France: 32 |
| Country: Number of subjects enrolled | Germany: 9 |
| Country: Number of subjects enrolled | Greece: 2 |
| Country: Number of subjects enrolled | Hungary: 37 |
| Country: Number of subjects enrolled | Italy: 19 |
| Country: Number of subjects enrolled | Latvia: 5 |

| | |
|--------------------------------------|------------------------|
| Country: Number of subjects enrolled | Netherlands: 11 |
| Country: Number of subjects enrolled | Norway: 1 |
| Country: Number of subjects enrolled | Poland: 12 |
| Country: Number of subjects enrolled | Russian Federation: 32 |
| Country: Number of subjects enrolled | Switzerland: 41 |
| Country: Number of subjects enrolled | United Kingdom: 34 |
| Worldwide total number of subjects | 359 |
| EEA total number of subjects | 226 |

Notes:

| Subjects enrolled per age group | |
|---|-----|
| In utero | 0 |
| Preterm newborn - gestational age < 37 wk | 0 |
| Newborns (0-27 days) | 0 |
| Infants and toddlers (28 days-23 months) | 0 |
| Children (2-11 years) | 0 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 354 |
| From 65 to 84 years | 5 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at 92 centers located in North America, Europe, and Australia from 16 November 2012 to 11 May 2015. The study consisted of a 24-week double-blind treatment period, a 108-week open-label treatment period, and a safety follow-up period.

Pre-assignment

Screening details:

Participants were to be randomly assigned in a 2:1:2:2:2 ratio to 1 of 5 treatment groups. Due to a misalignment error, some participants were erroneously assigned to incorrect treatment resulting in a final randomization ratio different from that originally stipulated in the protocol.

Period 1

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

Arms

| | |
|------------------------------|------------------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Placebo/Abrilumab 210 mg Q3M |

Arm description:

Participants randomized to receive placebo by subcutaneous injection on day 1, week 2, week 4, and every 4 weeks thereafter until week 24. During the open-label period, participants received abrilumab 210 mg once every 3 months (Q3M) for 108 weeks.

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

Dosage and administration details:

Placebo matching to abrilumab administered by subcutaneous injection

| | |
|------------------|---|
| Arm title | Abrilumab 7 mg Q4W/Abrilumab 210 mg Q3M |
|------------------|---|

Arm description:

Participants randomized to receive 7 mg abrilumab by subcutaneous injection on day 1, week 2, week 4, and every 4 weeks (Q4W) thereafter until week 24. During the open-label period, participants received abrilumab 210 mg once every 3 months for 108 weeks.

| | |
|--|------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Abrilumab |
| Investigational medicinal product code | AMG 181 |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Administered by subcutaneous injection.

| | |
|------------------|--|
| Arm title | Abrilumab 21 mg Q4W/Abrilumab 210 mg Q3M |
|------------------|--|

Arm description:

Participants randomized to receive 21 mg abrilumab by subcutaneous injection on day 1, week 2, week 4, and every 4 weeks thereafter until week 24. During the open-label period, participants received abrilumab 210 mg once every 3 months for 108 weeks.

| | |
|--|------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Abrilumab |
| Investigational medicinal product code | AMG 181 |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Administered by subcutaneous injection.

| | |
|------------------|--|
| Arm title | Abrilumab 70 mg Q4W/Abrilumab 210 mg Q3M |
|------------------|--|

Arm description:

Participants randomized to receive 70 mg abrilumab by subcutaneous injection on day 1, week 2, week 4, and every 4 weeks thereafter until week 24. During the open-label period, participants received abrilumab 210 mg once every 3 months for 108 weeks.

| | |
|--|------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Abrilumab |
| Investigational medicinal product code | AMG 181 |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Administered by subcutaneous injection.

| | |
|------------------|---------------------------------------|
| Arm title | Abrilumab 210 mg/Abrilumab 210 mg Q3M |
|------------------|---------------------------------------|

Arm description:

Participants randomized to receive a single dose of 210 mg abrilumab by subcutaneous injection on day 1, followed by placebo at week 2, week 4, and every 4 weeks thereafter until week 24. During the open-label period, participants received abrilumab 210 mg once every 3 months for 108 weeks.

| | |
|--|------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Abrilumab |
| Investigational medicinal product code | AMG 181 |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Administered by subcutaneous injection.

| Number of subjects in period 1 | Placebo/Abrilumab 210 mg Q3M | Abrilumab 7 mg Q4W/Abrilumab 210 mg Q3M | Abrilumab 21 mg Q4W/Abrilumab 210 mg Q3M |
|--------------------------------|------------------------------|---|--|
| | | | |
| Started | 117 | 22 | 40 |
| Received Treatment | 116 | 21 | 40 |
| Completed Week 8 Assessment | 106 | 18 | 38 |
| Entered Open-label Period | 100 | 19 | 36 |
| Completed | 84 | 15 | 27 |
| Not completed | 33 | 7 | 13 |
| Adverse event, serious fatal | 1 | - | - |
| Consent withdrawn by subject | 20 | 6 | 7 |
| Sponsor Decision | 3 | - | - |

| | | | |
|-------------------|---|---|---|
| Lost to follow-up | 9 | 1 | 6 |
|-------------------|---|---|---|

| Number of subjects in period 1 | Abrilumab 70 mg Q4W/Abrilumab 210 mg Q3M | Abrilumab 210 mg/Abrilumab 210 mg Q3M |
|---------------------------------------|--|---------------------------------------|
| Started | 100 | 80 |
| Received Treatment | 98 | 79 |
| Completed Week 8 Assessment | 94 | 76 |
| Entered Open-label Period | 88 | 68 |
| Completed | 62 | 55 |
| Not completed | 38 | 25 |
| Adverse event, serious fatal | 1 | - |
| Consent withdrawn by subject | 25 | 18 |
| Sponsor Decision | 2 | - |
| Lost to follow-up | 10 | 7 |

Baseline characteristics

Reporting groups

| | |
|---|--|
| Reporting group title | Placebo/Abrilumab 210 mg Q3M |
| Reporting group description: Participants randomized to receive placebo by subcutaneous injection on day 1, week 2, week 4, and every 4 weeks thereafter until week 24. During the open-label period, participants received abrilumab 210 mg once every 3 months (Q3M) for 108 weeks. | |
| Reporting group title | Abrilumab 7 mg Q4W/Abrilumab 210 mg Q3M |
| Reporting group description: Participants randomized to receive 7 mg abrilumab by subcutaneous injection on day 1, week 2, week 4, and every 4 weeks (Q4W) thereafter until week 24. During the open-label period, participants received abrilumab 210 mg once every 3 months for 108 weeks. | |
| Reporting group title | Abrilumab 21 mg Q4W/Abrilumab 210 mg Q3M |
| Reporting group description: Participants randomized to receive 21 mg abrilumab by subcutaneous injection on day 1, week 2, week 4, and every 4 weeks thereafter until week 24. During the open-label period, participants received abrilumab 210 mg once every 3 months for 108 weeks. | |
| Reporting group title | Abrilumab 70 mg Q4W/Abrilumab 210 mg Q3M |
| Reporting group description: Participants randomized to receive 70 mg abrilumab by subcutaneous injection on day 1, week 2, week 4, and every 4 weeks thereafter until week 24. During the open-label period, participants received abrilumab 210 mg once every 3 months for 108 weeks. | |
| Reporting group title | Abrilumab 210 mg/Abrilumab 210 mg Q3M |
| Reporting group description: Participants randomized to receive a single dose of 210 mg abrilumab by subcutaneous injection on day 1, followed by placebo at week 2, week 4, and every 4 weeks thereafter until week 24. During the open-label period, participants received abrilumab 210 mg once every 3 months for 108 weeks. | |

| Reporting group values | Placebo/Abrilumab 210 mg Q3M | Abrilumab 7 mg Q4W/Abrilumab 210 mg Q3M | Abrilumab 21 mg Q4W/Abrilumab 210 mg Q3M |
|---|------------------------------|---|--|
| Number of subjects | 117 | 22 | 40 |
| Age, Customized Units: Subjects | | | |
| 18 – 64 years | 113 | 22 | 40 |
| ≥ 65 years | 4 | 0 | 0 |
| Age Continuous Units: years | | | |
| arithmetic mean | 41.0 | 42.0 | 38.3 |
| standard deviation | ± 13.3 | ± 12.4 | ± 11.6 |
| Sex: Female, Male Units: Subjects | | | |
| Female | 36 | 8 | 12 |
| Male | 81 | 14 | 28 |
| Race/Ethnicity, Customized Units: Subjects | | | |
| Asian | 5 | 2 | 1 |
| White | 109 | 20 | 39 |
| Other | 3 | 0 | 0 |
| Ethnicity (NIH/OMB) Units: Subjects | | | |
| Hispanic or Latino | 4 | 0 | 2 |

| | | | |
|---|--------|--------|--------|
| Not Hispanic or Latino | 113 | 22 | 38 |
| Unknown or Not Reported | 0 | 0 | 0 |
| Any Prior Anti-Tumor Necrosis Factor (TNF) Use Units: Subjects | | | |
| Yes | 69 | 6 | 10 |
| No | 48 | 16 | 30 |
| Enrollment Prior to Protocol Amendment 3 Units: Subjects | | | |
| Yes | 76 | 0 | 0 |
| No | 41 | 22 | 40 |
| Duration of Ulcerative Colitis Units: years | | | |
| arithmetic mean | 7.83 | 9.07 | 7.05 |
| standard deviation | ± 5.58 | ± 6.57 | ± 5.39 |
| Total Mayo Score Units: years | | | |
| arithmetic mean | 8.9 | 8.1 | 8.6 |
| standard deviation | ± 1.5 | ± 1.4 | ± 1.7 |

| Reporting group values | Abrilumab 70 mg Q4W/Abrilumab 210 mg Q3M | Abrilumab 210 mg/Abrilumab 210 mg Q3M | Total |
|---|--|---------------------------------------|-------|
| Number of subjects | 100 | 80 | 359 |
| Age, Customized Units: Subjects | | | |
| 18 – 64 years | 99 | 80 | 354 |
| ≥ 65 years | 1 | 0 | 5 |
| Age Continuous Units: years | | | |
| arithmetic mean | 39.3 | 39.8 | - |
| standard deviation | ± 12.2 | ± 12.0 | |
| Sex: Female, Male Units: Subjects | | | |
| Female | 32 | 32 | 120 |
| Male | 68 | 48 | 239 |
| Race/Ethnicity, Customized Units: Subjects | | | |
| Asian | 7 | 1 | 16 |
| White | 89 | 78 | 335 |
| Other | 4 | 1 | 8 |
| Ethnicity (NIH/OMB) Units: Subjects | | | |
| Hispanic or Latino | 0 | 3 | 9 |
| Not Hispanic or Latino | 100 | 77 | 350 |
| Unknown or Not Reported | 0 | 0 | 0 |
| Any Prior Anti-Tumor Necrosis Factor (TNF) Use Units: Subjects | | | |
| Yes | 56 | 39 | 180 |
| No | 44 | 41 | 179 |
| Enrollment Prior to Protocol Amendment | | | |

| | | | |
|--------------------------------|--------|--------|-----|
| 3 | | | |
| Units: Subjects | | | |
| Yes | 58 | 38 | 172 |
| No | 42 | 42 | 187 |
| Duration of Ulcerative Colitis | | | |
| Units: years | | | |
| arithmetic mean | 9.39 | 9.44 | |
| standard deviation | ± 7.25 | ± 7.88 | - |
| Total Mayo Score | | | |
| Units: years | | | |
| arithmetic mean | 9.0 | 9.1 | |
| standard deviation | ± 1.5 | ± 1.4 | - |

End points

End points reporting groups

| | |
|---|--|
| Reporting group title | Placebo/Abrilumab 210 mg Q3M |
| Reporting group description: Participants randomized to receive placebo by subcutaneous injection on day 1, week 2, week 4, and every 4 weeks thereafter until week 24. During the open-label period, participants received abrilumab 210 mg once every 3 months (Q3M) for 108 weeks. | |
| Reporting group title | Abrilumab 7 mg Q4W/Abrilumab 210 mg Q3M |
| Reporting group description: Participants randomized to receive 7 mg abrilumab by subcutaneous injection on day 1, week 2, week 4, and every 4 weeks (Q4W) thereafter until week 24. During the open-label period, participants received abrilumab 210 mg once every 3 months for 108 weeks. | |
| Reporting group title | Abrilumab 21 mg Q4W/Abrilumab 210 mg Q3M |
| Reporting group description: Participants randomized to receive 21 mg abrilumab by subcutaneous injection on day 1, week 2, week 4, and every 4 weeks thereafter until week 24. During the open-label period, participants received abrilumab 210 mg once every 3 months for 108 weeks. | |
| Reporting group title | Abrilumab 70 mg Q4W/Abrilumab 210 mg Q3M |
| Reporting group description: Participants randomized to receive 70 mg abrilumab by subcutaneous injection on day 1, week 2, week 4, and every 4 weeks thereafter until week 24. During the open-label period, participants received abrilumab 210 mg once every 3 months for 108 weeks. | |
| Reporting group title | Abrilumab 210 mg/Abrilumab 210 mg Q3M |
| Reporting group description: Participants randomized to receive a single dose of 210 mg abrilumab by subcutaneous injection on day 1, followed by placebo at week 2, week 4, and every 4 weeks thereafter until week 24. During the open-label period, participants received abrilumab 210 mg once every 3 months for 108 weeks. | |

Primary: Percentage of Participants with Remission at Week 8

| | |
|--|---|
| End point title | Percentage of Participants with Remission at Week 8 |
| End point description: Remission was defined as a total Mayo Score ≤ 2 points, with no individual subscore > 1 point. The Mayo Score is a composite index of four items (stool frequency, rectal bleeding, rectosigmoidoscopy findings, and physician's global assessment), each graded semi-quantitatively on a score 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, ranging from 0 to 12 points. Higher scores represent more severe disease. The remission rate was calculated based on observed data (unadjusted remission rate) and also after applying a logistic regression model including the factors of treatment group, stratification factors (prior anti-TNF use and pre- versus post-Protocol Amendment 3) and baseline total Mayo Score (adjusted remission rate). The full analysis set includes randomized participants who received at least 1 dose of study drug. Remission rates were calculated using non-responder imputation. | |
| End point type | Primary |
| End point timeframe: Week 8 | |

| End point values | Placebo/Abrilumab 210 mg Q3M | Abrilumab 7 mg Q4W/Abrilumab 210 mg Q3M | Abrilumab 21 mg Q4W/Abrilumab 210 mg Q3M | Abrilumab 70 mg Q4W/Abrilumab 210 mg Q3M |
|-----------------------------------|------------------------------|---|--|--|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 116 | 21 | 40 | 98 |
| Units: percentage of participants | | | | |
| number (not applicable) | | | | |
| Unadjusted remission rate | 4.3 | 0.0 | 2.5 | 13.3 |
| Adjusted remission rate | 4.4 | 1.6 | 2.9 | 13.5 |

| End point values | Abrilumab 210 mg/Abrilumab 210 mg Q3M | | | |
|-----------------------------------|---------------------------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 79 | | | |
| Units: percentage of participants | | | | |
| number (not applicable) | | | | |
| Unadjusted remission rate | 12.7 | | | |
| Adjusted remission rate | 13.4 | | | |

Statistical analyses

| | |
|--|---|
| Statistical analysis title | Comparison of Abrilumab vs Placebo |
| Statistical analysis description: | |
| Comparisons between treatment groups were made using remission rates estimated from a logistic regression model adjusted for baseline total Mayo Score and stratification factors (prior vs no prior TNF antagonist use and enrollment pre- vs post-protocol amendment). | |
| Comparison groups | Placebo/Abrilumab 210 mg Q3M v Abrilumab 70 mg Q4W/Abrilumab 210 mg Q3M |
| Number of subjects included in analysis | 214 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[1] |
| P-value | = 0.021 ^[2] |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 3.35 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | 1.41 |
| upper limit | 7.95 |

Notes:

- [1] - The study was powered for formal statistical testing of the abrilumab 70 mg and 210 mg groups. To account for multiplicity of statistical testing, primary and key secondary end points for the 2 highest doses of abrilumab (70 and 210 mg) were tested at the end of the 8-week induction period under a sequential framework at a 2-sided significance level of 0.10 using the Bonferroni-based chain procedure.
- [2] - Adjusted for baseline total Mayo Score and stratification factors.

| | |
|-----------------------------------|-------------------------------|
| Statistical analysis title | Difference in Remission Rates |
|-----------------------------------|-------------------------------|

Statistical analysis description:

The difference in remission rates, estimated from a logistic regression model adjusted for baseline total Mayo Score and stratification factors (prior vs no prior TNF antagonist use and enrollment pre- vs post-protocol amendment).

| | |
|---|---|
| Comparison groups | Placebo/Abrilumab 210 mg Q3M v Abrilumab 70 mg Q4W/Abrilumab 210 mg Q3M |
| Number of subjects included in analysis | 214 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| Parameter estimate | Difference in Adjusted Remission Rates |
| Point estimate | 9 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | 1.6 |
| upper limit | 14.6 |

Statistical analysis title

Comparison of Abrilumab vs Placebo

Statistical analysis description:

Comparisons between treatment groups were made using remission rates from a logistic regression model adjusted for baseline total Mayo Score and stratification factors (prior vs no prior TNF antagonist use and enrollment pre- vs post-protocol amendment).

| | |
|---|--|
| Comparison groups | Placebo/Abrilumab 210 mg Q3M v Abrilumab 210 mg/Abrilumab 210 mg Q3M |
| Number of subjects included in analysis | 195 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[3] |
| P-value | = 0.03 ^[4] |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 3.33 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | 1.34 |
| upper limit | 8.26 |

Notes:

[3] - The study was powered for formal statistical testing of the abrilumab 70 mg and 210 mg groups. To account for multiplicity of statistical testing, primary and key secondary end points for the 2 highest doses of abrilumab (70 and 210 mg) were tested at the end of the 8-week induction period under a sequential framework at a 2-sided significance level of 0.10 using the Bonferroni-based chain procedure.

[4] - Adjusted for baseline total Mayo Score and stratification factors

Statistical analysis title

Difference in Remission Rates

Statistical analysis description:

The difference in remission rates, estimated from a logistic regression model adjusted for baseline total Mayo Score and stratification factors (prior vs no prior TNF antagonist use and enrollment pre- vs post-protocol amendment).

| | |
|-------------------|--|
| Comparison groups | Placebo/Abrilumab 210 mg Q3M v Abrilumab 210 mg/Abrilumab 210 mg Q3M |
|-------------------|--|

| | |
|---|--|
| Number of subjects included in analysis | 195 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| Parameter estimate | Difference in Adjusted Remission Rates |
| Point estimate | 8.9 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | 0.8 |
| upper limit | 14.9 |

| | |
|-----------------------------------|------------------------------------|
| Statistical analysis title | Comparison of Abrilumab vs Placebo |
|-----------------------------------|------------------------------------|

Statistical analysis description:

Comparisons between treatment groups were made using remission rates from a logistic regression model adjusted for baseline total Mayo Score and stratification factors (prior vs no prior TNF antagonist use and enrollment pre- vs post-protocol amendment).

| | |
|---|---|
| Comparison groups | Placebo/Abrilumab 210 mg Q3M v Abrilumab 21 mg Q4W/Abrilumab 210 mg Q3M |
| Number of subjects included in analysis | 156 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[5] |
| P-value | = 0.64 ^[6] |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 0.64 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | 0.13 |
| upper limit | 3.17 |

Notes:

[5] - Comparisons of abrilumab 21 mg with placebo were not included in the hypothesis testing procedure and were not adjusted for multiplicity.

[6] - Adjusted for baseline total Mayo Score and stratification factors

| | |
|-----------------------------------|-------------------------------|
| Statistical analysis title | Difference in Remission Rates |
|-----------------------------------|-------------------------------|

Statistical analysis description:

The difference in remission rates estimated from a logistic regression model adjusted for baseline total Mayo Score and stratification factors (prior vs no prior TNF antagonist use and enrollment pre- vs post-protocol amendment).

| | |
|---|---|
| Comparison groups | Placebo/Abrilumab 210 mg Q3M v Abrilumab 21 mg Q4W/Abrilumab 210 mg Q3M |
| Number of subjects included in analysis | 156 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[7] |
| Parameter estimate | Difference in Adjusted Remission Rates |
| Point estimate | -1.6 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | -5.2 |
| upper limit | 5.5 |

Notes:

[7] - Analysis was not part of the formal testing.

| | |
|-----------------------------------|------------------------------------|
| Statistical analysis title | Comparison of Abrilumab vs Placebo |
|-----------------------------------|------------------------------------|

Statistical analysis description:

Comparisons between treatment groups were made using remission rates from a logistic regression model adjusted for baseline total Mayo Score and stratification factors (prior vs no prior TNF antagonist use and enrollment pre- vs post-protocol amendment).

| | |
|---|--|
| Comparison groups | Placebo/Abrilumab 210 mg Q3M v Abrilumab 7 mg Q4W/Abrilumab 210 mg Q3M |
| Number of subjects included in analysis | 137 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[8] |
| P-value | = 0.49 ^[9] |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 0.34 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | 0.03 |
| upper limit | 4.33 |

Notes:

[8] - Comparisons of abrilumab 7 mg with placebo were not included in the hypothesis testing procedure and were not adjusted for multiplicity.

[9] - Adjusted for baseline total Mayo Score and stratification factors

| | |
|-----------------------------------|-------------------------------|
| Statistical analysis title | Difference in Remission Rates |
|-----------------------------------|-------------------------------|

Statistical analysis description:

The difference in remission rates estimated from a logistic regression model adjusted for baseline total Mayo Score and stratification factors (prior vs no prior TNF antagonist use and enrollment pre- vs post-protocol amendment).

| | |
|---|--|
| Comparison groups | Placebo/Abrilumab 210 mg Q3M v Abrilumab 7 mg Q4W/Abrilumab 210 mg Q3M |
| Number of subjects included in analysis | 137 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[10] |
| Parameter estimate | Difference in Adjusted Remission Rates |
| Point estimate | -2.9 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | -5.5 |
| upper limit | 5.4 |

Notes:

[10] - Analysis was not part of the formal testing.

Secondary: Percentage of Participants with Response at Week 8

| | |
|--|--|
| End point title | Percentage of Participants with Response at Week 8 |
| End point description: | |
| Response was defined by a decrease from baseline in the total Mayo Score of ≥ 3 points and $\geq 30\%$, with an accompanying decrease in the rectal bleeding subscore ≥ 1 point or an absolute rectal bleeding subscore = 0 or 1. The Mayo Score is a composite index of four items (stool frequency, rectal bleeding, rectosigmoidoscopy findings, and physician's global assessment); the total Mayo score ranges from 0 to 12 points, with higher scores representing more severe disease. The response rate was calculated based on observed data (unadjusted response rate) and also after applying a logistic regression model including the factors of treatment group, stratification factors (prior anti-TNF use and pre- versus post-Protocol Amendment 3) and baseline total Mayo Score (adjusted response rate). The full analysis set includes all randomized participants who received at least 1 dose of study drug. Both unadjusted and adjusted response rates were calculated using non-responder imputation. | |
| End point type | Secondary |
| End point timeframe: | |
| Baseline and week 8 | |

| End point values | Placebo/Abrilumab 210 mg Q3M | Abrilumab 7 mg Q4W/Abrilumab 210 mg Q3M | Abrilumab 21 mg Q4W/Abrilumab 210 mg Q3M | Abrilumab 70 mg Q4W/Abrilumab 210 mg Q3M |
|-----------------------------------|------------------------------|---|--|--|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 116 | 21 | 40 | 98 |
| Units: percentage of participants | | | | |
| number (not applicable) | | | | |
| Unadjusted response rate | 25.9 | 14.3 | 50.0 | 49.0 |
| Adjusted response rate | 26.0 | 12.3 | 47.2 | 49.4 |

| End point values | Abrilumab 210 mg/Abrilumab 210 mg Q3M | | | |
|-----------------------------------|---------------------------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 79 | | | |
| Units: percentage of participants | | | | |
| number (not applicable) | | | | |
| Unadjusted response rate | 46.8 | | | |
| Adjusted response rate | 47.4 | | | |

Statistical analyses

| | |
|---|---|
| Statistical analysis title | Comparison of Abrilumab vs Placebo |
| Statistical analysis description: | |
| Comparisons between treatment groups were made using response rates estimated from a logistic regression model adjusted for baseline total Mayo Score and stratification factors (prior vs no prior TNF antagonist use and enrollment pre- vs post-protocol amendment). | |
| Comparison groups | Placebo/Abrilumab 210 mg Q3M v Abrilumab 70 mg Q4W/Abrilumab 210 mg Q3M |

| | |
|---|-----------------------------|
| Number of subjects included in analysis | 214 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[11] |
| P-value | < 0.001 ^[12] |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 2.78 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | 1.71 |
| upper limit | 4.52 |

Notes:

[11] - If both comparisons of the primary endpoint reached statistical significance at 0.10, results from the 2 key secondary endpoints (response and mucosal healing at week 8) were to be sequentially (70 mg vs placebo then 210 mg vs placebo) tested at significance level of 0.05 independently of each other, according to the Bonferroni-based chain procedure.

[12] - Adjusted for baseline total Mayo Score and stratification factors.

| | |
|-----------------------------------|------------------------------|
| Statistical analysis title | Difference in Response Rates |
|-----------------------------------|------------------------------|

Statistical analysis description:

The difference in adjusted response rates, estimated from a logistic regression model adjusted for baseline total Mayo Score and stratification factors (prior vs no prior TNF antagonist use and enrollment pre- vs post-protocol amendment).

| | |
|---|---|
| Comparison groups | Placebo/Abrilumab 210 mg Q3M v Abrilumab 70 mg Q4W/Abrilumab 210 mg Q3M |
| Number of subjects included in analysis | 214 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| Parameter estimate | Difference in Adjusted Response Rates |
| Point estimate | 23.4 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | 11.8 |
| upper limit | 33.2 |

| | |
|-----------------------------------|------------------------------------|
| Statistical analysis title | Comparison on Abrilumab vs Placebo |
|-----------------------------------|------------------------------------|

Statistical analysis description:

Comparisons between treatment groups were made using response rates from a logistic regression model adjusted for baseline total Mayo Score and stratification factors (prior vs no prior TNF antagonist use and enrollment pre- vs post-protocol amendment).

| | |
|---|--|
| Comparison groups | Placebo/Abrilumab 210 mg Q3M v Abrilumab 210 mg/Abrilumab 210 mg Q3M |
| Number of subjects included in analysis | 195 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[13] |
| P-value | = 0.003 ^[14] |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 2.57 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | 1.53 |
| upper limit | 4.31 |

Notes:

[13] - If both comparisons of the primary endpoint reached statistical significance at 0.10, results from the 2 key secondary endpoints (response and mucosal healing at week 8) were to be sequentially (70 mg vs placebo then 210 mg vs placebo) tested at significance level of 0.05 independently of each other, according to the Bonferroni-based chain procedure.

[14] - Adjusted for baseline total Mayo Score and stratification factors.

| | |
|-----------------------------------|------------------------------|
| Statistical analysis title | Difference in Response rates |
|-----------------------------------|------------------------------|

Statistical analysis description:

The difference in adjusted response rates, estimated from a logistic regression model adjusted for baseline total Mayo Score and stratification factors (prior vs no prior TNF antagonist use and enrollment pre- vs post-protocol amendment).

| | |
|---|--|
| Comparison groups | Placebo/Abrilumab 210 mg Q3M v Abrilumab 210 mg/Abrilumab 210 mg Q3M |
| Number of subjects included in analysis | 195 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| Parameter estimate | Difference in Adjusted Response Rates |
| Point estimate | 21.4 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | 9 |
| upper limit | 31.8 |

| | |
|-----------------------------------|------------------------------------|
| Statistical analysis title | Comparison of Abrilumab vs Placebo |
|-----------------------------------|------------------------------------|

Statistical analysis description:

Comparisons between treatment groups were made using response rates from a logistic regression model adjusted for baseline total Mayo Score and stratification factors (prior vs no prior TNF antagonist use and enrollment pre- vs post-protocol amendment).

| | |
|---|---|
| Comparison groups | Placebo/Abrilumab 210 mg Q3M v Abrilumab 21 mg Q4W/Abrilumab 210 mg Q3M |
| Number of subjects included in analysis | 156 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[15] |
| P-value | = 0.024 ^[16] |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 2.54 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | 1.29 |
| upper limit | 5.02 |

Notes:

[15] - Comparisons of abrilumab 21 mg with placebo were not included in the hypothesis testing procedure and were not adjusted for multiplicity.

[16] - Adjusted for baseline total Mayo Score and stratification factors.

| | |
|---|---|
| Statistical analysis title | Difference in Response rates |
| Statistical analysis description: The difference in adjusted response rates, estimated from a logistic regression model adjusted for baseline total Mayo Score and stratification factors (prior vs no prior TNF antagonist use and enrollment pre- vs post-protocol amendment). | |
| Comparison groups | Placebo/Abrilumab 210 mg Q3M v Abrilumab 21 mg Q4W/Abrilumab 210 mg Q3M |
| Number of subjects included in analysis | 156 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[17] |
| Parameter estimate | Difference in Adjusted Response Rates |
| Point estimate | 21.2 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | 4.9 |
| upper limit | 34.1 |

Notes:

[17] - Analysis was not part of the formal testing.

| | |
|--|--|
| Statistical analysis title | Comparison of Abrilumab vs Placebo |
| Statistical analysis description: Comparisons between treatment groups were made using response rates from a logistic regression model adjusted for baseline total Mayo Score and stratification factors (prior vs no prior TNF antagonist use and enrollment pre- vs post-protocol amendment). | |
| Comparison groups | Placebo/Abrilumab 210 mg Q3M v Abrilumab 7 mg Q4W/Abrilumab 210 mg Q3M |
| Number of subjects included in analysis | 137 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[18] |
| P-value | = 0.18 ^[19] |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 0.4 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | 0.13 |
| upper limit | 1.22 |

Notes:

[18] - Comparisons of abrilumab 7 mg with placebo were not included in the hypothesis testing procedure and were not adjusted for multiplicity.

[19] - Adjusted for baseline total Mayo Score and stratification factors.

| | |
|---|--|
| Statistical analysis title | Difference in Response Rates |
| Statistical analysis description: The difference in adjusted response rates, estimated from a logistic regression model adjusted for baseline total Mayo Score and stratification factors (prior vs no prior TNF antagonist use and enrollment pre- vs post-protocol amendment). | |
| Comparison groups | Placebo/Abrilumab 210 mg Q3M v Abrilumab 7 mg Q4W/Abrilumab 210 mg Q3M |

| | |
|---|---------------------------------------|
| Number of subjects included in analysis | 137 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[20] |
| Parameter estimate | Difference in Adjusted Response Rates |
| Point estimate | -13.7 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | -24.4 |
| upper limit | 2.7 |

Notes:

[20] - Analysis was not part of the formal testing.

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 was defined using the rectosigmoidoscopy subscore of Mayo assessment as absolute subscore for rectosigmoidoscopy of 0 or 1. Flexible rectosigmoidoscopy was performed as part of the Mayo assessment, graded semi-quantitatively on a scale of 0 to 3 where 0 represents normal and higher score represents more severe disease status. The healing rate (percentage of participants with mucosal healing) was calculated based on observed data (unadjusted healing rate) and also after applying a logistic regression model including the factors of treatment group, stratification factors (prior anti-TNF use and pre- versus post-Protocol Amendment 3) and baseline rectosigmoidoscopy score (adjusted healing rate). The full analysis set includes all randomized participants who received at least 1 dose of study drug. Both unadjusted and adjusted healing rates were calculated using non-responder imputation.

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

End point timeframe:

Baseline and week 8

| End point values | Placebo/Abrilumab 210 mg Q3M | Abrilumab 7 mg Q4W/Abrilumab 210 mg Q3M | Abrilumab 21 mg Q4W/Abrilumab 210 mg Q3M | Abrilumab 70 mg Q4W/Abrilumab 210 mg Q3M |
|---|------------------------------|---|--|--|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 116 | 21 | 40 | 98 |
| Units: percentage of participants number (not applicable) | | | | |
| Unadjusted healing rate | 21.6 | 14.3 | 15.0 | 32.7 |
| Adjusted healing rate | 16.8 | 12.2 | 13.9 | 32.2 |

| End point values | Abrilumab 210 mg/Abrilumab 210 mg Q3M | | | |
|---|---------------------------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 79 | | | |
| Units: percentage of participants number (not applicable) | | | | |
| Unadjusted healing rate | 29.1 | | | |

| | | | | |
|-----------------------|------|--|--|--|
| Adjusted healing rate | 29.8 | | | |
|-----------------------|------|--|--|--|

Statistical analyses

| | |
|--|---|
| Statistical analysis title | Comparison of Abrilumab vs Placebo |
| Statistical analysis description: | |
| Comparisons between treatment groups were made using healing rates estimated from a logistic regression model adjusted for baseline rectosigmoidoscopy score and stratification factors (prior vs no prior TNF antagonist use and enrollment pre- vs post-protocol amendment). | |
| Comparison groups | Placebo/Abrilumab 210 mg Q3M v Abrilumab 70 mg Q4W/Abrilumab 210 mg Q3M |
| Number of subjects included in analysis | 214 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[21] |
| P-value | = 0.011 ^[22] |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 2.34 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | 1.35 |
| upper limit | 4.07 |

Notes:

[21] - If both comparisons of the primary endpoint reached statistical significance at 0.10, results from the 2 key secondary endpoints (response and mucosal healing at week 8) were to be sequentially (70 mg vs placebo then 210 mg vs placebo) tested at significance level of 0.05 independently of each other, according to the Bonferroni-based chain procedure.

[22] - Adjusted for baseline rectosigmoidoscopy score and stratification factors.

| | |
|---|---|
| Statistical analysis title | Difference in Mucosal Healing Rates |
| Statistical analysis description: | |
| The difference in adjusted healing rates, estimated from a logistic regression model adjusted for baseline rectosigmoidoscopy score and stratification factors (prior vs no prior TNF antagonist use and enrollment pre- vs post-protocol amendment). | |
| Comparison groups | Placebo/Abrilumab 210 mg Q3M v Abrilumab 70 mg Q4W/Abrilumab 210 mg Q3M |
| Number of subjects included in analysis | 214 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| Parameter estimate | Difference in Adjusted Healing Rates |
| Point estimate | 15.3 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | 4.8 |
| upper limit | 24 |

| | |
|--|--|
| Statistical analysis title | Comparison of Abrilumab vs Placebo |
| Statistical analysis description: | |
| Comparisons between treatment groups were made using healing rates from a logistic regression model adjusted for baseline rectosigmoidoscopy score and stratification factors (prior vs no prior TNF antagonist use and enrollment pre- vs post-protocol amendment). | |
| Comparison groups | Placebo/Abrilumab 210 mg Q3M v Abrilumab 210 mg/Abrilumab 210 mg Q3M |
| Number of subjects included in analysis | 195 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[23] |
| P-value | = 0.041 ^[24] |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 2.1 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | 1.15 |
| upper limit | 3.82 |

Notes:

[23] - If both comparisons of the primary endpoint reached statistical significance at 0.10, results from the 2 key secondary endpoints (response and mucosal healing at week 8) were to be sequentially (70 mg vs placebo then 210 mg vs placebo) tested at significance level of 0.05 independently of each other, according to the Bonferroni-based chain procedure.

[24] - Adjusted for baseline rectosigmoidoscopy score and stratification factors.

| | |
|---|--|
| Statistical analysis title | Difference in Mucosal Healing Rates |
| Statistical analysis description: | |
| The difference in adjusted healing rates, estimated from a logistic regression model adjusted for baseline rectosigmoidoscopy score and stratification factors (prior vs no prior TNF antagonist use and enrollment pre- vs post-protocol amendment). | |
| Comparison groups | Placebo/Abrilumab 210 mg Q3M v Abrilumab 210 mg/Abrilumab 210 mg Q3M |
| Number of subjects included in analysis | 195 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| Parameter estimate | Difference in Adjusted Healing Rates |
| Point estimate | 13 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | 1.7 |
| upper limit | 22.1 |

| | |
|--|---|
| Statistical analysis title | Comparison of Abrilumab vs Placebo |
| Statistical analysis description: | |
| Comparisons between treatment groups were made using healing rates from a logistic regression model adjusted for baseline rectosigmoidoscopy score and stratification factors (prior vs no prior TNF antagonist use and enrollment pre- vs post-protocol amendment). | |
| Comparison groups | Placebo/Abrilumab 210 mg Q3M v Abrilumab 21 mg Q4W/Abrilumab 210 mg Q3M |

| | |
|---|-----------------------------|
| Number of subjects included in analysis | 156 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[25] |
| P-value | = 0.68 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 0.8 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | 0.32 |
| upper limit | 1.97 |

Notes:

[25] - Comparisons of abrilumab 21 mg with placebo were not included in the hypothesis testing procedure and were not adjusted for multiplicity.

| | |
|-----------------------------------|-------------------------------------|
| Statistical analysis title | Difference in Mucosal Healing Rates |
|-----------------------------------|-------------------------------------|

Statistical analysis description:

The difference in adjusted healing rates, estimated from a logistic regression model adjusted for baseline rectosigmoidoscopy score and stratification factors (prior vs no prior TNF antagonist use and enrollment pre- vs post-protocol amendment).

| | |
|---|---|
| Comparison groups | Placebo/Abrilumab 210 mg Q3M v Abrilumab 21 mg Q4W/Abrilumab 210 mg Q3M |
| Number of subjects included in analysis | 156 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[26] |
| Parameter estimate | Difference in Adjusted Healing Rates |
| Point estimate | -3 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | -11.9 |
| upper limit | 9.4 |

Notes:

[26] - Analysis was not part of the formal testing.

| | |
|-----------------------------------|------------------------------------|
| Statistical analysis title | Comparison of Abrilumab vs Placebo |
|-----------------------------------|------------------------------------|

Statistical analysis description:

Comparisons between treatment groups were made using healing rates from a logistic regression model adjusted for baseline rectosigmoidoscopy score and stratification factors (prior vs no prior TNF antagonist use and enrollment pre- vs post-protocol amendment).

| | |
|---|--|
| Comparison groups | Placebo/Abrilumab 210 mg Q3M v Abrilumab 7 mg Q4W/Abrilumab 210 mg Q3M |
| Number of subjects included in analysis | 137 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[27] |
| P-value | = 0.6 ^[28] |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 0.69 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | 0.21 |
| upper limit | 2.22 |

Notes:

[27] - Comparisons of abrilumab 7 mg with placebo were not included in the hypothesis testing procedure and were not adjusted for multiplicity.

[28] - Adjusted for baseline rectosigmoidoscopy score and stratification factors.

| | |
|-----------------------------------|-------------------------------------|
| Statistical analysis title | Difference in Mucosal Healing Rates |
|-----------------------------------|-------------------------------------|

Statistical analysis description:

The difference in adjusted healing rates, estimated from a logistic regression model adjusted for baseline rectosigmoidoscopy score and stratification factors (prior vs no prior TNF antagonist use and enrollment pre- vs post-protocol amendment).

| | |
|---|--|
| Comparison groups | Placebo/Abrilumab 210 mg Q3M v Abrilumab 7 mg Q4W/Abrilumab 210 mg Q3M |
| Number of subjects included in analysis | 137 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[29] |
| Parameter estimate | Difference in Adjusted Healing Rates |
| Point estimate | -4.6 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | -14.9 |
| upper limit | 11.3 |

Notes:

[29] - Analysis was not part of the formal testing.

Secondary: Percentage of Participants with Sustained Remission at Week 8 and Week 24

| | |
|-----------------|---|
| End point title | Percentage of Participants with Sustained Remission at Week 8 and Week 24 |
|-----------------|---|

End point description:

Remission was defined as a total Mayo Score ≤ 2 points, with no individual subscore > 1 point. Sustained remission was defined as achieving the criteria for remission at both week 8 and week 24. The Mayo Score is a composite index of four items (stool frequency, rectal bleeding, rectosigmoidoscopy findings, and physician's global assessment); the total Mayo Score ranges from 0 to 12 points with higher scores representing more severe disease. The remission rate was calculated based on observed data (unadjusted remission rate) and also after applying a logistic regression model including the factors of treatment group, stratification factors (prior anti-TNF use and pre- versus post-Protocol Amendment 3) and baseline total Mayo Score (adjusted remission rate). The full analysis set includes all randomized participants who received at least 1 dose of study drug. Both non-adjusted and adjusted remission rates were calculated using non-responder imputation.

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

End point timeframe:

Week 8 and week 24

| End point values | Placebo/Abrilumab 210 mg Q3M | Abrilumab 7 mg Q4W/Abrilumab 210 mg Q3M | Abrilumab 21 mg Q4W/Abrilumab 210 mg Q3M | Abrilumab 70 mg Q4W/Abrilumab 210 mg Q3M |
|-----------------------------------|------------------------------|---|--|--|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 116 | 21 | 40 | 98 |
| Units: percentage of participants | | | | |
| number (not applicable) | | | | |
| Unadjusted remission rate | 2.6 | 0.0 | 2.5 | 8.2 |
| Adjusted remission rate | 3.3 | 1.6 | 2.8 | 9.1 |

| End point values | Abrilumab 210 mg/Abrilumab 210 mg Q3M | | | |
|-----------------------------------|---------------------------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 79 | | | |
| Units: percentage of participants | | | | |
| number (not applicable) | | | | |
| Unadjusted remission rate | 3.8 | | | |
| Adjusted remission rate | 4.3 | | | |

Statistical analyses

| Statistical analysis title | Comparison of Abrilumab vs Placebo |
|--|---|
| Statistical analysis description: | |
| Comparisons between treatment groups were made using sustained remission rates estimated from a logistic regression model adjusted for baseline total Mayo Score and stratification factors (prior vs no prior TNF antagonist use and enrollment pre- vs post-protocol amendment). | |
| Comparison groups | Placebo/Abrilumab 210 mg Q3M v Abrilumab 70 mg Q4W/Abrilumab 210 mg Q3M |
| Number of subjects included in analysis | 214 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.09 ^[30] |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 2.94 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | 1.03 |
| upper limit | 8.36 |

Notes:

[30] - Adjusted for baseline total Mayo Score and stratification factors.

| Statistical analysis title | Difference in Sustained Remission Rates |
|----------------------------|---|
|----------------------------|---|

Statistical analysis description:

The difference in adjusted sustained remission rates, estimated from a logistic regression model adjusted for baseline total Mayo Score and stratification factors (prior vs no prior TNF antagonist use

and enrollment pre- vs post-protocol amendment).

| | |
|---|---|
| Comparison groups | Placebo/Abrilumab 210 mg Q3M v Abrilumab 70 mg Q4W/Abrilumab 210 mg Q3M |
| Number of subjects included in analysis | 214 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| Parameter estimate | Difference in Adjusted Remission Rates |
| Point estimate | 5.8 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | -0.6 |
| upper limit | 10.4 |

| | |
|---|--|
| Statistical analysis title | Comparison of Abrilumab vs Placebo |
| Statistical analysis description: Comparisons between treatment groups were made using sustained remission rates from a logistic regression model adjusted for baseline total Mayo Score and stratification factors (prior vs no prior TNF antagonist use and enrollment pre- vs post-protocol amendment). | |
| Comparison groups | Placebo/Abrilumab 210 mg Q3M v Abrilumab 210 mg/Abrilumab 210 mg Q3M |
| Number of subjects included in analysis | 195 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.72 ^[31] |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 1.32 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | 0.38 |
| upper limit | 4.56 |

Notes:

[31] - Adjusted for baseline total Mayo Score and stratification factors.

| | |
|--|--|
| Statistical analysis title | Difference in Sustained Remission Rates |
| Statistical analysis description: The difference in adjusted sustained remission rates, estimated from a logistic regression model adjusted for baseline total Mayo Score and stratification factors (prior vs no prior TNF antagonist use and enrollment pre- vs post-protocol amendment). | |
| Comparison groups | Placebo/Abrilumab 210 mg Q3M v Abrilumab 210 mg/Abrilumab 210 mg Q3M |
| Number of subjects included in analysis | 195 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| Parameter estimate | Difference in Adjusted Remission Rates |
| Point estimate | 1 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | -4.7 |
| upper limit | 4.6 |

| | |
|-----------------------------------|-----------------------------------|
| Statistical analysis title | Comparison of Abilumab vs Placebo |
|-----------------------------------|-----------------------------------|

Statistical analysis description:

Comparisons between treatment groups were made using sustained remission rates from a logistic regression model adjusted for baseline total Mayo Score and stratification factors (prior vs no prior TNF antagonist use and enrollment pre- vs post-protocol amendment).

| | |
|---|--|
| Comparison groups | Placebo/Abilumab 210 mg Q3M v Abilumab 21 mg Q4W/Abilumab 210 mg Q3M |
| Number of subjects included in analysis | 156 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[32] |
| P-value | = 0.86 ^[33] |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 0.83 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | 0.16 |
| upper limit | 4.41 |

Notes:

[32] - Analysis was not part of the formal testing.

[33] - Adjusted for baseline total Mayo Score and stratification factors.

| | |
|-----------------------------------|---|
| Statistical analysis title | Difference in Sustained Remission Rates |
|-----------------------------------|---|

Statistical analysis description:

The difference in adjusted sustained remission rates estimated from a logistic regression model adjusted for baseline total Mayo Score and stratification factors (prior vs no prior TNF antagonist use and enrollment pre- vs post-protocol amendment).

| | |
|---|--|
| Comparison groups | Placebo/Abilumab 210 mg Q3M v Abilumab 21 mg Q4W/Abilumab 210 mg Q3M |
| Number of subjects included in analysis | 156 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[34] |
| Parameter estimate | Difference in Adjusted Remission Rates |
| Point estimate | -0.5 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | -3.9 |
| upper limit | 6.2 |

Notes:

[34] - Analysis was not part of the formal testing.

| | |
|-----------------------------------|-----------------------------------|
| Statistical analysis title | Comparison of Abilumab vs Placebo |
|-----------------------------------|-----------------------------------|

Statistical analysis description:

Comparisons between treatment groups were made using sustained remission rates from a logistic regression model adjusted for baseline total Mayo Score and stratification factors (prior vs no prior TNF antagonist use and enrollment pre- vs post-protocol amendment).

| | |
|---|--|
| Comparison groups | Placebo/Abrilumab 210 mg Q3M v Abrilumab 7 mg Q4W/Abrilumab 210 mg Q3M |
| Number of subjects included in analysis | 137 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[35] |
| P-value | = 0.64 ^[36] |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 0.49 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | 0.04 |
| upper limit | 6.31 |

Notes:

[35] - Analysis was not part of the formal testing.

[36] - Adjusted for baseline total Mayo Score and stratification factors.

| | |
|-----------------------------------|---|
| Statistical analysis title | Difference in Sustained Remission Rates |
|-----------------------------------|---|

Statistical analysis description:

The difference in adjusted sustained remission rates estimated from a logistic regression model adjusted for baseline total Mayo Score and stratification factors (prior vs no prior TNF antagonist use and enrollment pre- vs post-protocol amendment).

| | |
|---|--|
| Comparison groups | Placebo/Abrilumab 210 mg Q3M v Abrilumab 7 mg Q4W/Abrilumab 210 mg Q3M |
| Number of subjects included in analysis | 137 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[37] |
| Parameter estimate | Difference in Adjusted Remission Rates |
| Point estimate | -1.7 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | -4.2 |
| upper limit | 6.4 |

Notes:

[37] - Analysis was not part of the formal testing.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

24 weeks in the double-blind period and 108 weeks in the open-label period

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 20.1 |
|--------------------|------|

Reporting groups

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

Reporting group description:

Participants received placebo by subcutaneous injection on day 1, week 2, week 4, and every 4 weeks thereafter until week 24 during the double-blind (DB) treatment period.

| | |
|-----------------------|-------------------------------|
| Reporting group title | DB Period: Abrilumab 7 mg Q4W |
|-----------------------|-------------------------------|

Reporting group description:

Participants received 7 mg abrilumab by subcutaneous injection on day 1, week 2, week 4, and every 4 weeks (Q4W) thereafter until week 24 during the double-blind treatment period.

| | |
|-----------------------|--------------------------------|
| Reporting group title | DB Period: Abrilumab 21 mg Q4W |
|-----------------------|--------------------------------|

Reporting group description:

Participants received 21 mg abrilumab by subcutaneous injection on day 1, week 2, week 4, and every 4 weeks thereafter until week 24 during the double-blind treatment period.

| | |
|-----------------------|--------------------------------|
| Reporting group title | DB Period: Abrilumab 70 mg Q4W |
|-----------------------|--------------------------------|

Reporting group description:

Participants received 70 mg abrilumab by subcutaneous injection on day 1, week 2, week 4, and every 4 weeks thereafter until week 24 during the double-blind treatment period.

| | |
|-----------------------|-----------------------------|
| Reporting group title | DB Period: Abrilumab 210 mg |
|-----------------------|-----------------------------|

Reporting group description:

Participants received a single dose of 210 mg abrilumab by subcutaneous injection on day 1, followed by placebo at week 2, week 4, and every 4 weeks thereafter until week 24 during the double-blind treatment period.

| | |
|-----------------------|---|
| Reporting group title | OL Period: Placebo/Abrilumab 210 mg Q3M |
|-----------------------|---|

Reporting group description:

Participants who received placebo during the double-blind treatment period received abrilumab 210 mg once every 3 months (Q3M) for 108 weeks during the open-label (OL) treatment period.

| | |
|-----------------------|--|
| Reporting group title | OL Period: Abrilumab 7 mg Q4W/210 mg Q3M |
|-----------------------|--|

Reporting group description:

Participants who received 7 mg abrilumab Q4W in the DB treatment period received abrilumab 210 mg once every 3 months for 108 weeks during the open-label period.

| | |
|-----------------------|---|
| Reporting group title | OL Period: Abrilumab 21 mg Q4W/210 mg Q3M |
|-----------------------|---|

Reporting group description:

During the open-label period, participants who received 21 mg abrilumab Q4W during the DB treatment period received abrilumab 210 mg once every 3 months for 108 weeks.

| | |
|-----------------------|---|
| Reporting group title | OL Period: Abrilumab 70 mg Q4W/210 mg Q3M |
|-----------------------|---|

Reporting group description:

Participants who received 70 mg abrilumab Q4W during the DB treatment period received abrilumab 210 mg once every 3 months for 108 weeks during the open-label period.

| | |
|-----------------------|--|
| Reporting group title | OL Period: Abrilumab 210 mg/210 mg Q3M |
|-----------------------|--|

Reporting group description:

Participants who received 210 mg abrilumab during the DB treatment period received abrilumab 210 mg once every 3 months for 108 weeks during the open-label period.

| Serious adverse events | DB Period: Placebo | DB Period: Abrilumab 7 mg Q4W | DB Period: Abrilumab 21 mg Q4W |
|---|--------------------|-------------------------------------|--------------------------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 14 / 116 (12.07%) | 1 / 20 (5.00%) | 3 / 40 (7.50%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Epstein-Barr virus associated lymphoma | | | |
| subjects affected / exposed | 0 / 116 (0.00%) | 0 / 20 (0.00%) | 0 / 40 (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 |
| Immune system disorders | | | |
| Drug hypersensitivity | | | |
| subjects affected / exposed | 1 / 116 (0.86%) | 0 / 20 (0.00%) | 0 / 40 (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 |
| Sarcoidosis | | | |
| subjects affected / exposed | 0 / 116 (0.00%) | 0 / 20 (0.00%) | 0 / 40 (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 | | | |
| Pharyngeal haemorrhage | | | |
| subjects affected / exposed | 0 / 116 (0.00%) | 0 / 20 (0.00%) | 0 / 40 (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 |
| Investigations | | | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 0 / 116 (0.00%) | 0 / 20 (0.00%) | 0 / 40 (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 |
| Aspartate aminotransferase increased | | | |

| | | | |
|---|-----------------|----------------|----------------|
| subjects affected / exposed | 0 / 116 (0.00%) | 0 / 20 (0.00%) | 0 / 40 (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 alkaline phosphatase increased | | | |
| subjects affected / exposed | 0 / 116 (0.00%) | 0 / 20 (0.00%) | 0 / 40 (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 |
| Norovirus test positive | | | |
| subjects affected / exposed | 0 / 116 (0.00%) | 0 / 20 (0.00%) | 0 / 40 (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 | | | |
| Post lumbar puncture syndrome | | | |
| subjects affected / exposed | 1 / 116 (0.86%) | 0 / 20 (0.00%) | 0 / 40 (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 |
| Cardiac disorders | | | |
| Heart valve incompetence | | | |
| subjects affected / exposed | 0 / 116 (0.00%) | 0 / 20 (0.00%) | 0 / 40 (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 | | | |
| Migraine | | | |
| subjects affected / exposed | 0 / 116 (0.00%) | 0 / 20 (0.00%) | 0 / 40 (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 | 1 / 116 (0.86%) | 0 / 20 (0.00%) | 1 / 40 (2.50%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haemolytic anaemia | | | |

| | | | |
|---|-----------------|----------------|----------------|
| subjects affected / exposed | 0 / 116 (0.00%) | 0 / 20 (0.00%) | 0 / 40 (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 / 116 (0.00%) | 0 / 20 (0.00%) | 0 / 40 (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 | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 2 / 116 (1.72%) | 0 / 20 (0.00%) | 0 / 40 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Colitis | | | |
| subjects affected / exposed | 0 / 116 (0.00%) | 0 / 20 (0.00%) | 0 / 40 (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 | 5 / 116 (4.31%) | 0 / 20 (0.00%) | 1 / 40 (2.50%) |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diarrhoea | | | |
| subjects affected / exposed | 0 / 116 (0.00%) | 0 / 20 (0.00%) | 0 / 40 (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 dysplasia | | | |
| subjects affected / exposed | 0 / 116 (0.00%) | 0 / 20 (0.00%) | 0 / 40 (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 |
| Haemorrhoids | | | |
| subjects affected / exposed | 1 / 116 (0.86%) | 0 / 20 (0.00%) | 0 / 40 (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 |
| Ileus | | | |

| | | | |
|---|-----------------|----------------|----------------|
| subjects affected / exposed | 1 / 116 (0.86%) | 0 / 20 (0.00%) | 0 / 40 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Large intestinal obstruction | | | |
| subjects affected / exposed | 1 / 116 (0.86%) | 0 / 20 (0.00%) | 0 / 40 (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 |
| Megacolon | | | |
| subjects affected / exposed | 0 / 116 (0.00%) | 0 / 20 (0.00%) | 1 / 40 (2.50%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Proctalgia | | | |
| subjects affected / exposed | 0 / 116 (0.00%) | 0 / 20 (0.00%) | 0 / 40 (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 |
| Rectal haemorrhage | | | |
| subjects affected / exposed | 1 / 116 (0.86%) | 0 / 20 (0.00%) | 0 / 40 (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 |
| Skin and subcutaneous tissue disorders | | | |
| Pemphigoid | | | |
| subjects affected / exposed | 0 / 116 (0.00%) | 0 / 20 (0.00%) | 0 / 40 (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 | 1 / 116 (0.86%) | 0 / 20 (0.00%) | 0 / 40 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal colic | | | |
| subjects affected / exposed | 0 / 116 (0.00%) | 0 / 20 (0.00%) | 0 / 40 (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 | | | |
| Ankylosing spondylitis | | | |
| subjects affected / exposed | 0 / 116 (0.00%) | 0 / 20 (0.00%) | 0 / 40 (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 |
| Arthralgia | | | |
| subjects affected / exposed | 1 / 116 (0.86%) | 0 / 20 (0.00%) | 0 / 40 (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 |
| Arthritis | | | |
| subjects affected / exposed | 0 / 116 (0.00%) | 0 / 20 (0.00%) | 0 / 40 (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 |
| Osteoarthritis | | | |
| subjects affected / exposed | 0 / 116 (0.00%) | 0 / 20 (0.00%) | 0 / 40 (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 | | | |
| Abdominal abscess | | | |
| subjects affected / exposed | 0 / 116 (0.00%) | 0 / 20 (0.00%) | 0 / 40 (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 |
| Anal abscess | | | |
| subjects affected / exposed | 0 / 116 (0.00%) | 0 / 20 (0.00%) | 0 / 40 (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 |
| Anal infection | | | |
| subjects affected / exposed | 0 / 116 (0.00%) | 0 / 20 (0.00%) | 0 / 40 (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 |
| Cytomegalovirus infection | | | |
| subjects affected / exposed | 0 / 116 (0.00%) | 0 / 20 (0.00%) | 0 / 40 (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 |

| | | | |
|---|-----------------|----------------|----------------|
| Erysipelas | | | |
| subjects affected / exposed | 0 / 116 (0.00%) | 0 / 20 (0.00%) | 0 / 40 (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 | | | |
| subjects affected / exposed | 1 / 116 (0.86%) | 0 / 20 (0.00%) | 0 / 40 (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 |
| Gastroenteritis bacterial | | | |
| subjects affected / exposed | 0 / 116 (0.00%) | 0 / 20 (0.00%) | 0 / 40 (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 infection | | | |
| subjects affected / exposed | 0 / 116 (0.00%) | 0 / 20 (0.00%) | 0 / 40 (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 |
| Perineal abscess | | | |
| subjects affected / exposed | 0 / 116 (0.00%) | 0 / 20 (0.00%) | 0 / 40 (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 |
| Pharyngitis streptococcal | | | |
| subjects affected / exposed | 0 / 116 (0.00%) | 0 / 20 (0.00%) | 0 / 40 (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 / 116 (0.00%) | 0 / 20 (0.00%) | 0 / 40 (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 tuberculosis | | | |
| subjects affected / exposed | 0 / 116 (0.00%) | 0 / 20 (0.00%) | 0 / 40 (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 |
| Septic shock | | | |

| | | | |
|---|-----------------|----------------|----------------|
| subjects affected / exposed | 0 / 116 (0.00%) | 1 / 20 (5.00%) | 0 / 40 (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 |
| Skin infection | | | |
| subjects affected / exposed | 1 / 116 (0.86%) | 0 / 20 (0.00%) | 0 / 40 (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 |
| Tonsillitis | | | |
| subjects affected / exposed | 0 / 116 (0.00%) | 0 / 20 (0.00%) | 0 / 40 (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 / 116 (0.00%) | 0 / 20 (0.00%) | 0 / 40 (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 | DB Period: Abrilumab 70 mg Q4W | DB Period: Abrilumab 210 mg | OL Period: Placebo/Abrilumab 210 mg Q3M |
|---|--------------------------------------|--------------------------------|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 5 / 99 (5.05%) | 7 / 79 (8.86%) | 13 / 100 (13.00%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Epstein-Barr virus associated lymphoma | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 0 / 79 (0.00%) | 1 / 100 (1.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Immune system disorders | | | |
| Drug hypersensitivity | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 0 / 79 (0.00%) | 0 / 100 (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 |
| Sarcoidosis | | | |

| | | | |
|---|----------------|----------------|-----------------|
| subjects affected / exposed | 0 / 99 (0.00%) | 0 / 79 (0.00%) | 1 / 100 (1.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Pharyngeal haemorrhage | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 0 / 79 (0.00%) | 0 / 100 (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 |
| Investigations | | | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 1 / 79 (1.27%) | 0 / 100 (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 |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 1 / 79 (1.27%) | 0 / 100 (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 |
| Blood alkaline phosphatase increased | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 1 / 79 (1.27%) | 0 / 100 (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 |
| Norovirus test positive | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 0 / 79 (0.00%) | 0 / 100 (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 | | | |
| Post lumbar puncture syndrome | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 0 / 79 (0.00%) | 0 / 100 (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 | | | |
| Heart valve incompetence | | | |

| | | | |
|---|----------------|----------------|-----------------|
| subjects affected / exposed | 0 / 99 (0.00%) | 0 / 79 (0.00%) | 0 / 100 (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 | | | |
| Migraine | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 0 / 79 (0.00%) | 1 / 100 (1.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 0 / 79 (0.00%) | 2 / 100 (2.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haemolytic anaemia | | | |
| subjects affected / exposed | 1 / 99 (1.01%) | 0 / 79 (0.00%) | 0 / 100 (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 |
| Iron deficiency anaemia | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 0 / 79 (0.00%) | 1 / 100 (1.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 0 / 79 (0.00%) | 0 / 100 (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 / 99 (0.00%) | 0 / 79 (0.00%) | 1 / 100 (1.00%) |
| 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 | 4 / 99 (4.04%) | 2 / 79 (2.53%) | 6 / 100 (6.00%) |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 2 | 1 / 7 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|----------------|----------------|-----------------|
| Diarrhoea | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 0 / 79 (0.00%) | 0 / 100 (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 dysplasia | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 0 / 79 (0.00%) | 0 / 100 (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 |
| Haemorrhoids | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 0 / 79 (0.00%) | 0 / 100 (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 |
| Ileus | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 0 / 79 (0.00%) | 0 / 100 (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 |
| Large intestinal obstruction | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 0 / 79 (0.00%) | 0 / 100 (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 |
| Megacolon | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 0 / 79 (0.00%) | 0 / 100 (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 |
| Proctalgia | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 0 / 79 (0.00%) | 0 / 100 (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 |
| Rectal haemorrhage | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 0 / 79 (0.00%) | 0 / 100 (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 |
| Skin and subcutaneous tissue disorders | | | |

| | | | |
|---|----------------|----------------|-----------------|
| Pemphigoid | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 0 / 79 (0.00%) | 0 / 100 (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 / 99 (0.00%) | 0 / 79 (0.00%) | 0 / 100 (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 colic | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 0 / 79 (0.00%) | 1 / 100 (1.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Ankylosing spondylitis | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 0 / 79 (0.00%) | 0 / 100 (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 |
| Arthralgia | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 0 / 79 (0.00%) | 0 / 100 (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 |
| Arthritis | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 0 / 79 (0.00%) | 0 / 100 (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 |
| Osteoarthritis | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 0 / 79 (0.00%) | 1 / 100 (1.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Abdominal abscess | | | |

| | | | |
|---|----------------|----------------|-----------------|
| subjects affected / exposed | 0 / 99 (0.00%) | 0 / 79 (0.00%) | 0 / 100 (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 |
| Anal abscess | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 0 / 79 (0.00%) | 0 / 100 (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 |
| Anal infection | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 0 / 79 (0.00%) | 0 / 100 (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 |
| Cytomegalovirus infection | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 0 / 79 (0.00%) | 0 / 100 (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 |
| Erysipelas | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 1 / 79 (1.27%) | 0 / 100 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 3 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastroenteritis | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 1 / 79 (1.27%) | 0 / 100 (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 bacterial | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 0 / 79 (0.00%) | 0 / 100 (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 infection | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 0 / 79 (0.00%) | 0 / 100 (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 |
| Perineal abscess | | | |

| | | | |
|---|----------------|----------------|-----------------|
| subjects affected / exposed | 0 / 99 (0.00%) | 1 / 79 (1.27%) | 0 / 100 (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 |
| Pharyngitis streptococcal | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 0 / 79 (0.00%) | 0 / 100 (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 | 1 / 99 (1.01%) | 0 / 79 (0.00%) | 0 / 100 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary tuberculosis | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 0 / 79 (0.00%) | 0 / 100 (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 |
| Septic shock | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 0 / 79 (0.00%) | 0 / 100 (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 |
| Skin infection | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 0 / 79 (0.00%) | 0 / 100 (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 |
| Tonsillitis | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 0 / 79 (0.00%) | 0 / 100 (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 / 99 (0.00%) | 1 / 79 (1.27%) | 0 / 100 (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 |

| | | | |
|-------------------------------|------------|------------|------------|
| Serious adverse events | OL Period: | OL Period: | OL Period: |
|-------------------------------|------------|------------|------------|

| | Abrilumab 7 mg Q4W/210 mg Q3M | Abrilumab 21 mg Q4W/210 mg Q3M | Abrilumab 70 mg Q4W/210 mg Q3M |
|---|----------------------------------|-----------------------------------|-----------------------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 3 / 18 (16.67%) | 4 / 36 (11.11%) | 14 / 89 (15.73%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Epstein-Barr virus associated lymphoma | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 36 (0.00%) | 0 / 89 (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 |
| Immune system disorders | | | |
| Drug hypersensitivity | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 36 (0.00%) | 0 / 89 (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 |
| Sarcoidosis | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 36 (0.00%) | 0 / 89 (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 | | | |
| Pharyngeal haemorrhage | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 36 (0.00%) | 1 / 89 (1.12%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Investigations | | | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 36 (0.00%) | 0 / 89 (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 |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 36 (0.00%) | 0 / 89 (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 alkaline phosphatase increased | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 36 (0.00%) | 0 / 89 (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 |
| Norovirus test positive | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 36 (0.00%) | 0 / 89 (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 |
| Injury, poisoning and procedural complications | | | |
| Post lumbar puncture syndrome | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 36 (0.00%) | 0 / 89 (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 | | | |
| Heart valve incompetence | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 36 (0.00%) | 1 / 89 (1.12%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| Migraine | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 36 (0.00%) | 0 / 89 (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 / 18 (0.00%) | 1 / 36 (2.78%) | 0 / 89 (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 / 18 (0.00%) | 0 / 36 (0.00%) | 0 / 89 (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 / 18 (0.00%) | 0 / 36 (0.00%) | 0 / 89 (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 | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 36 (0.00%) | 0 / 89 (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 / 18 (0.00%) | 0 / 36 (0.00%) | 0 / 89 (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 | 0 / 18 (0.00%) | 2 / 36 (5.56%) | 4 / 89 (4.49%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 1 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diarrhoea | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 36 (0.00%) | 1 / 89 (1.12%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal dysplasia | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 36 (2.78%) | 0 / 89 (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 |
| Haemorrhoids | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 36 (0.00%) | 0 / 89 (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 |
| Ileus | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 36 (0.00%) | 0 / 89 (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 |
| Large intestinal obstruction | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 36 (0.00%) | 0 / 89 (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 |
| Megacolon | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 36 (0.00%) | 0 / 89 (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 |
| Proctalgia | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 36 (0.00%) | 1 / 89 (1.12%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Rectal haemorrhage | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 36 (0.00%) | 0 / 89 (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 |
| Skin and subcutaneous tissue disorders | | | |
| Pemphigoid | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 36 (0.00%) | 0 / 89 (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 / 18 (0.00%) | 0 / 36 (0.00%) | 0 / 89 (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 colic | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 36 (0.00%) | 0 / 89 (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 | | | |
| Ankylosing spondylitis | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 36 (0.00%) | 1 / 89 (1.12%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|----------------|----------------|----------------|
| Arthralgia | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 36 (0.00%) | 0 / 89 (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 |
| Arthritis | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 36 (0.00%) | 0 / 89 (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 |
| Osteoarthritis | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 36 (0.00%) | 0 / 89 (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 | | | |
| Abdominal abscess | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 36 (0.00%) | 1 / 89 (1.12%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Anal abscess | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 36 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Anal infection | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 36 (0.00%) | 1 / 89 (1.12%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cytomegalovirus infection | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 36 (0.00%) | 0 / 89 (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 |
| Erysipelas | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 36 (0.00%) | 0 / 89 (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 | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 36 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastroenteritis bacterial | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 36 (2.78%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal infection | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 36 (0.00%) | 1 / 89 (1.12%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Perineal abscess | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 36 (0.00%) | 0 / 89 (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 |
| Pharyngitis streptococcal | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 36 (0.00%) | 1 / 89 (1.12%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 36 (0.00%) | 0 / 89 (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 tuberculosis | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 36 (0.00%) | 1 / 89 (1.12%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Septic shock | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 36 (0.00%) | 0 / 89 (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 |
| Skin infection | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 36 (0.00%) | 0 / 89 (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 |
| Tonsillitis | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 36 (0.00%) | 1 / 89 (1.12%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 36 (0.00%) | 0 / 89 (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 | OL Period: Abrilumab 210 mg/210 mg Q3M | | |
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 6 / 68 (8.82%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Epstein-Barr virus associated lymphoma | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Immune system disorders | | | |
| Drug hypersensitivity | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Sarcoidosis | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory, thoracic and mediastinal disorders | | | |

| | | | |
|---|----------------|--|--|
| Pharyngeal haemorrhage | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Investigations | | | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Blood alkaline phosphatase increased | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Norovirus test positive | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Injury, poisoning and procedural complications | | | |
| Post lumbar puncture syndrome | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cardiac disorders | | | |
| Heart valve incompetence | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Nervous system disorders | | | |
| Migraine | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 68 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 1 / 68 (1.47%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Haemolytic anaemia | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Iron deficiency anaemia | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 1 / 68 (1.47%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Colitis | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Colitis ulcerative | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Diarrhoea | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal dysplasia | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 68 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Haemorrhoids | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Ileus | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Large intestinal obstruction | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Megacolon | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Proctalgia | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Rectal haemorrhage | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Skin and subcutaneous tissue disorders | | | |
| Pemphigoid | | | |
| subjects affected / exposed | 1 / 68 (1.47%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Renal and urinary disorders | | | |

| | | | |
|---|----------------|--|--|
| Nephrolithiasis | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Renal colic | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Ankylosing spondylitis | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Arthralgia | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Arthritis | | | |
| subjects affected / exposed | 1 / 68 (1.47%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Osteoarthritis | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infections and infestations | | | |
| Abdominal abscess | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Anal abscess | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | | |
|---|----------------|--|--|--|
| Anal infection | | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Cytomegalovirus infection | | | | |
| subjects affected / exposed | 1 / 68 (1.47%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Erysipelas | | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Gastroenteritis | | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Gastroenteritis bacterial | | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Gastrointestinal infection | | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Perineal abscess | | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pharyngitis streptococcal | | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pneumonia | | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 1 / 68 (1.47%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pulmonary tuberculosis | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Septic shock | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Skin infection | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Tonsillitis | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

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

| Non-serious adverse events | DB Period: Placebo | DB Period: Abrilumab 7 mg Q4W | DB Period: Abrilumab 21 mg Q4W |
|---|--------------------|-------------------------------------|--------------------------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 47 / 116 (40.52%) | 9 / 20 (45.00%) | 16 / 40 (40.00%) |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Lipoma | | | |

| | | | |
|---|--|--|---|
| subjects affected / exposed occurrences (all) | 0 / 116 (0.00%) 0 | 0 / 20 (0.00%) 0 | 0 / 40 (0.00%) 0 |
| Vascular disorders Hypertension subjects affected / exposed occurrences (all) | 1 / 116 (0.86%) 1 | 0 / 20 (0.00%) 0 | 0 / 40 (0.00%) 0 |
| Pregnancy, puerperium and perinatal conditions Pregnancy subjects affected / exposed occurrences (all) | 0 / 116 (0.00%) 0 | 0 / 20 (0.00%) 0 | 0 / 40 (0.00%) 0 |
| General disorders and administration site conditions Asthenia subjects affected / exposed occurrences (all) Fatigue subjects affected / exposed occurrences (all) Hyperthermia subjects affected / exposed occurrences (all) Influenza like illness subjects affected / exposed occurrences (all) Localised oedema subjects affected / exposed occurrences (all) | 3 / 116 (2.59%) 3 3 / 116 (2.59%) 3 0 / 116 (0.00%) 0 1 / 116 (0.86%) 1 0 / 116 (0.00%) 0 | 0 / 20 (0.00%) 0 0 / 20 (0.00%) 0 0 / 20 (0.00%) 0 0 / 20 (0.00%) 0 | 1 / 40 (2.50%) 1 1 / 40 (2.50%) 1 0 / 40 (0.00%) 0 1 / 40 (2.50%) 1 0 / 40 (0.00%) 0 |
| Immune system disorders Allergy to arthropod bite subjects affected / exposed occurrences (all) Food allergy subjects affected / exposed occurrences (all) | 0 / 116 (0.00%) 0 0 / 116 (0.00%) 0 | 0 / 20 (0.00%) 0 1 / 20 (5.00%) 1 | 0 / 40 (0.00%) 0 0 / 40 (0.00%) 0 |
| Respiratory, thoracic and mediastinal disorders | | | |

| | | | |
|---|----------------------|---------------------|---------------------|
| Cough subjects affected / exposed occurrences (all) | 2 / 116 (1.72%) 2 | 0 / 20 (0.00%) 0 | 0 / 40 (0.00%) 0 |
| Dyspnoea subjects affected / exposed occurrences (all) | 0 / 116 (0.00%) 0 | 0 / 20 (0.00%) 0 | 1 / 40 (2.50%) 1 |
| Investigations Blood phosphorus decreased subjects affected / exposed occurrences (all) | 0 / 116 (0.00%) 0 | 0 / 20 (0.00%) 0 | 0 / 40 (0.00%) 0 |
| Weight decreased subjects affected / exposed occurrences (all) | 1 / 116 (0.86%) 1 | 0 / 20 (0.00%) 0 | 0 / 40 (0.00%) 0 |
| Injury, poisoning and procedural complications Limb injury subjects affected / exposed occurrences (all) | 0 / 116 (0.00%) 0 | 0 / 20 (0.00%) 0 | 0 / 40 (0.00%) 0 |
| Congenital, familial and genetic disorders Phimosis subjects affected / exposed occurrences (all) | 0 / 116 (0.00%) 0 | 1 / 20 (5.00%) 1 | 0 / 40 (0.00%) 0 |
| Nervous system disorders Carpal tunnel syndrome subjects affected / exposed occurrences (all) | 0 / 116 (0.00%) 0 | 0 / 20 (0.00%) 0 | 0 / 40 (0.00%) 0 |
| Headache subjects affected / exposed occurrences (all) | 7 / 116 (6.03%) 8 | 1 / 20 (5.00%) 1 | 2 / 40 (5.00%) 5 |
| Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all) | 1 / 116 (0.86%) 1 | 1 / 20 (5.00%) 1 | 2 / 40 (5.00%) 2 |
| Lymphadenopathy subjects affected / exposed occurrences (all) | 0 / 116 (0.00%) 0 | 1 / 20 (5.00%) 1 | 0 / 40 (0.00%) 0 |
| Ear and labyrinth disorders | | | |

| | | | |
|--|----------------------|---------------------|---------------------|
| Vertigo subjects affected / exposed occurrences (all) | 0 / 116 (0.00%) 0 | 1 / 20 (5.00%) 1 | 0 / 40 (0.00%) 0 |
| Eye disorders Eye swelling subjects affected / exposed occurrences (all) | 0 / 116 (0.00%) 0 | 0 / 20 (0.00%) 0 | 0 / 40 (0.00%) 0 |
| Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all) | 3 / 116 (2.59%) 3 | 1 / 20 (5.00%) 1 | 3 / 40 (7.50%) 3 |
| Abdominal pain lower subjects affected / exposed occurrences (all) | 0 / 116 (0.00%) 0 | 0 / 20 (0.00%) 0 | 0 / 40 (0.00%) 0 |
| Aphthous ulcer subjects affected / exposed occurrences (all) | 0 / 116 (0.00%) 0 | 1 / 20 (5.00%) 1 | 0 / 40 (0.00%) 0 |
| Colitis ulcerative subjects affected / exposed occurrences (all) | 4 / 116 (3.45%) 4 | 0 / 20 (0.00%) 0 | 2 / 40 (5.00%) 2 |
| Diarrhoea subjects affected / exposed occurrences (all) | 1 / 116 (0.86%) 1 | 0 / 20 (0.00%) 0 | 3 / 40 (7.50%) 4 |
| Frequent bowel movements subjects affected / exposed occurrences (all) | 0 / 116 (0.00%) 0 | 0 / 20 (0.00%) 0 | 1 / 40 (2.50%) 1 |
| Gastrooesophageal reflux disease subjects affected / exposed occurrences (all) | 0 / 116 (0.00%) 0 | 0 / 20 (0.00%) 0 | 2 / 40 (5.00%) 2 |
| Haematochezia subjects affected / exposed occurrences (all) | 1 / 116 (0.86%) 1 | 0 / 20 (0.00%) 0 | 1 / 40 (2.50%) 1 |
| Nausea subjects affected / exposed occurrences (all) | 4 / 116 (3.45%) 5 | 0 / 20 (0.00%) 0 | 2 / 40 (5.00%) 2 |
| Vomiting | | | |

| | | | |
|--|----------------------|---------------------|---------------------|
| subjects affected / exposed occurrences (all) | 1 / 116 (0.86%) 1 | 0 / 20 (0.00%) 0 | 1 / 40 (2.50%) 1 |
| Skin and subcutaneous tissue disorders | | | |
| Acne | | | |
| subjects affected / exposed | 1 / 116 (0.86%) | 1 / 20 (5.00%) | 0 / 40 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Pruritus | | | |
| subjects affected / exposed | 2 / 116 (1.72%) | 1 / 20 (5.00%) | 0 / 40 (0.00%) |
| occurrences (all) | 2 | 1 | 0 |
| Pruritus generalised | | | |
| subjects affected / exposed | 0 / 116 (0.00%) | 0 / 20 (0.00%) | 0 / 40 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rash | | | |
| subjects affected / exposed | 3 / 116 (2.59%) | 1 / 20 (5.00%) | 0 / 40 (0.00%) |
| occurrences (all) | 3 | 1 | 0 |
| Skin ulcer | | | |
| subjects affected / exposed | 0 / 116 (0.00%) | 0 / 20 (0.00%) | 0 / 40 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Swelling face | | | |
| subjects affected / exposed | 0 / 116 (0.00%) | 0 / 20 (0.00%) | 0 / 40 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Urticaria | | | |
| subjects affected / exposed | 0 / 116 (0.00%) | 1 / 20 (5.00%) | 0 / 40 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Renal and urinary disorders | | | |
| Haematuria | | | |
| subjects affected / exposed | 1 / 116 (0.86%) | 0 / 20 (0.00%) | 0 / 40 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Proteinuria | | | |
| subjects affected / exposed | 0 / 116 (0.00%) | 0 / 20 (0.00%) | 0 / 40 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 5 / 116 (4.31%) | 0 / 20 (0.00%) | 4 / 40 (10.00%) |
| occurrences (all) | 6 | 0 | 4 |
| Back pain | | | |

| | | | |
|---|----------------------|----------------------|----------------------|
| subjects affected / exposed occurrences (all) | 4 / 116 (3.45%) 4 | 1 / 20 (5.00%) 1 | 0 / 40 (0.00%) 0 |
| Joint swelling subjects affected / exposed occurrences (all) | 1 / 116 (0.86%) 1 | 1 / 20 (5.00%) 1 | 1 / 40 (2.50%) 1 |
| Rheumatic disorder subjects affected / exposed occurrences (all) | 0 / 116 (0.00%) 0 | 0 / 20 (0.00%) 0 | 0 / 40 (0.00%) 0 |
| Infections and infestations | | | |
| Candida infection subjects affected / exposed occurrences (all) | 0 / 116 (0.00%) 0 | 2 / 20 (10.00%) 2 | 0 / 40 (0.00%) 0 |
| Conjunctivitis subjects affected / exposed occurrences (all) | 1 / 116 (0.86%) 1 | 0 / 20 (0.00%) 0 | 0 / 40 (0.00%) 0 |
| Gastroenteritis subjects affected / exposed occurrences (all) | 2 / 116 (1.72%) 2 | 0 / 20 (0.00%) 0 | 0 / 40 (0.00%) 0 |
| Influenza subjects affected / exposed occurrences (all) | 4 / 116 (3.45%) 4 | 2 / 20 (10.00%) 2 | 0 / 40 (0.00%) 0 |
| Nasopharyngitis subjects affected / exposed occurrences (all) | 7 / 116 (6.03%) 7 | 0 / 20 (0.00%) 0 | 6 / 40 (15.00%) 6 |
| Upper respiratory tract infection subjects affected / exposed occurrences (all) | 2 / 116 (1.72%) 3 | 0 / 20 (0.00%) 0 | 0 / 40 (0.00%) 0 |
| Urinary tract infection subjects affected / exposed occurrences (all) | 0 / 116 (0.00%) 0 | 0 / 20 (0.00%) 0 | 0 / 40 (0.00%) 0 |
| Metabolism and nutrition disorders | | | |
| Dehydration subjects affected / exposed occurrences (all) | 0 / 116 (0.00%) 0 | 0 / 20 (0.00%) 0 | 1 / 40 (2.50%) 1 |
| Weight gain poor | | | |

| | | | |
|-----------------------------|-----------------|----------------|----------------|
| subjects affected / exposed | 0 / 116 (0.00%) | 1 / 20 (5.00%) | 0 / 40 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |

| Non-serious adverse events | DB Period: Abrilumab 70 mg Q4W | DB Period: Abrilumab 210 mg | OL Period: Placebo/Abrilumab 210 mg Q3M |
|---|--------------------------------------|--------------------------------|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 55 / 99 (55.56%) | 35 / 79 (44.30%) | 55 / 100 (55.00%) |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Lipoma | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 0 / 79 (0.00%) | 0 / 100 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 5 / 99 (5.05%) | 0 / 79 (0.00%) | 1 / 100 (1.00%) |
| occurrences (all) | 5 | 0 | 1 |
| Pregnancy, puerperium and perinatal conditions | | | |
| Pregnancy | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 0 / 79 (0.00%) | 0 / 100 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 3 / 99 (3.03%) | 1 / 79 (1.27%) | 1 / 100 (1.00%) |
| occurrences (all) | 4 | 1 | 1 |
| Fatigue | | | |
| subjects affected / exposed | 8 / 99 (8.08%) | 3 / 79 (3.80%) | 1 / 100 (1.00%) |
| occurrences (all) | 8 | 3 | 1 |
| Hyperthermia | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 1 / 79 (1.27%) | 0 / 100 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Influenza like illness | | | |
| subjects affected / exposed | 2 / 99 (2.02%) | 1 / 79 (1.27%) | 2 / 100 (2.00%) |
| occurrences (all) | 2 | 1 | 6 |
| Localised oedema | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 0 / 79 (0.00%) | 0 / 100 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Immune system disorders | | | |

| | | | |
|---|------------------------|-----------------------|----------------------|
| Allergy to arthropod bite subjects affected / exposed occurrences (all) | 0 / 99 (0.00%) 0 | 0 / 79 (0.00%) 0 | 1 / 100 (1.00%) 3 |
| Food allergy subjects affected / exposed occurrences (all) | 0 / 99 (0.00%) 0 | 0 / 79 (0.00%) 0 | 0 / 100 (0.00%) 0 |
| Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) | 5 / 99 (5.05%) 5 | 2 / 79 (2.53%) 2 | 2 / 100 (2.00%) 2 |
| Dyspnoea subjects affected / exposed occurrences (all) | 0 / 99 (0.00%) 0 | 2 / 79 (2.53%) 2 | 0 / 100 (0.00%) 0 |
| Investigations Blood phosphorus decreased subjects affected / exposed occurrences (all) | 1 / 99 (1.01%) 1 | 0 / 79 (0.00%) 0 | 0 / 100 (0.00%) 0 |
| Weight decreased subjects affected / exposed occurrences (all) | 0 / 99 (0.00%) 0 | 0 / 79 (0.00%) 0 | 0 / 100 (0.00%) 0 |
| Injury, poisoning and procedural complications Limb injury subjects affected / exposed occurrences (all) | 0 / 99 (0.00%) 0 | 0 / 79 (0.00%) 0 | 0 / 100 (0.00%) 0 |
| Congenital, familial and genetic disorders Phimosis subjects affected / exposed occurrences (all) | 0 / 99 (0.00%) 0 | 0 / 79 (0.00%) 0 | 0 / 100 (0.00%) 0 |
| Nervous system disorders Carpal tunnel syndrome subjects affected / exposed occurrences (all) | 0 / 99 (0.00%) 0 | 0 / 79 (0.00%) 0 | 0 / 100 (0.00%) 0 |
| Headache subjects affected / exposed occurrences (all) | 11 / 99 (11.11%) 14 | 8 / 79 (10.13%) 11 | 3 / 100 (3.00%) 4 |
| Blood and lymphatic system disorders | | | |

| | | | |
|--|---------------------|---------------------|-------------------------|
| Anaemia subjects affected / exposed occurrences (all) | 2 / 99 (2.02%) 2 | 2 / 79 (2.53%) 2 | 4 / 100 (4.00%) 5 |
| Lymphadenopathy subjects affected / exposed occurrences (all) | 0 / 99 (0.00%) 0 | 0 / 79 (0.00%) 0 | 0 / 100 (0.00%) 0 |
| Ear and labyrinth disorders Vertigo subjects affected / exposed occurrences (all) | 0 / 99 (0.00%) 0 | 0 / 79 (0.00%) 0 | 0 / 100 (0.00%) 0 |
| Eye disorders Eye swelling subjects affected / exposed occurrences (all) | 0 / 99 (0.00%) 0 | 0 / 79 (0.00%) 0 | 0 / 100 (0.00%) 0 |
| Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all) | 1 / 99 (1.01%) 2 | 1 / 79 (1.27%) 2 | 8 / 100 (8.00%) 8 |
| Abdominal pain lower subjects affected / exposed occurrences (all) | 1 / 99 (1.01%) 1 | 0 / 79 (0.00%) 0 | 1 / 100 (1.00%) 1 |
| Aphthous ulcer subjects affected / exposed occurrences (all) | 0 / 99 (0.00%) 0 | 0 / 79 (0.00%) 0 | 0 / 100 (0.00%) 0 |
| Colitis ulcerative subjects affected / exposed occurrences (all) | 7 / 99 (7.07%) 8 | 6 / 79 (7.59%) 7 | 17 / 100 (17.00%) 18 |
| Diarrhoea subjects affected / exposed occurrences (all) | 3 / 99 (3.03%) 3 | 5 / 79 (6.33%) 5 | 2 / 100 (2.00%) 2 |
| Frequent bowel movements subjects affected / exposed occurrences (all) | 0 / 99 (0.00%) 0 | 0 / 79 (0.00%) 0 | 0 / 100 (0.00%) 0 |
| Gastrooesophageal reflux disease subjects affected / exposed occurrences (all) | 2 / 99 (2.02%) 2 | 1 / 79 (1.27%) 1 | 2 / 100 (2.00%) 2 |
| Haematochezia | | | |

| | | | |
|--|---------------------|---------------------|----------------------|
| subjects affected / exposed occurrences (all) | 1 / 99 (1.01%) 1 | 0 / 79 (0.00%) 0 | 0 / 100 (0.00%) 0 |
| Nausea subjects affected / exposed occurrences (all) | 4 / 99 (4.04%) 4 | 5 / 79 (6.33%) 5 | 2 / 100 (2.00%) 2 |
| Vomiting subjects affected / exposed occurrences (all) | 3 / 99 (3.03%) 3 | 2 / 79 (2.53%) 2 | 4 / 100 (4.00%) 5 |
| Skin and subcutaneous tissue disorders | | | |
| Acne subjects affected / exposed occurrences (all) | 2 / 99 (2.02%) 2 | 0 / 79 (0.00%) 0 | 2 / 100 (2.00%) 3 |
| Pruritus subjects affected / exposed occurrences (all) | 1 / 99 (1.01%) 1 | 3 / 79 (3.80%) 3 | 3 / 100 (3.00%) 3 |
| Pruritus generalised subjects affected / exposed occurrences (all) | 0 / 99 (0.00%) 0 | 0 / 79 (0.00%) 0 | 0 / 100 (0.00%) 0 |
| Rash subjects affected / exposed occurrences (all) | 4 / 99 (4.04%) 4 | 1 / 79 (1.27%) 1 | 5 / 100 (5.00%) 6 |
| Skin ulcer subjects affected / exposed occurrences (all) | 0 / 99 (0.00%) 0 | 0 / 79 (0.00%) 0 | 0 / 100 (0.00%) 0 |
| Swelling face subjects affected / exposed occurrences (all) | 0 / 99 (0.00%) 0 | 0 / 79 (0.00%) 0 | 0 / 100 (0.00%) 0 |
| Urticaria subjects affected / exposed occurrences (all) | 0 / 99 (0.00%) 0 | 0 / 79 (0.00%) 0 | 1 / 100 (1.00%) 1 |
| Renal and urinary disorders | | | |
| Haematuria subjects affected / exposed occurrences (all) | 0 / 99 (0.00%) 0 | 0 / 79 (0.00%) 0 | 0 / 100 (0.00%) 0 |
| Proteinuria | | | |

| | | | |
|--|---------------------|---------------------|----------------------|
| subjects affected / exposed occurrences (all) | 0 / 99 (0.00%) 0 | 0 / 79 (0.00%) 0 | 0 / 100 (0.00%) 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 11 / 99 (11.11%) | 6 / 79 (7.59%) | 11 / 100 (11.00%) |
| occurrences (all) | 18 | 6 | 11 |
| Back pain | | | |
| subjects affected / exposed | 2 / 99 (2.02%) | 1 / 79 (1.27%) | 5 / 100 (5.00%) |
| occurrences (all) | 2 | 1 | 6 |
| Joint swelling | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 0 / 79 (0.00%) | 1 / 100 (1.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Rheumatic disorder | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 0 / 79 (0.00%) | 0 / 100 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Infections and infestations | | | |
| Candida infection | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 0 / 79 (0.00%) | 1 / 100 (1.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Conjunctivitis | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 0 / 79 (0.00%) | 1 / 100 (1.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Gastroenteritis | | | |
| subjects affected / exposed | 4 / 99 (4.04%) | 0 / 79 (0.00%) | 2 / 100 (2.00%) |
| occurrences (all) | 5 | 0 | 2 |
| Influenza | | | |
| subjects affected / exposed | 2 / 99 (2.02%) | 0 / 79 (0.00%) | 3 / 100 (3.00%) |
| occurrences (all) | 2 | 0 | 4 |
| Nasopharyngitis | | | |
| subjects affected / exposed | 9 / 99 (9.09%) | 8 / 79 (10.13%) | 9 / 100 (9.00%) |
| occurrences (all) | 10 | 9 | 13 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 4 / 99 (4.04%) | 1 / 79 (1.27%) | 5 / 100 (5.00%) |
| occurrences (all) | 5 | 1 | 5 |
| Urinary tract infection | | | |

| | | | |
|---|---------------------|---------------------|----------------------|
| subjects affected / exposed occurrences (all) | 3 / 99 (3.03%) 3 | 0 / 79 (0.00%) 0 | 1 / 100 (1.00%) 1 |
| Metabolism and nutrition disorders Dehydration subjects affected / exposed occurrences (all) | 0 / 99 (0.00%) 0 | 0 / 79 (0.00%) 0 | 0 / 100 (0.00%) 0 |
| Weight gain poor subjects affected / exposed occurrences (all) | 0 / 99 (0.00%) 0 | 0 / 79 (0.00%) 0 | 0 / 100 (0.00%) 0 |

| Non-serious adverse events | OL Period: Abrilumab 7 mg Q4W/210 mg Q3M | OL Period: Abrilumab 21 mg Q4W/210 mg Q3M | OL Period: Abrilumab 70 mg Q4W/210 mg Q3M |
|---|--|---|---|
| Total subjects affected by non-serious adverse events subjects affected / exposed | 10 / 18 (55.56%) | 19 / 36 (52.78%) | 53 / 89 (59.55%) |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) Lipoma subjects affected / exposed occurrences (all) | 1 / 18 (5.56%) 1 | 0 / 36 (0.00%) 0 | 0 / 89 (0.00%) 0 |
| Vascular disorders Hypertension subjects affected / exposed occurrences (all) | 0 / 18 (0.00%) 0 | 0 / 36 (0.00%) 0 | 0 / 89 (0.00%) 0 |
| Pregnancy, puerperium and perinatal conditions Pregnancy subjects affected / exposed occurrences (all) | 1 / 18 (5.56%) 1 | 0 / 36 (0.00%) 0 | 0 / 89 (0.00%) 0 |
| General disorders and administration site conditions Asthenia subjects affected / exposed occurrences (all) | 1 / 18 (5.56%) 1 | 0 / 36 (0.00%) 0 | 4 / 89 (4.49%) 5 |
| Fatigue subjects affected / exposed occurrences (all) | 0 / 18 (0.00%) 0 | 1 / 36 (2.78%) 1 | 1 / 89 (1.12%) 1 |
| Hyperthermia subjects affected / exposed occurrences (all) | 1 / 18 (5.56%) 3 | 0 / 36 (0.00%) 0 | 1 / 89 (1.12%) 1 |
| Influenza like illness | | | |

| | | | |
|---|---------------------|---------------------|---------------------|
| subjects affected / exposed occurrences (all) | 1 / 18 (5.56%) 1 | 0 / 36 (0.00%) 0 | 4 / 89 (4.49%) 5 |
| Localised oedema subjects affected / exposed occurrences (all) | 1 / 18 (5.56%) 1 | 0 / 36 (0.00%) 0 | 0 / 89 (0.00%) 0 |
| Immune system disorders Allergy to arthropod bite subjects affected / exposed occurrences (all) | 1 / 18 (5.56%) 1 | 0 / 36 (0.00%) 0 | 0 / 89 (0.00%) 0 |
| Food allergy subjects affected / exposed occurrences (all) | 0 / 18 (0.00%) 0 | 0 / 36 (0.00%) 0 | 0 / 89 (0.00%) 0 |
| Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) | 0 / 18 (0.00%) 0 | 1 / 36 (2.78%) 1 | 4 / 89 (4.49%) 4 |
| Dyspnoea subjects affected / exposed occurrences (all) | 1 / 18 (5.56%) 1 | 0 / 36 (0.00%) 0 | 0 / 89 (0.00%) 0 |
| Investigations Blood phosphorus decreased subjects affected / exposed occurrences (all) | 1 / 18 (5.56%) 1 | 0 / 36 (0.00%) 0 | 0 / 89 (0.00%) 0 |
| Weight decreased subjects affected / exposed occurrences (all) | 1 / 18 (5.56%) 1 | 0 / 36 (0.00%) 0 | 3 / 89 (3.37%) 3 |
| Injury, poisoning and procedural complications Limb injury subjects affected / exposed occurrences (all) | 1 / 18 (5.56%) 1 | 0 / 36 (0.00%) 0 | 0 / 89 (0.00%) 0 |
| Congenital, familial and genetic disorders Phimosi subjects affected / exposed occurrences (all) | 0 / 18 (0.00%) 0 | 0 / 36 (0.00%) 0 | 0 / 89 (0.00%) 0 |
| Nervous system disorders | | | |

| | | | |
|---|----------------------|------------------------|------------------------|
| Carpal tunnel syndrome subjects affected / exposed occurrences (all) | 1 / 18 (5.56%) 2 | 0 / 36 (0.00%) 0 | 0 / 89 (0.00%) 0 |
| Headache subjects affected / exposed occurrences (all) | 2 / 18 (11.11%) 2 | 1 / 36 (2.78%) 1 | 5 / 89 (5.62%) 5 |
| Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all) | 1 / 18 (5.56%) 1 | 3 / 36 (8.33%) 5 | 6 / 89 (6.74%) 7 |
| Lymphadenopathy subjects affected / exposed occurrences (all) | 0 / 18 (0.00%) 0 | 0 / 36 (0.00%) 0 | 0 / 89 (0.00%) 0 |
| Ear and labyrinth disorders Vertigo subjects affected / exposed occurrences (all) | 0 / 18 (0.00%) 0 | 0 / 36 (0.00%) 0 | 1 / 89 (1.12%) 1 |
| Eye disorders Eye swelling subjects affected / exposed occurrences (all) | 1 / 18 (5.56%) 1 | 0 / 36 (0.00%) 0 | 0 / 89 (0.00%) 0 |
| Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all) | 1 / 18 (5.56%) 1 | 3 / 36 (8.33%) 3 | 6 / 89 (6.74%) 6 |
| Abdominal pain lower subjects affected / exposed occurrences (all) | 1 / 18 (5.56%) 1 | 0 / 36 (0.00%) 0 | 1 / 89 (1.12%) 1 |
| Aphthous ulcer subjects affected / exposed occurrences (all) | 0 / 18 (0.00%) 0 | 0 / 36 (0.00%) 0 | 1 / 89 (1.12%) 1 |
| Colitis ulcerative subjects affected / exposed occurrences (all) | 4 / 18 (22.22%) 4 | 11 / 36 (30.56%) 15 | 22 / 89 (24.72%) 24 |
| Diarrhoea subjects affected / exposed occurrences (all) | 0 / 18 (0.00%) 0 | 2 / 36 (5.56%) 4 | 5 / 89 (5.62%) 6 |

| | | | |
|--|---------------------|---------------------|---------------------|
| Frequent bowel movements subjects affected / exposed occurrences (all) | 1 / 18 (5.56%) 1 | 1 / 36 (2.78%) 1 | 0 / 89 (0.00%) 0 |
| Gastrooesophageal reflux disease subjects affected / exposed occurrences (all) | 0 / 18 (0.00%) 0 | 0 / 36 (0.00%) 0 | 0 / 89 (0.00%) 0 |
| Haematochezia subjects affected / exposed occurrences (all) | 1 / 18 (5.56%) 1 | 1 / 36 (2.78%) 3 | 0 / 89 (0.00%) 0 |
| Nausea subjects affected / exposed occurrences (all) | 1 / 18 (5.56%) 1 | 1 / 36 (2.78%) 2 | 5 / 89 (5.62%) 5 |
| Vomiting subjects affected / exposed occurrences (all) | 1 / 18 (5.56%) 1 | 2 / 36 (5.56%) 2 | 0 / 89 (0.00%) 0 |
| Skin and subcutaneous tissue disorders | | | |
| Acne subjects affected / exposed occurrences (all) | 0 / 18 (0.00%) 0 | 0 / 36 (0.00%) 0 | 0 / 89 (0.00%) 0 |
| Pruritus subjects affected / exposed occurrences (all) | 1 / 18 (5.56%) 1 | 0 / 36 (0.00%) 0 | 1 / 89 (1.12%) 1 |
| Pruritus generalised subjects affected / exposed occurrences (all) | 1 / 18 (5.56%) 1 | 0 / 36 (0.00%) 0 | 1 / 89 (1.12%) 1 |
| Rash subjects affected / exposed occurrences (all) | 0 / 18 (0.00%) 0 | 0 / 36 (0.00%) 0 | 1 / 89 (1.12%) 2 |
| Skin ulcer subjects affected / exposed occurrences (all) | 1 / 18 (5.56%) 1 | 0 / 36 (0.00%) 0 | 0 / 89 (0.00%) 0 |
| Swelling face subjects affected / exposed occurrences (all) | 1 / 18 (5.56%) 1 | 0 / 36 (0.00%) 0 | 0 / 89 (0.00%) 0 |
| Urticaria | | | |

| | | | |
|--|---------------------|---------------------|---------------------|
| subjects affected / exposed occurrences (all) | 0 / 18 (0.00%) 0 | 1 / 36 (2.78%) 1 | 1 / 89 (1.12%) 1 |
| Renal and urinary disorders | | | |
| Haematuria | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 36 (0.00%) | 0 / 89 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Proteinuria | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 36 (0.00%) | 0 / 89 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 2 / 18 (11.11%) | 3 / 36 (8.33%) | 9 / 89 (10.11%) |
| occurrences (all) | 2 | 3 | 11 |
| Back pain | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 36 (0.00%) | 8 / 89 (8.99%) |
| occurrences (all) | 0 | 0 | 8 |
| Joint swelling | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 36 (0.00%) | 0 / 89 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rheumatic disorder | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 36 (0.00%) | 0 / 89 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Infections and infestations | | | |
| Candida infection | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 36 (0.00%) | 0 / 89 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Conjunctivitis | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 36 (0.00%) | 0 / 89 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Gastroenteritis | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 3 / 36 (8.33%) | 3 / 89 (3.37%) |
| occurrences (all) | 0 | 4 | 3 |
| Influenza | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 1 / 36 (2.78%) | 2 / 89 (2.25%) |
| occurrences (all) | 1 | 1 | 4 |
| Nasopharyngitis | | | |

| | | | |
|---|---------------------|---------------------|----------------------|
| subjects affected / exposed occurrences (all) | 0 / 18 (0.00%) 0 | 1 / 36 (2.78%) 1 | 5 / 89 (5.62%) 10 |
| Upper respiratory tract infection subjects affected / exposed occurrences (all) | 0 / 18 (0.00%) 0 | 2 / 36 (5.56%) 2 | 5 / 89 (5.62%) 6 |
| Urinary tract infection subjects affected / exposed occurrences (all) | 1 / 18 (5.56%) 1 | 0 / 36 (0.00%) 0 | 1 / 89 (1.12%) 1 |
| Metabolism and nutrition disorders Dehydration subjects affected / exposed occurrences (all) | 1 / 18 (5.56%) 1 | 0 / 36 (0.00%) 0 | 0 / 89 (0.00%) 0 |
| Weight gain poor subjects affected / exposed occurrences (all) | 0 / 18 (0.00%) 0 | 0 / 36 (0.00%) 0 | 0 / 89 (0.00%) 0 |

| | | | |
|--|--|--|--|
| Non-serious adverse events | OL Period: Abrilumab 210 mg/210 mg Q3M | | |
| Total subjects affected by non-serious adverse events subjects affected / exposed | 26 / 68 (38.24%) | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) Lipoma subjects affected / exposed occurrences (all) | 0 / 68 (0.00%) 0 | | |
| Vascular disorders Hypertension subjects affected / exposed occurrences (all) | 1 / 68 (1.47%) 1 | | |
| Pregnancy, puerperium and perinatal conditions Pregnancy subjects affected / exposed occurrences (all) | 0 / 68 (0.00%) 0 | | |
| General disorders and administration site conditions Asthenia subjects affected / exposed occurrences (all) Fatigue | 1 / 68 (1.47%) 1 | | |

| | | | |
|---|---|--|--|
| <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>1 / 68 (1.47%)</p> <p>1</p> | | |
| <p>Hyperthermia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>0 / 68 (0.00%)</p> <p>0</p> | | |
| <p>Influenza like illness</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>0 / 68 (0.00%)</p> <p>0</p> | | |
| <p>Localised oedema</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>0 / 68 (0.00%)</p> <p>0</p> | | |
| <p>Immune system disorders</p> <p>Allergy to arthropod bite</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Food allergy</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>0 / 68 (0.00%)</p> <p>0</p> <p>0 / 68 (0.00%)</p> <p>0</p> | | |
| <p>Respiratory, thoracic and mediastinal disorders</p> <p>Cough</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Dyspnoea</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>1 / 68 (1.47%)</p> <p>1</p> <p>0 / 68 (0.00%)</p> <p>0</p> | | |
| <p>Investigations</p> <p>Blood phosphorus decreased</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Weight decreased</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>0 / 68 (0.00%)</p> <p>0</p> <p>1 / 68 (1.47%)</p> <p>1</p> | | |
| <p>Injury, poisoning and procedural complications</p> <p>Limb injury</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>0 / 68 (0.00%)</p> <p>0</p> | | |

| | | | |
|--|---|--|--|
| Congenital, familial and genetic disorders Phimosis subjects affected / exposed occurrences (all) | 0 / 68 (0.00%) 0 | | |
| Nervous system disorders Carpal tunnel syndrome subjects affected / exposed occurrences (all) Headache subjects affected / exposed occurrences (all) | 0 / 68 (0.00%) 0 4 / 68 (5.88%) 4 | | |
| Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all) Lymphadenopathy subjects affected / exposed occurrences (all) | 2 / 68 (2.94%) 2 1 / 68 (1.47%) 1 | | |
| Ear and labyrinth disorders Vertigo subjects affected / exposed occurrences (all) | 0 / 68 (0.00%) 0 | | |
| Eye disorders Eye swelling subjects affected / exposed occurrences (all) | 0 / 68 (0.00%) 0 | | |
| Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all) Abdominal pain lower subjects affected / exposed occurrences (all) Aphthous ulcer subjects affected / exposed occurrences (all) Colitis ulcerative | 0 / 68 (0.00%) 0 0 / 68 (0.00%) 0 0 / 68 (0.00%) 0 | | |

| | | | |
|--|-----------------|--|--|
| subjects affected / exposed | 8 / 68 (11.76%) | | |
| occurrences (all) | 9 | | |
| Diarrhoea | | | |
| subjects affected / exposed | 1 / 68 (1.47%) | | |
| occurrences (all) | 1 | | |
| Frequent bowel movements | | | |
| subjects affected / exposed | 1 / 68 (1.47%) | | |
| occurrences (all) | 1 | | |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | |
| occurrences (all) | 0 | | |
| Haematochezia | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | |
| occurrences (all) | 0 | | |
| Nausea | | | |
| subjects affected / exposed | 1 / 68 (1.47%) | | |
| occurrences (all) | 1 | | |
| Vomiting | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | |
| occurrences (all) | 0 | | |
| Skin and subcutaneous tissue disorders | | | |
| Acne | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | |
| occurrences (all) | 0 | | |
| Pruritus | | | |
| subjects affected / exposed | 2 / 68 (2.94%) | | |
| occurrences (all) | 3 | | |
| Pruritus generalised | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | |
| occurrences (all) | 0 | | |
| Rash | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | |
| occurrences (all) | 0 | | |
| Skin ulcer | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | |
| occurrences (all) | 0 | | |

| | | | |
|---|---------------------|--|--|
| Swelling face subjects affected / exposed occurrences (all) | 0 / 68 (0.00%) 0 | | |
| Urticaria subjects affected / exposed occurrences (all) | 0 / 68 (0.00%) 0 | | |
| Renal and urinary disorders Haematuria subjects affected / exposed occurrences (all) | 0 / 68 (0.00%) 0 | | |
| Proteinuria subjects affected / exposed occurrences (all) | 0 / 68 (0.00%) 0 | | |
| Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) | 1 / 68 (1.47%) 1 | | |
| Back pain subjects affected / exposed occurrences (all) | 0 / 68 (0.00%) 0 | | |
| Joint swelling subjects affected / exposed occurrences (all) | 1 / 68 (1.47%) 1 | | |
| Rheumatic disorder subjects affected / exposed occurrences (all) | 0 / 68 (0.00%) 0 | | |
| Infections and infestations Candida infection subjects affected / exposed occurrences (all) | 0 / 68 (0.00%) 0 | | |
| Conjunctivitis subjects affected / exposed occurrences (all) | 1 / 68 (1.47%) 1 | | |
| Gastroenteritis subjects affected / exposed occurrences (all) | 1 / 68 (1.47%) 2 | | |

| | | | |
|------------------------------------|----------------|--|--|
| Influenza | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | |
| occurrences (all) | 0 | | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 6 / 68 (8.82%) | | |
| occurrences (all) | 10 | | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | |
| occurrences (all) | 0 | | |
| Urinary tract infection | | | |
| subjects affected / exposed | 1 / 68 (1.47%) | | |
| occurrences (all) | 1 | | |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | |
| occurrences (all) | 0 | | |
| Weight gain poor | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | |
| occurrences (all) | 0 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|--|
| 01 June 2012 | <p>Amendment 1 introduced changes that incorporated feedback received from regulatory authorities in Europe and the US. Briefly:</p> <ul style="list-style-type: none">- The subject population at study entry was limited to subjects who had an inadequate response to, or intolerance to, immunomodulators or anti-TNF agents.- Methods of birth control were added.- The safety follow-up period was extended from 12 months to 24 months.- Immunomodulators were to be withdrawn in all subjects at week 8.- Recommendations for withdrawal of open-label AMG 181 during the open-label period were added.- The use of concomitant medications during the study was clarified.- Hepatotoxicity rules on stopping of and rechallenge with investigational product were added.- In compliance with a requirement contained in the then-current version of the European Union Clinical Trial Directive, the safety reporting language in Protocol Section 9.2.2 ("Reporting Procedures for Serious Adverse Events") was updated. The reporting timeline for the investigator to report serious adverse events to Amgen upon knowledge of the event was changed to within 24 hours. Language that limited the types of serious adverse events the investigator was to report to Amgen after the end of study was deleted.- In the statistical considerations section, the statistical method proposed for the primary analysis was changed to an IPW GEE model. The lists of covariates and subgroup analyses were updated.- Other minor changes included corrections of typographical errors and small edits to clarify intent. |
| 11 February 2013 | <p>Amendment 2 introduced the following changes:</p> <ul style="list-style-type: none">- The protocol was amended to ensure that the study was adequately sized to evaluate the primary endpoint of the study in light of results from a phase 3 study of vedolizumab in subjects with Ulcerative Colitis (Feagan et al, 2012). The assumptions for sample size were updated accordingly with the type I error rate adjusted to a 2-sided alpha level of 0.10 that resulted in a 14% increase in the study sample size. The enrollment of subjects with any prior exposure to anti-TNF agents was limited to approximately 50% in order to assess the efficacy of AMG 181 in both anti-TNF agent naïve and anti-TNF agent exposed subjects.- Minor updates were made to Section 2 (Background and Rationale).- Minor clarifications and corrections were made to eligibility criteria.- Clarifications and corrections were made to Section 7 (Study Procedures).- Reasons for removal of subjects from the study were updated in Section 8 (Removal and Replacement of Subjects) and Section 9 (Safety Data Collection, Recording, and Reporting).- Updates to Section 9 (Safety Data Collection, Recording, and Reporting) were made to ensure that adverse event reporting and reports of lactation followed the sponsor's standard procedures.- Typographic and formatting errors were corrected throughout the Protocol. |

| | |
|-------------------|---|
| 25 September 2013 | <p>Amendment 3 introduced the following changes:</p> <ul style="list-style-type: none"> • A systematic misalignment between the IP packaging and the IPIM occurred such that subjects enrolled prior to Protocol Amendment 3 were randomly assigned to treatment groups at ratios different from those stipulated in the Protocol. A higher proportion of subjects received placebo and some subjects received a dose higher than they were randomly assigned. All subjects were expected to have received a dose level defined by the Protocol. No increased safety risks were identified for any subjects. Changes to Statistical Considerations were made as summarized below: <ul style="list-style-type: none"> - Neither the randomization nor study blind was compromised and the intent-to-treat principle was maintained. The full analysis consisted of all randomized subjects who had received at least 1 dose of IP. Subjects enrolled under Amendment 3 were to be analyzed according to their IVRS randomized treatment group. Subjects enrolled prior to Amendment 3 were to be analyzed according to the randomly assigned yet erroneous treatment as the result of the systemic misalignment. - Due to the unintended difference in the randomization ratio and the disproportion of subjects in treatment arms prior to Amendment 3, a linear trend test was no longer appropriate. The primary and key secondary endpoints were to be tested under a sequential framework for the 2 highest doses of AMG 181. The total sample size of 360 with the unintended final randomization allocation had approximately 87% and 84% power to detect differences between the AMG 181 70 mg and 210 mg groups vs placebo using a 0.10 2-sided test. - The AMG 181 70 mg group vs the placebo group was to be tested prior to AMG 181 210 mg group vs placebo group analyses. • Clarifications to Study Design were done. • Inclusion Criteria were updated such that at non-US sites, subjects who demonstrated an inadequate response to, loss of response to, or intolerance to corticosteroids were to be allowed in the study. |
|-------------------|---|

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

| Date | Interruption | Restart date |
|--------------|--|------------------|
| 12 July 2013 | Routine PK analyses by the unblinded clinical pharmacology group reported a systematic inconsistency in expected exposures for the 7 mg and 21 mg dose cohorts. The study was immediately paused for investigation, which showed a consistent discrepancy between the IP instruction manual (IPIM) description of vial positions and the actual vial positions in the IP package. Once the discrepancy was corrected and affected patients completed their double-blind treatment period, the study resumed enrollment and randomization per protocol. | 06 December 2013 |

Notes:

Limitations and caveats

None reported