



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
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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
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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
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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
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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
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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
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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 standard deviation	7.83 ± 5.58	9.07 ± 6.57	7.05 ± 5.39
Total Mayo Score Units: years arithmetic mean standard deviation	8.9 ± 1.5	8.1 ± 1.4	8.6 ± 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 standard deviation	39.3 ± 12.2	39.8 ± 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
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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
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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
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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
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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
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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
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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
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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
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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			
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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
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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
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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
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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
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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
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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
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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 Abrilumab vs Placebo
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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 21 mg Q4W/Abrilumab 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
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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 21 mg Q4W/Abrilumab 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 Abrilumab vs Placebo
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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
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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
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	20.1
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Reporting groups

Reporting group title	DB Period: Placebo
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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
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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
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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
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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
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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
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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
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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
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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
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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
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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:
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	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	1 / 99 (1.01%)	0 / 79 (0.00%)	0 / 100 (0.00%)
occurrences (all)	1	0	0
Nausea			
subjects affected / exposed	4 / 99 (4.04%)	5 / 79 (6.33%)	2 / 100 (2.00%)
occurrences (all)	4	5	2
Vomiting			
subjects affected / exposed	3 / 99 (3.03%)	2 / 79 (2.53%)	4 / 100 (4.00%)
occurrences (all)	3	2	5
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	2 / 99 (2.02%)	0 / 79 (0.00%)	2 / 100 (2.00%)
occurrences (all)	2	0	3
Pruritus			
subjects affected / exposed	1 / 99 (1.01%)	3 / 79 (3.80%)	3 / 100 (3.00%)
occurrences (all)	1	3	3
Pruritus generalised			
subjects affected / exposed	0 / 99 (0.00%)	0 / 79 (0.00%)	0 / 100 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	4 / 99 (4.04%)	1 / 79 (1.27%)	5 / 100 (5.00%)
occurrences (all)	4	1	6
Skin ulcer			
subjects affected / exposed	0 / 99 (0.00%)	0 / 79 (0.00%)	0 / 100 (0.00%)
occurrences (all)	0	0	0
Swelling face			
subjects affected / exposed	0 / 99 (0.00%)	0 / 79 (0.00%)	0 / 100 (0.00%)
occurrences (all)	0	0	0
Urticaria			
subjects affected / exposed	0 / 99 (0.00%)	0 / 79 (0.00%)	1 / 100 (1.00%)
occurrences (all)	0	0	1
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	0 / 99 (0.00%)	0 / 79 (0.00%)	0 / 100 (0.00%)
occurrences (all)	0	0	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	1 / 18 (5.56%)	1 / 36 (2.78%)	0 / 89 (0.00%)
occurrences (all)	1	1	0
Gastrooesophageal reflux disease subjects affected / exposed	0 / 18 (0.00%)	0 / 36 (0.00%)	0 / 89 (0.00%)
occurrences (all)	0	0	0
Haematochezia subjects affected / exposed	1 / 18 (5.56%)	1 / 36 (2.78%)	0 / 89 (0.00%)
occurrences (all)	1	3	0
Nausea subjects affected / exposed	1 / 18 (5.56%)	1 / 36 (2.78%)	5 / 89 (5.62%)
occurrences (all)	1	2	5
Vomiting subjects affected / exposed	1 / 18 (5.56%)	2 / 36 (5.56%)	0 / 89 (0.00%)
occurrences (all)	1	2	0
Skin and subcutaneous tissue disorders			
Acne subjects affected / exposed	0 / 18 (0.00%)	0 / 36 (0.00%)	0 / 89 (0.00%)
occurrences (all)	0	0	0
Pruritus subjects affected / exposed	1 / 18 (5.56%)	0 / 36 (0.00%)	1 / 89 (1.12%)
occurrences (all)	1	0	1
Pruritus generalised subjects affected / exposed	1 / 18 (5.56%)	0 / 36 (0.00%)	1 / 89 (1.12%)
occurrences (all)	1	0	1
Rash subjects affected / exposed	0 / 18 (0.00%)	0 / 36 (0.00%)	1 / 89 (1.12%)
occurrences (all)	0	0	2
Skin ulcer subjects affected / exposed	1 / 18 (5.56%)	0 / 36 (0.00%)	0 / 89 (0.00%)
occurrences (all)	1	0	0
Swelling face subjects affected / exposed	1 / 18 (5.56%)	0 / 36 (0.00%)	0 / 89 (0.00%)
occurrences (all)	1	0	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		

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

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	Amendment 1 introduced changes that incorporated feedback received from regulatory authorities in Europe and the US. Briefly: - 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	Amendment 2 introduced the following changes: - 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	Amendment 3 introduced the following changes: • 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: - 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.
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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