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GENERIC DRUG NAME / COMPOUND NUMBER: Fezakinumab / ILV-094

PROTOCOL NO.: 3199K1-2001 (B1981001)

PROTOCOL TITLE: A Randomized, Parallel, Double-Blind, Placebo-Controlled Study to Evaluate the Efficacy and Safety of ILV-094 Administered Subcutaneously to Subjects With Active Rheumatoid Arthritis on a Stable Background of Methotrexate

Study Centers: Forty-six (46) centers took part in the study and randomized subjects: 5 in Belgium, 4 in Columbia, 2 in Croatia, 4 in Hungary, 7 in Japan, 1 in Mexico, 7 in Romania, 7 in Russian Federation and 9 in the United States (US).

Study Initiation and Final Completion Dates: 18 June 2009 and 18 February 2011

Phase of Development: Phase 2

Study Objectives:

- To assess the safety and efficacy of different dose regimens of fezakinumab compared with placebo, administered subcutaneously (SC) to subjects with active rheumatoid arthritis (RA) on a background of methotrexate.

METHODS

Study Design:

This was a Phase 2, multicenter, parallel-group, placebo-controlled, randomized, double-blind study. The subjects were stratified by anti-tumor necrosis factor (TNF) agent prior use (yes/no) and geographic region of the site (Japan/non-Japan). The study was divided into 2 sequential parts for enrollment. Enrollment of subjects in the second part of the study started after enrollment in the first part was completed.

In the first part of enrollment, subjects were to be equally randomized (1:1:1 ratio) at Baseline (Day 1) into 1 of 3 groups:

- 100 mg fezakinumab every 2 weeks (Q2W) SC;
- 100 mg fezakinumab every 4 weeks (Q4W) SC (alternating fezakinumab 100 mg and placebo Q2W);
- Placebo Q2W SC.

In the second part of enrollment, additional subjects were to be randomized (2:1 ratio) at Baseline (Day 1) into 1 of 2 groups:

- 200 mg fezakinumab Q2W SC;
- Placebo Q2W SC.

The subjects received their first dose of study treatment at Baseline (Day 1), consisting of a 2-fold loading dose to ensure that steady-state exposure was reached faster. Study treatment was then administered Q2W and the subjects received their last dose of study treatment at Week 10. They were evaluated for 12 weeks after their last dose of study treatment, ie, until Week 22. The subjects who discontinued prematurely might have initiated an alternative treatment if appropriate but were also evaluated over the 12-week period after their last dose of study treatment.

Table 1 and Table 2 summarize the schedule of activities.

Table 1. Study Flowchart 1: Screening Through Week 22 Follow-Up

Study Period	Screening	Baseline	Treatment Period						Follow-Up Period		
Study Visit Day	Screening	Day 1	Day 14[a]	Day 28[a]	Day 42[a]	Day 56[a]	Day 70[a]	Day 84[a]	Follow-Up Day 98[b]	Follow-Up Day 126[b]	Follow-Up/ Final Visit Day 154[b]
Study Visit Week	Up to W-4	W0	W2	W4	W6	W8	W10	W12	W14	W18	W22
Informed consent	X										
Inclusion/exclusion criteria	X	X									
Demography	X										
Medical history	X										
Prior/concomitant treatments and medications	X	X	X	X	X	X	X	X	X	X	X
Physical examination	X	X	X	X	X	X	X	X	X	X	X
Vital signs[c]	X	X	X	X	X	X	X	X	X	X	X
Complete Joint Assessment (28-joints)	X	X	X	X	X	X	X	X	X[d]	X[d]	X[d]
Physician and Patient global assessment of RA		X	X	X	X	X	X	X	X[d]	X[d]	X[d]
Tuberculosis test[e]	X										
Chest radiograph (PA and lateral)[e]	X										
ECG (12-lead)	X										
Laboratory evaluations[f, g]	X	X	X	X	X	X	X	X	X	X	X
Urine pregnancy test (women only, local laboratory)[g, h]	X	X	X	X	X	X	X	X	X	X	X
CRP (central laboratory) and ESR (local laboratory)	X	X	X	X	X	X	X	X	X[d]	X[d]	X[d]
HIV, HBsAg, and HCV[g]	X										
Randomization		X									
Study treatment administration[h]		X	X	X	X	X	X				
Serum sample for PK[i]		X	X	X	X	X	X	X	X	X	X
Serum sample for anti-fezakinumab antibodies[i]		X						X			X
Blood sample for PD biomarkers[j]		X	X	X	X	X	X	X	X[d]	X[d]	X[d]
Blood sample for PGt[k]		X									
Blood sample for PGx[k]		X		X		X		X			X[d]

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Study Visit Day	Screening	Day 1	Day 14[a]	Day 28[a]	Day 42[a]	Day 56[a]	Day 70[a]	Day 84[a]	Follow-Up Day 98[b]	Follow-Up Day 126[b]	Follow-Up/ Final Visit Day 154[b]
Study Visit Week	Up to W-4	W0	W2	W4	W6	W8	W10	W12	W14	W18	W22
Pain VAS		X	X	X	X	X	X	X	X[d]	X[d]	X[d]
General health VAS		X	X	X	X	X	X	X	X[d]	X[d]	X[d]
HAQ-DI		X	X	X	X	X	X	X	X[d]	X[d]	X[d]
SF-36		X		X		X		X			
FACIT-Fatigue		X		X		X		X			
Adverse events[l]	X----------X										
Conclusion of treatment phase								X			
Conclusion of subject participation											X

CCP = cyclic citrullinated peptide; CRP = C-reactive protein; ECG = electrocardiogram; ESR = erythrocyte sedimentation rate; FACIT-Fatigue = Functional Assessment of Chronic Illness Therapy -Fatigue; HAQ-DI = Health Assessment Questionnaire Disability Index; HBsAg = hepatitis B surface antigen; HCV = hepatitis C virus; HIV = human immunodeficiency virus; IEC = independent ethics committee; IL = interleukin; IRB = institutional review board; PA = posteroanterior; PD = pharmacodynamics; PGt = pharmacogenetic; PGx = pharmacogenomic; PK = pharmacokinetic; RA = rheumatoid arthritis; RF = rheumatoid factor; SAA = serum amyloid A; SF-36= Short Form 36; TNF = tumor necrosis factor; VAS = visual analog scale; W = week.

a. Study Week 2 to Week 12 visits occurred within a window of ±3 days of the projected visit date.
b. Follow-up Week 14 to Week 22 visits occurred within a window of ±6 days of the projected visit date.
c. Vital signs included height (in cm), weight (in kg), sitting blood pressure, pulse rate (after sitting for 5 minutes) and temperature (oral, axillary, or tympanic). Height was recorded at the Screening visit only.
d. These tests or assessments were required during the follow-up period visits only if the subject had not initiated a prohibited treatment that could alter RA activity.
e. Tuberculosis test was performed at Screening, unless a tuberculosis test was performed within 4 weeks prior to Baseline and the results were available. Chest x-ray was performed at Screening, unless a chest radiograph was performed within 3 months prior to Baseline and the results were available.
f. Samples for laboratory evaluations, including hematology, blood chemistry, urinalysis, and coagulation tests, to be collected after an 8-hour fast.
g. All screening laboratory results (including HIV, HBsAg, and HCV) and any repeat laboratory tests were reviewed prior to randomization.
h. If a urine pregnancy test was positive, subject was withdrawn from study. For all women, a negative pregnancy test result must be available for eligibility assessment and prior to the administration of TA at Baseline and at Weeks 2, 4, 6, 8 and 10.
i. Blood samples for fezakinumab PK analysis and anti-fezakinumab antibodies were collected prior to the study treatment administration on Day 1 (predose) and also preferably prior to the study treatment administration of each visit during the treatment period.
j. Biomarkers to be evaluated included SAA, TNF, anti-CCP, RF (total RF), IL-6, IL-22, IL-17, IL-12, and IL-23. RF was evaluated at Baseline and Week 12 only.
k. Prior to collection of PGt and PGx samples, subjects signed and dated a separate IRB/IEC approved consent. PGt and PGx samples were collected prior to

Table 1. Study Flowchart 1: Screening Through Week 22 Follow-Up

Study Period	Screening	Baseline	Treatment Period						Follow-Up Period		
Study Visit Day	Screening	Day 1	Day 14[a]	Day 28[a]	Day 42[a]	Day 56[a]	Day 70[a]	Day 84[a]	Follow-Up Day 98[b]	Follow-Up Day 126[b]	Follow-Up/ Final Visit Day 154[b]
Study Visit Week	Up to W-4	W0	W2	W4	W6	W8	W10	W12	W14	W18	W22

study treatment administration on Day 1 (predose).

l. Adverse events were collected from the signing of the informed consent form to conclusion of subject participation.

Table 2. Study Flowchart 2: Early Termination and Follow-Up

Study Period	**Early Termination and Follow-up Period**			
Study Visit Week	**Early Termination Visit (if Discontinuation Prior to Week 12)[a]**	**Early Termination Follow-Up Visit (4 weeks After the Last Dose[b])**	**Early Termination Follow-Up Visit (8 weeks After the Last Dose[b])**	**Early Termination Follow-Up Visit/Final Visit (12 Weeks After the Last Dose[b])**
Concomitant treatments and medications	X	X	X	X
Physical examination	X	X	X	X
Vital signs[c]	X	X	X	X
Complete Joint Assessment (28-joints)	X			
Physician and Patient Global Assessment of RA	X			
Laboratory evaluations[d]	X	X	X	X
Urine pregnancy test (women only, local laboratory)	X	X	X	X
CRP (central laboratory) and ESR (local laboratory)	X			
Serum sample for PK	X	X	X	X
Serum sample for anti-fezakinumab antibodies	X			X
Blood sample for PD biomarkers[e]	X			
Pain VAS	X			
General health VAS	X			
HAQ-DI	X			
Adverse events[f]	X----------X			
Conclusion of treatment phase	X			
Conclusion of subject participation				X

CCP = cyclic citrullinated peptide; CRP = C-reactive protein; ESR = erythrocyte sedimentation rate; HAQ-DI = Health Assessment Questionnaire Disability Index; IL = interleukin; PD = pharmacodynamics; PK = pharmacokinetic; RA = rheumatoid arthritis; RF = rheumatoid factor; SAA = serum amyloid A; TNF = tumor necrosis factor; VAS = visual analog scale.

a. Early termination visit for subjects who discontinued prior to Week 12 visit.
b. Early termination follow-up visits occurred within a window of ±6 days of the projected visit date.
c. Vital signs included weight (in kg), sitting blood pressure, pulse rate (after sitting for 5 minutes) and temperature (oral, axillary, or tympanic).
d. Samples for laboratory evaluations, including hematology, blood chemistry, urinalysis, and coagulation tests to be collected after an 8-hour fast.
e. Biomarkers to be evaluated included SAA, TNF, anti-CCP, RF (total RF), IL-6, IL-22, IL-17, IL-12, and IL-23.
f. Adverse events to be collected from the signing of the informed consent form to conclusion of subject participation.

Number of Subjects (Planned and Analyzed):

The number of randomized subjects planned for this study was 180, based on 40 subjects in each of the 3 fezakinumab groups and 60 subjects in the placebo group.

Three hundred twenty two (322) subjects were assigned to treatment; 108 subjects were screening failures with 18 subjects not randomized who were eligible. In total, 196 subjects were randomized to receive study treatment, including 39 subjects in the 100 mg fezakinumab Q4W group, 42 subjects in the 100 mg fezakinumab Q2W group, 49 subjects in the 200 mg fezakinumab Q2W group, and 66 subjects in the placebo group. One (1) subject randomized to the 200 mg fezakinumab Q2W group did not receive any dose of study treatment. Thus, a total of 195 subjects received at least 1 dose of study treatment: 9 in Belgium, 26 in Columbia, 13 in Croatia, 25 in Hungary, 28 in Japan, 6 in Mexico, 19 in Romania, 25 in the Russian Federation, 44 in the US. All 195 subjects were included in the safety and modified intent-to-treat (mITT) populations.

Diagnosis and Main Criteria for Inclusion:

Subjects who met the American College of Rheumatology (ACR) 1987 revised criteria for classification of RA for at least 6 months prior to Screening, with active RA at the time of Screening and Baseline consisting of ≥5 swollen and ≥5 tender joints (28-joint count) and at least 1 of the following at Screening: C-reactive protein (CRP) ≥10 mg/L or Erythrocyte Sedimentation Rate (ESR) ≥28 mm/h and who were receiving methotrexate for at least 12 weeks, with a stable route and dose (up to 25 mg weekly) for at least 8 weeks prior to the Baseline visit were included in the study.

Main Exclusion Criteria: Subjects with other rheumatic diseases, cancer or history of cancer (other than cutaneous basal cell carcinoma and squamous cell carcinoma or in situ cervical cancer) and any prior use of B cell-depleting therapy were excluded from the study.

Study Treatment:

Study treatments in this study were fezakinumab and placebo available as lyophilized powder. Subjects enrolled in the first part were randomly assigned to receive 100 mg fezakinumab Q2W, Q4W or placebo. In the second part of enrollment, subjects were randomly assigned to receive 200 mg fezakinumab Q2W SC or placebo Q2W SC. The study site personnel administered the study treatment to the subjects SC in the arms, the thighs, or the abdomen. Study treatment administrations were to be done preferably at the same location.

Subjects participated in the study for approximately 26 weeks. This included a screening period of up to 4 weeks, a 12-week treatment period (last administration of study treatment at Week 10) and a 10-week follow-up period (12 weeks after the last study treatment administration).

Efficacy Endpoints:

Primary Efficacy Endpoint:

The primary efficacy endpoint was ACR20 at Week 12. ACR is a commonly accepted efficacy composite variable that uses tender and swollen joint count, patient global assessment, physician global assessment, patient pain visual analog scale (VAS), Health Assessment Questionnaire (HAQ) and CRP. ACR20 represents a 20% improvement from Baseline and was calculated by the Sponsor.

Secondary Efficacy Endpoints:

- ACR20 at all time points other than Week 12.
- ACR50 (50% improvement from Baseline).
- ACR70 (70% improvement from Baseline).
- Disease Activity Score (DAS) 28. DAS 28 is a weighted calculation of the 28-joint count for tenderness and swelling, CRP, ESR, and general health VAS.
- Tender Joints Assessment. Joint assessors assessed 28 joints for tenderness as follows: 0= no tenderness; 1= any tenderness; JR = joint replacement; NE = not evaluable. For consistency, the same assessor should have, if possible, evaluated the number of tender joints at each visit.
- Swollen Joints Assessment. Joint assessors assessed 28 joints for swelling as follows: 0= no swelling; 1= any swelling; JR = joint replacement; NE = not evaluable. For consistency, the same assessor should have, if possible, evaluated the number of swollen joints at each visit.
- Physician Global Assessment and Patient Global Assessment of Disease Activity on a 0 to 10 Scale. The physician global assessment and patient global assessment were to be completed independently in a manner that did not bias the Investigator or the subject.
- Pain VAS (0 to 100 mm).
- General health VAS (0 to 100 mm).
- Quality of life and physical function as assessed by the Health Assessment Questionnaire Disability Index (HAQ-DI). This validated instrument was available in several languages. The appropriate language form was used for each participating country.
- General quality of life as assessed by the Short Form 36 (SF-36).
- Fatigue as assessed by the Functional Assessment of Chronic Illness Therapy -Fatigue (FACIT-Fatigue).

- European League Against Rheumatism (EULAR) response as derived from DAS 28.

The efficacy assessments were well-accepted endpoints for evaluating active RA.

Safety Evaluations: The safety of fezakinumab was determined using the following assessments: monitoring of adverse events (AEs) (including infectious and noninfectious AEs, infectious and noninfectious serious AEs [SAEs], medically important infections [defined as infections that required parenteral anti-infective agents and/or hospitalization] and injection site reactions [ISRs]), physical examinations, vital signs, and laboratory determinations. Blood samples to determine anti-fezakinumab antibodies were also collected for immunogenicity analysis.

Statistical Methods:

Analysis Populations:

There were 3 efficacy analysis populations used in this study.

Modified Intent-to-treat Population: A mITT population, defined as all randomized subjects who received at least 1 dose (even partial) of study treatment, was the primary population for efficacy analyses.

Per-protocol or Valid for Efficacy Population: A per-protocol population, or valid for efficacy (VFE) population, was defined as a subset of mITT that did not have protocol deviations that might have had a significant impact on the efficacy endpoints.

Follow-up Analysis Population: A follow-up analysis population was defined as all randomized subjects who completed the 12-week treatment period and had follow-up efficacy measurement(s).

Efficacy Analysis:

ACR20 at Week 12 was the primary endpoint. The ACR measurements (ACR20, ACR50, and ACR70) are the commonly accepted efficacy composite variables for RA. The primary efficacy analysis was performed when the treatment period had been concluded for all the subjects. For categorical variables such as ACR20/50/70, the comparison of fezakinumab groups versus placebo was made using the Cochran-Mantel-Haenszel test stratified by anti-TNF agent prior use (yes/no) and geographic region of the site (Japan/non-Japan). For continuous variables such as DAS 28, change from Baseline was analyzed using an analysis of covariance (ANCOVA) with treatment, anti-TNF agent prior use (yes/no) and geographic region of the site (Japan/non-Japan) as factors, and Baseline as a covariate. DAS 28 was a weighted calculation of the 28-joint counts for tenderness and swelling, CRP, and general health VAS.

Safety Analysis: Safety analysis was performed for the mITT population using observed data. Continuous variables were summarized and analyzed using ANCOVA by study time points, with a baseline value as the baseline covariate. Incidences of AEs were analyzed using Fisher's exact test.

RESULTS

Subject Disposition and Demography:

Table 3 summarizes the disposition of subjects and the populations evaluated. In total, 196 subjects were randomized to receive study treatment, including 39 subjects in the 100 mg fezakinumab Q4W group, 42 subjects in the 100 mg fezakinumab Q2W group, 49 subjects in the 200 mg fezakinumab Q2W group, and 66 subjects in the placebo group. One (1) subject who was randomized to the 200 mg fezakinumab Q2W group did not receive any dose of study treatment. Thus, a total of 195 subjects received at least 1 dose of study treatment and were included in the safety and mITT populations. Of those, 5 subjects were randomized despite not fulfilling eligibility requirements. Of the 195 subjects randomized, 122 subjects were randomized to Part 1 and 73 subjects were randomized to Part 2.

The subjects treated with placebo were enrolled in 2 study parts, but the outcomes from the placebo groups were observationally similar in general, although the proportion of ACR20 responders to placebo was numerically slightly larger in Part 1 of the study compared to Part 2. Therefore, unless stated otherwise, the placebo group in the analysis results refers to the combined placebo groups from Parts 1 and 2.

Table 4 summarizes the primary reasons (number of subjects [n], %) for withdrawal from the treatment phase of the study. Table 5 summarizes the primary reasons (n, %) for withdrawal from the follow-up phase of the study. The clinical significance of the statistical significance of the overall difference between groups who completed/discontinued was unclear.

Table 3. Summary of Populations Evaluation

Population Group	Placebo	100 mg Fezakinumab Q4W	100 mg Fezakinumab Q2W	200 mg Fezakinumab Q2W	Total
Randomized population	66	39	42	49	196
Randomized and not treated				1	1
Safety/mITT population	66	39	42	48	195
Not eligible but randomized			3	2	5
Study treatment permanently discontinued	12	3	1	7	23
Per protocol population	56	34	34	41	165
Follow-up population	49	36	40	41	166

mITT = modified intent-to-treat, Q2W = every 2 weeks, Q4W = every 4 weeks.

Table 4. Summary of Conclusion of Subject Participation From Treatment Phase - Safety Population

Conclusion Status Reason[a]	Overall p-Value	Treatment Sequence: Placebo N=66	100 mg Fezakinumab Q4W N=39	100 mg Fezakinumab Q2W N=42	200 mg Fezakinumab Q2W N=48	Total N=195
Total		66 (100)	39 (100)	42 (100)	48 (100)	195 (100)
Completed	0.054	54 (81.8)	36 (92.3)	41 (97.6)	41 (85.4)	172 (88.2)
Treatment phase completed	0.054	54 (81.8)	36 (92.3)	41 (97.6)	41 (85.4)	172 (88.2)
Discontinued	0.054	12 (18.2)	3 (7.7)	1 (2.4)	7 (14.6)	23 (11.8)
Adverse event	0.270	3 (4.5)	1 (2.6)	0	0	4 (2.1)
Lost to follow-up	0.662	0	0	0	1 (2.1)	1 (0.5)
Protocol violation	0.366	3 (4.5)	0	1 (2.4)	0	4 (2.1)
Subject request	0.085	4 (6.1)	0	0	4 (8.3)	8 (4.1)
Unsatisfactory response - efficacy	0.560	2 (3.0)	2 (5.1)	0	2 (4.2)	6 (3.1)

Overall p-value: Refers to number of subjects data. Fisher's Exact Test p-value (2-tail).
N = number of subjects, Q2W = every 2 weeks, Q4W = every 4 weeks.
a. Total discontinued was the sum of individual reasons since they were mutually exclusive by subject.

Table 5. Summary of Conclusion of Subject Participation From Follow-up Phase - Safety Population

Conclusion Status Reason[a]	Overall p-Value	Treatment Sequence: Placebo N=66	Treatment Sequence: 100 mg Fezakinumab Q4W N=39	Treatment Sequence: 100 mg Fezakinumab Q2W N=42	Treatment Sequence: 200 mg Fezakinumab Q2W N=48	Total N=195
Total		66 (100)	39 (100)	42 (100)	48 (100)	195 (100)
Completed	0.025*	60 (90.9)	39 (100)	41 (97.6)	41 (85.4)	181 (92.8)
Follow-up phase completed	0.025*	60 (90.9)	39 (100)	41 (97.6)	41 (85.4)	181 (92.8)
Discontinued	0.025*	6 (9.1)	0	1 (2.4)	7 (14.6)	14 (7.2)
Lost to follow-up	0.144	0	0	0	2 (4.2)	2 (1.0)
Other	1.000	1 (1.5)	0	0	0	1 (0.5)
Subject request	0.297	5 (7.6)	0	1 (2.4)	3 (6.3)	9 (4.6)
Unsatisfactory response - efficacy	0.144	0	0	0	2 (4.2)	2 (1.0)

Statistical significance at the $p<0.05$, $p<0.01$, $p<0.001$ levels is denoted by *, **, *** respectively.
Overall p-value: Refers to number of subjects data. Fisher's Exact Test p-value (2-tail).
N = number of subjects, Q2W = every 2 weeks, Q4W = every 4 weeks.
a. Total discontinued was the sum of individual reasons since they were mutually exclusive by subject.

A summary of the subjects' demographic and baseline characteristics is presented in Table 6. The safety population of 195 subjects consisted of 39 male and 156 female subjects with an age range of 23 to 81 years, and a mean age of 57 years. Data from all 195 subjects were included in the safety analyses. Demographic and baseline characteristics were generally similar across the treatment groups. Although no formal statistical analyses were carried out, some differences between treatment groups were noticeable: fewer subjects (8.33% of subjects) in the 200 mg fezakinumab Q2W group compared with subjects in the other groups (range from 19.49% to 28.57% of subjects) had received prior anti-TNF medication; as Mexico and Romania did not take part in the first enrollment phase no subjects in Mexico or Romania received fezakinumab at the 100 mg dose level; subjects in the 100 mg fezakinumab Q4W group had a longer mean disease duration (9.74 years) compared with subjects in the other groups (mean range from 6.07 to 7.80 years).

Table 6. Demographic and Baseline Characteristics Summary - Safety Population

Characteristic	Treatment Sequence				Total (N=195)
	Placebo (N=66)	100 mg Fezakinumab Q4W (N=39)	100 mg Fezakinumab Q2W (N=42)	200 mg Fezakinumab Q2W (N=48)	
Age (year)					
N	66	39	42	48	195
Mean	56.91	59.95	55.14	54.90	56.64
Standard deviation	11.01	10.30	10.80	11.11	10.93
Minimum	28.00	40.00	23.00	26.00	23.00
Maximum	81.00	79.00	72.00	77.00	81.00
Median	58.00	60.00	56.00	55.00	57.00
Sex, n (%)					
Female	53 (80.30)	34 (87.18)	31 (73.81)	38 (79.17)	156 (80.00)
Male	13 (19.70)	5 (12.82)	11 (26.19)	10 (20.83)	39 (20.00)
Race, n (%)					
Asian	10 (15.15)	5 (12.82)	7 (16.67)	6 (12.50)	28 (14.36)
Black or African American	1 (1.52)	1 (2.56)	0	0	2 (1.03)
Other	9 (13.64)	4 (10.26)	6 (14.29)	8 (16.67)	27 (13.85)
White	46 (69.70)	29 (74.36)	29 (69.05)	34 (70.83)	138 (70.77)
Ethnicity, n (%)					
Hispanic or Latino	12 (18.18)	9 (23.08)	11 (26.19)	10 (20.83)	42 (21.54)
Non-Hispanic and Non-Latino	54 (81.82)	30 (76.92)	31 (73.81)	38 (79.17)	153 (78.46)
Baseline height (cm)					
N	66	39	42	48	195
Mean	162.33	161.65	163.20	160.69	161.98
Standard deviation	7.88	8.28	8.85	9.17	8.48
Minimum	150.20	145.00	146.50	145.00	145.00
Maximum	185.00	184.00	180.00	189.00	189.00
Median	160.00	160.60	163.50	159.50	160.60
Baseline weight (kg)					
N	66	39	42	48	195
Mean	70.69	72.09	75.01	72.02	72.23
Standard deviation	17.44	16.84	16.82	17.28	17.09
Minimum	40.20	43.10	45.10	42.60	40.20
Maximum	120.00	106.30	115.10	130.60	130.60
Median	68.00	71.00	72.55	69.40	70.00

Table 6. Demographic and Baseline Characteristics Summary - Safety Population

Characteristic	Treatment Sequence				Total (N=195)
	Placebo (N=66)	100 mg Fezakinumab Q4W (N=39)	100 mg Fezakinumab Q2W (N=42)	200 mg Fezakinumab Q2W (N=48)	
Body Mass Index (kg/m^2)					
N	66	39	42	48	195
Mean	26.54	27.50	27.90	27.58	27.28
Standard deviation	5.78	5.92	5.56	5.76	5.74
Minimum	15.50	18.60	18.60	18.60	15.50
Maximum	43.40	40.30	40.30	49.60	49.60
Median	24.80	27.90	27.90	27.90	27.90

N/n = number of subject, Q2W = every 2 weeks, Q4W = every 4 weeks.

Efficacy Results:

Primary Efficacy Results:

ACR20 at Week 12:

Table 7 provides the analysis of ACR20 responders at Week 12 for the mITT population. No statistically significant differences in ACR20 responders were observed between any of the groups using last observation carried forward (LOCF) imputation, observed data, or non-responder imputation. Therefore, the study did not meet its primary efficacy objective regarding the statistical superiority of at least 1 of the 3 dose regimens compared to placebo in terms of ACR20 at Week 12. The ACR20 (LOCF) of 50% in the placebo group was substantially higher than that expected and was not exceeded numerically in any fezakinumab treatment group.

Table 7. Analysis of ACR20 Responders at Week 12, mITT Population

Data Types	Treatment	n/N	Observed Rate (Exact 95% CI) (%)	p-Value[a]			Treatment Difference (95% CI)[b] (%)		
				vs Placebo	vs 100mg Fezakinumab Q4W	vs 100mg Fezakinumab Q2W	vs Placebo	vs 100mg Fezakinumab Q4W	vs 100mg Fezakinumab Q2W
LOCF	Placebo	33/66	50.0(37.4, 62.6)						
	100mg fezakinumab Q4W	17/39	43.6(27.8, 60.4)	0.558			-5.9(-25.0, 13.3)		
	100mg fezakinumab Q2W	16/42	38.1(23.6, 54.4)	0.251	0.659		-11.4(-30.1, 7.3)	-4.9(-25.9, 16.0)	
	200mg fezakinumab Q2W	24/48	50.0(35.2, 64.8)	0.707	0.929	0.391	-3.7(-21.7, 14.4)	1.0(-19.7, 21.6)	9.5(-10.5, 29.5)
Observed	Placebo	31/55	56.4(42.3, 69.7)						
	100mg fezakinumab Q4W	16/36	44.4(27.9, 61.9)	0.352			-9.8(-29.6, 9.9)		
	100mg fezakinumab Q2W	16/41	39.0(24.2, 55.5)	0.116	0.652		-16.5(-36.0, 3.0)	-5.2(-26.3, 15.9)	
	200mg fezakinumab Q2W	23/42	54.8(38.7, 70.2)	0.672	0.837	0.211	-4.5(-24.8, 15.7)	2.5(-19.7, 24.6)	15.0(-7.1, 37.1)
NRI[c]	Placebo	31/65	47.7(35.1, 60.5)						
	100mg fezakinumab Q4W	16/39	41.0(25.6, 57.9)	0.549			-6.0(-25.1, 13.1)		
	100mg fezakinumab Q2W	16/42	38.1(23.6, 54.4)	0.354	0.820		-9.2(-27.9, 9.5)	-2.5(-23.4, 18.4)	
	200mg fezakinumab Q2W	23/48	47.9(33.3, 62.8)	0.750	0.875	0.496	-3.1(-21.3, 15.0)	1.7(-18.9, 22.3)	7.5(-12.5, 27.5)

Missing data with a prior and posterior value were not imputed.
ACR = American College of Rheumatology, CI = confidence interval, LOCF = last observation carried forward, mITT = modified intent-to-treat, N/n = number of subject, NRI = Non-Responder Imputation, Q2W = every 2 weeks, Q4W = every 4 weeks, TNF = tumor necrosis factor, vs = versus.

a. p-Values from a 2-sided stratified Cochran-Mantel-Haenszel test by anti-TNF prior use and geographic region of the site.
b. Treatment group differences and the corresponding CIs adjusted for stratification are calculated using the Cochran method.
c. Subjects are defined as non-responders for any given time point after subject withdrawal.

Secondary Efficacy Results:

ACR20 at All Time Points:

In the analysis of ACR20 responders for the mITT population using LOCF imputation, no statistically significant differences between the groups were observed for any week, except for the 100 mg fezakinumab Q2W versus the 100 mg fezakinumab Q4W group at Week 6 and the 200 mg fezakinumab Q2W versus the 100 mg fezakinumab Q4W group at Week 10 (Table 8).

ACR50:

In the analysis of ACR50 responders for the mITT population using LOCF imputation, no statistically significant differences between the groups were observed for any week (Table 9).

ACR70:

In the analysis of ACR70 responders for the mITT population using LOCF imputation, no statistically significant differences between the groups were observed for any week (Table 10).

Table 8. Analysis of ACR20 Responder by Study Week, mITT Population, LOCF

Study Week	Treatment	n/N	Observed Rate (Exact 95% CI) (%)	p-Value[a]			Treatment Difference (95% CI)[b] (%)		
				vs Placebo	vs 100mg Fezakinumab Q4W	vs 100mg Fezakinumab Q2W	vs Placebo	vs 100mg Fezakinumab Q4W	vs 100mg Fezakinumab Q2W
Week 2	Placebo	12/66	18.2(9.8, 29.6)						
	100mg fezakinumab Q4W	7/39	17.9(7.5, 33.5)	0.991			-0.1(-14.8, 14.7)		
	100mg fezakinumab Q2W	6/42	14.3(5.4, 28.5)	0.518	0.606		-4.8(-18.4, 8.8)	-4.3(-19.8, 11.2)	
	200mg fezakinumab Q2W	7/48	14.6(6.1, 27.8)	0.630	0.640	0.781	-3.5(-16.9, 9.8)	-3.9(-19.2, 11.4)	2.1(-11.5, 15.8)
Week 4	Placebo	16/66	24.2(14.5, 36.4)						
	100mg fezakinumab Q4W	13/39	33.3(19.1, 50.2)	0.295			9.4(-8.3, 27.0)		
	100mg fezakinumab Q2W	9/42	21.4(10.3, 36.8)	0.686	0.222		-3.4(-19.3, 12.5)	-12.4(-31.4, 6.6)	
	200mg fezakinumab Q2W	13/48	27.1(15.3, 41.8)	0.772	0.393	0.582	2.5(-13.2, 18.2)	-8.8(-28.0, 10.4)	5.2(-12.0, 22.5)
Week 6	Placebo	22/66	33.3(22.2, 46.0)						
	100mg fezakinumab Q4W	18/39	46.2(30.1, 62.8)	0.201			12.8(-6.5, 32.0)		
	100mg fezakinumab Q2W	10/42	23.8(12.1, 39.5)	0.256	0.036		-10.4(-27.3, 6.5)	-22.6(-42.7, -2.5)	
	200mg fezakinumab Q2W	19/48	39.6(25.8, 54.7)	0.519	0.491	0.135	6.1(-11.4, 23.5)	-7.6(-28.3, 13.0)	15.6(-2.4, 33.6)
Week 8	Placebo	21/66	31.8(20.9, 44.4)						
	100mg fezakinumab Q4W	19/39	48.7(32.4, 65.2)	0.094			16.7(-1.9, 35.2)		
	100mg fezakinumab Q2W	14/42	33.3(19.6, 49.5)	0.760	0.223		2.8(-14.4, 20.1)	-13.0(-33.4, 7.4)	
	200mg fezakinumab Q2W	17/48	35.4(22.2, 50.5)	0.950	0.199	0.798	0.6(-16.8, 18.0)	-14.1(-33.9, 5.7)	-2.6(-21.8, 16.5)
Week 10	Placebo	28/66	42.4(30.3, 55.2)						
	100mg fezakinumab Q4W	22/39	56.4(39.6, 72.2)	0.185			13.6(-5.9, 33.0)		
	100mg fezakinumab Q2W	18/42	42.9(27.7, 59.0)	0.982	0.269		0.2(-18.8, 19.3)	-12.5(-34.1, 9.0)	
	200mg fezakinumab Q2W	15/48	31.3(18.7, 46.3)	0.223	0.014	0.196	-11.6(-29.0, 5.8)	-27.1(-47.1, -7.1)	-14.0(-33.8, 5.9)
Week 12	Placebo	33/66	50.0(37.4, 62.6)						
	100mg fezakinumab Q4W	17/39	43.6(27.8, 60.4)	0.558			-5.9(-25.0, 13.3)		
	100mg fezakinumab Q2W	16/42	38.1(23.6, 54.4)	0.251	0.659		-11.4(-30.1, 7.3)	-4.9(-25.9, 16.0)	
	200mg fezakinumab Q2W	24/48	50.0(35.2, 64.8)	0.707	0.929	0.391	-3.7(-21.7, 14.4)	1.0(-19.7, 21.6)	9.5(-10.5, 29.5)

ACR = American College of Rheumatology, CI = confidence interval, LOCF = last observation carried forward, mITT = modified intent-to-treat, N/n = number of subject, Q2W = every 2 weeks, Q4W = every 4 weeks, TNF = tumor necrosis factor, vs = versus.

a. p-Values from a 2-sided stratified Cochran-Mantel-Haenszel test by anti-TNF prior use and geographic region of the site.

b. Treatment group differences and the corresponding CIs adjusted for stratification are calculated using the Cochran method.

Table 9. Analysis of ACR50 Responder by Study Week, mITT Population, LOCF

Study Week	Treatment	n/N	Observed Rate (Exact 95% CI) (%)	p-Value[a]			Treatment Difference (95% CI)[b](%)		
				vs Placebo	vs 100mg Fezakinumab Q4W	vs 100mg Fezakinumab Q2W	vs Placebo	vs 100mg Fezakinumab Q4W	vs 100mg Fezakinumab Q2W
Week 2	Placebo	2/66	3.0(0.4, 10.5)						
	100mg fezakinumab Q4W	1/39	2.6(0.1, 13.5)	0.885			-0.5(-6.8, 5.8)		
	100mg fezakinumab Q2W	4/42	9.5(2.7, 22.6)	0.180	0.209		6.1(-3.4, 15.6)	6.8(-2.9, 16.4)	
	200mg fezakinumab Q2W	0/48	0.0(0.0, 7.4)	0.277	0.244	0.053	-2.7(-6.5, 1.1)	-2.8(-8.2, 2.6)	-8.7(-17.2, -0.3)
Week 4	Placebo	4/66	6.1(1.7, 14.8)						
	100mg fezakinumab Q4W	3/39	7.7(1.6, 20.9)	0.740			1.7(-7.9, 11.3)		
	100mg fezakinumab Q2W	3/42	7.1(1.5, 19.5)	0.934	0.995		0.4(-9.3, 10.1)	-0.0(-11.0, 11.0)	
	200mg fezakinumab Q2W	2/48	4.2(0.5, 14.3)	0.876	0.412	0.521	-0.6(-7.7, 6.4)	-4.3(-14.9, 6.3)	-3.3(-13.0, 6.4)
Week 6	Placebo	6/66	9.1(3.4, 18.7)						
	100mg fezakinumab Q4W	3/39	7.7(1.6, 20.9)	0.842			-1.1(-11.4, 9.2)		
	100mg fezakinumab Q2W	6/42	14.3(5.4, 28.5)	0.509	0.359		4.1(-8.1, 16.3)	6.6(-6.2, 19.3)	
	200mg fezakinumab Q2W	6/48	12.5(4.7, 25.2)	0.504	0.604	0.982	4.0(-7.0, 15.0)	3.5(-9.1, 16.2)	0.2(-13.1, 13.4)
Week 8	Placebo	5/66	7.6(2.5, 16.8)						
	100mg fezakinumab Q4W	5/39	12.8(4.3, 27.4)	0.373			5.4(-6.3, 17.0)		
	100mg fezakinumab Q2W	2/42	4.8(0.6, 16.2)	0.499	0.239		-3.4(-12.0, 5.2)	-7.4(-18.7, 3.8)	
	200mg fezakinumab Q2W	7/48	14.6(6.1, 27.8)	0.244	0.954	0.092	7.0(-4.2, 18.3)	-0.4(-14.9, 14.0)	10.9(0.1, 21.6)
Week 10	Placebo	12/66	18.2(9.8, 29.6)						
	100mg fezakinumab Q4W	7/39	17.9(7.5, 33.5)	0.979			-0.2(-15.0, 14.6)		
	100mg fezakinumab Q2W	4/42	9.5(2.7, 22.6)	0.166	0.254		-9.8(-21.8, 2.2)	-8.9(-22.7, 5.0)	
	200mg fezakinumab Q2W	9/48	18.8(8.9, 32.6)	0.947	0.862	0.123	0.5(-13.2, 14.2)	-1.5(-17.4, 14.4)	11.8(-0.1, 23.7)
Week 12	Placebo	10/66	15.2(7.5, 26.1)						
	100mg fezakinumab Q4W	9/39	23.1(11.1, 39.3)	0.286			8.3(-7.1, 23.8)		
	100mg fezakinumab Q2W	6/42	14.3(5.4, 28.5)	0.822	0.348		-1.6(-15.0, 11.8)	-8.3(-25.0, 8.3)	
	200mg fezakinumab Q2W	7/48	14.6(6.1, 27.8)	0.986	0.171	0.928	-0.1(-12.3, 12.1)	-11.7(-28.2, 4.8)	0.7(-13.1, 14.5)

ACR = American College of Rheumatology, CI = confidence interval, LOCF = last observation carried forward, mITT = modified intent-to-treat, N/n = number of subject, Q2W = every 2 weeks, Q4W = every 4 weeks, TNF = tumor necrosis factor, vs = versus.

a. p-Values from a 2-sided stratified Cochran-Mantel-Haenszel test by anti-TNF prior use and geographic region of the site.

b. Treatment group differences and the corresponding CIs adjusted for stratification are calculated using the Cochran method.

Table 10. Analysis of ACR70 Responder by Study Week, mITT Population, LOCF

Study Week	Treatment	n/N	Observed Rate (Exact 95% CI) (%)	p-Value[a]			Treatment Difference (95% CI)[b] (%)		
				vs Placebo	vs 100mg Fezakinumab Q4W	vs 100mg Fezakinumab Q2W	vs Placebo	vs 100mg Fezakinumab Q4W	vs 100mg Fezakinumab Q2W
Week 2	Placebo	0/66	0.0(0.0, 5.4)						
	100mg fezakinumab Q4W	1/39	2.6(0.1, 13.5)	0.205			2.5(-2.3, 7.4)		
	100mg fezakinumab Q2W	1/42	2.4(0.1, 12.6)	0.188	0.958		2.5(-2.3, 7.3)	0.2(-6.6, 7.0)	
	200mg fezakinumab Q2W	0/48	0.0(0.0, 7.4)		0.244	0.227	0.0(0.0, 0.0)	-2.8(-8.2, 2.6)	-2.9(-8.4, 2.7)
Week 4	Placebo	1/66	1.5(0.0, 8.2)						
	100mg fezakinumab Q4W	1/39	2.6(0.1, 13.5)	0.699			1.1(-4.5, 6.6)		
	100mg fezakinumab Q2W	3/42	7.1(1.5, 19.5)	0.155	0.330		5.4(-3.0, 13.8)	4.8(-4.3, 13.9)	
	200mg fezakinumab Q2W	0/48	0.0(0.0, 7.4)	0.546	0.244	0.071	-1.0(-2.9, 0.9)	-2.8(-8.2, 2.6)	-7.3(-15.4, 0.9)
Week 6	Placebo	0/66	0.0(0.0, 5.4)						
	100mg fezakinumab Q4W	1/39	2.6(0.1, 13.5)	0.205			2.5(-2.3, 7.4)		
	100mg fezakinumab Q2W	1/42	2.4(0.1, 12.6)	0.269	0.907		2.2(-1.8, 6.1)	-0.4(-6.3, 5.5)	
	200mg fezakinumab Q2W	1/48	2.1(0.1, 11.1)	0.280	0.723	0.891	2.0(-1.6, 5.6)	-1.2(-7.3, 5.0)	0.4(-4.0, 4.9)
Week 8	Placebo	0/66	0.0(0.0, 5.4)						
	100mg fezakinumab Q4W	1/39	2.6(0.1, 13.5)	0.205			2.5(-2.3, 7.4)		
	100mg fezakinumab Q2W	0/42	0.0(0.0, 8.4)		0.335		0.0(0.0, 0.0)	-2.4(-7.0, 2.2)	
	200mg fezakinumab Q2W	2/48	4.2(0.5, 14.3)	0.125	0.828	0.245	4.0(-1.3, 9.4)	0.9(-6.4, 8.2)	3.9(-1.2, 9.1)
Week 10	Placebo	0/66	0.0(0.0, 5.4)						
	100mg fezakinumab Q4W	2/39	5.1(0.6, 17.3)	0.071			5.0(-1.7, 11.8)		
	100mg fezakinumab Q2W	1/42	2.4(0.1, 12.6)	0.317	0.510		2.0(-1.2, 5.1)	-2.8(-10.0, 4.4)	
	200mg fezakinumab Q2W	1/48	2.1(0.1, 11.1)	0.280	0.329	0.414	2.0(-1.6, 5.6)	-4.0(-12.0, 4.1)	1.9(-1.5, 5.4)
Week 12	Placebo	3/66	4.5(0.9, 12.7)						
	100mg fezakinumab Q4W	2/39	5.1(0.6, 17.3)	0.892			0.6(-7.6, 8.8)		
	100mg fezakinumab Q2W	2/42	4.8(0.6, 16.2)	0.903	0.964		-0.5(-8.3, 7.2)	-0.2(-9.0, 8.5)	
	200mg fezakinumab Q2W	1/48	2.1(0.1, 11.1)	0.625	0.329	0.780	-1.7(-7.2, 3.8)	-4.0(-12.0, 4.1)	-0.9(-7.5, 5.6)

ACR = American College of Rheumatology, CI = confidence interval, LOCF = last observation carried forward, mITT = modified intent-to-treat, N/n = number of subject, Q2W = every 2 weeks, Q4W = every 4 weeks, TNF = tumor necrosis factor, vs = versus.

a. p-Values from a 2-sided stratified Cochran-Mantel-Haenszel test by anti-TNF prior use and geographic region of the site.

b. Treatment group differences and the corresponding CIs adjusted for stratification are calculated using the Cochran method.

DAS 28:

For the mITT population using LOCF imputation within treatment comparisons revealed statistically significant changes from Baseline in DAS 28 (CRP and ESR based) for all groups at all weeks (Table 11 and Table 12). No statistically significant differences in the change from Baseline in DAS 28 (CRP and ESR based) between the groups were observed at any week (Table 13 and Table 14).

Table 11. Descriptive Summary Statistics and Within Treatment Comparison for DAS28 (CRP Based), mITT Population, LOCF

								Change From Baseline						
Study Week	**Treatment**	**N**	**Mean**	**SD**	**Median**	**Min**	**Max**	**N**	**Mean**	**SD**	**Median**	**Min**	**Max**	**p-Value[a]**
Baseline	Placebo	65	5.6	0.8	5.7	4.4	7.2							
	100mg fezakinumab Q4W	39	5.5	0.9	5.7	3.9	7.3							
	100mg fezakinumab Q2W	42	5.3	0.8	5.3	3.8	7.3							
	200mg fezakinumab Q2W	48	5.5	0.8	5.4	3.6	7.1							
Week 2	Placebo	66	5.1	1.0	5.1	2.2	7.4	65	-0.5	0.8	-0.4	-3.1	1.1	<.001
	100mg fezakinumab Q4W	39	5.1	1.1	5.0	1.4	7.4	39	-0.5	0.8	-0.5	-2.9	1.4	<.001
	100mg fezakinumab Q2W	42	4.9	1.4	5.0	1.2	7.3	42	-0.5	0.9	-0.2	-3.1	1.3	0.002
	200mg fezakinumab Q2W	48	5.2	1.0	5.1	3.2	7.5	48	-0.2	0.6	-0.1	-2.0	1.6	0.006
Week 4	Placebo	66	4.9	1.1	4.9	2.0	7.5	65	-0.7	0.9	-0.6	-3.4	0.7	<.001
	100mg fezakinumab Q4W	39	4.8	0.9	4.9	2.2	6.7	39	-0.7	0.9	-0.6	-2.3	1.4	<.001
	100mg fezakinumab Q2W	42	4.6	1.4	4.9	1.1	7.2	42	-0.7	1.0	-0.4	-3.0	1.1	<.001
	200mg fezakinumab Q2W	48	5.0	1.1	4.9	2.4	8.1	48	-0.5	0.7	-0.4	-2.1	1.1	<.001
Week 6	Placebo	66	4.7	1.2	4.8	2.1	7.6	65	-0.9	0.9	-0.8	-3.9	0.7	<.001
	100mg fezakinumab Q4W	39	4.4	1.2	4.4	1.4	6.6	39	-1.1	0.9	-1.1	-2.9	1.4	<.001
	100mg fezakinumab Q2W	42	4.6	1.2	4.5	1.9	7.4	42	-0.7	0.9	-0.4	-2.5	0.8	<.001
	200mg fezakinumab Q2W	48	4.6	1.2	4.6	1.6	8.1	48	-0.9	0.9	-0.8	-3.3	1.1	<.001
Week 8	Placebo	66	4.6	1.3	4.4	1.6	7.3	65	-1.0	1.1	-1.0	-3.9	1.1	<.001
	100mg fezakinumab Q4W	39	4.4	1.1	4.2	1.3	6.8	39	-1.1	0.9	-1.1	-3.1	0.7	<.001
	100mg fezakinumab Q2W	42	4.4	1.2	4.3	2.1	6.9	42	-0.9	1.0	-0.6	-3.1	1.1	<.001
	200mg fezakinumab Q2W	48	4.4	1.3	4.5	1.8	8.1	48	-1.0	0.9	-0.9	-3.4	1.1	<.001
Week 10	Placebo	66	4.5	1.3	4.4	1.9	7.6	65	-1.1	1.1	-1.0	-3.9	0.9	<.001
	100mg fezakinumab Q4W	39	4.2	1.2	4.1	1.4	6.6	39	-1.3	0.9	-1.4	-3.0	1.0	<.001
	100mg fezakinumab Q2W	42	4.4	1.2	4.5	1.5	7.3	42	-0.9	1.1	-0.6	-3.6	1.0	<.001
	200mg fezakinumab Q2W	48	4.5	1.3	4.7	1.6	8.1	48	-1.0	1.0	-0.8	-3.1	1.7	<.001
Week 12	Placebo	66	4.4	1.3	4.2	1.7	7.7	65	-1.2	1.1	-1.1	-4.3	1.3	<.001
	100mg fezakinumab Q4W	39	4.2	1.4	4.0	1.7	8.2	39	-1.3	1.1	-1.3	-3.2	0.9	<.001
	100mg fezakinumab Q2W	42	4.3	1.3	4.3	1.7	7.2	42	-1.0	1.1	-1.0	-3.1	1.3	<.001
	200mg fezakinumab Q2W	48	4.4	1.3	4.5	1.5	8.1	48	-1.1	1.1	-1.0	-3.4	2.1	<.001

CRP = C-reactive protein, DAS = disease activity score, LOCF = last observation carried forward, Max = maximum, Min = minimum, mITT = modified intent-to-treat, N = number of subject, Q2W = every 2 weeks, Q4W = every 4 weeks, SD = standard deviation.
a. p-Value from a 2-sided paired T-test.

Table 12. Descriptive Summary Statistics and Within Treatment Comparison for DAS28 (ESR Based), mITT Population, LOCF

								Change From Baseline						
Study Week	**Treatment**	**N**	**Mean**	**SD**	**Median**	**Min**	**Max**	**N**	**Mean**	**SD**	**Median**	**Min**	**Max**	**p-Value[a]**
Baseline	Placebo	65	6.4	0.7	6.4	4.6	7.8							
	100mg fezakinumab Q4W	39	6.4	0.8	6.5	5.2	8.4							
	100mg fezakinumab Q2W	42	6.2	0.7	6.2	4.9	7.4							
	200mg fezakinumab Q2W	48	6.3	0.8	6.3	4.5	7.7							
Week 2	Placebo	66	5.8	1.1	5.8	2.2	8.2	65	-0.6	0.8	-0.5	-2.7	0.9	<.001
	100mg fezakinumab Q4W	39	5.9	1.1	5.8	2.7	8.5	39	-0.5	0.7	-0.5	-2.8	0.9	<.001
	100mg fezakinumab Q2W	42	5.6	1.4	5.6	1.7	7.7	42	-0.6	1.0	-0.4	-3.7	1.9	<.001
	200mg fezakinumab Q2W	48	5.9	0.8	5.9	4.0	7.8	48	-0.4	0.6	-0.3	-2.3	1.6	<.001
Week 4	Placebo	66	5.5	1.3	5.7	1.8	8.2	65	-0.9	1.0	-0.7	-3.7	0.8	<.001
	100mg fezakinumab Q4W	39	5.6	0.9	5.6	3.5	8.2	39	-0.8	0.8	-0.7	-2.2	1.6	<.001
	100mg fezakinumab Q2W	42	5.3	1.3	5.6	2.0	7.7	42	-0.8	1.0	-0.5	-3.6	0.8	<.001
	200mg fezakinumab Q2W	48	5.7	0.9	5.7	3.5	8.3	48	-0.6	0.8	-0.5	-2.6	0.7	<.001
Week 6	Placebo	66	5.4	1.3	5.3	2.0	8.1	65	-1.0	1.0	-0.9	-3.9	0.9	<.001
	100mg fezakinumab Q4W	39	5.2	1.1	5.1	2.5	7.8	39	-1.2	0.8	-1.2	-3.0	0.7	<.001
	100mg fezakinumab Q2W	42	5.3	1.2	5.4	1.9	7.8	42	-0.8	1.0	-0.7	-3.3	1.3	<.001
	200mg fezakinumab Q2W	48	5.2	1.2	5.3	2.6	8.3	48	-1.0	1.0	-1.0	-3.8	0.9	<.001
Week 8	Placebo	66	5.3	1.3	5.1	1.9	8.1	65	-1.1	1.1	-0.9	-3.8	1.1	<.001
	100mg fezakinumab Q4W	39	5.2	1.1	5.0	2.4	7.8	39	-1.2	0.9	-1.1	-3.0	0.5	<.001
	100mg fezakinumab Q2W	42	5.0	1.3	5.0	1.0	7.4	42	-1.1	1.2	-1.0	-4.8	1.3	<.001
	200mg fezakinumab Q2W	48	5.1	1.2	5.2	2.4	8.3	48	-1.1	1.0	-1.1	-3.9	0.6	<.001
Week 10	Placebo	66	5.2	1.4	5.1	2.0	7.6	65	-1.2	1.2	-1.1	-3.9	0.8	<.001
	100mg fezakinumab Q4W	39	5.0	1.2	4.9	2.5	7.8	39	-1.4	0.9	-1.5	-2.9	0.6	<.001
	100mg fezakinumab Q2W	42	5.0	1.3	5.1	1.9	7.6	42	-1.1	1.2	-0.9	-4.1	1.1	<.001
	200mg fezakinumab Q2W	48	5.1	1.3	5.2	1.3	8.3	48	-1.1	1.1	-0.9	-3.7	1.6	<.001
Week 12	Placebo	66	5.1	1.3	4.9	2.1	7.6	65	-1.3	1.1	-1.3	-3.9	0.8	<.001
	100mg fezakinumab Q4W	39	5.0	1.4	4.8	2.7	8.6	39	-1.3	1.0	-1.5	-3.0	0.4	<.001
	100mg fezakinumab Q2W	42	5.0	1.3	4.9	1.4	7.6	42	-1.1	1.2	-1.1	-4.4	1.2	<.001
	200mg fezakinumab Q2W	48	5.1	1.3	5.2	2.5	8.3	48	-1.2	1.2	-1.1	-4.4	2.1	<.001

DAS = disease activity score, ESR = erythrocyte sedimentation rate, LOCF = last observation carried forward, Max = maximum, Min = minimum, mITT = modified intent-to-treat, N = number of subject, Q2W = every 2 weeks, Q4W = every 4 weeks, SD = standard deviation.
a. p-Value from a 2-sided paired T-test.

Table 13. Descriptive Summary Statistics and Between Treatment Comparisons (ANCOVA), for Change From Baseline in DAS28 (CRP Based), mITT Population, LOCF

Study Week	Treatment	N	Mean	Comparator	N	Mean	Adjusted Mean Diff[a] (SE)	95% CI[a]	p-Value[a]
Week 2	100mg fezakinumab Q4W	39	-0.5	Placebo	65	-0.5	0.1 (0.2)	-0.2, 0.4	0.670
	100mg fezakinumab Q2W	42	-0.5	Placebo	65	-0.5	0.1 (0.2)	-0.2, 0.4	0.713
	200mg fezakinumab Q2W	48	-0.2	Placebo	65	-0.5	0.3 (0.1)	-0.0, 0.6	0.075
	100mg fezakinumab Q2W	42	-0.5	100mg fezakinumab Q4W	39	-0.5	-0.0 (0.2)	-0.4, 0.3	0.953
	200mg fezakinumab Q2W	48	-0.2	100mg fezakinumab Q4W	39	-0.5	0.2 (0.2)	-0.1, 0.5	0.236
	200mg fezakinumab Q2W	48	-0.2	100mg fezakinumab Q2W	42	-0.5	0.2 (0.2)	-0.1, 0.5	0.209
Week 4	100mg fezakinumab Q4W	39	-0.7	Placebo	65	-0.7	0.0 (0.2)	-0.3, 0.4	0.894
	100mg fezakinumab Q2W	42	-0.7	Placebo	65	-0.7	0.0 (0.2)	-0.3, 0.4	0.843
	200mg fezakinumab Q2W	48	-0.5	Placebo	65	-0.7	0.2 (0.2)	-0.1, 0.6	0.186
	100mg fezakinumab Q2W	42	-0.7	100mg fezakinumab Q4W	39	-0.7	0.0 (0.2)	-0.4, 0.4	0.955
	200mg fezakinumab Q2W	48	-0.5	100mg fezakinumab Q4W	39	-0.7	0.2 (0.2)	-0.2, 0.6	0.294
	200mg fezakinumab Q2W	48	-0.5	100mg fezakinumab Q2W	42	-0.7	0.2 (0.2)	-0.2, 0.6	0.317
Week 6	100mg fezakinumab Q4W	39	-1.1	Placebo	65	-0.9	-0.2 (0.2)	-0.6, 0.2	0.312
	100mg fezakinumab Q2W	42	-0.7	Placebo	65	-0.9	0.2 (0.2)	-0.2, 0.5	0.307
	200mg fezakinumab Q2W	48	-0.9	Placebo	65	-0.9	-0.0 (0.2)	-0.4, 0.3	0.925
	100mg fezakinumab Q2W	42	-0.7	100mg fezakinumab Q4W	39	-1.1	0.4 (0.2)	-0.0, 0.8	0.068
	200mg fezakinumab Q2W	48	-0.9	100mg fezakinumab Q4W	39	-1.1	0.2 (0.2)	-0.2, 0.6	0.388
	200mg fezakinumab Q2W	48	-0.9	100mg fezakinumab Q2W	42	-0.7	-0.2 (0.2)	-0.6, 0.2	0.301
Week 8	100mg fezakinumab Q4W	39	-1.1	Placebo	65	-1.0	-0.1 (0.2)	-0.5, 0.3	0.581
	100mg fezakinumab Q2W	42	-0.9	Placebo	65	-1.0	0.0 (0.2)	-0.4, 0.4	0.989
	200mg fezakinumab Q2W	48	-1.0	Placebo	65	-1.0	0.0 (0.2)	-0.4, 0.4	0.996
	100mg fezakinumab Q2W	42	-0.9	100mg fezakinumab Q4W	39	-1.1	0.1 (0.2)	-0.3, 0.6	0.608
	200mg fezakinumab Q2W	48	-1.0	100mg fezakinumab Q4W	39	-1.1	0.1 (0.2)	-0.3, 0.5	0.603
	200mg fezakinumab Q2W	48	-1.0	100mg fezakinumab Q2W	42	-0.9	-0.0 (0.2)	-0.4, 0.4	0.993
Week 10	100mg fezakinumab Q4W	39	-1.3	Placebo	65	-1.1	-0.2 (0.2)	-0.6, 0.2	0.354
	100mg fezakinumab Q2W	42	-0.9	Placebo	65	-1.1	0.1 (0.2)	-0.3, 0.5	0.565
	200mg fezakinumab Q2W	48	-1.0	Placebo	65	-1.1	0.1 (0.2)	-0.3, 0.5	0.501
	100mg fezakinumab Q2W	42	-0.9	100mg fezakinumab Q4W	39	-1.3	0.3 (0.2)	-0.1, 0.8	0.176
	200mg fezakinumab Q2W	48	-1.0	100mg fezakinumab Q4W	39	-1.3	0.3 (0.2)	-0.1, 0.8	0.144
	200mg fezakinumab Q2W	48	-1.0	100mg fezakinumab Q2W	42	-0.9	0.0 (0.2)	-0.4, 0.5	0.947

Table 13. Descriptive Summary Statistics and Between Treatment Comparisons (ANCOVA), for Change From Baseline in DAS28 (CRP Based), mITT Population, LOCF

Study Week	Treatment	N	Mean	Comparator	N	Mean	Adjusted Mean Diff[a] (SE)	95% CI[a]	p-Value[a]
Week 12	100mg fezakinumab Q4W	39	-1.3	Placebo	65	-1.2	-0.0 (0.2)	-0.5, 0.4	0.846
	100mg fezakinumab Q2W	42	-1.0	Placebo	65	-1.2	0.1 (0.2)	-0.3, 0.6	0.520
	200mg fezakinumab Q2W	48	-1.1	Placebo	65	-1.2	0.2 (0.2)	-0.3, 0.6	0.434
	100mg fezakinumab Q2W	42	-1.0	100mg fezakinumab Q4W	39	-1.3	0.2 (0.2)	-0.3, 0.7	0.453
	200mg fezakinumab Q2W	48	-1.1	100mg fezakinumab Q4W	39	-1.3	0.2 (0.2)	-0.3, 0.7	0.382
	200mg fezakinumab Q2W	48	-1.1	100mg fezakinumab Q2W	42	-1.0	0.0 (0.2)	-0.4, 0.5	0.919

ANCOVA = analysis of covariance, CI = confidence interval, CRP = C-reactive protein, DAS = disease activity score, Diff = difference, LOCF = last observation carried forward, mITT = modified intent-to-treat, N = number of subject, Q2W = every 2 weeks, Q4W = every 4 weeks, SE = standard error, TNF = tumor necrosis factor.

a. From the ANCOVA model: change = baseline + anti-TNF prior use + region + treatment.

Table 14. Descriptive Summary Statistics and Between Treatment Comparisons (ANCOVA) for Change From Baseline in DAS28 (ESR Based), mITT Population, LOCF

Study Week	Treatment	N	Mean	Comparator	N	Mean	Adjusted Mean Diff[a] (SE)	95% CI[a]	p-Value[a]
Week 2	100mg fezakinumab Q4W	39	-0.5	Placebo	65	-0.6	0.1 (0.2)	-0.3, 0.4	0.691
	100mg fezakinumab Q2W	42	-0.6	Placebo	65	-0.6	0.0 (0.2)	-0.3, 0.3	0.918
	200mg fezakinumab Q2W	48	-0.4	Placebo	65	-0.6	0.2 (0.2)	-0.1, 0.5	0.144
	100mg fezakinumab Q2W	42	-0.6	100mg fezakinumab Q4W	39	-0.5	-0.0 (0.2)	-0.4, 0.3	0.789
	200mg fezakinumab Q2W	48	-0.4	100mg fezakinumab Q4W	39	-0.5	0.2 (0.2)	-0.2, 0.5	0.354
	200mg fezakinumab Q2W	48	-0.4	100mg fezakinumab Q2W	42	-0.6	0.2 (0.2)	-0.1, 0.6	0.225
Week 4	100mg fezakinumab Q4W	39	-0.8	Placebo	65	-0.9	0.1 (0.2)	-0.3, 0.5	0.582
	100mg fezakinumab Q2W	42	-0.8	Placebo	65	-0.9	0.1 (0.2)	-0.3, 0.4	0.782
	200mg fezakinumab Q2W	48	-0.6	Placebo	65	-0.9	0.3 (0.2)	-0.1, 0.6	0.140
	100mg fezakinumab Q2W	42	-0.8	100mg fezakinumab Q4W	39	-0.8	-0.1 (0.2)	-0.5, 0.4	0.801
	200mg fezakinumab Q2W	48	-0.6	100mg fezakinumab Q4W	39	-0.8	0.2 (0.2)	-0.2, 0.6	0.425
	200mg fezakinumab Q2W	48	-0.6	100mg fezakinumab Q2W	42	-0.8	0.2 (0.2)	-0.2, 0.6	0.286
Week 6	100mg fezakinumab Q4W	39	-1.2	Placebo	65	-1.0	-0.2 (0.2)	-0.6, 0.2	0.256
	100mg fezakinumab Q2W	42	-0.8	Placebo	65	-1.0	0.1 (0.2)	-0.2, 0.5	0.457
	200mg fezakinumab Q2W	48	-1.0	Placebo	65	-1.0	-0.0 (0.2)	-0.4, 0.3	0.792
	100mg fezakinumab Q2W	42	-0.8	100mg fezakinumab Q4W	39	-1.2	0.4 (0.2)	-0.1, 0.8	0.091
	200mg fezakinumab Q2W	48	-1.0	100mg fezakinumab Q4W	39	-1.2	0.2 (0.2)	-0.2, 0.6	0.408
	200mg fezakinumab Q2W	48	-1.0	100mg fezakinumab Q2W	42	-0.8	-0.2 (0.2)	-0.6, 0.2	0.353
Week 8	100mg fezakinumab Q4W	39	-1.2	Placebo	65	-1.1	-0.1 (0.2)	-0.5, 0.3	0.687
	100mg fezakinumab Q2W	42	-1.1	Placebo	65	-1.1	-0.1 (0.2)	-0.5, 0.3	0.677
	200mg fezakinumab Q2W	48	-1.1	Placebo	65	-1.1	-0.0 (0.2)	-0.4, 0.4	0.852
	100mg fezakinumab Q2W	42	-1.1	100mg fezakinumab Q4W	39	-1.2	-0.0 (0.2)	-0.5, 0.5	0.994
	200mg fezakinumab Q2W	48	-1.1	100mg fezakinumab Q4W	39	-1.2	0.0 (0.2)	-0.4, 0.5	0.833
	200mg fezakinumab Q2W	48	-1.1	100mg fezakinumab Q2W	42	-1.1	0.1 (0.2)	-0.4, 0.5	0.826
Week 10	100mg fezakinumab Q4W	39	-1.4	Placebo	65	-1.2	-0.2 (0.2)	-0.6, 0.3	0.481
	100mg fezakinumab Q2W	42	-1.1	Placebo	65	-1.2	0.1 (0.2)	-0.3, 0.5	0.655
	200mg fezakinumab Q2W	48	-1.1	Placebo	65	-1.2	0.1 (0.2)	-0.3, 0.5	0.659
	100mg fezakinumab Q2W	42	-1.1	100mg fezakinumab Q4W	39	-1.4	0.3 (0.3)	-0.2, 0.8	0.300
	200mg fezakinumab Q2W	48	-1.1	100mg fezakinumab Q4W	39	-1.4	0.3 (0.2)	-0.2, 0.7	0.294
	200mg fezakinumab Q2W	48	-1.1	100mg fezakinumab Q2W	42	-1.1	-0.0 (0.2)	-0.5, 0.5	0.984
Week 12	100mg fezakinumab Q4W	39	-1.3	Placebo	65	-1.3	-0.0 (0.2)	-0.5, 0.4	0.912

Table 14. Descriptive Summary Statistics and Between Treatment Comparisons (ANCOVA) for Change From Baseline in DAS28 (ESR Based), mITT Population, LOCF

Study Week	Treatment	N	Mean	Comparator	N	Mean	Adjusted Mean Diff[a] (SE)	95% CI[a]	p-Value[a]
	100mg fezakinumab Q2W	42	-1.1	Placebo	65	-1.3	0.1 (0.2)	-0.3, 0.6	0.524
	200mg fezakinumab Q2W	48	-1.2	Placebo	65	-1.3	0.1 (0.2)	-0.3, 0.6	0.543
	100mg fezakinumab Q2W	42	-1.1	100mg fezakinumab Q4W	39	-1.3	0.2 (0.3)	-0.3, 0.7	0.503
	200mg fezakinumab Q2W	48	-1.2	100mg fezakinumab Q4W	39	-1.3	0.2 (0.2)	-0.3, 0.6	0.521
	200mg fezakinumab Q2W	48	-1.2	100mg fezakinumab Q2W	42	-1.1	-0.0 (0.2)	-0.5, 0.5	0.962

ANCOVA = analysis of covariance, CI = confidence interval, DAS = disease activity score, Diff = difference, ESR = erythrocyte sedimentation rate, LOCF = last observation carried forward, mITT = modified intent-to-treat, N = number of subject, Q2W = every 2 weeks, Q4W = every 4 weeks, SE = standard error, TNF = tumor necrosis factor.

a. From the ANCOVA model: change = baseline + anti-TNF prior use + region + treatment.

Tender Joints Assessment:

For the mITT population using LOCF imputation within treatment comparisons revealed statistically significant changes from Baseline in the total number of tender joints for all groups at all weeks (Table 15). No statistically significant differences in the change from Baseline in the total number of tender joints between the groups were observed at any week (Table 16).

Swollen Joints Assessment:

For the mITT population using LOCF imputation within treatment comparisons revealed statistically significant changes from Baseline in the total number of swollen joints for all groups at all weeks (Table 17). No statistically significant differences in the change from Baseline in the total number of swollen joints between the groups were observed at any week (Table 18).

Table 15. Descriptive Summary Statistics and Within Treatment Comparison for Total Number of Tender Joints, mITT Population, LOCF

								Change From Baseline						
Study Week	**Treatment**	**N**	**Mean**	**SD**	**Median**	**Min**	**Max**	**N**	**Mean**	**SD**	**Median**	**Min**	**Max**	**p-Value[a]**
Baseline	Placebo	66	13.4	5.2	13.0	5.0	26.0							
	100mg fezakinumab Q4W	39	13.2	6.3	12.0	5.0	28.0							
	100mg fezakinumab Q2W	42	12.3	5.9	10.0	5.0	27.0							
	200mg fezakinumab Q2W	48	14.4	5.9	14.3	5.0	28.0							
Week 2	Placebo	66	11.1	6.0	10.0	0.0	28.0	66	-2.4	4.2	-2.0	-15.0	6.0	<.001
	100mg fezakinumab Q4W	39	10.9	7.1	9.0	0.0	28.0	39	-2.3	4.7	-3.0	-11.4	15.0	0.003
	100mg fezakinumab Q2W	42	10.8	7.8	8.5	0.0	28.0	42	-1.5	4.3	-1.0	-10.0	10.0	0.028
	200mg fezakinumab Q2W	48	12.5	6.4	10.5	4.0	28.0	48	-1.9	4.5	-2.0	-13.0	17.0	0.004
Week 4	Placebo	66	10.4	6.6	10.0	0.0	26.0	66	-3.0	5.0	-2.0	-17.0	10.0	<.001
	100mg fezakinumab Q4W	39	9.5	7.1	7.0	1.0	28.0	39	-3.7	5.7	-4.0	-15.6	11.0	<.001
	100mg fezakinumab Q2W	42	9.5	6.7	9.3	0.0	28.0	42	-2.8	4.7	-3.0	-15.0	8.0	<.001
	200mg fezakinumab Q2W	48	11.2	6.5	10.0	2.0	28.0	48	-3.2	4.8	-2.5	-17.0	8.0	<.001
Week 6	Placebo	66	9.5	7.1	8.0	0.0	28.0	66	-3.9	5.0	-4.0	-17.0	7.0	<.001
	100mg fezakinumab Q4W	39	8.1	7.5	6.0	0.0	28.0	39	-5.1	5.1	-5.4	-16.6	10.0	<.001
	100mg fezakinumab Q2W	42	9.2	7.8	7.0	0.0	28.0	42	-3.0	5.5	-4.0	-13.0	14.9	0.001
	200mg fezakinumab Q2W	48	9.3	6.4	8.5	0.0	28.0	48	-5.1	5.2	-4.7	-22.0	8.0	<.001
Week 8	Placebo	66	9.2	7.2	6.5	0.0	27.0	66	-4.2	6.5	-4.0	-21.0	16.0	<.001
	100mg fezakinumab Q4W	39	7.8	7.2	6.0	0.0	28.0	39	-5.4	4.7	-5.4	-17.0	7.0	<.001
	100mg fezakinumab Q2W	42	7.9	7.2	6.0	0.0	28.0	42	-4.3	5.2	-4.5	-16.0	11.0	<.001
	200mg fezakinumab Q2W	48	9.3	6.6	8.8	0.0	28.0	48	-5.1	5.1	-4.0	-21.0	3.0	<.001
Week 10	Placebo	66	8.4	7.0	6.5	0.0	28.0	66	-5.1	5.8	-4.5	-17.0	11.0	<.001
	100mg fezakinumab Q4W	39	7.2	6.9	4.0	0.0	25.0	39	-6.0	5.6	-6.5	-18.0	13.0	<.001
	100mg fezakinumab Q2W	42	8.0	7.1	6.0	0.0	28.0	42	-4.2	5.5	-4.7	-15.0	10.0	<.001
	200mg fezakinumab Q2W	48	9.5	7.0	7.5	0.0	28.0	48	-4.9	5.7	-5.0	-22.0	14.0	<.001
Week 12	Placebo	66	7.7	6.4	7.0	0.0	28.0	66	-5.7	5.6	-5.0	-18.0	11.0	<.001
	100mg fezakinumab Q4W	39	7.4	8.0	4.0	0.0	28.0	39	-5.8	5.4	-6.0	-16.0	6.0	<.001
	100mg fezakinumab Q2W	42	7.8	7.7	5.5	0.0	28.0	42	-4.5	5.3	-5.0	-17.0	8.0	<.001
	200mg fezakinumab Q2W	48	9.2	7.0	7.0	0.0	28.0	48	-5.2	6.4	-5.0	-22.0	16.2	<.001

LOCF = last observation carried forward, Max = maximum, Min = minimum, mITT = modified intent-to-treat, N = number of subject, Q2W = every 2 weeks, Q4W = every 4 weeks, SD = standard deviation.

a. p-Value from a 2-sided paired T-test.

Table 16. Descriptive Summary Statistics and Between Treatment Comparisons (ANCOVA) for Change From Baseline in Total Number of Tender Joints, mITT Population, LOCF

Study Week	Treatment	N	Mean	Comparator	N	Mean	Adjusted Mean Diff[a] (SE)	95% CI[a]	p-Value[a]
Week 2	100mg fezakinumab Q4W	39	-2.3	Placebo	66	-2.4	0.0 (0.9)	-1.7, 1.8	0.967
	100mg fezakinumab Q2W	42	-1.5	Placebo	66	-2.4	0.7 (0.9)	-1.0, 2.5	0.395
	200mg fezakinumab Q2W	48	-1.9	Placebo	66	-2.4	0.6 (0.8)	-1.1, 2.2	0.506
	100mg fezakinumab Q2W	42	-1.5	100mg fezakinumab Q4W	39	-2.3	0.7 (1.0)	-1.2, 2.6	0.472
	200mg fezakinumab Q2W	48	-1.9	100mg fezakinumab Q4W	39	-2.3	0.5 (1.0)	-1.4, 2.4	0.584
	200mg fezakinumab Q2W	48	-1.9	100mg fezakinumab Q2W	42	-1.5	-0.2 (0.9)	-2.0, 1.7	0.848
Week 4	100mg fezakinumab Q4W	39	-3.7	Placebo	66	-3.0	-0.7 (1.0)	-2.7, 1.2	0.457
	100mg fezakinumab Q2W	42	-2.8	Placebo	66	-3.0	0.0 (1.0)	-1.9, 1.9	0.997
	200mg fezakinumab Q2W	48	-3.2	Placebo	66	-3.0	0.0 (0.9)	-1.8, 1.9	0.964
	100mg fezakinumab Q2W	42	-2.8	100mg fezakinumab Q4W	39	-3.7	0.7 (1.1)	-1.4, 2.9	0.499
	200mg fezakinumab Q2W	48	-3.2	100mg fezakinumab Q4W	39	-3.7	0.8 (1.1)	-1.3, 2.9	0.465
	200mg fezakinumab Q2W	48	-3.2	100mg fezakinumab Q2W	42	-2.8	0.0 (1.1)	-2.1, 2.1	0.971
Week 6	100mg fezakinumab Q4W	39	-5.1	Placebo	66	-3.9	-1.2 (1.0)	-3.3, 0.8	0.234
	100mg fezakinumab Q2W	42	-3.0	Placebo	66	-3.9	0.7 (1.0)	-1.3, 2.7	0.483
	200mg fezakinumab Q2W	48	-5.1	Placebo	66	-3.9	-1.0 (1.0)	-2.9, 1.0	0.322
	100mg fezakinumab Q2W	42	-3.0	100mg fezakinumab Q4W	39	-5.1	2.0 (1.2)	-0.3, 4.2	0.090
	200mg fezakinumab Q2W	48	-5.1	100mg fezakinumab Q4W	39	-5.1	0.3 (1.1)	-2.0, 2.5	0.816
	200mg fezakinumab Q2W	48	-5.1	100mg fezakinumab Q2W	42	-3.0	-1.7 (1.1)	-3.9, 0.5	0.129
Week 8	100mg fezakinumab Q4W	39	-5.4	Placebo	66	-4.2	-1.2 (1.1)	-3.4, 0.9	0.258
	100mg fezakinumab Q2W	42	-4.3	Placebo	66	-4.2	-0.4 (1.1)	-2.6, 1.7	0.677
	200mg fezakinumab Q2W	48	-5.1	Placebo	66	-4.2	-0.5 (1.0)	-2.5, 1.6	0.656
	100mg fezakinumab Q2W	42	-4.3	100mg fezakinumab Q4W	39	-5.4	0.8 (1.2)	-1.6, 3.2	0.512
	200mg fezakinumab Q2W	48	-5.1	100mg fezakinumab Q4W	39	-5.4	0.8 (1.2)	-1.5, 3.1	0.509
	200mg fezakinumab Q2W	48	-5.1	100mg fezakinumab Q2W	42	-4.3	-0.0 (1.2)	-2.3, 2.3	0.989
Week 10	100mg fezakinumab Q4W	39	-6.0	Placebo	66	-5.1	-1.0 (1.1)	-3.2, 1.2	0.369
	100mg fezakinumab Q2W	42	-4.2	Placebo	66	-5.1	0.5 (1.1)	-1.7, 2.7	0.647
	200mg fezakinumab Q2W	48	-4.9	Placebo	66	-5.1	0.6 (1.1)	-1.5, 2.6	0.601
	100mg fezakinumab Q2W	42	-4.2	100mg fezakinumab Q4W	39	-6.0	1.5 (1.2)	-0.9, 3.9	0.223
	200mg fezakinumab Q2W	48	-4.9	100mg fezakinumab Q4W	39	-6.0	1.6 (1.2)	-0.8, 3.9	0.196
	200mg fezakinumab Q2W	48	-4.9	100mg fezakinumab Q2W	42	-4.2	0.1 (1.2)	-2.3, 2.4	0.965
Week 12	100mg fezakinumab Q4W	39	-5.8	Placebo	66	-5.7	-0.1 (1.1)	-2.3, 2.1	0.935

Table 16. Descriptive Summary Statistics and Between Treatment Comparisons (ANCOVA) for Change From Baseline in Total Number of Tender Joints, mITT Population, LOCF

Study Week	Treatment	N	Mean	Comparator	N	Mean	Adjusted Mean Diff[a] (SE)	95% CI[a]	p-Value[a]
	100mg fezakinumab Q2W	42	-4.5	Placebo	66	-5.7	0.9 (1.1)	-1.3, 3.0	0.439
	200mg fezakinumab Q2W	48	-5.2	Placebo	66	-5.7	0.9 (1.1)	-1.2, 3.0	0.383
	100mg fezakinumab Q2W	42	-4.5	100mg fezakinumab Q4W	39	-5.8	0.9 (1.2)	-1.5, 3.4	0.447
	200mg fezakinumab Q2W	48	-5.2	100mg fezakinumab Q4W	39	-5.8	1.0 (1.2)	-1.4, 3.4	0.398
	200mg fezakinumab Q2W	48	-5.2	100mg fezakinumab Q2W	42	-4.5	0.1 (1.2)	-2.3, 2.4	0.949

ANCOVA = analysis of covariance, CI = confidence interval, Diff = difference, LOCF = last observation carried forward, mITT = modified intent-to-treat, N = number of subject, Q2W = every 2 weeks, Q4W = every 4 weeks, SE = standard error, TNF = tumor necrosis factor.

a. From the ANCOVA model: change = baseline + anti-TNF prior use + region + treatment.

Table 17. Descriptive Summary Statistics and Within Treatment Comparison for Total Number of Swollen Joints, mITT Population, LOCF

								Change From Baseline						
Study Week	**Treatment**	**N**	**Mean**	**SD**	**Median**	**Min**	**Max**	**N**	**Mean**	**SD**	**Median**	**Min**	**Max**	**p-Value[a]**
Baseline	Placebo	66	10.2	3.8	9.0	5.0	22.0							
	100mg fezakinumab Q4W	39	10.0	4.6	7.0	5.0	20.0							
	100mg fezakinumab Q2W	42	9.4	4.6	7.5	5.0	25.0							
	200mg fezakinumab Q2W	48	10.0	4.1	9.0	5.0	23.0							
Week 2	Placebo	66	8.2	5.0	7.0	0.0	24.0	66	-1.9	3.3	-1.5	-12.0	6.0	<.001
	100mg fezakinumab Q4W	39	8.4	5.2	7.0	0.0	23.0	39	-1.6	3.7	-2.0	-12.0	8.0	0.011
	100mg fezakinumab Q2W	42	6.9	5.2	6.0	0.0	23.0	42	-2.5	3.3	-2.0	-13.0	6.0	<.001
	200mg fezakinumab Q2W	48	8.0	4.7	6.5	0.0	25.0	48	-2.0	3.8	-2.0	-12.0	5.0	<.001
Week 4	Placebo	66	7.0	4.9	6.0	0.0	23.0	66	-3.2	3.4	-3.0	-12.0	4.0	<.001
	100mg fezakinumab Q4W	39	6.8	5.1	5.2	1.0	22.0	39	-3.1	4.5	-3.0	-15.0	9.0	<.001
	100mg fezakinumab Q2W	42	5.8	5.0	4.0	0.0	22.0	42	-3.6	3.0	-4.0	-13.0	5.0	<.001
	200mg fezakinumab Q2W	48	7.0	5.0	6.0	0.0	25.9	48	-3.0	4.7	-3.0	-14.0	10.4	<.001
Week 6	Placebo	66	6.6	5.3	6.0	0.0	23.0	66	-3.5	3.9	-4.0	-12.0	7.0	<.001
	100mg fezakinumab Q4W	39	5.7	5.4	4.0	0.0	27.0	39	-4.3	4.4	-5.0	-15.0	7.0	<.001
	100mg fezakinumab Q2W	42	6.0	5.8	4.5	0.0	25.0	42	-3.4	4.1	-4.0	-13.0	9.0	<.001
	200mg fezakinumab Q2W	48	5.9	5.1	5.0	0.0	25.9	48	-4.0	4.6	-4.0	-16.0	10.4	<.001
Week 8	Placebo	66	6.4	5.4	5.0	0.0	24.0	66	-3.8	4.4	-4.0	-14.0	8.0	<.001
	100mg fezakinumab Q4W	39	6.0	6.0	4.0	0.0	27.0	39	-4.0	4.2	-4.0	-15.0	7.0	<.001
	100mg fezakinumab Q2W	42	5.0	4.9	4.0	0.0	20.0	42	-4.3	3.4	-4.5	-12.0	4.0	<.001
	200mg fezakinumab Q2W	48	5.6	5.2	4.0	0.0	25.9	48	-4.4	4.8	-4.0	-19.0	10.4	<.001
Week 10	Placebo	66	5.9	5.8	4.0	0.0	23.0	66	-4.2	4.7	-5.0	-15.0	8.0	<.001
	100mg fezakinumab Q4W	39	5.4	5.5	3.0	0.0	27.0	39	-4.6	4.1	-5.0	-13.0	7.0	<.001
	100mg fezakinumab Q2W	42	5.2	5.2	5.0	0.0	25.0	42	-4.2	3.7	-5.0	-12.0	4.0	<.001
	200mg fezakinumab Q2W	48	5.9	5.8	4.0	0.0	25.9	48	-4.1	5.4	-4.0	-20.0	10.4	<.001
Week 12	Placebo	66	5.5	5.6	4.0	0.0	26.0	66	-4.7	4.8	-5.0	-16.0	12.0	<.001
	100mg fezakinumab Q4W	39	5.6	5.9	4.0	0.0	27.0	39	-4.4	4.9	-5.0	-16.0	7.0	<.001
	100mg fezakinumab Q2W	42	5.0	5.3	4.0	0.0	23.0	42	-4.3	3.9	-4.0	-12.0	5.0	<.001
	200mg fezakinumab Q2W	48	5.5	5.9	4.0	0.0	25.9	48	-4.5	5.7	-4.5	-20.0	11.8	<.001

LOCF = last observation carried forward, Max = maximum, Min = minimum, mITT = modified intent-to-treat, N = number of subject, Q2W = every 2 weeks, Q4W = every 4 weeks, SD = standard deviation.

a. p-Value from a 2-sided paired T-test.

Table 18. Descriptive Summary Statistics and Between Treatment Comparisons (ANCOVA) for Change From Baseline in Total Number of Swollen Joints, mITT Population, LOCF

Study Week	Treatment	N	Mean	Comparator	N	Mean	Adjusted Mean Diff[a] (SE)	95% CI[a]	p-Value[a]
Week 2	100mg fezakinumab Q4W	39	-1.6	Placebo	66	-1.9	0.3 (0.7)	-1.1, 1.7	0.636
	100mg fezakinumab Q2W	42	-2.5	Placebo	66	-1.9	-0.7 (0.7)	-2.0, 0.7	0.339
	200mg fezakinumab Q2W	48	-2.0	Placebo	66	-1.9	0.0 (0.7)	-1.3, 1.3	0.968
	100mg fezakinumab Q2W	42	-2.5	100mg fezakinumab Q4W	39	-1.6	-1.0 (0.8)	-2.5, 0.5	0.202
	200mg fezakinumab Q2W	48	-2.0	100mg fezakinumab Q4W	39	-1.6	-0.3 (0.8)	-1.8, 1.2	0.685
	200mg fezakinumab Q2W	48	-2.0	100mg fezakinumab Q2W	42	-2.5	0.7 (0.8)	-0.8, 2.2	0.358
Week 4	100mg fezakinumab Q4W	39	-3.1	Placebo	66	-3.2	-0.0 (0.8)	-1.5, 1.5	0.974
	100mg fezakinumab Q2W	42	-3.6	Placebo	66	-3.2	-0.6 (0.8)	-2.1, 0.9	0.405
	200mg fezakinumab Q2W	48	-3.0	Placebo	66	-3.2	0.2 (0.7)	-1.3, 1.6	0.796
	100mg fezakinumab Q2W	42	-3.6	100mg fezakinumab Q4W	39	-3.1	-0.6 (0.9)	-2.3, 1.1	0.477
	200mg fezakinumab Q2W	48	-3.0	100mg fezakinumab Q4W	39	-3.1	0.2 (0.8)	-1.4, 1.9	0.796
	200mg fezakinumab Q2W	48	-3.0	100mg fezakinumab Q2W	42	-3.6	0.8 (0.8)	-0.8, 2.4	0.318
Week 6	100mg fezakinumab Q4W	39	-4.3	Placebo	66	-3.5	-0.7 (0.8)	-2.4, 0.9	0.386
	100mg fezakinumab Q2W	42	-3.4	Placebo	66	-3.5	-0.0 (0.8)	-1.7, 1.6	0.962
	200mg fezakinumab Q2W	48	-4.0	Placebo	66	-3.5	-0.5 (0.8)	-2.0, 1.1	0.569
	100mg fezakinumab Q2W	42	-3.4	100mg fezakinumab Q4W	39	-4.3	0.7 (0.9)	-1.1, 2.5	0.458
	200mg fezakinumab Q2W	48	-4.0	100mg fezakinumab Q4W	39	-4.3	0.3 (0.9)	-1.5, 2.1	0.760
	200mg fezakinumab Q2W	48	-4.0	100mg fezakinumab Q2W	42	-3.4	-0.4 (0.9)	-2.2, 1.3	0.644
Week 8	100mg fezakinumab Q4W	39	-4.0	Placebo	66	-3.8	-0.2 (0.8)	-1.9, 1.4	0.788
	100mg fezakinumab Q2W	42	-4.3	Placebo	66	-3.8	-0.9 (0.8)	-2.5, 0.8	0.294
	200mg fezakinumab Q2W	48	-4.4	Placebo	66	-3.8	-0.5 (0.8)	-2.0, 1.1	0.561
	100mg fezakinumab Q2W	42	-4.3	100mg fezakinumab Q4W	39	-4.0	-0.6 (0.9)	-2.5, 1.2	0.491
	200mg fezakinumab Q2W	48	-4.4	100mg fezakinumab Q4W	39	-4.0	-0.2 (0.9)	-2.0, 1.5	0.793
	200mg fezakinumab Q2W	48	-4.4	100mg fezakinumab Q2W	42	-4.3	0.4 (0.9)	-1.4, 2.2	0.651
Week 10	100mg fezakinumab Q4W	39	-4.6	Placebo	66	-4.2	-0.4 (0.9)	-2.2, 1.4	0.648
	100mg fezakinumab Q2W	42	-4.2	Placebo	66	-4.2	-0.2 (0.9)	-2.0, 1.5	0.795
	200mg fezakinumab Q2W	48	-4.1	Placebo	66	-4.2	0.3 (0.9)	-1.4, 2.0	0.705
	100mg fezakinumab Q2W	42	-4.2	100mg fezakinumab Q4W	39	-4.6	0.2 (1.0)	-1.8, 2.2	0.855
	200mg fezakinumab Q2W	48	-4.1	100mg fezakinumab Q4W	39	-4.6	0.7 (1.0)	-1.2, 2.7	0.447
	200mg fezakinumab Q2W	48	-4.1	100mg fezakinumab Q2W	42	-4.2	0.6 (1.0)	-1.3, 2.5	0.564
Week 12	100mg fezakinumab Q4W	39	-4.4	Placebo	66	-4.7	0.3 (0.9)	-1.5, 2.1	0.745

Table 18. Descriptive Summary Statistics and Between Treatment Comparisons (ANCOVA) for Change From Baseline in Total Number of Swollen Joints, mITT Population, LOCF

Study Week	Treatment	N	Mean	Comparator	N	Mean	Adjusted Mean Diff[a] (SE)	95% CI[a]	p-Value[a]
	100mg fezakinumab Q2W	42	-4.3	Placebo	66	-4.7	-0.1 (0.9)	-1.9, 1.7	0.922
	200mg fezakinumab Q2W	48	-4.5	Placebo	66	-4.7	0.6 (0.9)	-1.2, 2.3	0.519
	100mg fezakinumab Q2W	42	-4.3	100mg fezakinumab Q4W	39	-4.4	-0.4 (1.0)	-2.4, 1.6	0.703
	200mg fezakinumab Q2W	48	-4.5	100mg fezakinumab Q4W	39	-4.4	0.3 (1.0)	-1.7, 2.2	0.790
	200mg fezakinumab Q2W	48	-4.5	100mg fezakinumab Q2W	42	-4.3	0.7 (1.0)	-1.3, 2.6	0.506

ANCOVA = analysis of covariance, CI = confidence interval, Diff = difference, LOCF = last observation carried forward, mITT = modified intent-to-treat, N = number of subject, Q2W = every 2 weeks, Q4W = every 4 weeks, SE = standard error, TNF = tumor necrosis factor.

a. From the ANCOVA model: change = baseline + anti-TNF prior use + region + treatment.

Physician Global Assessment of Disease Activity:

For the mITT population using LOCF imputation, within treatment comparisons revealed statistically significant changes from Baseline in the physician global assessment of disease activity for all groups at all weeks (Table 19). No statistically significant differences in the change from Baseline in the physician global assessment of disease activity between the groups were observed at any week (Table 20).

Patient Global Assessment of Disease Activity:

For the mITT population using LOCF imputation within treatment comparisons revealed statistically significant changes from Baseline in the patient global assessment of disease activity for all groups at all weeks, except for the 100 mg fezakinumab Q2W group at Week 2 and the 200 mg fezakinumab Q2W group at Week 2 and at Week 4 (Table 21). With few exceptions, no statistically significant differences in the change from Baseline in the patient global assessment of disease activity between the groups were observed at any week (Table 22).

Table 19. Descriptive Summary Statistics and Within Treatment Comparison for Physician Global Assessment of Disease Activity, mITT Population, LOCF

								Change From Baseline						
Study Week	**Treatment**	**N**	**Mean**	**SD**	**Median**	**Min**	**Max**	**N**	**Mean**	**SD**	**Median**	**Min**	**Max**	**p-Value[a]**
Baseline	Placebo	66	6.2	1.6	6.0	2.0	9.0							
	100mg fezakinumab Q4W	39	6.3	1.5	6.0	3.0	9.0							
	100mg fezakinumab Q2W	42	6.0	1.7	6.0	1.0	9.0							
	200mg fezakinumab Q2W	48	6.0	1.6	6.0	3.0	9.0							
Week 2	Placebo	66	5.4	1.9	6.0	1.0	9.0	66	-0.9	1.6	-1.0	-6.0	4.0	<.001
	100mg fezakinumab Q4W	39	5.2	1.8	5.0	0.0	8.0	39	-1.1	1.7	-1.0	-6.0	3.0	<.001
	100mg fezakinumab Q2W	42	5.1	2.1	5.0	0.0	9.0	42	-1.0	1.7	-0.5	-5.0	2.0	<.001
	200mg fezakinumab Q2W	48	5.1	1.7	5.0	2.0	9.0	48	-0.9	1.2	-1.0	-4.0	1.0	<.001
Week 4	Placebo	66	4.7	1.9	5.0	1.0	8.0	66	-1.5	1.7	-1.5	-5.0	2.0	<.001
	100mg fezakinumab Q4W	39	4.9	1.8	5.0	1.0	8.0	39	-1.4	2.0	-1.0	-6.0	3.0	<.001
	100mg fezakinumab Q2W	42	4.6	2.2	5.0	0.0	8.0	42	-1.4	1.9	-1.0	-7.0	2.0	<.001
	200mg fezakinumab Q2W	48	4.9	1.9	5.0	1.0	9.0	48	-1.1	1.5	-1.0	-5.0	2.0	<.001
Week 6	Placebo	66	4.4	1.8	4.0	0.0	9.0	66	-1.8	1.6	-2.0	-6.0	2.0	<.001
	100mg fezakinumab Q4W	39	4.5	1.9	4.0	0.0	8.0	39	-1.8	1.8	-1.0	-6.0	1.0	<.001
	100mg fezakinumab Q2W	42	4.3	1.8	4.0	0.0	8.0	42	-1.8	2.0	-2.0	-6.0	2.0	<.001
	200mg fezakinumab Q2W	48	4.3	2.0	4.0	0.0	9.0	48	-1.7	1.7	-2.0	-5.0	1.0	<.001
Week 8	Placebo	66	4.5	2.1	4.0	0.0	9.0	66	-1.7	2.2	-2.0	-6.0	4.0	<.001
	100mg fezakinumab Q4W	39	3.9	1.6	4.0	0.0	8.0	39	-2.4	1.7	-2.0	-6.0	0.0	<.001
	100mg fezakinumab Q2W	42	3.9	1.9	4.0	0.0	8.0	42	-2.2	1.8	-2.0	-7.0	2.0	<.001
	200mg fezakinumab Q2W	48	4.1	2.0	4.0	0.0	9.0	48	-1.9	1.7	-2.0	-6.0	1.0	<.001
Week 10	Placebo	66	4.2	2.3	4.0	1.0	9.0	66	-2.0	2.3	-2.0	-7.0	5.0	<.001
	100mg fezakinumab Q4W	39	3.6	1.7	4.0	0.0	8.0	39	-2.7	2.0	-2.0	-6.0	0.0	<.001
	100mg fezakinumab Q2W	42	3.9	1.9	4.0	0.0	8.0	42	-2.2	2.0	-2.5	-7.0	2.0	<.001
	200mg fezakinumab Q2W	48	4.2	2.3	4.0	0.0	9.0	48	-1.8	1.9	-2.0	-6.0	1.0	<.001
Week 12	Placebo	66	4.0	2.2	4.0	1.0	9.0	66	-2.3	2.2	-2.0	-6.0	4.0	<.001
	100mg fezakinumab Q4W	39	3.7	2.1	3.0	0.0	8.0	39	-2.6	2.2	-3.0	-8.0	1.0	<.001
	100mg fezakinumab Q2W	42	3.6	1.9	3.5	0.0	8.0	42	-2.5	2.1	-2.0	-7.0	3.0	<.001
	200mg fezakinumab Q2W	48	3.9	2.1	4.0	0.0	10.0	48	-2.1	1.9	-2.0	-7.0	1.0	<.001

LOCF = last observation carried forward, Max = maximum, Min = minimum, mITT = modified intent-to-treat, N = number of subject, Q2W = every 2 weeks, Q4W = every 4 weeks, SD = standard deviation.

a. p-Value from a 2-sided paired T-test.

Table 20. Descriptive Summary Statistics and Between Treatment Comparisons (ANCOVA for Change From Baseline in Physician Global Assessment of Disease Activity, mITT Population, LOCF

Study Week	Treatment	N	Mean	Comparator	N	Mean	Adjusted Mean Diff[a] (SE)	95% CI[a]	p-Value[a]
Week 2	100mg fezakinumab Q4W	39	-1.1	Placebo	66	-0.9	-0.2 (0.3)	-0.8, 0.4	0.542
	100mg fezakinumab Q2W	42	-1.0	Placebo	66	-0.9	-0.2 (0.3)	-0.7, 0.4	0.605
	200mg fezakinumab Q2W	48	-0.9	Placebo	66	-0.9	-0.1 (0.3)	-0.7, 0.5	0.761
	100mg fezakinumab Q2W	42	-1.0	100mg fezakinumab Q4W	39	-1.1	0.0 (0.3)	-0.6, 0.7	0.926
	200mg fezakinumab Q2W	48	-0.9	100mg fezakinumab Q4W	39	-1.1	0.1 (0.3)	-0.5, 0.7	0.765
	200mg fezakinumab Q2W	48	-0.9	100mg fezakinumab Q2W	42	-1.0	0.1 (0.3)	-0.6, 0.7	0.837
Week 4	100mg fezakinumab Q4W	39	-1.4	Placebo	66	-1.5	0.2 (0.3)	-0.4, 0.9	0.510
	100mg fezakinumab Q2W	42	-1.4	Placebo	66	-1.5	0.0 (0.3)	-0.6, 0.7	0.911
	200mg fezakinumab Q2W	48	-1.1	Placebo	66	-1.5	0.4 (0.3)	-0.3, 1.0	0.269
	100mg fezakinumab Q2W	42	-1.4	100mg fezakinumab Q4W	39	-1.4	-0.2 (0.4)	-0.9, 0.5	0.618
	200mg fezakinumab Q2W	48	-1.1	100mg fezakinumab Q4W	39	-1.4	0.1 (0.4)	-0.6, 0.8	0.716
	200mg fezakinumab Q2W	48	-1.1	100mg fezakinumab Q2W	42	-1.4	0.3 (0.4)	-0.4, 1.0	0.376
Week 6	100mg fezakinumab Q4W	39	-1.8	Placebo	66	-1.8	0.1 (0.3)	-0.6, 0.7	0.778
	100mg fezakinumab Q2W	42	-1.8	Placebo	66	-1.8	-0.0 (0.3)	-0.7, 0.6	0.885
	200mg fezakinumab Q2W	48	-1.7	Placebo	66	-1.8	0.1 (0.3)	-0.6, 0.7	0.868
	100mg fezakinumab Q2W	42	-1.8	100mg fezakinumab Q4W	39	-1.8	-0.1 (0.4)	-0.9, 0.6	0.702
	200mg fezakinumab Q2W	48	-1.7	100mg fezakinumab Q4W	39	-1.8	-0.0 (0.4)	-0.7, 0.7	0.908
	200mg fezakinumab Q2W	48	-1.7	100mg fezakinumab Q2W	42	-1.8	0.1 (0.4)	-0.6, 0.8	0.778
Week 8	100mg fezakinumab Q4W	39	-2.4	Placebo	66	-1.7	-0.6 (0.4)	-1.3, 0.1	0.094
	100mg fezakinumab Q2W	42	-2.2	Placebo	66	-1.7	-0.6 (0.3)	-1.2, 0.1	0.114
	200mg fezakinumab Q2W	48	-1.9	Placebo	66	-1.7	-0.2 (0.3)	-0.9, 0.4	0.490
	100mg fezakinumab Q2W	42	-2.2	100mg fezakinumab Q4W	39	-2.4	0.0 (0.4)	-0.7, 0.8	0.909
	200mg fezakinumab Q2W	48	-1.9	100mg fezakinumab Q4W	39	-2.4	0.4 (0.4)	-0.4, 1.1	0.341
	200mg fezakinumab Q2W	48	-1.9	100mg fezakinumab Q2W	42	-2.2	0.3 (0.4)	-0.4, 1.1	0.398
Week 10	100mg fezakinumab Q4W	39	-2.7	Placebo	66	-2.0	-0.6 (0.4)	-1.4, 0.2	0.117
	100mg fezakinumab Q2W	42	-2.2	Placebo	66	-2.0	-0.3 (0.4)	-1.0, 0.5	0.514
	200mg fezakinumab Q2W	48	-1.8	Placebo	66	-2.0	0.2 (0.4)	-0.6, 0.9	0.631
	100mg fezakinumab Q2W	42	-2.2	100mg fezakinumab Q4W	39	-2.7	0.4 (0.4)	-0.5, 1.2	0.398
	200mg fezakinumab Q2W	48	-1.8	100mg fezakinumab Q4W	39	-2.7	0.8 (0.4)	-0.0, 1.6	0.060
	200mg fezakinumab Q2W	48	-1.8	100mg fezakinumab Q2W	42	-2.2	0.4 (0.4)	-0.4, 1.2	0.303
Week 12	100mg fezakinumab Q4W	39	-2.6	Placebo	66	-2.3	-0.3 (0.4)	-1.1, 0.5	0.477

Table 20. Descriptive Summary Statistics and Between Treatment Comparisons (ANCOVA for Change From Baseline in Physician Global Assessment of Disease Activity, mITT Population, LOCF

Study Week	Treatment	N	Mean	Comparator	N	Mean	Adjusted Mean Diff[a] (SE)	95% CI[a]	p-Value[a]
	100mg fezakinumab Q2W	42	-2.5	Placebo	66	-2.3	-0.3 (0.4)	-1.1, 0.4	0.408
	200mg fezakinumab Q2W	48	-2.1	Placebo	66	-2.3	0.1 (0.4)	-0.7, 0.8	0.833
	100mg fezakinumab Q2W	42	-2.5	100mg fezakinumab Q4W	39	-2.6	-0.0 (0.4)	-0.9, 0.8	0.928
	200mg fezakinumab Q2W	48	-2.1	100mg fezakinumab Q4W	39	-2.6	0.4 (0.4)	-0.5, 1.2	0.396
	200mg fezakinumab Q2W	48	-2.1	100mg fezakinumab Q2W	42	-2.5	0.4 (0.4)	-0.4, 1.2	0.341

ANCOVA = analysis of covariance, CI = confidence interval, Diff = difference, LOCF = last observation carried forward, mITT = modified intent-to-treat, N = number of subject, Q2W = every 2 weeks, Q4W = every 4 weeks, SE = standard error, TNF = tumor necrosis factor.

a. From the ANCOVA model: change = baseline + anti-TNF prior use + region + treatment.

Table 21. Descriptive Summary Statistics and Within Treatment Comparison for Patient Global Assessment of Disease Activity, mITT Population, LOCF

								Change From Baseline						
Study Week	**Treatment**	**N**	**Mean**	**SD**	**Median**	**Min**	**Max**	**N**	**Mean**	**SD**	**Median**	**Min**	**Max**	**p-Value[a]**
Baseline	Placebo	66	6.2	1.8	6.0	2.0	10.0							
	100mg fezakinumab Q4W	39	6.0	1.8	6.0	3.0	10.0							
	100mg fezakinumab Q2W	42	6.3	1.7	6.5	2.0	10.0							
	200mg fezakinumab Q2W	48	5.9	2.1	6.0	2.0	10.0							
Week 2	Placebo	66	5.5	2.3	5.0	1.0	10.0	66	-0.7	1.8	-1.0	-5.0	4.0	0.003
	100mg fezakinumab Q4W	39	5.5	2.1	6.0	1.0	10.0	39	-0.6	1.7	0.0	-6.0	3.0	0.045
	100mg fezakinumab Q2W	42	5.6	2.4	6.0	0.0	9.0	42	-0.7	2.3	0.0	-6.0	4.0	0.061
	200mg fezakinumab Q2W	48	5.7	2.2	6.0	1.0	10.0	48	-0.2	1.6	0.0	-3.0	4.0	0.407
Week 4	Placebo	66	5.2	2.1	5.0	1.0	9.0	66	-1.0	1.9	-1.0	-5.0	4.0	<.001
	100mg fezakinumab Q4W	39	5.0	2.2	5.0	1.0	10.0	39	-1.0	2.2	-1.0	-6.0	4.0	0.008
	100mg fezakinumab Q2W	42	5.6	2.2	6.0	0.0	10.0	42	-0.7	1.9	0.0	-6.0	4.0	0.017
	200mg fezakinumab Q2W	48	5.5	2.0	5.5	1.0	10.0	48	-0.3	1.6	0.0	-3.0	5.0	0.182
Week 6	Placebo	66	5.0	2.0	4.5	1.0	10.0	66	-1.2	2.1	-1.0	-6.0	5.0	<.001
	100mg fezakinumab Q4W	39	4.7	2.2	5.0	1.0	10.0	39	-1.3	1.8	-1.0	-6.0	2.0	<.001
	100mg fezakinumab Q2W	42	5.4	1.8	5.5	2.0	8.0	42	-1.0	1.8	-0.5	-5.0	3.0	0.002
	200mg fezakinumab Q2W	48	5.1	2.1	5.0	1.0	10.0	48	-0.8	1.9	-1.0	-5.0	6.0	0.007
Week 8	Placebo	66	5.1	2.1	5.0	1.0	9.0	66	-1.0	2.2	-1.0	-5.0	5.0	<.001
	100mg fezakinumab Q4W	39	4.6	2.3	4.0	1.0	10.0	39	-1.5	2.0	-1.0	-6.0	3.0	<.001
	100mg fezakinumab Q2W	42	5.5	1.9	5.0	2.0	9.0	42	-0.8	1.9	-1.0	-5.0	4.0	0.010
	200mg fezakinumab Q2W	48	4.8	2.0	5.0	1.0	9.0	48	-1.1	2.0	-1.0	-5.0	4.0	<.001
Week 10	Placebo	66	5.0	2.3	5.0	1.0	10.0	66	-1.1	2.3	-1.0	-6.0	5.0	<.001
	100mg fezakinumab Q4W	39	4.0	2.4	3.0	0.0	10.0	39	-2.1	2.2	-2.0	-7.0	2.0	<.001
	100mg fezakinumab Q2W	42	5.2	2.1	5.0	1.0	9.0	42	-1.1	2.3	-1.0	-5.0	6.0	0.004
	200mg fezakinumab Q2W	48	5.0	2.2	5.0	1.0	10.0	48	-0.8	1.8	-1.0	-5.0	3.0	0.004
Week 12	Placebo	66	4.7	2.1	5.0	1.0	9.0	66	-1.5	2.2	-1.5	-6.0	6.0	<.001
	100mg fezakinumab Q4W	39	4.5	2.4	4.0	0.0	10.0	39	-1.6	2.2	-1.0	-7.0	2.0	<.001
	100mg fezakinumab Q2W	42	5.0	2.0	5.0	1.0	9.0	42	-1.3	2.4	-1.0	-6.0	4.0	0.001
	200mg fezakinumab Q2W	48	4.8	2.2	5.0	1.0	10.0	48	-1.1	2.0	-1.0	-6.0	2.0	<.001

LOCF = last observation carried forward, Max = maximum, Min = minimum, mITT = modified intent-to-treat, N = number of subject, Q2W = every 2 weeks, Q4W = every 4 weeks. SD = standard deviation.

a. p-Value from a 2-sided paired T-test.

Table 22. Descriptive Summary Statistics and Between Treatment Comparisons (ANCOVA) for Change From Baseline in Patient Global Assessment of Disease Acitivity, mITT Population, LOCF

Study Week	Treatment	N	Mean	Comparator	N	Mean	Adjusted Mean Diff[a] (SE)	95% CI[a]	p-Value[a]
Week 2	100mg fezakinumab Q4W	39	-0.6	Placebo	66	-0.7	0.1 (0.4)	-0.6, 0.8	0.772
	100mg fezakinumab Q2W	42	-0.7	Placebo	66	-0.7	0.0 (0.4)	-0.7, 0.7	0.959
	200mg fezakinumab Q2W	48	-0.2	Placebo	66	-0.7	0.5 (0.3)	-0.2, 1.2	0.160
	100mg fezakinumab Q2W	42	-0.7	100mg fezakinumab Q4W	39	-0.6	-0.1 (0.4)	-0.9, 0.7	0.829
	200mg fezakinumab Q2W	48	-0.2	100mg fezakinumab Q4W	39	-0.6	0.4 (0.4)	-0.4, 1.1	0.330
	200mg fezakinumab Q2W	48	-0.2	100mg fezakinumab Q2W	42	-0.7	0.5 (0.4)	-0.3, 1.2	0.228
Week 4	100mg fezakinumab Q4W	39	-1.0	Placebo	66	-1.0	-0.1 (0.4)	-0.8, 0.6	0.832
	100mg fezakinumab Q2W	42	-0.7	Placebo	66	-1.0	0.3 (0.3)	-0.4, 1.0	0.424
	200mg fezakinumab Q2W	48	-0.3	Placebo	66	-1.0	0.6 (0.3)	-0.1, 1.3	0.075
	100mg fezakinumab Q2W	42	-0.7	100mg fezakinumab Q4W	39	-1.0	0.4 (0.4)	-0.4, 1.1	0.368
	200mg fezakinumab Q2W	48	-0.3	100mg fezakinumab Q4W	39	-1.0	0.7 (0.4)	-0.1, 1.4	0.077
	200mg fezakinumab Q2W	48	-0.3	100mg fezakinumab Q2W	42	-0.7	0.3 (0.4)	-0.4, 1.1	0.393
Week 6	100mg fezakinumab Q4W	39	-1.3	Placebo	66	-1.2	-0.1 (0.4)	-0.9, 0.6	0.687
	100mg fezakinumab Q2W	42	-1.0	Placebo	66	-1.2	0.3 (0.4)	-0.4, 1.0	0.394
	200mg fezakinumab Q2W	48	-0.8	Placebo	66	-1.2	0.3 (0.3)	-0.4, 1.0	0.386
	100mg fezakinumab Q2W	42	-1.0	100mg fezakinumab Q4W	39	-1.3	0.4 (0.4)	-0.3, 1.2	0.263
	200mg fezakinumab Q2W	48	-0.8	100mg fezakinumab Q4W	39	-1.3	0.4 (0.4)	-0.3, 1.2	0.254
	200mg fezakinumab Q2W	48	-0.8	100mg fezakinumab Q2W	42	-1.0	-0.0 (0.4)	-0.8, 0.8	0.990
Week 8	100mg fezakinumab Q4W	39	-1.5	Placebo	66	-1.0	-0.5 (0.4)	-1.2, 0.2	0.184
	100mg fezakinumab Q2W	42	-0.8	Placebo	66	-1.0	0.3 (0.4)	-0.4, 1.0	0.430
	200mg fezakinumab Q2W	48	-1.1	Placebo	66	-1.0	-0.2 (0.4)	-0.9, 0.5	0.567
	100mg fezakinumab Q2W	42	-0.8	100mg fezakinumab Q4W	39	-1.5	0.8 (0.4)	-0.0, 1.6	0.058
	200mg fezakinumab Q2W	48	-1.1	100mg fezakinumab Q4W	39	-1.5	0.3 (0.4)	-0.5, 1.1	0.461
	200mg fezakinumab Q2W	48	-1.1	100mg fezakinumab Q2W	42	-0.8	-0.5 (0.4)	-1.3, 0.3	0.217
Week 10	100mg fezakinumab Q4W	39	-2.1	Placebo	66	-1.1	-1.0 (0.4)	-1.8, -0.2	0.020
	100mg fezakinumab Q2W	42	-1.1	Placebo	66	-1.1	0.1 (0.4)	-0.7, 0.9	0.763
	200mg fezakinumab Q2W	48	-0.8	Placebo	66	-1.1	0.2 (0.4)	-0.6, 0.9	0.659
	100mg fezakinumab Q2W	42	-1.1	100mg fezakinumab Q4W	39	-2.1	1.1 (0.5)	0.2, 2.0	0.017
	200mg fezakinumab Q2W	48	-0.8	100mg fezakinumab Q4W	39	-2.1	1.1 (0.4)	0.3, 2.0	0.010
	200mg fezakinumab Q2W	48	-0.8	100mg fezakinumab Q2W	42	-1.1	0.1 (0.4)	-0.8, 0.9	0.909
Week 12	100mg fezakinumab Q4W	39	-1.6	Placebo	66	-1.5	-0.1 (0.4)	-0.9, 0.7	0.752

Table 22. Descriptive Summary Statistics and Between Treatment Comparisons (ANCOVA) for Change From Baseline in Patient Global Assessment of Disease Acitivity, mITT Population, LOCF

Study Week	Treatment	N	Mean	Comparator	N	Mean	Adjusted Mean Diff[a] (SE)	95% CI[a]	p-Value[a]
	100mg fezakinumab Q2W	42	-1.3	Placebo	66	-1.5	0.3 (0.4)	-0.5, 1.1	0.444
	200mg fezakinumab Q2W	48	-1.1	Placebo	66	-1.5	0.3 (0.4)	-0.5, 1.0	0.437
	100mg fezakinumab Q2W	42	-1.3	100mg fezakinumab Q4W	39	-1.6	0.4 (0.4)	-0.4, 1.3	0.335
	200mg fezakinumab Q2W	48	-1.1	100mg fezakinumab Q4W	39	-1.6	0.4 (0.4)	-0.4, 1.3	0.327
	200mg fezakinumab Q2W	48	-1.1	100mg fezakinumab Q2W	42	-1.3	-0.0 (0.4)	-0.8, 0.8	0.991

ANCOVA = analysis of covariance, CI = confidence interval, Diff = difference, LOCF = last observation carried forward, mITT = modified intent-to-treat, N = number of subject, Q2W = every 2 weeks, Q4W = every 4 weeks, SE = standard error, TNF = tumor necrosis factor.

a. From the ANCOVA model: change = baseline + anti-TNF prior use + region + treatment.

Pain VAS:

With few exceptions, within treatment comparisons revealed statistically significant changes from Baseline in pain VAS for all groups at all weeks (Table 23). With few exceptions, no statistically significant differences in the change from Baseline in pain VAS between the groups were observed at any week (Table 24).

General Health VAS:

For the mITT population using LOCF with few exceptions, within treatment comparisons revealed statistically significant changes from Baseline in general health VAS for all groups at all weeks (Table 25). With few exceptions, no statistically significant differences in the change from Baseline in general health VAS between the groups were observed at any week (Table 26).

Table 23. Descriptive Summary Statistics and Within Treatment Comparison for Pain VAS, mITT Population, LOCF

								Change From Baseline						
Study Week	**Treatment**	**N**	**Mean**	**SD**	**Median**	**Min**	**Max**	**N**	**Mean**	**SD**	**Median**	**Min**	**Max**	**p-Value[a]**
Baseline	Placebo	66	58.0	21.2	58.0	9.0	96.0							
	100mg fezakinumab Q4W	39	56.0	19.1	55.0	18.0	95.0							
	100mg fezakinumab Q2W	42	56.6	18.7	58.5	15.0	92.0							
	200mg fezakinumab Q2W	48	56.5	23.6	55.0	9.0	98.0							
Week 2	Placebo	66	49.8	23.5	50.0	2.0	98.0	66	-8.3	17.8	-6.0	-57.0	46.0	<.001
	100mg fezakinumab Q4W	39	48.3	24.0	47.0	6.0	96.0	39	-7.8	18.5	-3.0	-63.0	16.0	0.012
	100mg fezakinumab Q2W	42	51.7	23.7	55.5	2.0	97.0	42	-4.9	19.6	-3.0	-55.0	26.0	0.114
	200mg fezakinumab Q2W	48	52.3	21.5	52.0	5.0	86.0	48	-4.2	18.8	-2.5	-66.0	49.0	0.125
Week 4	Placebo	66	46.8	23.7	42.0	3.0	97.0	66	-11.2	17.7	-8.0	-59.0	25.0	<.001
	100mg fezakinumab Q4W	39	45.9	23.9	46.0	8.0	97.0	39	-10.1	21.8	-8.0	-52.0	39.0	0.006
	100mg fezakinumab Q2W	42	54.7	22.0	59.0	1.0	89.0	42	-1.9	18.4	-1.0	-58.0	42.0	0.506
	200mg fezakinumab Q2W	48	52.6	20.7	54.0	2.0	93.0	48	-3.9	18.3	-5.5	-59.0	32.0	0.144
Week 6	Placebo	66	48.8	23.6	45.5	1.0	96.0	66	-9.3	19.3	-9.0	-54.0	55.0	<.001
	100mg fezakinumab Q4W	39	45.2	23.5	45.5	3.0	96.0	39	-10.8	24.4	-13.0	-53.0	53.0	0.009
	100mg fezakinumab Q2W	42	48.8	18.9	49.5	5.0	86.0	42	-7.8	18.7	-6.0	-49.0	23.0	0.010
	200mg fezakinumab Q2W	48	46.7	21.7	51.0	2.0	93.0	48	-9.8	21.8	-6.0	-62.0	52.0	0.003
Week 8	Placebo	66	47.3	24.4	44.5	2.0	96.0	66	-10.8	22.5	-10.5	-57.0	55.0	<.001
	100mg fezakinumab Q4W	39	38.9	23.5	40.0	3.0	95.0	39	-17.1	21.8	-17.0	-57.0	53.0	<.001
	100mg fezakinumab Q2W	42	49.0	22.8	52.0	6.0	90.0	42	-7.6	25.3	-3.0	-60.0	37.0	0.057
	200mg fezakinumab Q2W	48	44.1	21.2	49.5	2.0	93.0	48	-12.5	23.1	-8.0	-63.0	36.0	<.001
Week 10	Placebo	66	45.2	26.1	43.5	2.0	96.0	66	-12.9	22.7	-12.5	-68.0	47.0	<.001
	100mg fezakinumab Q4W	39	37.7	24.6	38.0	2.0	96.0	39	-18.3	23.7	-19.0	-55.0	53.0	<.001
	100mg fezakinumab Q2W	42	46.2	24.0	47.0	3.0	93.0	42	-10.5	28.2	-9.0	-59.0	78.0	0.021
	200mg fezakinumab Q2W	48	44.7	23.5	50.5	1.0	93.0	48	-11.8	24.1	-10.0	-67.0	52.0	0.001
Week 12	Placebo	66	44.0	25.0	41.5	2.0	96.0	66	-14.1	22.0	-12.5	-67.0	55.0	<.001
	100mg fezakinumab Q4W	39	39.9	23.9	41.5	0.0	94.0	39	-16.1	24.0	-13.0	-59.0	53.0	<.001
	100mg fezakinumab Q2W	42	44.9	22.4	47.5	3.0	95.5	42	-11.8	23.1	-10.0	-62.0	33.0	0.002
	200mg fezakinumab Q2W	48	42.6	19.9	45.0	2.0	93.0	48	-14.0	23.7	-9.0	-74.0	31.0	<.001

LOCF = last observation carried forward, Max = maximum, Min = minimum, mITT = modified intent-to-treat, N = number of subject, Q2W = every 2 weeks, Q4W = every 4 weeks, SD = standard deviation, VAS = visual analog scale.

a. p-Value from a 2-sided paired T-test.

Table 24. Descriptive Summary Statistics and Between Treatment Comparisons (ANCOVA) for Change From Baseline in Pain VAS, mITT Population, LOCF

Study Week	Treatment	N	Mean	Comparator	N	Mean	Adjusted Mean Diff[a] (SE)	95% CI[a]	p-Value[a]
Week 2	100mg fezakinumab Q4W	39	-7.8	Placebo	66	-8.3	0.0 (3.6)	-7.0, 7.1	0.993
	100mg fezakinumab Q2W	42	-4.9	Placebo	66	-8.3	2.7 (3.5)	-4.2, 9.6	0.440
	200mg fezakinumab Q2W	48	-4.2	Placebo	66	-8.3	4.1 (3.4)	-2.5, 10.8	0.222
	100mg fezakinumab Q2W	42	-4.9	100mg fezakinumab Q4W	39	-7.8	2.7 (3.9)	-5.1, 10.4	0.498
	200mg fezakinumab Q2W	48	-4.2	100mg fezakinumab Q4W	39	-7.8	4.1 (3.8)	-3.4, 11.7	0.285
	200mg fezakinumab Q2W	48	-4.2	100mg fezakinumab Q2W	42	-4.9	1.4 (3.8)	-6.0, 8.9	0.706
Week 4	100mg fezakinumab Q4W	39	-10.1	Placebo	66	-11.2	0.5 (3.6)	-6.6, 7.6	0.885
	100mg fezakinumab Q2W	42	-1.9	Placebo	66	-11.2	8.7 (3.5)	1.8, 15.6	0.014
	200mg fezakinumab Q2W	48	-3.9	Placebo	66	-11.2	7.1 (3.4)	0.4, 13.8	0.037
	100mg fezakinumab Q2W	42	-1.9	100mg fezakinumab Q4W	39	-10.1	8.2 (4.0)	0.4, 16.0	0.040
	200mg fezakinumab Q2W	48	-3.9	100mg fezakinumab Q4W	39	-10.1	6.6 (3.8)	-1.0, 14.2	0.088
	200mg fezakinumab Q2W	48	-3.9	100mg fezakinumab Q2W	42	-1.9	-1.6 (3.8)	-9.1, 5.9	0.679
Week 6	100mg fezakinumab Q4W	39	-10.8	Placebo	66	-9.3	-2.5 (3.8)	-10.0, 5.1	0.518
	100mg fezakinumab Q2W	42	-7.8	Placebo	66	-9.3	0.7 (3.7)	-6.6, 8.1	0.845
	200mg fezakinumab Q2W	48	-9.8	Placebo	66	-9.3	-1.0 (3.6)	-8.1, 6.1	0.779
	100mg fezakinumab Q2W	42	-7.8	100mg fezakinumab Q4W	39	-10.8	3.2 (4.2)	-5.1, 11.5	0.448
	200mg fezakinumab Q2W	48	-9.8	100mg fezakinumab Q4W	39	-10.8	1.5 (4.1)	-6.6, 9.5	0.722
	200mg fezakinumab Q2W	48	-9.8	100mg fezakinumab Q2W	42	-7.8	-1.7 (4.1)	-9.7, 6.3	0.667
Week 8	100mg fezakinumab Q4W	39	-17.1	Placebo	66	-10.8	-7.4 (4.2)	-15.7, 0.8	0.078
	100mg fezakinumab Q2W	42	-7.6	Placebo	66	-10.8	2.3 (4.1)	-5.8, 10.4	0.573
	200mg fezakinumab Q2W	48	-12.5	Placebo	66	-10.8	-2.3 (4.0)	-10.2, 5.5	0.558
	100mg fezakinumab Q2W	42	-7.6	100mg fezakinumab Q4W	39	-17.1	9.8 (4.6)	0.6, 18.9	0.036
	200mg fezakinumab Q2W	48	-12.5	100mg fezakinumab Q4W	39	-17.1	5.1 (4.5)	-3.8, 14.0	0.257
	200mg fezakinumab Q2W	48	-12.5	100mg fezakinumab Q2W	42	-7.6	-4.6 (4.5)	-13.4, 4.1	0.298
Week 10	100mg fezakinumab Q4W	39	-18.3	Placebo	66	-12.9	-6.4 (4.5)	-15.4, 2.5	0.157
	100mg fezakinumab Q2W	42	-10.5	Placebo	66	-12.9	1.6 (4.4)	-7.2, 10.3	0.724
	200mg fezakinumab Q2W	48	-11.8	Placebo	66	-12.9	0.6 (4.3)	-7.9, 9.0	0.893
	100mg fezakinumab Q2W	42	-10.5	100mg fezakinumab Q4W	39	-18.3	8.0 (5.0)	-1.9, 17.9	0.111
	200mg fezakinumab Q2W	48	-11.8	100mg fezakinumab Q4W	39	-18.3	7.0 (4.9)	-2.6, 16.6	0.151
	200mg fezakinumab Q2W	48	-11.8	100mg fezakinumab Q2W	42	-10.5	-1.0 (4.8)	-10.5, 8.5	0.837
Week 12	100mg fezakinumab Q4W	39	-16.1	Placebo	66	-14.1	-3.0 (4.2)	-11.3, 5.2	0.469

Table 24. Descriptive Summary Statistics and Between Treatment Comparisons (ANCOVA) for Change From Baseline in Pain VAS, mITT Population, LOCF

Study Week	Treatment	N	Mean	Comparator	N	Mean	Adjusted Mean Diff[a] (SE)	95% CI[a]	p-Value[a]
	100mg fezakinumab Q2W	42	-11.8	Placebo	66	-14.1	1.2 (4.1)	-6.8, 9.3	0.760
	200mg fezakinumab Q2W	48	-14.0	Placebo	66	-14.1	-0.0 (3.9)	-7.8, 7.8	0.993
	100mg fezakinumab Q2W	42	-11.8	100mg fezakinumab Q4W	39	-16.1	4.3 (4.6)	-4.8, 13.3	0.354
	200mg fezakinumab Q2W	48	-14.0	100mg fezakinumab Q4W	39	-16.1	3.0 (4.5)	-5.8, 11.8	0.505
	200mg fezakinumab Q2W	48	-14.0	100mg fezakinumab Q2W	42	-11.8	-1.3 (4.4)	-10.0, 7.5	0.772

ANCOVA = analysis of covariance, CI = confidence interval, Diff = difference, LOCF = last observation carried forward, mITT = modified intent-to-treat, N = number of subject, Q2W = every 2 weeks, Q4W = every 4 weeks, SE = standard error, TNF = tumor necrosis factor, VAS = visual analog scale.

a. From the ANCOVA model: change = baseline + anti-TNF prior use + region + treatment.

Table 25. Descriptive Summary Statistics and Within Treatment Comparison for General Health VAS, mITT Population, LOCF

								Change From Baseline						
Study Week	**Treatment**	**N**	**Mean**	**SD**	**Median**	**Min**	**Max**	**N**	**Mean**	**SD**	**Median**	**Min**	**Max**	**p-Value[a]**
Baseline	Placebo	65	60.8	18.4	60.0	15.0	100.0							
	100mg fezakinumab Q4W	39	59.2	21.2	56.0	19.0	98.0							
	100mg fezakinumab Q2W	42	61.0	16.4	61.5	24.0	97.0							
	200mg fezakinumab Q2W	48	57.7	20.7	55.0	7.0	94.0							
Week 2	Placebo	66	54.1	22.4	52.0	5.0	98.0	65	-7.1	18.6	-6.0	-57.0	32.0	0.003
	100mg fezakinumab Q4W	39	52.5	23.0	46.0	7.0	96.0	39	-6.6	20.1	-4.0	-58.0	47.0	0.046
	100mg fezakinumab Q2W	42	53.0	23.7	57.0	1.0	97.0	42	-8.0	19.9	-2.0	-68.0	35.0	0.013
	200mg fezakinumab Q2W	48	54.8	19.8	54.0	4.0	83.0	48	-2.9	12.1	-2.5	-26.0	33.0	0.103
Week 4	Placebo	66	48.8	23.0	47.5	4.0	98.0	65	-12.3	17.3	-11.0	-60.0	29.0	<.001
	100mg fezakinumab Q4W	39	48.2	22.9	49.0	4.0	92.0	39	-11.0	24.3	-12.0	-56.0	47.0	0.007
	100mg fezakinumab Q2W	42	54.3	23.1	59.5	1.0	96.0	42	-6.7	22.6	-3.0	-63.0	42.0	0.062
	200mg fezakinumab Q2W	48	52.9	20.2	54.0	3.0	96.0	48	-4.8	15.2	-3.0	-40.0	26.0	0.034
Week 6	Placebo	66	50.7	22.0	49.5	4.0	98.0	65	-10.4	17.3	-10.0	-61.0	23.0	<.001
	100mg fezakinumab Q4W	39	42.4	21.9	40.0	5.0	96.0	39	-16.8	20.1	-13.0	-58.0	29.0	<.001
	100mg fezakinumab Q2W	42	52.5	19.4	53.0	13.0	96.0	42	-8.5	22.0	-3.0	-60.0	30.0	0.016
	200mg fezakinumab Q2W	48	48.8	21.9	52.0	1.0	96.0	48	-8.9	18.5	-10.5	-52.0	30.0	0.002
Week 8	Placebo	66	47.5	24.1	48.0	1.0	98.0	65	-13.2	21.4	-11.0	-68.0	44.5	<.001
	100mg fezakinumab Q4W	39	40.4	23.8	40.0	0.0	94.0	39	-18.8	20.7	-13.0	-58.0	32.0	<.001
	100mg fezakinumab Q2W	42	50.3	22.2	51.0	10.0	95.0	42	-10.7	23.2	-9.5	-65.0	29.0	0.005
	200mg fezakinumab Q2W	48	45.4	21.5	50.5	1.0	96.0	48	-12.3	20.0	-13.5	-59.0	30.0	<.001
Week 10	Placebo	66	48.4	25.7	48.0	3.0	98.0	65	-12.5	20.8	-12.0	-60.0	51.0	<.001
	100mg fezakinumab Q4W	39	38.9	22.2	39.0	3.0	94.0	39	-20.2	21.9	-14.0	-63.0	28.0	<.001
	100mg fezakinumab Q2W	42	46.9	24.0	45.0	7.0	89.0	42	-14.1	26.6	-7.5	-71.0	22.0	0.001
	200mg fezakinumab Q2W	48	45.7	23.3	48.0	1.0	96.0	48	-12.0	17.0	-10.5	-56.0	24.0	<.001
Week 12	Placebo	66	47.6	25.4	49.5	3.0	98.0	65	-13.3	19.3	-12.0	-71.0	26.0	<.001
	100mg fezakinumab Q4W	39	40.6	23.0	42.0	0.0	94.0	39	-18.6	22.1	-12.0	-66.0	34.0	<.001
	100mg fezakinumab Q2W	42	47.4	22.0	50.0	2.0	96.5	42	-13.6	26.1	-6.5	-72.0	32.0	0.002
	200mg fezakinumab Q2W	48	43.2	21.4	43.0	3.0	96.0	48	-14.5	21.1	-10.5	-71.0	24.0	<.001

LOCF = last observation carried forward, Max = maximum, Min = minimum, mITT = modified intent-to-treat, N = number of subject, Q2W = every 2 weeks, Q4W = every 4 weeks, SD = standard deviation, VAS = visual analog scale.

a. p-Value from a 2-sided paired T-test.

Table 26. Descriptive Summary Statistics and Between Treatment Comparisons (ANCOVA) for Change From Baseline in General Health VAS, mITT Population, LOCF

Study Week	Treatment	N	Mean	Comparator	N	Mean	Adjusted Mean Diff[a] (SE)	95% CI[a]	p-Value[a]
Week 2	100mg fezakinumab Q4W	39	-6.6	Placebo	65	-7.1	0.2 (3.5)	-6.6, 7.1	0.948
	100mg fezakinumab Q2W	42	-8.0	Placebo	65	-7.1	-1.1 (3.4)	-7.8, 5.6	0.752
	200mg fezakinumab Q2W	48	-2.9	Placebo	65	-7.1	3.9 (3.3)	-2.6, 10.4	0.239
	100mg fezakinumab Q2W	42	-8.0	100mg fezakinumab Q4W	39	-6.6	-1.3 (3.8)	-8.8, 6.2	0.734
	200mg fezakinumab Q2W	48	-2.9	100mg fezakinumab Q4W	39	-6.6	3.7 (3.7)	-3.7, 11.0	0.325
	200mg fezakinumab Q2W	48	-2.9	100mg fezakinumab Q2W	42	-8.0	5.0 (3.7)	-2.3, 12.2	0.179
Week 4	100mg fezakinumab Q4W	39	-11.0	Placebo	65	-12.3	0.9 (3.8)	-6.5, 8.3	0.804
	100mg fezakinumab Q2W	42	-6.7	Placebo	65	-12.3	5.4 (3.7)	-1.9, 12.6	0.144
	200mg fezakinumab Q2W	48	-4.8	Placebo	65	-12.3	7.1 (3.6)	0.1, 14.1	0.047
	100mg fezakinumab Q2W	42	-6.7	100mg fezakinumab Q4W	39	-11.0	4.5 (4.1)	-3.7, 12.6	0.282
	200mg fezakinumab Q2W	48	-4.8	100mg fezakinumab Q4W	39	-11.0	6.2 (4.0)	-1.7, 14.1	0.126
	200mg fezakinumab Q2W	48	-4.8	100mg fezakinumab Q2W	42	-6.7	1.7 (4.0)	-6.1, 9.6	0.668
Week 6	100mg fezakinumab Q4W	39	-16.8	Placebo	65	-10.4	-7.1 (3.6)	-14.2, 0.1	0.054
	100mg fezakinumab Q2W	42	-8.5	Placebo	65	-10.4	1.9 (3.6)	-5.2, 8.9	0.602
	200mg fezakinumab Q2W	48	-8.9	Placebo	65	-10.4	0.5 (3.4)	-6.3, 7.3	0.893
	100mg fezakinumab Q2W	42	-8.5	100mg fezakinumab Q4W	39	-16.8	8.9 (4.0)	1.0, 16.8	0.027
	200mg fezakinumab Q2W	48	-8.9	100mg fezakinumab Q4W	39	-16.8	7.5 (3.9)	-0.1, 15.2	0.054
	200mg fezakinumab Q2W	48	-8.9	100mg fezakinumab Q2W	42	-8.5	-1.4 (3.9)	-9.0, 6.2	0.718
Week 8	100mg fezakinumab Q4W	39	-18.8	Placebo	65	-13.2	-6.2 (4.1)	-14.2, 1.8	0.129
	100mg fezakinumab Q2W	42	-10.7	Placebo	65	-13.2	2.2 (4.0)	-5.6, 10.0	0.579
	200mg fezakinumab Q2W	48	-12.3	Placebo	65	-13.2	0.4 (3.8)	-7.2, 8.0	0.919
	100mg fezakinumab Q2W	42	-10.7	100mg fezakinumab Q4W	39	-18.8	8.4 (4.5)	-0.4, 17.2	0.062
	200mg fezakinumab Q2W	48	-12.3	100mg fezakinumab Q4W	39	-18.8	6.6 (4.3)	-2.0, 15.1	0.132
	200mg fezakinumab Q2W	48	-12.3	100mg fezakinumab Q2W	42	-10.7	-1.8 (4.3)	-10.3, 6.7	0.673
Week 10	100mg fezakinumab Q4W	39	-20.2	Placebo	65	-12.5	-8.3 (4.2)	-16.6, 0.0	0.050
	100mg fezakinumab Q2W	42	-14.1	Placebo	65	-12.5	-1.8 (4.1)	-9.9, 6.3	0.669
	200mg fezakinumab Q2W	48	-12.0	Placebo	65	-12.5	-0.3 (4.0)	-8.1, 7.6	0.946
	100mg fezakinumab Q2W	42	-14.1	100mg fezakinumab Q4W	39	-20.2	6.5 (4.6)	-2.6, 15.6	0.160
	200mg fezakinumab Q2W	48	-12.0	100mg fezakinumab Q4W	39	-20.2	8.0 (4.5)	-0.8, 16.9	0.076
	200mg fezakinumab Q2W	48	-12.0	100mg fezakinumab Q2W	42	-14.1	1.5 (4.5)	-7.3, 10.3	0.738
Week 12	100mg fezakinumab Q4W	39	-18.6	Placebo	65	-13.3	-6.0 (4.2)	-14.2, 2.2	0.152

Table 26. Descriptive Summary Statistics and Between Treatment Comparisons (ANCOVA) for Change From Baseline in General Health VAS, mITT Population, LOCF

Study Week	Treatment	N	Mean	Comparator	N	Mean	Adjusted Mean Diff[a] (SE)	95% CI[a]	p-Value[a]
	100mg fezakinumab Q2W	42	-13.6	Placebo	65	-13.3	-0.4 (4.1)	-8.4, 7.7	0.927
	200mg fezakinumab Q2W	48	-14.5	Placebo	65	-13.3	-2.4 (4.0)	-10.2, 5.4	0.551
	100mg fezakinumab Q2W	42	-13.6	100mg fezakinumab Q4W	39	-18.6	5.6 (4.6)	-3.4, 14.7	0.222
	200mg fezakinumab Q2W	48	-14.5	100mg fezakinumab Q4W	39	-18.6	3.6 (4.5)	-5.2, 12.4	0.416
	200mg fezakinumab Q2W	48	-14.5	100mg fezakinumab Q2W	42	-13.6	-2.0 (4.4)	-10.7, 6.7	0.654

ANCOVA = analysis of covariance, CI = confidence interval, Diff = difference, LOCF = last observation carried forward, mITT = modified intent-to-treat, N = number of subject, Q2W = every 2 weeks, Q4W = every 4 weeks, SE = standard error, TNF = tumor necrosis factor, VAS = visual analog scale.

a. From the ANCOVA model: change = baseline + anti-TNF prior use + region + treatment.

Quality of Life and Physical Function as Assessed by the HAQ-DI:

For the mITT population using LOCF imputation with few exceptions, within treatment comparisons revealed statistically significant changes from Baseline in the HAQ-DI for all groups at all weeks (Table 27). No statistically significant differences in the change From Baseline in the HAQ-DI between the groups were observed at any week (Table 28).

Table 27. Descriptive Summary Statistics and Within Treatment Comparison for HAQ-DI, mITT Population, LOCF

								Change From Baseline						
Study Week	**Treatment**	**N**	**Mean**	**SD**	**Median**	**Min**	**Max**	**N**	**Mean**	**SD**	**Median**	**Min**	**Max**	**p-Value[a]**
Baseline	Placebo	66	1.4	0.7	1.4	0.0	2.8							
	100mg fezakinumab Q4W	39	1.3	0.7	1.4	0.1	2.9							
	100mg fezakinumab Q2W	42	1.3	0.6	1.3	0.0	2.9							
	200mg fezakinumab Q2W	48	1.3	0.7	1.4	0.0	2.5							
Week 2	Placebo	66	1.3	0.7	1.4	0.0	2.8	66	-0.1	0.4	-0.1	-1.1	1.0	0.033
	100mg fezakinumab Q4W	39	1.3	0.7	1.1	0.1	2.5	39	-0.1	0.4	-0.1	-1.5	1.1	0.243
	100mg fezakinumab Q2W	42	1.2	0.7	1.3	0.0	2.8	42	-0.1	0.4	0.0	-1.5	0.6	0.139
	200mg fezakinumab Q2W	48	1.3	0.6	1.3	0.0	2.5	48	-0.1	0.3	-0.1	-1.3	0.9	0.190
Week 4	Placebo	66	1.3	0.7	1.4	0.0	2.6	66	-0.1	0.4	-0.1	-1.3	1.0	0.004
	100mg fezakinumab Q4W	39	1.1	0.6	1.1	0.0	2.5	39	-0.2	0.5	-0.1	-1.4	1.4	0.011
	100mg fezakinumab Q2W	42	1.3	0.7	1.4	0.0	2.8	42	-0.1	0.5	0.0	-2.1	0.8	0.402
	200mg fezakinumab Q2W	48	1.2	0.7	1.1	0.0	2.9	48	-0.1	0.4	-0.1	-1.4	1.3	0.032
Week 6	Placebo	66	1.2	0.7	1.3	0.0	2.6	66	-0.2	0.4	-0.1	-1.3	0.5	<.001
	100mg fezakinumab Q4W	39	1.1	0.7	1.1	0.0	2.6	39	-0.2	0.5	-0.3	-1.3	1.3	0.022
	100mg fezakinumab Q2W	42	1.2	0.6	1.3	0.0	2.9	42	-0.1	0.5	0.0	-1.5	0.8	0.211
	200mg fezakinumab Q2W	48	1.2	0.7	1.0	0.0	2.9	48	-0.2	0.5	-0.1	-1.4	1.3	0.011
Week 8	Placebo	66	1.2	0.6	1.3	0.0	2.6	66	-0.2	0.4	-0.1	-1.8	0.6	<.001
	100mg fezakinumab Q4W	39	1.1	0.7	1.1	0.0	2.6	39	-0.2	0.5	-0.1	-1.6	1.0	0.010
	100mg fezakinumab Q2W	42	1.2	0.7	1.3	0.0	2.8	42	-0.2	0.5	0.0	-1.9	0.6	0.035
	200mg fezakinumab Q2W	48	1.1	0.7	1.0	0.0	2.9	48	-0.2	0.5	-0.2	-1.4	1.3	<.001
Week 10	Placebo	66	1.2	0.7	1.2	0.0	2.6	66	-0.2	0.5	-0.1	-2.0	1.1	<.001
	100mg fezakinumab Q4W	39	1.1	0.7	1.0	0.0	2.6	39	-0.3	0.5	-0.4	-1.3	1.0	0.002
	100mg fezakinumab Q2W	42	1.2	0.7	1.3	0.0	2.6	42	-0.2	0.5	-0.1	-2.1	0.9	0.032
	200mg fezakinumab Q2W	48	1.1	0.7	1.0	0.0	2.9	48	-0.2	0.4	-0.1	-1.1	1.3	0.001
Week 12	Placebo	66	1.2	0.7	1.3	0.0	2.6	66	-0.2	0.4	-0.1	-1.4	1.3	<.001
	100mg fezakinumab Q4W	39	1.1	0.7	1.0	0.0	2.6	39	-0.3	0.6	-0.3	-1.4	1.0	0.006
	100mg fezakinumab Q2W	42	1.1	0.7	1.2	0.0	2.5	42	-0.2	0.6	-0.1	-2.1	1.1	0.028
	200mg fezakinumab Q2W	48	1.1	0.7	1.0	0.0	2.9	48	-0.2	0.5	-0.2	-1.4	1.3	0.001

HAQ-DI = Health Assessment Questionnaire Disability Index, LOCF = last observation carried forward, Max = maximum, Min = minimum, mITT = modified intent-to-treat, N = number of subject, Q2W = every 2 weeks, Q4W = every 4 weeks, SD = standard deviation.

a. p-Value from a 2-sided paired T-test.

Table 28. Descriptive Summary Statistics and Between Treatment Comparisons (ANCOVA) for Change From Baseline in HAQ-DI, mITT Population, LOCF

Study Week	Treatment	N	Mean	Comparator	N	Mean	Adjusted Mean Diff[a] (SE)	95% CI[a]	p-Value[a]
Week 2	100mg fezakinumab Q4W	39	-0.1	Placebo	66	-0.1	0.0 (0.1)	-0.1, 0.2	0.884
	100mg fezakinumab Q2W	42	-0.1	Placebo	66	-0.1	-0.0 (0.1)	-0.2, 0.1	0.956
	200mg fezakinumab Q2W	48	-0.1	Placebo	66	-0.1	0.0 (0.1)	-0.1, 0.2	0.751
	100mg fezakinumab Q2W	42	-0.1	100mg fezakinumab Q4W	39	-0.1	-0.0 (0.1)	-0.2, 0.2	0.856
	200mg fezakinumab Q2W	48	-0.1	100mg fezakinumab Q4W	39	-0.1	0.0 (0.1)	-0.2, 0.2	0.886
	200mg fezakinumab Q2W	48	-0.1	100mg fezakinumab Q2W	42	-0.1	0.0 (0.1)	-0.1, 0.2	0.739
Week 4	100mg fezakinumab Q4W	39	-0.2	Placebo	66	-0.1	-0.1 (0.1)	-0.2, 0.1	0.419
	100mg fezakinumab Q2W	42	-0.1	Placebo	66	-0.1	0.1 (0.1)	-0.1, 0.2	0.479
	200mg fezakinumab Q2W	48	-0.1	Placebo	66	-0.1	-0.0 (0.1)	-0.2, 0.2	0.953
	100mg fezakinumab Q2W	42	-0.1	100mg fezakinumab Q4W	39	-0.2	0.1 (0.1)	-0.1, 0.3	0.174
	200mg fezakinumab Q2W	48	-0.1	100mg fezakinumab Q4W	39	-0.2	0.1 (0.1)	-0.1, 0.3	0.482
	200mg fezakinumab Q2W	48	-0.1	100mg fezakinumab Q2W	42	-0.1	-0.1 (0.1)	-0.2, 0.1	0.481
Week 6	100mg fezakinumab Q4W	39	-0.2	Placebo	66	-0.2	-0.0 (0.1)	-0.2, 0.1	0.773
	100mg fezakinumab Q2W	42	-0.1	Placebo	66	-0.2	0.1 (0.1)	-0.1, 0.2	0.342
	200mg fezakinumab Q2W	48	-0.2	Placebo	66	-0.2	-0.0 (0.1)	-0.2, 0.2	0.921
	100mg fezakinumab Q2W	42	-0.1	100mg fezakinumab Q4W	39	-0.2	0.1 (0.1)	-0.1, 0.3	0.269
	200mg fezakinumab Q2W	48	-0.2	100mg fezakinumab Q4W	39	-0.2	0.0 (0.1)	-0.2, 0.2	0.856
	200mg fezakinumab Q2W	48	-0.2	100mg fezakinumab Q2W	42	-0.1	-0.1 (0.1)	-0.3, 0.1	0.334
Week 8	100mg fezakinumab Q4W	39	-0.2	Placebo	66	-0.2	-0.1 (0.1)	-0.2, 0.1	0.549
	100mg fezakinumab Q2W	42	-0.2	Placebo	66	-0.2	0.0 (0.1)	-0.2, 0.2	0.934
	200mg fezakinumab Q2W	48	-0.2	Placebo	66	-0.2	-0.1 (0.1)	-0.2, 0.1	0.447
	100mg fezakinumab Q2W	42	-0.2	100mg fezakinumab Q4W	39	-0.2	0.1 (0.1)	-0.1, 0.3	0.537
	200mg fezakinumab Q2W	48	-0.2	100mg fezakinumab Q4W	39	-0.2	-0.0 (0.1)	-0.2, 0.2	0.910
	200mg fezakinumab Q2W	48	-0.2	100mg fezakinumab Q2W	42	-0.2	-0.1 (0.1)	-0.3, 0.1	0.450
Week 10	100mg fezakinumab Q4W	39	-0.3	Placebo	66	-0.2	-0.0 (0.1)	-0.2, 0.1	0.657
	100mg fezakinumab Q2W	42	-0.2	Placebo	66	-0.2	0.0 (0.1)	-0.1, 0.2	0.753
	200mg fezakinumab Q2W	48	-0.2	Placebo	66	-0.2	-0.0 (0.1)	-0.2, 0.2	0.987
	100mg fezakinumab Q2W	42	-0.2	100mg fezakinumab Q4W	39	-0.3	0.1 (0.1)	-0.1, 0.3	0.495
	200mg fezakinumab Q2W	48	-0.2	100mg fezakinumab Q4W	39	-0.3	0.0 (0.1)	-0.2, 0.2	0.689
	200mg fezakinumab Q2W	48	-0.2	100mg fezakinumab Q2W	42	-0.2	-0.0 (0.1)	-0.2, 0.2	0.760
Week 12	100mg fezakinumab Q4W	39	-0.3	Placebo	66	-0.2	-0.1 (0.1)	-0.2, 0.1	0.548

Table 28. Descriptive Summary Statistics and Between Treatment Comparisons (ANCOVA) for Change From Baseline in HAQ-DI, mITT Population, LOCF

Study Week	Treatment	N	Mean	Comparator	N	Mean	Adjusted Mean Diff[a] (SE)	95% CI[a]	p-Value[a]
	100mg fezakinumab Q2W	42	-0.2	Placebo	66	-0.2	-0.0 (0.1)	-0.2, 0.2	0.909
	200mg fezakinumab Q2W	48	-0.2	Placebo	66	-0.2	-0.0 (0.1)	-0.2, 0.2	0.762
	100mg fezakinumab Q2W	42	-0.2	100mg fezakinumab Q4W	39	-0.3	0.0 (0.1)	-0.2, 0.3	0.658
	200mg fezakinumab Q2W	48	-0.2	100mg fezakinumab Q4W	39	-0.3	0.0 (0.1)	-0.2, 0.2	0.769
	200mg fezakinumab Q2W	48	-0.2	100mg fezakinumab Q2W	42	-0.2	-0.0 (0.1)	-0.2, 0.2	0.870

ANCOVA = analysis of covariance, CI = confidence interval, Diff = difference, HAQ-DI = Health Assessment Questionnaire Disability Index, LOCF = last observation carried forward, mITT = modified intent-to-treat, N = number of subject, Q2W = every 2 weeks, Q4W = every 4 weeks, SE = standard error, TNF = tumor necrosis factor.

a. From the ANCOVA model: change = baseline + anti-TNF prior use + region + treatment.

General Quality of Life as Assessed by the SF-36:

For the mITT population using LOCF imputation with few exceptions, within treatment comparisons revealed statistically significant changes from Baseline in the SF-36 physical component summary for all groups at all weeks (Table 29). No statistically significant differences in the change from Baseline in the SF-36 physical component summary between the groups were observed at any week (Table 30).

With few exceptions, within treatment comparisons revealed no statistically significant changes from Baseline in the SF-36 mental component summary for any groups at any weeks (Table 31). No statistically significant differences in the change from Baseline in the mental component summary between the groups were observed at any week (Table 32).

Table 29. Descriptive Summary Statistics and Within Treatment Comparison for SF-36 Physical Component Summary, mITT Population, LOCF

								Change From Baseline						
Study Week	**Treatment**	**N**	**Mean**	**SD**	**Median**	**Min**	**Max**	**N**	**Mean**	**SD**	**Median**	**Min**	**Max**	**p-Value[a]**
Baseline	Placebo	65	33.8	7.8	32.1	19.8	50.0							
	100mg fezakinumab Q4W	39	34.9	5.8	34.0	18.5	48.3							
	100mg fezakinumab Q2W	42	34.8	6.6	34.0	21.2	54.8							
	200mg fezakinumab Q2W	48	34.4	8.3	33.6	19.2	57.3							
Week 4	Placebo	66	36.0	8.2	35.0	19.6	57.3	65	2.3	7.1	0.4	-14.6	20.9	0.012
	100mg fezakinumab Q4W	39	36.9	8.5	37.2	13.8	56.2	39	2.0	6.3	3.0	-18.1	15.6	0.051
	100mg fezakinumab Q2W	42	36.0	8.6	34.3	21.8	60.8	42	1.3	5.9	-0.5	-5.8	22.5	0.174
	200mg fezakinumab Q2W	48	36.5	7.7	36.1	22.1	53.1	48	2.1	5.4	0.6	-9.3	21.8	0.009
Week 8	Placebo	66	35.8	7.5	34.7	19.8	55.5	65	2.1	6.5	1.6	-19.9	19.1	0.011
	100mg fezakinumab Q4W	39	37.3	8.5	36.9	20.4	57.2	39	2.4	5.9	3.5	-13.6	16.0	0.016
	100mg fezakinumab Q2W	42	36.6	7.1	35.8	24.7	52.2	42	1.9	7.5	3.2	-15.3	19.5	0.115
	200mg fezakinumab Q2W	48	36.9	8.1	36.5	22.1	53.1	48	2.5	6.2	1.9	-13.6	15.5	0.007
Week 12	Placebo	66	36.7	7.7	35.6	19.8	57.5	65	3.0	6.2	1.8	-9.0	21.3	<.001
	100mg fezakinumab Q4W	39	37.6	8.6	36.1	18.9	56.6	39	2.7	6.8	1.6	-13.0	19.0	0.019
	100mg fezakinumab Q2W	42	36.3	8.7	36.4	11.5	55.8	42	1.5	9.1	1.5	-32.9	17.5	0.294
	200mg fezakinumab Q2W	48	37.1	9.4	38.5	17.1	57.3	48	2.7	6.3	1.7	-8.4	19.0	0.004

LOCF = last observation carried forward, Max = maximum, Min = minimum, mITT = modified intent-to-treat, N = number of subject, Q2W = every 2 weeks, Q4W = every 4 weeks, SD = standard deviation, SF-36 = Short Form 36.

a. p-Value from a 2-sided paired T-test.

Table 30. Descriptive Summary Statistics and Between Treatment Comparisons (ANCOVA) for Change From Baseline in SF-36 Physical Component Summary, mITT Population, LOCF

Study Week	Treatment	N	Mean	Comparator	N	Mean	Adjusted Mean Diff[a] (SE)	95% CI[a]	p-Value[a]
Week 4	100mg fezakinumab Q4W	39	2.0	Placebo	65	2.3	0.0 (1.2)	-2.4, 2.5	0.988
	100mg fezakinumab Q2W	42	1.3	Placebo	65	2.3	-0.8 (1.2)	-3.2, 1.6	0.516
	200mg fezakinumab Q2W	48	2.1	Placebo	65	2.3	-0.0 (1.2)	-2.3, 2.3	0.971
	100mg fezakinumab Q2W	42	1.3	100mg fezakinumab Q4W	39	2.0	-0.8 (1.4)	-3.5, 1.9	0.553
	200mg fezakinumab Q2W	48	2.1	100mg fezakinumab Q4W	39	2.0	-0.1 (1.3)	-2.7, 2.5	0.963
	200mg fezakinumab Q2W	48	2.1	100mg fezakinumab Q2W	42	1.3	0.7 (1.3)	-1.8, 3.3	0.570
Week 8	100mg fezakinumab Q4W	39	2.4	Placebo	65	2.1	0.7 (1.2)	-1.7, 3.1	0.580
	100mg fezakinumab Q2W	42	1.9	Placebo	65	2.1	0.3 (1.2)	-2.1, 2.6	0.813
	200mg fezakinumab Q2W	48	2.5	Placebo	65	2.1	0.3 (1.2)	-2.0, 2.6	0.800
	100mg fezakinumab Q2W	42	1.9	100mg fezakinumab Q4W	39	2.4	-0.4 (1.3)	-3.0, 2.2	0.769
	200mg fezakinumab Q2W	48	2.5	100mg fezakinumab Q4W	39	2.4	-0.4 (1.3)	-3.0, 2.2	0.769
	200mg fezakinumab Q2W	48	2.5	100mg fezakinumab Q2W	42	1.9	0.0 (1.3)	-2.5, 2.6	0.994
Week 12	100mg fezakinumab Q4W	39	2.7	Placebo	65	3.0	0.1 (1.4)	-2.7, 2.8	0.969
	100mg fezakinumab Q2W	42	1.5	Placebo	65	3.0	-1.1 (1.3)	-3.8, 1.5	0.406
	200mg fezakinumab Q2W	48	2.7	Placebo	65	3.0	-0.3 (1.3)	-2.8, 2.3	0.841
	100mg fezakinumab Q2W	42	1.5	100mg fezakinumab Q4W	39	2.7	-1.2 (1.5)	-4.2, 1.8	0.438
	200mg fezakinumab Q2W	48	2.7	100mg fezakinumab Q4W	39	2.7	-0.3 (1.5)	-3.2, 2.6	0.831
	200mg fezakinumab Q2W	48	2.7	100mg fezakinumab Q2W	42	1.5	0.9 (1.5)	-2.0, 3.7	0.556

ANCOVA = analysis of covariance, CI = confidence interval, Diff = difference, LOCF = last observation carried forward, mITT = modified intent-to-treat, N = number of subject, Q2W = every 2 weeks, Q4W = every 4 weeks, SE = standard error, SF-36 = Short Form 36, TNF = tumor necrosis factor.

a. From the ANCOVA model: change = baseline + anti-TNF prior use + region + treatment.

Table 31. Descriptive Summary Statistics and Within Treatment Comparison for SF-36 Mental Component Summary, mITT Population, LOCF

								Change From Baseline						
Study Week	**Treatment**	**N**	**Mean**	**SD**	**Median**	**Min**	**Max**	**N**	**Mean**	**SD**	**Median**	**Min**	**Max**	**p-Value[a]**
Baseline	Placebo	65	40.5	12.3	39.3	13.8	62.5							
	100mg fezakinumab Q4W	39	42.0	12.0	39.8	13.1	70.2							
	100mg fezakinumab Q2W	42	41.2	11.0	38.8	18.3	64.3							
	200mg fezakinumab Q2W	48	41.1	13.0	40.7	15.4	67.4							
Week 4	Placebo	66	42.7	12.4	44.6	15.3	64.0	65	2.2	8.8	0.1	-19.8	33.7	0.050
	100mg fezakinumab Q4W	39	43.0	13.0	43.5	11.9	66.3	39	1.1	8.3	1.2	-13.6	16.5	0.428
	100mg fezakinumab Q2W	42	41.0	12.2	38.7	13.9	62.9	42	-0.2	9.5	0.2	-20.1	16.8	0.890
	200mg fezakinumab Q2W	48	40.3	12.4	42.1	8.4	64.5	48	-0.8	8.1	-0.2	-36.0	19.6	0.493
Week 8	Placebo	66	44.5	11.3	45.0	20.3	65.2	65	4.1	8.9	1.6	-10.4	28.9	<.001
	100mg fezakinumab Q4W	39	44.8	12.0	42.6	15.2	67.6	39	2.8	8.2	3.1	-11.4	18.5	0.041
	100mg fezakinumab Q2W	42	43.1	11.9	42.0	20.1	66.1	42	1.9	8.3	2.1	-20.1	24.6	0.139
	200mg fezakinumab Q2W	48	42.9	11.3	43.6	19.4	63.6	48	1.8	8.0	0.4	-20.7	20.3	0.132
Week 12	Placebo	66	43.2	11.8	44.4	20.3	64.2	65	2.7	8.9	1.5	-16.7	29.9	0.017
	100mg fezakinumab Q4W	39	44.2	11.7	44.2	17.1	63.1	39	2.3	9.0	1.5	-14.1	25.1	0.124
	100mg fezakinumab Q2W	42	44.2	12.6	42.8	23.3	69.7	42	3.0	9.2	2.4	-19.5	28.5	0.038
	200mg fezakinumab Q2W	48	44.5	9.8	44.6	26.2	62.9	48	3.4	9.2	3.2	-26.3	28.0	0.014

LOCF = last observation carried forward, Max = maximum, Min = minimum, mITT = modified intent-to-treat, N = number of subject, Q2W = every 2 weeks, Q4W = every 4 weeks, SD = standard deviation, SF-36 = Short Form 36.

a. p-Value from a 2-sided paired T-test.

Table 32. Descriptive Summary Statistics and Between Treatment Comparisons (ANCOVA) for Change From Baseline in SF-36 Mental Component Summary, mITT Population, LOCF

Study Week	Treatment	N	Mean	Comparator	N	Mean	Adjusted Mean Diff[a] (SE)	95% CI[a]	p-Value[a]
Week 4	100mg fezakinumab Q4W	39	1.1	Placebo	65	2.2	-0.8 (1.7)	-4.2, 2.5	0.614
	100mg fezakinumab Q2W	42	-0.2	Placebo	65	2.2	-2.2 (1.6)	-5.5, 1.0	0.175
	200mg fezakinumab Q2W	48	-0.8	Placebo	65	2.2	-2.9 (1.6)	-6.0, 0.3	0.072
	100mg fezakinumab Q2W	42	-0.2	100mg fezakinumab Q4W	39	1.1	-1.4 (1.8)	-5.0, 2.2	0.453
	200mg fezakinumab Q2W	48	-0.8	100mg fezakinumab Q4W	39	1.1	-2.0 (1.8)	-5.6, 1.5	0.261
	200mg fezakinumab Q2W	48	-0.8	100mg fezakinumab Q2W	42	-0.2	-0.6 (1.8)	-4.1, 2.9	0.721
Week 8	100mg fezakinumab Q4W	39	2.8	Placebo	65	4.1	-0.9 (1.6)	-4.0, 2.1	0.547
	100mg fezakinumab Q2W	42	1.9	Placebo	65	4.1	-2.1 (1.5)	-5.1, 1.0	0.182
	200mg fezakinumab Q2W	48	1.8	Placebo	65	4.1	-2.1 (1.5)	-5.1, 0.8	0.152
	100mg fezakinumab Q2W	42	1.9	100mg fezakinumab Q4W	39	2.8	-1.1 (1.7)	-4.5, 2.3	0.520
	200mg fezakinumab Q2W	48	1.8	100mg fezakinumab Q4W	39	2.8	-1.2 (1.7)	-4.5, 2.1	0.479
	200mg fezakinumab Q2W	48	1.8	100mg fezakinumab Q2W	42	1.9	-0.1 (1.7)	-3.3, 3.2	0.962
Week 12	100mg fezakinumab Q4W	39	2.3	Placebo	65	2.7	-0.0 (1.6)	-3.3, 3.2	0.983
	100mg fezakinumab Q2W	42	3.0	Placebo	65	2.7	0.4 (1.6)	-2.7, 3.6	0.783
	200mg fezakinumab Q2W	48	3.4	Placebo	65	2.7	1.0 (1.6)	-2.1, 4.1	0.518
	100mg fezakinumab Q2W	42	3.0	100mg fezakinumab Q4W	39	2.3	0.5 (1.8)	-3.1, 4.0	0.792
	200mg fezakinumab Q2W	48	3.4	100mg fezakinumab Q4W	39	2.3	1.0 (1.8)	-2.4, 4.5	0.554
	200mg fezakinumab Q2W	48	3.4	100mg fezakinumab Q2W	42	3.0	0.6 (1.7)	-2.9, 4.0	0.746

ANCOVA = analysis of covariance, CI = confidence interval, Diff = difference, LOCF = last observation carried forward, mITT = modified intent-to-treat, N = number of subject, Q2W = every 2 weeks, Q4W = every 4 weeks, SE = standard error, SF-36 = Short Form 36, TNF = tumor necrosis factor.

a. From the ANCOVA model: change = baseline + anti-TNF prior use + region + treatment.

Fatigue as Assessed by the FACIT-Fatigue:

For the mITT population using LOCF imputation with few exceptions, within treatment comparisons revealed statistically significant changes from Baseline in FACIT-Fatigue for all groups at all weeks (Table 33). No statistically significant differences in the change from Baseline in FACIT-Fatigue between the groups were observed at any week (Table 34).

Table 33. Descriptive Summary Statistics and Within Treatment Comparison for FACIT, mITT Population, LOCF

								Change From Baseline						
Study Week	**Treatment**	**N**	**Mean**	**SD**	**Median**	**Min**	**Max**	**N**	**Mean**	**SD**	**Median**	**Min**	**Max**	**p-Value[a]**
Baseline	Placebo	66	29.1	10.9	30.0	2.0	49.0							
	100mg fezakinumab Q4W	39	30.9	10.9	33.0	1.0	48.0							
	100mg fezakinumab Q2W	42	30.6	9.4	31.5	7.0	49.0							
	200mg fezakinumab Q2W	48	29.2	11.7	26.5	7.0	52.0							
Week 4	Placebo	66	31.7	10.7	31.0	2.0	50.0	66	2.6	7.8	1.5	-15.0	27.0	0.008
	100mg fezakinumab Q4W	39	33.6	11.3	36.0	2.0	52.0	39	2.7	6.9	1.0	-10.0	27.0	0.020
	100mg fezakinumab Q2W	42	32.6	9.8	31.5	12.0	47.0	42	2.0	7.0	1.0	-15.0	21.0	0.067
	200mg fezakinumab Q2W	48	30.7	10.6	33.0	8.0	52.0	48	1.5	7.4	0.0	-11.0	22.0	0.157
Week 8	Placebo	66	32.7	10.8	32.5	2.0	52.0	66	3.6	8.6	1.0	-12.0	30.0	0.001
	100mg fezakinumab Q4W	39	33.7	10.4	35.0	2.0	52.0	39	2.8	6.8	1.0	-12.0	21.0	0.015
	100mg fezakinumab Q2W	42	32.1	9.9	33.0	3.0	50.0	42	1.5	9.3	1.5	-41.0	18.0	0.296
	200mg fezakinumab Q2W	48	32.3	10.7	33.5	7.0	52.0	48	3.2	7.9	1.5	-13.0	25.0	0.008
Week 12	Placebo	66	33.3	9.4	32.5	2.0	52.0	66	4.2	8.4	3.0	-16.0	30.0	<.001
	100mg fezakinumab Q4W	39	34.3	9.5	35.0	3.0	52.0	39	3.4	6.9	3.0	-8.0	24.0	0.004
	100mg fezakinumab Q2W	42	32.4	9.5	34.0	11.0	49.0	42	1.8	8.7	2.0	-24.0	20.0	0.198
	200mg fezakinumab Q2W	48	33.2	10.9	34.5	7.0	52.0	48	4.0	7.4	2.0	-8.0	26.0	<.001

FACIT = Functional Assessment of Chronic Illness Therapy, LOCF = last observation carried forward, Max = maximum, Min = minimum, mITT = modified intent-to-treat, N = number of subject, Q2W = every 2 weeks, Q4W = every 4 weeks, SD = standard deviation.

a. p-Value from a 2-sided paired T-test.

Table 34. Descriptive Summary Statistics and Between Treatment Comparisons (ANCOVA) for Change From Baseline in FACIT, mITT Population, LOCF

Study Week	Treatment	N	Mean	Comparator	N	Mean	Adjusted Mean Diff[a] (SE)	95% CI[a]	p-Value[a]
Week 4	100mg fezakinumab Q4W	39	2.7	Placebo	66	2.6	0.5 (1.4)	-2.3, 3.2	0.730
	100mg fezakinumab Q2W	42	2.0	Placebo	66	2.6	-0.2 (1.4)	-2.9, 2.5	0.870
	200mg fezakinumab Q2W	48	1.5	Placebo	66	2.6	-1.1 (1.3)	-3.7, 1.5	0.421
	100mg fezakinumab Q2W	42	2.0	100mg fezakinumab Q4W	39	2.7	-0.7 (1.5)	-3.7, 2.3	0.646
	200mg fezakinumab Q2W	48	1.5	100mg fezakinumab Q4W	39	2.7	-1.5 (1.5)	-4.5, 1.4	0.303
	200mg fezakinumab Q2W	48	1.5	100mg fezakinumab Q2W	42	2.0	-0.8 (1.5)	-3.8, 2.1	0.572
Week 8	100mg fezakinumab Q4W	39	2.8	Placebo	66	3.6	-0.2 (1.5)	-3.3, 2.8	0.877
	100mg fezakinumab Q2W	42	1.5	Placebo	66	3.6	-1.5 (1.5)	-4.5, 1.4	0.315
	200mg fezakinumab Q2W	48	3.2	Placebo	66	3.6	-0.5 (1.4)	-3.4, 2.3	0.710
	100mg fezakinumab Q2W	42	1.5	100mg fezakinumab Q4W	39	2.8	-1.3 (1.7)	-4.6, 2.1	0.451
	200mg fezakinumab Q2W	48	3.2	100mg fezakinumab Q4W	39	2.8	-0.3 (1.6)	-3.5, 2.9	0.855
	200mg fezakinumab Q2W	48	3.2	100mg fezakinumab Q2W	42	1.5	1.0 (1.6)	-2.2, 4.2	0.550
Week 12	100mg fezakinumab Q4W	39	3.4	Placebo	66	4.2	-0.2 (1.4)	-3.0, 2.6	0.870
	100mg fezakinumab Q2W	42	1.8	Placebo	66	4.2	-2.0 (1.4)	-4.7, 0.7	0.152
	200mg fezakinumab Q2W	48	4.0	Placebo	66	4.2	-0.1 (1.3)	-2.7, 2.6	0.963
	100mg fezakinumab Q2W	42	1.8	100mg fezakinumab Q4W	39	3.4	-1.8 (1.6)	-4.8, 1.3	0.260
	200mg fezakinumab Q2W	48	4.0	100mg fezakinumab Q4W	39	3.4	0.2 (1.5)	-2.8, 3.2	0.912
	200mg fezakinumab Q2W	48	4.0	100mg fezakinumab Q2W	42	1.8	1.9 (1.5)	-1.0, 4.9	0.202

ANCOVA = analysis of covariance, CI = confidence interval, Diff = difference, FACIT-Fatigue = Functional Assessment of Chronic Illness Therapy-Fatigue, LOCF = last observation carried forward, mITT = modified intent-to-treat, N = number of subject, Q2W = every 2 weeks, Q4W = every 4 weeks, SE = standard error, TNF = tumor necrosis factor.

a. From the ANCOVA model: change = baseline + anti-TNF prior use + region + treatment.

EULAR Response as Derived From DAS 28:

For the mITT population using LOCF imputation the proportion of subjects who achieved a EULAR response was not statistically significantly different between the groups at any week, except for the 100 mg fezakinumab Q2W versus the 100 mg fezakinumab Q4W group at Week 6 (Table 35).

Table 35. Number (%) of Subjects Achieving EULAR Response, mITT Population, LOCF

						p-Value[a]		
Timepoint	**Treatment**	**N**	**Good n (%)**	**Moderate n (%)**	**None n (%)**	**vs Placebo**	**vs 100mg Fezakinumab Q4W**	**vs 100mg Fezakinumab Q2W**
Week 2	Placebo	65	3 (4.6%)	15 (23.1%)	47 (72.3%)			
	100mg fezakinumab Q4W	39	1 (2.6%)	10 (25.6%)	28 (71.8%)	0.900		
	100mg fezakinumab Q2W	42	5 (11.9%)	7 (16.7%)	30 (71.4%)	0.522	0.534	
	200mg fezakinumab Q2W	48	0 (0.0%)	9 (18.8%)	39 (81.3%)	0.147	0.206	0.070
Week 4	Placebo	65	4 (6.2%)	20 (30.8%)	41 (63.1%)			
	100mg fezakinumab Q4W	39	2 (5.1%)	13 (33.3%)	24 (61.5%)	0.936		
	100mg fezakinumab Q2W	42	6 (14.3%)	9 (21.4%)	27 (64.3%)	0.625	0.685	
	200mg fezakinumab Q2W	48	1 (2.1%)	15 (31.3%)	32 (66.7%)	0.586	0.340	0.212
Week 6	Placebo	65	7 (10.8%)	27 (41.5%)	31 (47.7%)			
	100mg fezakinumab Q4W	39	4 (10.3%)	20 (51.3%)	15 (38.5%)	0.455		
	100mg fezakinumab Q2W	42	4 (9.5%)	11 (26.2%)	27 (64.3%)	0.145	0.050	
	200mg fezakinumab Q2W	48	5 (10.4%)	18 (37.5%)	25 (52.1%)	0.660	0.428	0.160
Week 8	Placebo	65	8 (12.3%)	29 (44.6%)	28 (43.1%)			
	100mg fezakinumab Q4W	39	5 (12.8%)	18 (46.2%)	16 (41.0%)	0.757		
	100mg fezakinumab Q2W	42	4 (9.5%)	16 (38.1%)	22 (52.4%)	0.408	0.374	
	200mg fezakinumab Q2W	48	8 (16.7%)	19 (39.6%)	21 (43.8%)	0.983	0.992	0.422
Week 10	Placebo	65	13 (20.0%)	28 (43.1%)	24 (36.9%)			
	100mg fezakinumab Q4W	39	6 (15.4%)	22 (56.4%)	11 (28.2%)	0.743		
	100mg fezakinumab Q2W	42	6 (14.3%)	15 (35.7%)	21 (50.0%)	0.188	0.148	
	200mg fezakinumab Q2W	48	7 (14.6%)	21 (43.8%)	20 (41.7%)	0.385	0.304	0.552
Week 12	Placebo	65	12 (18.5%)	33 (50.8%)	20 (30.8%)			
	100mg fezakinumab Q4W	39	11 (28.2%)	16 (41.0%)	12 (30.8%)	0.494		
	100mg fezakinumab Q2W	42	7 (16.7%)	18 (42.9%)	17 (40.5%)	0.421	0.235	
	200mg fezakinumab Q2W	48	9 (18.8%)	20 (41.7%)	19 (39.6%)	0.418	0.268	0.957

EULAR = European League Response Against Rheumatism, LOCF = last observation carried forward, mITT = modified intent-to-treat, N/n = number of subject, Q2W = every 2 weeks, Q4W = every 4 weeks, TNF = tumor necrosis factor, vs = versus.

a. p-Value from a 2-sided stratified Cochran-Mantel-Haenszel row mean test by anti-TNF prior use and and geographic region of the site.

Safety Results:

Treatment-Emergent AEs (TEAEs) Excluding Infections and Injection Site Reactions:

For calculating treatment-emergent events, the treatment-emergent period was defined as the period from administration of the first dose of study treatment until 12 weeks after the last dose of study treatment.

The numbers (%) of all subjects with TEAEs that occurred during the study are provided in Table 36. TEAEs were reported in a total of 96 subjects (49.2%) consisting of 24 subjects (50.0%) in the 200 mg fezakinumab Q2W group, 22 subjects (52.4%) in the 100 mg fezakinumab Q2W group, 22 subjects (56.4%) in the 100 mg fezakinumab Q4W group, and 28 subjects (42.4%) in the placebo group.

The most common TEAEs (incidence ≥5% of the subjects in total) were diarrhea and nausea. Other common TEAEs (incidence ≥5% of the subjects in at least 1 fezakinumab group) were alanine aminotransferase increased, hypertension, headache, arthralgia, vomiting, rheumatoid arthritis, stomatitis, food poisoning, joint range of motion decreased, musculoskeletal pain, myalgia, and seasonal allergy. There were no statistically significant differences in the incidence of any TEAEs between the groups with 2 exceptions: reproductive system and breast disorders (3 subjects [6.3%] in the 200 mg fezakinumab Q2W group, 2 subjects [5.1%] in the 100 mg fezakinumab Q4W group and no subjects in the other groups) and seasonal allergy (2 subjects [5.1%] in the 100 mg fezakinumab Q4W group and no subjects in the other groups). In most cases, TEAEs were mild to moderate.

Treatment-Related TEAEs Excluding Infections and Injection Site Reactions:

In 41 of the total of 96 subjects with TEAEs, the events were considered to be related to the study treatment: 14 subjects (29.2%) in the 200 mg fezakinumab Q2W group, 8 subjects (19.0%) in the 100 mg fezakinumab Q2W group, 8 subjects (20.5%) in the 100 mg fezakinumab Q4W group, and 11 subjects (16.7%) in the placebo group (Table 37).

Table 36. Number (%) of Subjects Reporting TEAEs Excluding Infections and Injection Site Reactions - Safety Population

System Organ Class[a] Preferred Term	Overall p-Value	Treatment				
		Placebo N=66	100 mg Fezakinumab Q4W N=39	100 mg Fezakinumab Q2W N=42	200 mg Fezakinumab Q2W N=48	Total N=195
Any adverse event	0.538	28 (42.4)	22 (56.4)	22 (52.4)	24 (50.0)	96 (49.2)
Blood and lymphatic system disorders	0.360	4 (6.1)	2 (5.1)	0	1 (2.1)	7 (3.6)
Anaemia	0.700	2 (3.0)	0	0	1 (2.1)	3 (1.5)
Leukocytosis	0.200	0	1 (2.6)	0	0	1 (0.5)
Leukopenia	1.000	1 (1.5)	0	0	0	1 (0.5)
Lymphadenopathy	0.200	0	1 (2.6)	0	0	1 (0.5)
Neutropenia	1.000	1 (1.5)	0	0	0	1 (0.5)
Neutrophilia	0.200	0	1 (2.6)	0	0	1 (0.5)
Cardiac disorders	0.550	2 (3.0)	0	0	0	2 (1.0)
Atrial fibrillation	1.000	1 (1.5)	0	0	0	1 (0.5)
Mitral valve incompetence	1.000	1 (1.5)	0	0	0	1 (0.5)
Tachycardia paroxysmal	1.000	1 (1.5)	0	0	0	1 (0.5)
Ear and labyrinth disorders	0.473	0	1 (2.6)	1 (2.4)	1 (2.1)	3 (1.5)
Cerumen impaction	0.662	0	0	0	1 (2.1)	1 (0.5)
Vertigo	0.231	0	1 (2.6)	1 (2.4)	0	2 (1.0)
Endocrine disorders	0.662	0	0	0	1 (2.1)	1 (0.5)
Hypothyroidism	0.662	0	0	0	1 (2.1)	1 (0.5)
Eye disorders	0.678	2 (3.0)	1 (2.6)	3 (7.1)	1 (2.1)	7 (3.6)
Blepharitis	0.662	0	0	0	1 (2.1)	1 (0.5)
Cataract	0.200	0	1 (2.6)	0	0	1 (0.5)
Conjunctivitis	1.000	1 (1.5)	0	0	0	1 (0.5)
Conjunctivitis allergic	0.833	1 (1.5)	0	1 (2.4)	0	2 (1.0)
Dry eye	0.833	1 (1.5)	0	1 (2.4)	0	2 (1.0)
Eye irritation	0.415	0	0	1 (2.4)	0	1 (0.5)
Hypermetropia	0.415	0	0	1 (2.4)	0	1 (0.5)
Ocular hyperaemia	0.415	0	0	1 (2.4)	0	1 (0.5)
Presbyopia	0.415	0	0	1 (2.4)	0	1 (0.5)
Vision blurred	0.231	0	1 (2.6)	1 (2.4)	0	2 (1.0)
Visual acuity reduced	0.662	0	0	0	1 (2.1)	1 (0.5)
Gastrointestinal disorders	0.692	11 (16.7)	10 (25.6)	8 (19.0)	11 (22.9)	40 (20.5)
Abdominal pain upper	0.144	0	0	0	2 (4.2)	2 (1.0)
Abdominal tenderness	0.200	0	1 (2.6)	0	0	1 (0.5)

Table 36. Number (%) of Subjects Reporting TEAEs Excluding Infections and Injection Site Reactions - Safety Population

System Organ Class[a] Preferred Term	Overall p-Value	Treatment				
		Placebo N=66	100 mg Fezakinumab Q4W N=39	100 mg Fezakinumab Q2W N=42	200 mg Fezakinumab Q2W N=48	Total N=195
Cheilitis	0.415	0	0	1 (2.4)	0	1 (0.5)
Constipation	0.833	1 (1.5)	0	1 (2.4)	0	2 (1.0)
Diarrhoea	1.000	4 (6.1)	2 (5.1)	3 (7.1)	3 (6.3)	12 (6.2)
Dyspepsia	0.924	1 (1.5)	1 (2.6)	1 (2.4)	2 (4.2)	5 (2.6)
Flatulence	1.000	1 (1.5)	0	0	0	1 (0.5)
Food poisoning	0.300	1 (1.5)	2 (5.1)	0	0	3 (1.5)
Gastritis	0.200	0	1 (2.6)	0	0	1 (0.5)
Gastrooesophageal reflux disease	0.231	0	1 (2.6)	1 (2.4)	0	2 (1.0)
Nausea	0.419	4 (6.1)	1 (2.6)	4 (9.5)	1 (2.1)	10 (5.1)
Pancreatitis acute	1.000	1 (1.5)	0	0	0	1 (0.5)
Stomatitis	0.364	1 (1.5)	0	1 (2.4)	3 (6.3)	5 (2.6)
Toothache	0.200	0	1 (2.6)	0	0	1 (0.5)
Umbilical hernia	0.200	0	1 (2.6)	0	0	1 (0.5)
Vomiting	0.722	2 (3.0)	1 (2.6)	3 (7.1)	2 (4.2)	8 (4.1)
General disorders and administration site conditions	0.701	6 (9.1)	2 (5.1)	4 (9.5)	2 (4.2)	14 (7.2)
Asthenia	0.139	0	0	2 (4.8)	2 (4.2)	4 (2.1)
Chest discomfort	1.000	1 (1.5)	0	0	0	1 (0.5)
Fatigue	0.550	2 (3.0)	0	0	0	2 (1.0)
Gait disturbance	1.000	1 (1.5)	0	0	0	1 (0.5)
Injection site haematoma	1.000	1 (1.5)	0	0	0	1 (0.5)
Injection site haemorrhage	0.200	0	1 (2.6)	0	0	1 (0.5)
Oedema	0.415	0	0	1 (2.4)	0	1 (0.5)
Pain	0.200	0	1 (2.6)	0	0	1 (0.5)
Pyrexia	0.911	2 (3.0)	0	1 (2.4)	1 (2.1)	4 (2.1)
Hepatobiliary disorders	1.000	1 (1.5)	0	0	0	1 (0.5)
Bile duct obstruction	1.000	1 (1.5)	0	0	0	1 (0.5)
Cholangitis	1.000	1 (1.5)	0	0	0	1 (0.5)
Cholelithiasis	1.000	1 (1.5)	0	0	0	1 (0.5)
Immune system disorders	0.039*	0	2 (5.1)	0	0	2 (1.0)
Seasonal allergy	0.039*	0	2 (5.1)	0	0	2 (1.0)

Table 36. Number (%) of Subjects Reporting TEAEs Excluding Infections and Injection Site Reactions - Safety Population

System Organ Class[a] Preferred Term	Overall p-Value	Treatment				
		Placebo N=66	100 mg Fezakinumab Q4W N=39	100 mg Fezakinumab Q2W N=42	200 mg Fezakinumab Q2W N=48	Total N=195
Injury, poisoning and procedural complications	0.932	4 (6.1)	2 (5.1)	2 (4.8)	4 (8.3)	12 (6.2)
Arthropod sting	0.662	0	0	0	1 (2.1)	1 (0.5)
Concussion	0.415	0	0	1 (2.4)	0	1 (0.5)
Contusion	0.239	0	1 (2.6)	2 (4.8)	1 (2.1)	4 (2.1)
Excoriation	1.000	1 (1.5)	0	0	0	1 (0.5)
Fall	0.231	0	1 (2.6)	1 (2.4)	0	2 (1.0)
Injury	0.662	0	0	0	1 (2.1)	1 (0.5)
Joint dislocation	0.200	0	1 (2.6)	0	0	1 (0.5)
Joint injury	0.686	1 (1.5)	1 (2.6)	0	0	2 (1.0)
Laceration	1.000	1 (1.5)	0	0	0	1 (0.5)
Limb injury	0.550	2 (3.0)	0	0	0	2 (1.0)
Muscle rupture	0.662	0	0	0	1 (2.1)	1 (0.5)
Muscle strain	1.000	1 (1.5)	0	0	0	1 (0.5)
Synovial rupture	0.662	0	0	0	1 (2.1)	1 (0.5)
Thermal burn	1.000	1 (1.5)	0	0	0	1 (0.5)
Investigations	0.691	3 (4.5)	4 (10.3)	3 (7.1)	4 (8.3)	14 (7.2)
Alanine aminotransferase increased	0.236	0	2 (5.1)	1 (2.4)	2 (4.2)	5 (2.6)
Aspartate aminotransferase increased	0.286	0	1 (2.6)	2 (4.8)	2 (4.2)	5 (2.6)
Blood pressure increased	0.700	2 (3.0)	0	0	1 (2.1)	3 (1.5)
Blood thyroid stimulating hormone decreased	0.415	0	0	1 (2.4)	0	1 (0.5)
Cardiac murmur	0.330	0	1 (2.6)	0	1 (2.1)	2 (1.0)
Coagulation test abnormal	1.000	1 (1.5)	0	0	0	1 (0.5)
Liver function test abnormal	0.200	0	1 (2.6)	0	0	1 (0.5)
Metabolism and nutrition disorders	0.206	4 (6.1)	3 (7.7)	0	1 (2.1)	8 (4.1)
Decreased appetite	0.200	0	1 (2.6)	0	0	1 (0.5)
Hypercalcaemia	0.200	0	1 (2.6)	0	0	1 (0.5)
Hypercholesterolaemia	0.550	2 (3.0)	0	0	0	2 (1.0)
Hyperglycaemia	0.891	1 (1.5)	1 (2.6)	0	1 (2.1)	3 (1.5)
Hypoglycaemia	0.200	0	1 (2.6)	0	0	1 (0.5)
Hypokalaemia	0.686	1 (1.5)	1 (2.6)	0	0	2 (1.0)

Table 36. Number (%) of Subjects Reporting TEAEs Excluding Infections and Injection Site Reactions - Safety Population

System Organ Class[a] Preferred Term	Overall p-Value	Treatment				
		Placebo N=66	100 mg Fezakinumab Q4W N=39	100 mg Fezakinumab Q2W N=42	200 mg Fezakinumab Q2W N=48	Total N=195
Musculoskeletal and connective tissue disorders	0.122	6 (9.1)	7 (17.9)	11 (26.2)	7 (14.6)	31 (15.9)
Arthralgia	0.345	2 (3.0)	0	3 (7.1)	3 (6.3)	8 (4.1)
Back pain	0.286	0	1 (2.6)	2 (4.8)	2 (4.2)	5 (2.6)
Bone pain	0.415	0	0	1 (2.4)	0	1 (0.5)
Groin pain	0.200	0	1 (2.6)	0	0	1 (0.5)
Joint range of motion decreased	0.057	0	2 (5.1)	1 (2.4)	0	3 (1.5)
Joint swelling	1.000	1 (1.5)	0	0	0	1 (0.5)
Muscle spasms	0.436	0	0	1 (2.4)	1 (2.1)	2 (1.0)
Muscular weakness	0.200	0	1 (2.6)	0	0	1 (0.5)
Musculoskeletal discomfort	1.000	1 (1.5)	0	0	0	1 (0.5)
Musculoskeletal pain	0.057	0	2 (5.1)	1 (2.4)	0	3 (1.5)
Myalgia	0.114	0	2 (5.1)	0	1 (2.1)	3 (1.5)
Osteoarthritis	0.200	0	1 (2.6)	0	0	1 (0.5)
Pain in extremity	0.686	1 (1.5)	1 (2.6)	0	0	2 (1.0)
Rheumatoid arthritis	0.407	1 (1.5)	1 (2.6)	3 (7.1)	1 (2.1)	6 (3.1)
Rotator cuff syndrome	0.200	0	1 (2.6)	0	0	1 (0.5)
Tendonitis	0.231	0	1 (2.6)	1 (2.4)	0	2 (1.0)
Trigger finger	0.415	0	0	1 (2.4)	0	1 (0.5)
Neoplasms benign, malignant and unspecified (including cysts and polyps)	0.200	0	1 (2.6)	0	0	1 (0.5)
Acoustic neuroma	0.200	0	1 (2.6)	0	0	1 (0.5)
Nervous system disorders	0.854	8 (12.1)	3 (7.7)	3 (7.1)	5 (10.4)	19 (9.7)
Disturbance in attention	1.000	1 (1.5)	0	0	0	1 (0.5)
Dizziness	0.270	3 (4.5)	1 (2.6)	0	0	4 (2.1)
Headache	0.355	1 (1.5)	1 (2.6)	2 (4.8)	4 (8.3)	8 (4.1)
Paraesthesia	0.415	0	0	1 (2.4)	0	1 (0.5)
Presyncope	0.200	0	1 (2.6)	0	0	1 (0.5)
Sciatica	1.000	1 (1.5)	0	0	0	1 (0.5)
Somnolence	0.408	1 (1.5)	0	0	2 (4.2)	3 (1.5)
Syncope	1.000	1 (1.5)	0	0	0	1 (0.5)
Tremor	1.000	1 (1.5)	0	0	0	1 (0.5)

Table 36. Number (%) of Subjects Reporting TEAEs Excluding Infections and Injection Site Reactions - Safety Population

System Organ Class[a] Preferred Term	Overall p-Value	Treatment				
		Placebo N=66	100 mg Fezakinumab Q4W N=39	100 mg Fezakinumab Q2W N=42	200 mg Fezakinumab Q2W N=48	Total N=195
Psychiatric disorders	0.605	1 (1.5)	0	2 (4.8)	1 (2.1)	4 (2.1)
Depression	0.436	0	0	1 (2.4)	1 (2.1)	2 (1.0)
Emotional distress	0.415	0	0	1 (2.4)	0	1 (0.5)
Listless	1.000	1 (1.5)	0	0	0	1 (0.5)
Renal and urinary disorders	0.956	2 (3.0)	1 (2.6)	2 (4.8)	2 (4.2)	7 (3.6)
Calculus urinary	0.200	0	1 (2.6)	0	0	1 (0.5)
Costovertebral angle tenderness	0.415	0	0	1 (2.4)	0	1 (0.5)
Dysuria	0.144	0	0	0	2 (4.2)	2 (1.0)
Haematuria	0.415	0	0	1 (2.4)	0	1 (0.5)
Micturition urgency	1.000	1 (1.5)	0	0	0	1 (0.5)
Pollakiuria	0.662	0	0	0	1 (2.1)	1 (0.5)
Urinary incontinence	1.000	1 (1.5)	0	0	0	1 (0.5)
Reproductive system and breast disorders	0.044*	0	2 (5.1)	0	3 (6.3)	5 (2.6)
Benign prostatic hyperplasia	0.200	0	1 (2.6)	0	0	1 (0.5)
Breast tenderness	0.200	0	1 (2.6)	0	0	1 (0.5)
Calculus prostatic	0.200	0	1 (2.6)	0	0	1 (0.5)
Menorrhagia	0.662	0	0	0	1 (2.1)	1 (0.5)
Prostatitis	0.200	0	1 (2.6)	0	0	1 (0.5)
Uterine haemorrhage	0.662	0	0	0	1 (2.1)	1 (0.5)
Vulvovaginal pruritus	0.662	0	0	0	1 (2.1)	1 (0.5)
Respiratory, thoracic and mediastinal disorders	0.107	5 (7.6)	1 (2.6)	6 (14.3)	1 (2.1)	13 (6.7)
Asthma	1.000	1 (1.5)	0	0	0	1 (0.5)
Bronchospasm	0.415	0	0	1 (2.4)	0	1 (0.5)
Cough	1.000	1 (1.5)	0	0	1 (2.1)	2 (1.0)
Dyspnoea	1.000	1 (1.5)	0	0	0	1 (0.5)
Epistaxis	0.415	0	0	1 (2.4)	0	1 (0.5)
Hiccups	0.415	0	0	1 (2.4)	0	1 (0.5)
Nasal congestion	0.415	0	0	1 (2.4)	0	1 (0.5)
Nasal oedema	0.415	0	0	1 (2.4)	0	1 (0.5)
Oropharyngeal pain	1.000	1 (1.5)	0	0	0	1 (0.5)
Paranasal sinus hypersecretion	0.200	0	1 (2.6)	0	0	1 (0.5)

Table 36. Number (%) of Subjects Reporting TEAEs Excluding Infections and Injection Site Reactions - Safety Population

System Organ Class[a] Preferred Term	Overall p-Value	Treatment				
		Placebo N=66	100 mg Fezakinumab Q4W N=39	100 mg Fezakinumab Q2W N=42	200 mg Fezakinumab Q2W N=48	Total N=195
Pharyngeal erythema	0.200	0	1 (2.6)	0	0	1 (0.5)
Rales	0.833	1 (1.5)	0	1 (2.4)	0	2 (1.0)
Rhonchi	1.000	1 (1.5)	0	0	0	1 (0.5)
Sinus congestion	1.000	1 (1.5)	0	0	0	1 (0.5)
Skin and subcutaneous tissue disorders	0.633	6 (9.1)	5 (12.8)	2 (4.8)	5 (10.4)	18 (9.2)
Acne	1.000	1 (1.5)	0	0	1 (2.1)	2 (1.0)
Alopecia	0.330	0	1 (2.6)	0	1 (2.1)	2 (1.0)
Dermatitis	0.200	0	1 (2.6)	0	0	1 (0.5)
Dermatitis contact	0.200	0	1 (2.6)	0	0	1 (0.5)
Eczema	0.436	0	0	1 (2.4)	1 (2.1)	2 (1.0)
Eczema weeping	1.000	1 (1.5)	0	0	0	1 (0.5)
Erythema	0.686	1 (1.5)	1 (2.6)	0	0	2 (1.0)
Hair colour changes	1.000	1 (1.5)	0	0	0	1 (0.5)
Hyperhidrosis	0.662	0	0	0	1 (2.1)	1 (0.5)
Photosensitivity reaction	0.415	0	0	1 (2.4)	0	1 (0.5)
Psoriasis	0.200	0	1 (2.6)	0	0	1 (0.5)
Rash	1.000	1 (1.5)	0	0	0	1 (0.5)
Skin ulcer	1.000	1 (1.5)	0	0	1 (2.1)	2 (1.0)
Urticaria	0.662	0	0	0	1 (2.1)	1 (0.5)
Vascular disorders	0.396	3 (4.5)	3 (7.7)	0	2 (4.2)	8 (4.1)
Hypertension	0.517	1 (1.5)	2 (5.1)	0	1 (2.1)	4 (2.1)
Hypotension	0.662	0	0	0	1 (2.1)	1 (0.5)
Peripheral ischaemia	1.000	1 (1.5)	0	0	0	1 (0.5)
Phlebitis	1.000	1 (1.5)	0	0	0	1 (0.5)
Varicose ulceration	0.200	0	1 (2.6)	0	0	1 (0.5)

Table 36. Number (%) of Subjects Reporting TEAEs Excluding Infections and Injection Site Reactions - Safety Population

System Organ Class[a] Preferred Term	Overall p-Value	Treatment				
		Placebo N=66	100 mg Fezakinumab Q4W N=39	100 mg Fezakinumab Q2W N=42	200 mg Fezakinumab Q2W N=48	Total N=195

Statistical significance at the $p<0.05$, $p<0.01$, $p<0.001$ levels is denoted by *, **, *** respectively.
Lag time of 12 weeks was added to treatment period (Therapy start - Therapy stop) for calculating treatment-emergent events.
Classifications of adverse events are based on the Medical Dictionary for Regulatory Activities (MedDRA).
Overall p-value: Refers to number of subjects data. Fisher's Exact Test p-value (2-tail).
Adverse events and serious adverse events are not separated out.
N = number of subjects with serious adverse events, Q2W = every 2 weeks, Q4W = every 4 weeks, TEAE = treatment-emergent adverse events.

a. Totals for the number of subjects at a higher level were not necessarily the sum of those at the lower levels since a subject may have reported ≥2 different adverse events within the higher level category.

Table 37. Number (%) of Subjects Reporting TEAEs (Treatment-Related) Excluding Infections and Injection Site Reactions - Safety Population

System Organ Class[a] Preferred Term	Overall p-Value	Treatment				
		Placebo N=66	100 mg Fezakinumab Q4W N=39	100 mg Fezakinumab Q2W N=42	200 mg Fezakinumab Q2W N=48	Total N=195
Any adverse event	0.538	11 (16.7)	8 (20.5)	8 (19.0)	14 (29.2)	41 (21.0)
Blood and lymphatic system disorders	0.360	2 (3.0)	0	0	0	2 (1.0)
Leukopenia	1.000	1 (1.5)	0	0	0	1 (0.5)
Neutropenia	1.000	1 (1.5)	0	0	0	1 (0.5)
Ear and labyrinth disorders	0.473	0	0	1 (2.4)	0	1 (0.5)
Vertigo	0.231	0	0	1 (2.4)	0	1 (0.5)
Eye disorders	0.678	1 (1.5)	0	0	1 (2.1)	2 (1.0)
Blepharitis	0.662	0	0	0	1 (2.1)	1 (0.5)
Conjunctivitis allergic	0.833	1 (1.5)	0	0	0	1 (0.5)
Gastrointestinal disorders	0.692	2 (3.0)	2 (5.1)	4 (9.5)	5 (10.4)	13 (6.7)
Abdominal pain upper	0.144	0	0	0	1 (2.1)	1 (0.5)
Diarrhoea	1.000	1 (1.5)	1 (2.6)	1 (2.4)	1 (2.1)	4 (2.1)
Dyspepsia	0.924	0	1 (2.6)	1 (2.4)	1 (2.1)	3 (1.5)
Nausea	0.419	0	0	2 (4.8)	0	2 (1.0)
Stomatitis	0.364	1 (1.5)	0	0	2 (4.2)	3 (1.5)
Vomiting	0.722	0	0	1 (2.4)	0	1 (0.5)
General disorders and administration site conditions	0.701	3 (4.5)	1 (2.6)	2 (4.8)	2 (4.2)	8 (4.1)
Asthenia	0.139	0	0	1 (2.4)	2 (4.2)	3 (1.5)
Fatigue	0.550	2 (3.0)	0	0	0	2 (1.0)
Injection site haemorrhage	0.200	0	1 (2.6)	0	0	1 (0.5)
Pyrexia	0.911	1 (1.5)	0	1 (2.4)	0	2 (1.0)
Investigations	0.691	0	1 (2.6)	1 (2.4)	2 (4.2)	4 (2.1)
Alanine aminotransferase increased	0.236	0	1 (2.6)	0	2 (4.2)	3 (1.5)
Aspartate aminotransferase increased	0.286	0	1 (2.6)	1 (2.4)	2 (4.2)	4 (2.1)
Metabolism and nutrition disorders	0.206	2 (3.0)	0	0	0	2 (1.0)
Hypercholesterolaemia	0.550	2 (3.0)	0	0	0	2 (1.0)
Musculoskeletal and connective tissue disorders	0.122	1 (1.5)	2 (5.1)	0	2 (4.2)	5 (2.6)
Arthralgia	0.345	0	0	0	1 (2.1)	1 (0.5)
Myalgia	0.114	0	2 (5.1)	0	1 (2.1)	3 (1.5)
Pain in extremity	0.686	1 (1.5)	0	0	0	1 (0.5)
Rheumatoid arthritis	0.407	0	0	0	1 (2.1)	1 (0.5)

Table 37. Number (%) of Subjects Reporting TEAEs (Treatment-Related) Excluding Infections and Injection Site Reactions - Safety Population

System Organ Class[a] Preferred Term	Overall p-Value	Treatment				
		Placebo N=66	100 mg Fezakinumab Q4W N=39	100 mg Fezakinumab Q2W N=42	200 mg Fezakinumab Q2W N=48	Total N=195
Rotator cuff syndrome	0.200	0	1 (2.6)	0	0	1 (0.5)
Nervous system disorders	0.854	2 (3.0)	1 (2.6)	2 (4.8)	4 (8.3)	9 (4.6)
Dizziness	0.270	2 (3.0)	1 (2.6)	0	0	3 (1.5)
Headache	0.355	1 (1.5)	0	1 (2.4)	3 (6.3)	5 (2.6)
Paraesthesia	0.415	0	0	1 (2.4)	0	1 (0.5)
Somnolence	0.408	0	0	0	2 (4.2)	2 (1.0)
Psychiatric disorders	0.605	0	0	0	1 (2.1)	1 (0.5)
Depression	0.436	0	0	0	1 (2.1)	1 (0.5)
Renal and urinary disorders	0.956	1 (1.5)	0	0	1 (2.1)	2 (1.0)
Dysuria	0.144	0	0	0	1 (2.1)	1 (0.5)
Micturition urgency	1.000	1 (1.5)	0	0	0	1 (0.5)
Reproductive system and breast disorders	0.044*	0	0	0	2 (4.2)	2 (1.0)
Uterine haemorrhage	0.662	0	0	0	1 (2.1)	1 (0.5)
Vulvovaginal pruritus	0.662	0	0	0	1 (2.1)	1 (0.5)
Respiratory, thoracic and mediastinal disorders	0.107	2 (3.0)	1 (2.6)	1 (2.4)	0	4 (2.1)
Cough	1.000	1 (1.5)	0	0	0	1 (0.5)
Hiccups	0.415	0	0	1 (2.4)	0	1 (0.5)
Paranasal sinus hypersecretion	0.200	0	1 (2.6)	0	0	1 (0.5)
Sinus congestion	1.000	1 (1.5)	0	0	0	1 (0.5)
Skin and subcutaneous tissue disorders	0.633	1 (1.5)	2 (5.1)	0	4 (8.3)	7 (3.6)
Acne	1.000	0	0	0	1 (2.1)	1 (0.5)
Alopecia	0.330	0	1 (2.6)	0	1 (2.1)	2 (1.0)
Eczema	0.436	0	0	0	1 (2.1)	1 (0.5)
Erythema	0.686	1 (1.5)	1 (2.6)	0	0	2 (1.0)
Hyperhidrosis	0.662	0	0	0	1 (2.1)	1 (0.5)
Vascular disorders	0.396	0	0	0	1 (2.1)	1 (0.5)
Hypotension	0.662	0	0	0	1 (2.1)	1 (0.5)

Table 37. Number (%) of Subjects Reporting TEAEs (Treatment-Related) Excluding Infections and Injection Site Reactions - Safety Population

System Organ Class[a] Preferred Term	Overall p-Value	Treatment				
		Placebo N=66	100 mg Fezakinumab Q4W N=39	100 mg Fezakinumab Q2W N=42	200 mg Fezakinumab Q2W N=48	Total N=195

Overall p-value: Refers to number of subjects data. Fisher's Exact Test p-value (2-tail).
Statistical significance at the $p<0.05$, $p<0.01$, $p<0.001$ levels is denoted by *, **, *** respectively.
Lag time of 12 weeks was added to treatment period (Therapy start - Therapy stop) for calculating treatment-emergent events.
Classifications of adverse events were based on the Medical Dictionary for Regulatory Activities (MedDRA).
Adverse events and serious adverse events are not separated out.
N = number of subjects with serious adverse events, Q2W = every 2 weeks, Q4W = every 4 weeks, TEAE = treatment-emergent adverse events.

a. Totals for the number of subjects at a higher level were not necessarily the sum of those at the lower levels since a subject may have reported ≥2 different adverse events within the higher level category.

Treatment-Emergent Infections:

The numbers (%) of all subjects with treatment-emergent infections that occurred during the study are provided in Table 38. Treatment-emergent infections were reported in a total of 70 subjects (35.9%): 15 subjects (31.3%) in the 200 mg fezakinumab Q2W group, 17 subjects (40.5%) in the 100 mg fezakinumab Q2W group, 17 subjects (43.6%) in the 100 mg fezakinumab Q4W group, and 21 subjects (31.8%) in the placebo group.

The most common treatment-emergent infections (incidence ≥5% of the subjects in total) were nasopharyngitis and upper respiratory tract infection. Other common treatment-emergent infections (incidence ≥5% of the subjects in at least 1 fezakinumab group) were oral herpes, bronchitis, cellulitis and urinary tract infection. There were no statistically significant differences in the incidence of treatment-emergent infections between the groups. In most cases, treatment-emergent infections were mild.

Treatment-Emergent Infections (Treatment-Related):

Table 39 summarizes all treatment-emergent infections (treatment-related). In 39 of the total of 70 subjects who had treatment-emergent infections, the infection was considered to be possibly or definitely related to treatment with the study treatment: 9 subjects (18.8%) in the 200 mg fezakinumab Q2W group, 8 subjects (19.0%) in the 100 mg fezakinumab Q2W group, 10 subjects (25.6%) in the 100 mg fezakinumab Q4W group, and 12 subjects (18.2%) in the placebo group.

Table 38. Number (%) of Subjects Reporting Treatment-Emergent Infections - Safety Population

System Organ Class[a] Preferred Term	Overall p-Value	Treatment				
		Placebo N=66	100 mg Fezakinumab Q4W N=39	100 mg Fezakinumab Q2W N=42	200 mg Fezakinumab Q2W N=48	Total N=195
Any adverse event	0.515	21 (31.8)	17 (43.6)	17 (40.5)	15 (31.3)	70 (35.9)
Eye disorders	0.415	0	0	1 (2.4)	0	1 (0.5)
Conjunctivitis	0.415	0	0	1 (2.4)	0	1 (0.5)
Gastrointestinal disorders	1.000	1 (1.5)	0	0	0	1 (0.5)
Apical granuloma	1.000	1 (1.5)	0	0	0	1 (0.5)
Infections and infestations	0.462	19 (28.8)	17 (43.6)	15 (35.7)	15 (31.3)	66 (33.8)
Bronchitis	0.124	4 (6.1)	1 (2.6)	0	0	5 (2.6)
Bronchitis bacterial	0.415	0	0	1 (2.4)	0	1 (0.5)
Cellulitis	0.300	1 (1.5)	2 (5.1)	0	0	3 (1.5)
Cystitis	0.200	0	1 (2.6)	0	0	1 (0.5)
Diarrhoea infectious	0.415	0	0	1 (2.4)	0	1 (0.5)
Diverticulitis	0.662	0	0	0	1 (2.1)	1 (0.5)
Fungal skin infection	1.000	1 (1.5)	0	0	0	1 (0.5)
Gastroenteritis	0.893	2 (3.0)	1 (2.6)	2 (4.8)	1 (2.1)	6 (3.1)
Herpes zoster	0.837	2 (3.0)	1 (2.6)	0	1 (2.1)	4 (2.1)
Infected skin ulcer	0.200	0	1 (2.6)	0	0	1 (0.5)
Infection	0.415	0	0	1 (2.4)	0	1 (0.5)
Influenza	0.221	3 (4.5)	0	0	0	3 (1.5)
Lower respiratory tract infection	1.000	1 (1.5)	0	0	0	1 (0.5)
Nasopharyngitis	0.445	2 (3.0)	2 (5.1)	4 (9.5)	4 (8.3)	12 (6.2)
Oral herpes	0.108	1 (1.5)	0	3 (7.1)	0	4 (2.1)
Pharyngitis	0.333	0	1 (2.6)	1 (2.4)	2 (4.2)	4 (2.1)
Respiratory tract infection	1.000	1 (1.5)	0	0	0	1 (0.5)
Rhinitis	1.000	1 (1.5)	0	0	0	1 (0.5)
Staphylococcal infection	1.000	1 (1.5)	0	0	0	1 (0.5)
Testicular abscess	1.000	1 (1.5)	0	0	0	1 (0.5)
Tinea pedis	0.436	0	0	1 (2.4)	1 (2.1)	2 (1.0)
Tinea versicolour	0.662	0	0	0	1 (2.1)	1 (0.5)
Tooth abscess	0.686	1 (1.5)	1 (2.6)	0	0	2 (1.0)
Tooth infection	0.200	0	1 (2.6)	0	0	1 (0.5)
Tracheitis	1.000	1 (1.5)	0	0	0	1 (0.5)
Tracheobronchitis	0.415	0	0	1 (2.4)	0	1 (0.5)

Table 38. Number (%) of Subjects Reporting Treatment-Emergent Infections - Safety Population

System Organ Class[a] Preferred Term	Overall p-Value	Treatment				
		Placebo N=66	100 mg Fezakinumab Q4W N=39	100 mg Fezakinumab Q2W N=42	200 mg Fezakinumab Q2W N=48	Total N=195
Upper respiratory tract infection	0.546	4 (6.1)	4 (10.3)	1 (2.4)	3 (6.3)	12 (6.2)
Urinary tract infection	0.926	2 (3.0)	2 (5.1)	2 (4.8)	2 (4.2)	8 (4.1)
Vaginal infection	0.662	0	0	0	1 (2.1)	1 (0.5)
Viral diarrhoea	0.415	0	0	1 (2.4)	0	1 (0.5)
Viral infection	0.662	0	0	0	1 (2.1)	1 (0.5)
Viral upper respiratory tract infection	0.662	0	0	0	1 (2.1)	1 (0.5)
Vulvovaginal candidiasis	0.415	0	0	1 (2.4)	0	1 (0.5)
Musculoskeletal and connective tissue disorders	1.000	1 (1.5)	0	0	0	1 (0.5)
Bursitis	1.000	1 (1.5)	0	0	0	1 (0.5)
Respiratory, thoracic and mediastinal disorders	0.231	0	1 (2.6)	1 (2.4)	0	2 (1.0)
Oropharyngeal pain	0.231	0	1 (2.6)	1 (2.4)	0	2 (1.0)
Vascular disorders	0.200	0	1 (2.6)	0	0	1 (0.5)
Varicose ulceration	0.200	0	1 (2.6)	0	0	1 (0.5)

Lag time of 12 weeks was added to treatment period (Therapy start - Therapy stop) for calculating treatment-emergent events.
Classifications of adverse events are based on the Medical Dictionary for Regulatory Activities (MedDRA).
Overall p-value: Refers to number of subjects data. Fisher's Exact Test p-value (2-tail).
Adverse events and serious adverse events are not separated out.
N = number of subjects with serious adverse events, Q2W = every 2 weeks, Q4W = every 4 weeks.

a. Totals for the number of subjects at a higher level were not necessarily the sum of those at the lower levels since a subject may have reported ≥2 different adverse events within the higher level category.

Table 39. Number (%) of Subjects Reporting Treatment-Emergent Infection (Treatment-Related) - Safety Population

System Organ Class[a] Preferred Term	Overall p-Value	Treatment				
		Placebo N=66	100 mg Fezakinumab Q4W N=39	100 mg Fezakinumab Q2W N=42	200 mg Fezakinumab Q2W N=48	Total N=195
Any adverse event	0.515	12 (18.2)	10 (25.6)	8 (19.0)	9 (18.8)	39 (20.0)
Infections and infestations	0.462	12 (18.2)	10 (25.6)	8 (19.0)	9 (18.8)	39 (20.0)
Bronchitis	0.124	3 (4.5)	0	0	0	3 (1.5)
Cellulitis	0.300	0	1 (2.6)	0	0	1 (0.5)
Cystitis	0.200	0	1 (2.6)	0	0	1 (0.5)
Diarrhoea infectious	0.415	0	0	1 (2.4)	0	1 (0.5)
Gastroenteritis	0.893	2 (3.0)	1 (2.6)	0	0	3 (1.5)
Herpes zoster	0.837	2 (3.0)	1 (2.6)	0	1 (2.1)	4 (2.1)
Infection	0.415	0	0	1 (2.4)	0	1 (0.5)
Influenza	0.221	2 (3.0)	0	0	0	2 (1.0)
Nasopharyngitis	0.445	0	1 (2.6)	3 (7.1)	2 (4.2)	6 (3.1)
Oral herpes	0.108	1 (1.5)	0	1 (2.4)	0	2 (1.0)
Pharyngitis	0.333	0	0	0	1 (2.1)	1 (0.5)
Testicular abscess	1.000	1 (1.5)	0	0	0	1 (0.5)
Tinea pedis	0.436	0	0	1 (2.4)	1 (2.1)	2 (1.0)
Tinea versicolour	0.662	0	0	0	1 (2.1)	1 (0.5)
Tracheitis	1.000	1 (1.5)	0	0	0	1 (0.5)
Tracheobronchitis	0.415	0	0	1 (2.4)	0	1 (0.5)
Upper respiratory tract infection	0.546	4 (6.1)	3 (7.7)	0	2 (4.2)	9 (4.6)
Urinary tract infection	0.926	1 (1.5)	2 (5.1)	0	1 (2.1)	4 (2.1)
Vaginal infection	0.662	0	0	0	1 (2.1)	1 (0.5)
Vulvovaginal candidiasis	0.415	0	0	1 (2.4)	0	1 (0.5)
Respiratory, thoracic and mediastinal disorders	0.231	0	1 (2.6)	0	0	1 (0.5)
Oropharyngeal pain	0.231	0	1 (2.6)	0	0	1 (0.5)
Vascular disorders	0.200	0	1 (2.6)	0	0	1 (0.5)
Varicose ulceration	0.200	0	1 (2.6)	0	0	1 (0.5)

Overall p-value: Refers to number of subjects data. Fisher's Exact Test p-value (2-tail).
Lag time of 12 weeks was added to treatment period (Therapy start - Therapy stop) for calculating treatment-emergent events.
Classifications of adverse events were based on the Medical Dictionary for Regulatory Activities (MedDRA).
Adverse events and serious adverse events are not separated out.
N = number of subjects with serious adverse events, Q2W = every 2 weeks, Q4W = every 4 weeks.

Table 39. Number (%) of Subjects Reporting Treatment-Emergent Infection (Treatment-Related) - Safety Population

a. Totals for the number of subjects at a higher level were not necessarily the sum of those at the lower levels since a subject may have reported ≥2 different adverse events within the higher level category.

Serious AEs (SAEs) Excluding Infections and Injection Site Reactions:

Eight (8) subjects (4.1%) reported a total of 15 SAEs excluding infections and ISRs during this study: 1 subject (2.1%) in the 200 mg fezakinumab Q2W group, 1 subject (2.6%) in the 100 mg fezakinumab Q4W group, and 6 subjects (9.1%) in the placebo group (Table 40).

SAE Infections:

A total of 3 subjects (1.5%) reported infections that qualified as SAEs during this study: 1 subject in the 100 mg fezakinumab Q4W group and 1 subject in the placebo group (2.6% and 1.5%, respectively) each reported cellulitis, and 1 subject (1.5%) in the placebo group reported testicular abscess (Table 41).

Treatment-Related SAE: Data not available.

Table 40. Number (%) of Subjects Reporting Serious Adverse Events Excluding Infections and Injection Site Reactions - Safety Population

System Organ Class[a] Preferred Term	Overall p-Value	Treatment				
		Placebo N=66	100 mg Fezakinumab Q4W N=39	100 mg Fezakinumab Q2W N=42	200 mg Fezakinumab Q2W N=48	Total N=195
Any adverse event	0.115	6 (9.1)	1 (2.6)	0	1 (2.1)	8 (4.1)
Blood and lymphatic system disorders	1.000	1 (1.5)	0	0	0	1 (0.5)
Anaemia	1.000	1 (1.5)	0	0	0	1 (0.5)
Cardiac disorders	1.000	1 (1.5)	0	0	0	1 (0.5)
Atrial fibrillation	1.000	1 (1.5)	0	0	0	1 (0.5)
Gastrointestinal disorders	1.000	1 (1.5)	0	0	0	1 (0.5)
Pancreatitis acute	1.000	1 (1.5)	0	0	0	1 (0.5)
General disorders and administration site conditions	1.000	1 (1.5)	0	0	0	1 (0.5)
Gait disturbance	1.000	1 (1.5)	0	0	0	1 (0.5)
Hepatobiliary disorders	1.000	1 (1.5)	0	0	0	1 (0.5)
Bile duct obstruction	1.000	1 (1.5)	0	0	0	1 (0.5)
Cholangitis	1.000	1 (1.5)	0	0	0	1 (0.5)
Cholelithiasis	1.000	1 (1.5)	0	0	0	1 (0.5)
Injury, poisoning and procedural complications	0.330	0	1 (2.6)	0	1 (2.1)	2 (1.0)
Fall	0.200	0	1 (2.6)	0	0	1 (0.5)
Joint dislocation	0.200	0	1 (2.6)	0	0	1 (0.5)
Road traffic accident	0.662	0	0	0	1 (2.1)	1 (0.5)
Metabolism and nutrition disorders	1.000	1 (1.5)	0	0	0	1 (0.5)
Hypokalaemia	1.000	1 (1.5)	0	0	0	1 (0.5)
Musculoskeletal and connective tissue disorders	1.000	1 (1.5)	0	0	0	1 (0.5)
Rheumatoid arthritis	1.000	1 (1.5)	0	0	0	1 (0.5)
Nervous system disorders	0.550	2 (3.0)	0	0	0	2 (1.0)
Dizziness	1.000	1 (1.5)	0	0	0	1 (0.5)
Syncope	1.000	1 (1.5)	0	0	0	1 (0.5)
Vascular disorders	1.000	1 (1.5)	0	0	0	1 (0.5)
Peripheral ischaemia	1.000	1 (1.5)	0	0	0	1 (0.5)

Overall p-value: Refers to number of subjects data. Fisher's Exact Test p-value (2-tail).
Classifications of adverse events are based on the Medical Dictionary for Regulatory Activities (MedDRA).
N = number of subjects with serious adverse events, Q2W = every 2 weeks, Q4W = every 4 weeks.

a. Totals for the number of subjects at a higher level were not necessarily the sum of those at the lower levels since a subject may have reported ≥2 different adverse events within the higher level category.

Table 41. Number (%) of Subjects Reporting Serious Adverse Events Infections - Safety Population

System Organ Class[a] Preferred Term	Overall p-Value	Treatment				
		Placebo N=66	100 mg Fezakinumab Q4W N=39	100 mg Fezakinumab Q2W N=42	200 mg Fezakinumab Q2W N=48	Total N=195
Any adverse event	0.542	2 (3.0)	1 (2.6)	0	0	3 (1.5)
Infections and infestations	0.542	2 (3.0)	1 (2.6)	0	0	3 (1.5)
Cellulitis	0.686	1 (1.5)	1 (2.6)	0	0	2 (1.0)
Testicular abscess	1.000	1 (1.5)	0	0	0	1 (0.5)

Overall p-value: Refers to number of subjects data. Fisher's Exact Test p-value (2-tail).
Classifications of adverse events are based on the Medical Dictionary for Regulatory Activities (MedDRA).
N = number of subjects; Q2W = every 2 weeks, Q4W = every 4 weeks.

a. Totals for the number of subjects at a higher level were not necessarily the sum of those at the lower levels since a subject may have reported ≥2 different adverse events within the higher level category.

Discontinuations due to AEs: A total of 4 subjects reported AEs leading to discontinuation from the study treatment: 1 subject in the 100 mg fezakinumab Q4W group and 3 subjects in the placebo group (1 of the subjects in the placebo group also discontinued from the study due to AEs) (Table 42 and Table 43).

Death: No subjects died during this study.

Table 42. Number (%) of Subjects Reporting Adverse Events Causing Permanent Discontinuation of Study Treatment Excluding Infections and Injection Site Reactions - Safety Population

System Organ Class[a] Preferred Term	Overall p-Value	Treatment				
		Placebo N=66	100 mg Fezakinumab Q4W N=39	100 mg Fezakinumab Q2W N=42	200 mg Fezakinumab Q2W N=48	Total N=195
Any adverse event	0.542	2 (3.0)	1 (2.6)	0	0	3 (1.5)
Gastrointestinal disorders	1.000	1 (1.5)	0	0	0	1 (0.5)
Pancreatitis acute	1.000	1 (1.5)	0	0	0	1 (0.5)
Investigations	0.200	0	1 (2.6)	0	0	1 (0.5)
Liver function test abnormal	0.200	0	1 (2.6)	0	0	1 (0.5)
Nervous system disorders	1.000	1 (1.5)	0	0	0	1 (0.5)
Headache	1.000	1 (1.5)	0	0	0	1 (0.5)

Overall p-value: Refers to number of subjects data. Fisher's Exact Test p-value (2-tail).
Classifications of adverse events are based on the Medical Dictionary for Regulatory Activities (MedDRA).
N = number of subjects; Q2W = every 2 weeks, Q4W = every 4 weeks.
a. Totals for the number of subjects at a higher level were not necessarily the sum of those at the lower levels since a subject may have reported ≥2 different adverse events within the higher level category.

Table 43. Number (%) of Subjects Reporting Infections Causing Permanent Discontinuation of Study Treatment - Safety Population

System Organ Class[a] Preferred Term	Overall p-Value	Treatment				
		Placebo N=66	100 mg Fezakinumab Q4W N=39	100 mg Fezakinumab Q2W N=42	200 mg Fezakinumab Q2W N=48	Total N=195
Any adverse event	1.000	1 (1.5)	0	0	0	1 (0.5)
Infections and infestations	1.000	1 (1.5)	0	0	0	1 (0.5)
Lower respiratory infection	1.000	1 (1.5)	0	0	0	1 (0.5)

Overall p-value: Refers to number of subjects data. Fisher's Exact Test p-value (2-tail).
Classifications of adverse events are based on the Medical Dictionary for Regulatory Activities (MedDRA).
N = number of subjects; Q2W = every 2 weeks, Q4W = every 4 weeks.
a. Totals for the number of subjects at a higher level were not necessarily the sum of those at the lower levels since a subject may have reported ≥2 different adverse events within the higher level category.

CONCLUSIONS:

Fezakinumab is a human monoclonal antibody that is a potent inhibitor of interleukin (IL)-22 and is being developed for the treatment of RA. The purpose of this phase 2, multicenter, parallel-group, placebo-controlled, randomized, double-blind study was to evaluate the efficacy and safety of fezakinumab in subjects with active RA while receiving a stable background of methotrexate.

A total of 195 subjects were randomized and treated with study treatment and were included in the safety analysis. Efficacy analyses were performed for the mITT population (195 subjects), the per-protocol population (165 subjects), and the follow-up population (166 subjects).

The efficacy results were as follows:

- None of the 3 fezakinumab dose regimens evaluated were statistically significantly different from placebo with respect to the primary efficacy endpoint ACR20 so the study did not meet its primary efficacy objective regarding the statistical superiority of at least 1 of the 3 dose regimens compared to placebo in terms of ACR20 at Week 12.

- Statistically significant differences between the groups were shown at some time points (Weeks 2, 4, 6, 8, 10, or 12) for the secondary endpoints ACR20, EULAR response, patient global assessment of disease activity, pain VAS, and general health VAS. Consistent trends regarding better efficacy of 1 of the 3 fezakinumab dose regimen or time point of the measurement could not be detected. For the other secondary efficacy and health outcomes endpoints, no statistically significant differences between the groups were observed for any week.

Fezakinumab was generally well tolerated at doses of 100 mg fezakinumab Q2W SC, 100 mg fezakinumab Q4W SC, and 200 mg fezakinumab Q2W SC during the 12-week treatment period (last administration of study treatment at Week 10). No AEs attributed to treatment with fezakinumab were identified. However, due to the small number of subjects who received fezakinumab in this study, the safety data for this study needs to be interpreted with caution.