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PROPRIETARY DRUG NAME®/GENERIC DRUG NAME: Xeljanz ®/ Tofacitinib citrate

PROTOCOL NO.: A3921041

PROTOCOL TITLE: A Long-Term, Open-Label Study of CP-690,550 to Confirm the Safety Following Long-Term Administration of CP-690,550 in the Treatment of Rheumatoid Arthritis

Study Center(s): There were a total of 56 centers in Japan.

Study Initiation Date and Final Completion Dates: 18 April 2008 to 25 December 2013

Phase of Development: Phase 3

Study Objective(s):

Primary Objective

To determine the long-term safety and tolerability of CP-690,550 for rheumatoid arthritis (RA) patients who had completed a qualifying CP-690,550 study.

Secondary Objectives

- To evaluate the persistence of efficacy of CP-690,550 for treatment of RA patients who had completed a qualifying CP-690,550 study.
- To evaluate quality of life (QOL) and functional status in these patients with long-term administration of CP-690,550.

METHODS

Study Design: This was a Phase 3, multi-center, open-label, non-comparative, long-term study. The estimated sample size was 480 patients who had completed a previous qualifying controlled CP-690,550 study in Japan. The subjects had been treated at 1 of various doses in the qualifying study: CP-690,550 (1, 3, 5, and 10 mg, twice daily (BID) or placebo for Study A3921039 [Note 1], and CP-690,550 (1, 3, 5, 10 and 15 mg, BID) or placebo for Study

Note [1]: The Study A3921039 was a Phase 2, randomized, double-blind, placebo-controlled, multicenter study to confirm dose responsiveness following 12 weeks of the administration of CP-690,550 (1, 3, 5, and 10 mg, BID) or placebo in patients with active RA inadequately controlled with methotrexate (MTX) alone, in a 12-week add-on therapy with MTX.

A3921040 [Note 2], and CP-690,550 (5 and 10 mg, BID) or placebo for Study A3921044 [Note 3]. The subjects, who received CP-690,550 in the qualifying studies, increased, maintained or decreased dose upon entry into Study A3921041. The subjects who received placebo (CP-690,550 0 mg) in the Studies A3921039 and A3921040 could have received initially CP-690,550 5 mg BID in Study A3921041.

There was no screening visit in this study. For individual Japanese patients participation in this study was to be initiated on the day of the final visit (i.e. last dose) of their participation in their qualifying study (Studies A3921039, A3921040, and A3921044). That is, the final visit of the qualifying randomized study could be combined with the baseline visit for this study. If it was the same day, the investigator instructed the subject to begin dosing in this study on the next morning. If the date of study initiation was not the same as the date of the final visit of the qualifying study, the study was to be initiated within 7 days of the final visit of the qualifying study. This study was to be continued up to 6 months after marketing approval in Japan as a clinical study period (until preparation to supply CP-690,550 to patients). The study duration was changed to until 3 months after CP-690,550 became commercially available in Japan or until CP-690,550 was commercially supplied to patients at the sites.

All subjects were to initiate CP-690,550 treatment in this study at a daily dose of 10 mg (5 mg BID) of CP-690,550. The dosage could be increased from 5 mg BID to 10 mg BID, reduced from 10 mg BID to 5 mg BID, or temporarily discontinued (up to 28 consecutive days) based on consideration of the risks and benefits to the subject.

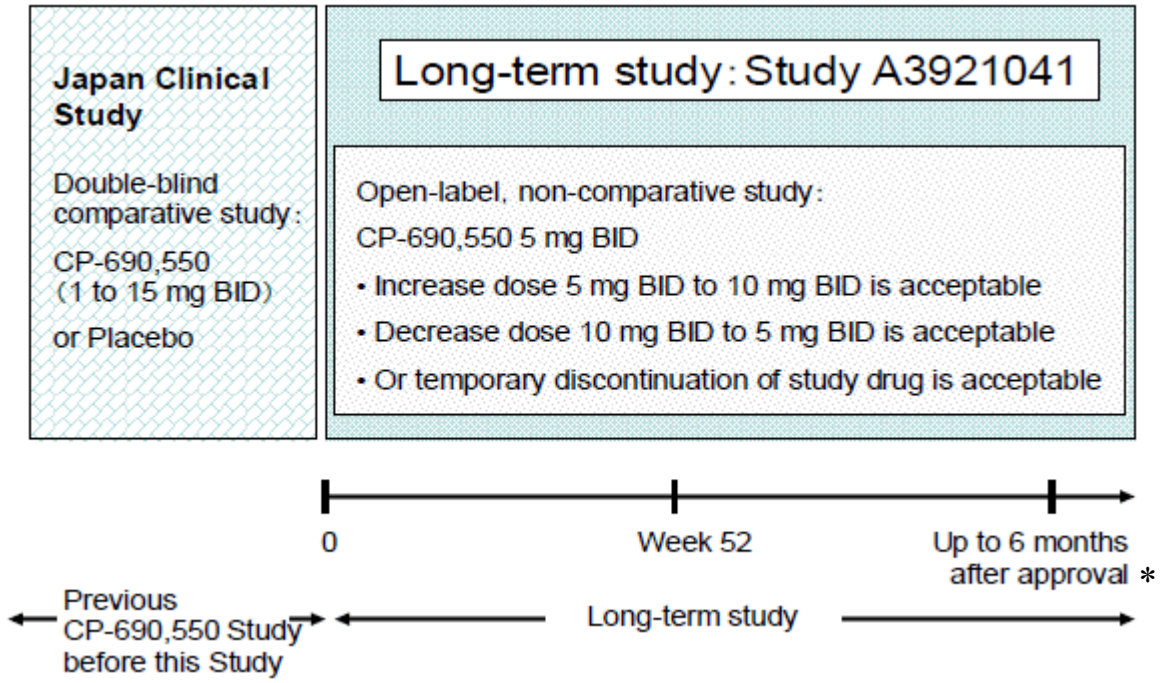
The baseline data of the prior randomized studies of CP-690,550 were used as baseline for safety and efficacy evaluation in this study.

The study design is presented in Figure 1.

Note [2]: The Study A3921040 was a Phase 2, randomized, double-blind, placebo-controlled, multicenter study to confirm dose responsiveness following 12 weeks of the administration of CP-690,550 (1, 3, 5, 10 and 15 mg, BID) or placebo in patients with active RA inadequately responding to at least 1 disease-modifying antirheumatic drug (DMARD).

Note [3]: The Study A3921044 was a Phase 3 randomized, 2-year, double-blind, placebo-controlled, parallel group study to compare the efficacy of CP-690,550 in doses of 5 mg BID and 10 mg BID versus placebo for the treatment of signs and symptoms of RA in patients with active RA on a stable background of MTX.

Figure 1. Study Design



BID = twice daily.
*The study duration was changed from "up to 6 months after approval" to "until 3 months after CP-690,550 became commercially available in Japan or until CP-690,550 was commercially supplied to patients at the sites".

The schedule activity in this study is presented in Table 1. As an example, from baseline of the long-term study to Week 84 visit, end of treatment or early termination.

Table 1. Schedule of Activities

	Items	Baseline Day 0	Visit points (Long-term)																	End of Treatment **(Early term)**
			W2 **(A)**	W4 (A)	W8 (A)	W12 (B)	W16 (C)	W20 (C)	W24 (D)	W28 (C)	W32 (C)	W36 (E)	W40 (C)	W44 (C)	W48 (F)	W52 (C)	W60 (E)	W72 (G)	W84 (E)	
Informed Consent		X																		
Patient background	Eligibility confirmation (e.g., inclusion/exclusion criteria)	X																		
	Background investigation (e.g., complications, medical history, treatment conditions) [1]	X													X			X		X
	Questions/Examinations by physician (physical examination, joint palpation) [2]	X	X	X	X	X			X			X			X		X	X	X	X
	Questions/Examinations by physician (including lung and heart auscultation)						X	X		X	X		X	X		X	will be performed as a standard test [10]			
Observation items	ACR Assessments [3]	X	X	X	X	X			X			X			X		X	X	X	X
	DAS 28-3 (CRP), DAS 28-4 (ESR)	X	X	X	X	X			X			X			X		X	X	X	X
	QOL (SF-36v2)	X				X			X						X			X		X
	HAQ-DI	X	X	X	X	X			X			X			X		X	X	X	X
	Body weight, Vital signs (sitting blood pressure/ pulse rate, axillary body temperature)	X	X	X	X	X			X			X			X		X	X	X	X
	Adverse events assessment	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Lab tests	Tuberculosis test [4]	X																		
	ESR (Westergren method)	X	X	X	X	X			X			X			X		X	X	X	X
	CRP (C-reactive protein)	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
	Hematology [5]	X	X	X	X	X			X			X			X		X	X	X	X
	Biochemistry: standard (fasting) [6]	X	X	X	X	X			X			X			X		X	X	X	X
	Biochemistry: hematological including differential [10]						X	X		X	X		X	X		X	will be performed as a standard test [10]			
	Biochemistry: lipid special (fasting) [7]	X				X			X			X			X		X	X	X	X
	Pregnancy test (serum) [8]	X				X			X			X			X		X	X	X	X
	Urinalysis (general/pregnancy) [8]	X	X	X	X	X			X			X			X		X	X	X	X
	Standard 12-lead ECG	X							X						X			X		X
	SpO_2	X	X	X	X	X			X			X			X		X	X	X	X
	Radiographs of hands and feet[11]								X						X					X
	Chest X-rays	X													X					X
	HBcAb, HBsAb[12]																	X		
	HBV-DNA quantitative test, HBsAg[13]																	X		
	Sub set markers of lymphocytes (FACS analysis)[14]														X		X	X	X	X
suppl	Study drug dispensing	X				X			X			X			X		X	X	X	
	Study drug recovery, remaining drug check		X	X	X	X			X			X			X		X	X	X	X

Items	Baseline Day 0	Visit points (Long-term)																	End of Treatment **(Early term)**
		W2 **(A)**	W4 (A)	W8 (A)	W12 (B)	W16 (C)	W20 (C)	W24 (D)	W28 (C)	W32 (C)	W36 (E)	W40 (C)	W44 (C)	W48 (F)	W52 (C)	W60 (E)	W72 (G)	W84 (E)	
Confirmation of concomitant medications	X	X	X	X	X			X			X			X		X	X	X	X
Instructions on the use of drugs [9]	X	X	X	X	X			X			X			X		X	X	X	

W = Week, ACR = American College of Rheumatology, DAS = disease activity score, CRP = C-reactive protein, ESR = erythrocyte sedimentation rate, QOL = quality of life, SF-36 = SF-36 health survey, HAQ-DI = Health Assessment Questionnaire-Disability Index, ECG = electrocardiogram, SpO_2 = transcutaneous arterial oxygen saturation.

1. Medical history, complications, treatment conditions, etc. utilized qualifying study data. Cardiovascular Risk Factor Assessment included smoking status, average weekly alcohol consumption, family history of premature coronary heart disease (CHD), and waist circumference. This information was to be updated at annual visits (Week 48, 72 etc.).
2. Questioning/examination by physician consisted of weight, examination of heart, lungs, abdomen, and lymph nodes. At Baseline and Week 96/early termination was monitored carefully.
3. ACR Assessments included Tender /Painful Joint Count (68), Swollen Joint Count (66), Patient Assessment of Arthritis Pain (VAS), Patient Global Assessment of Arthritis (VAS), Physician Global Assessment of Arthritis (VAS), HAQ-DI.
4. Confirmation of tuberculosis infection by means of QuantiFERON®-TB or tuberculin skin test was performed only if a tuberculin test had not been performed during the qualifying study (the assessment of tuberculin test was to be made within 48-72 hours).
5. WBC; differential WBC; RBC; hemoglobin; hematocrit; reticulocytes; platelet count
6. Biochemistry tests (standard): protein, total bilirubin, albumin, ALP, BUN, creatinine, blood glucose, AST, ALT, LDH, Na^+, K^+, Cl^-, Ca^{++}, HCO_3^- (all measured at fasting at least 9 hours after eating).
7. Biochemistry tests (lipid): T-Chol, LDL, HDL, TG, Apolipoprotein A-I and A-II, Apolipoprotein B (all measured at fasting at least 9 hours after eating).
8. Pregnancy tests were performed for women of child bearing potential (serum FSH [test] was optional). Urinalysis was performed using dipsticks and, if a clinically significant abnormality was observed or at the discretion of the investigator, additional examination by means of, for example, microscopy was performed.
9. The final visit of the qualifying randomized study could be combined with the baseline visit for this study. If it was the same day, the investigator instructed the subject to begin dosing in the next morning. Subjects were instructed to return the remaining study medication every three months and at the end of treatment (including visit after discontinuation).
10. Visit for ensuring safety of patients was added as patient status dictated. Questions/examinations (including lung and heart auscultation), CRP, hematological biochemistry including differential (serum creatinine, AST, ALT and albumin etc.) were confirmed.
11. Only subjects who had enrolled in and completed qualifying study A3921044 had radiographs of the wrists/hands and feet (not subjects from studies A3921039 or A3921040). Radiographs were read and scored centrally; images were acquired at Week 24, Week 48, thereafter every 48 weeks and end of treatment/early termination. Patients whose radiographs had been acquired within 24 weeks from the end of treatment/early termination were not to be repeated at the end of treatment/early termination.
12. Measured at a first visit after the IRB approval of this protocol amendment. Subjects with HBcAb positive had to be tested for HBsAb.
13. Subjects with HBcAb positive and HBsAb negative had to discontinue the study and take the examination of HBV-DNA and HBsAg.
14. Sub set markers of lymphocytes; Lymphocytes cell surface markers (CD3+, CD4+, CD8+, CD19+, CD3-/CD16+/CD56+, CD3+/CD16+/CD56+, CD16+/CD56+, CD16+/CD56-, CD16-/CD56+, CD16-/CD56-) were measured at E (48 weeks or later), F and G visits.

Number of Subjects (Planned and Analyzed): The estimated sample size was 480 subjects. Actual number enrolled was 486 subjects (113 subjects from A3921039, 291 subjects from A3921040, and 82 subjects from A3921044). The 105 subjects who were exposed to 10 mg

BID for more than or equal to 84 days in total within the long-term safety study (A3921041) were grouped into CP-690,550 10 mg BID, and the remaining 381 subjects were grouped into CP-690,550 5 mg BID.

Diagnosis and Main Criteria for Inclusion: The subjects were at least 20 years of age. The subjects had to have participated in a qualifying clinical study of CP-690,550 and completed the study as required. If methotrexate (MTX) was being used concomitantly, a folic acid preparation had [also] to be used concomitantly.

Study Treatment: In this study, subjects initially received CP-690,550 5 mg BID administered orally. CP-690,550 1 mg tablets were supplied until around June 2009. The dose could be reduced from 5 mg BID to 1 mg BID - 4 mg BID as prescribed in the original protocol prior to Protocol Amendment 2 (Protocol Version 3; Dated 09 March 2009). After Protocol Amendment 2, CP-690,550 1 mg tablets were changed to 5 mg tablets after supplying them to each site. The dosing regimen was changed to state that the dose could be increased from 5 mg BID to 10 mg BID, reduced from 10 mg BID to 5 mg BID, or temporarily discontinued based on consideration of the risks and benefits to the patient.

At each visit, the investigator instructed the subject to take the CP-690,550 dose, twice daily separated by 12±2 hours with a cup of water (about 200 mL), without chewing. The final visit of the qualifying randomized study could be combined with the baseline visit for this study. If it was the same day, the investigator instructed the subject to begin dosing in this study on the next morning.

Efficacy Endpoints: The efficacy endpoints included:

- American College of Rheumatology (ACR) 20, ACR50, and ACR70 response rates
- Actual values and changes from baseline (of the qualifying randomized studies) of the 7 components of the ACR core set
  - Tender/Painful Joint Count (68)
  - Swollen Joint Count (66)
  - Patient Assessment of Arthritis Pain (visual analogue scale: VAS)
  - Patient Global Assessment of Arthritis (VAS)
  - Physician Global Assessment of Arthritis (VAS)
  - Health Assessment Questionnaire-Disability Index (HAQ-DI)
  - C-reactive protein (CRP)
- Disease Activity Score (DAS) assessment using the DAS28-3 (CRP) and DAS28-4 (erythrocyte sedimentation rate [ESR])

- Radiographs of hands and feet (for the subjects from the qualifying study A3921044)
- SF-36 health survey

Safety Evaluations: Safety was assessed by adverse events, clinical laboratory tests, vital signs (sitting blood pressure, pulse rate, axillary temperature), standard 12-lead electrocardiograms (ECGs). Evaluations were made at specified time points from baseline through last subject visit.

Statistical Methods: No formal hypothesis tests were conducted. The full analysis set (FAS) included all subjects enrolled in this study who had been part of a qualifying study, and who received at least 1 dose of open-label study medication in Study A3921041. The analysis of safety was the primary analysis. The safety analysis set was the same as the FAS. The previous study baseline data were used as baseline data, unless otherwise noted. All the safety and efficacy data were summarized descriptively through appropriate data tabulations, descriptive statistics, and graphical presentations. The qualifying study baseline data were used as a baseline data, unless otherwise noted.

RESULTS

Subject Disposition and Demography: Subject disposition is shown in Table 2. A total of 486 subjects were assigned to study treatment and all of them were treated. Of those, 113 subjects were from A3921039, 291 subjects were from A3921040, and 82 subjects were from A3921044. A total of 308 (63.4%) subjects completed the study, and 178 (36.6%) subjects were discontinued from the study. The primary reason of study discontinuation was adverse events regardless of whether or not they were treatment emergent. A total of 123 subjects were discontinued from the study by reason of adverse events (110 subjects had adverse events considered related to study drug and 13 subjects had adverse events considered not related).

All 486 subjects who received at least 1 dose of the study drug were evaluated for efficacy and safety measures. All subjects were to initiate at a daily dose of 10 mg (5 mg BID) of CP-690,550. The CP-690,550 dose could be increased, reduced or temporarily discontinued based on the investigator's assessment of the risks and benefits to the subject's condition.

Subjects who were exposed to 10 mg BID for more than or equal to 84 days in total within the long-term safety study (A3921041) were grouped into CP-690,550 10 mg BID in the tables and figures. Other subjects were grouped into CP-690,550 5 mg BID. As mentioned above, the dosing could be adjusted based on the investigator's assessment of the risks and benefits to the subject's condition, therefore the study was not designed to perform a comparison between the CP-690,550 5 mg BID group and 10 mg BID group in this study. In addition, the subjects often changed CP-690,550 dose between the qualifying study and Study A3921041. Their responses may have changed after entry into Study A3921041 and CP-690,550 dose could be increased after Week 12 in this study. Therefore the Week 12 data were focused as turning point in efficacy evaluation in this study.

Table 2. Subject Disposition

	CP-690,550		
Number (%) of Subjects	5 mg BID	10 mg BID	Total
Assigned to study treatment	381	105	486
Treated	381	105	486
Completed	242 (63.5)	66 (62.9)	308 (63.4)
Discontinued	139 (36.5)	39 (37.1)	178 (36.6)
Analyzed for efficacy			
Full analysis set	381 (100.0)	105 (100.0)	486 (100.0)
Analyzed for safety			
Adverse events	381 (100.0)	105 (100.0)	486 (100.0)
Laboratory data	381 (100.0)	105 (100.0)	486 (100.0)

BID = twice daily.

The demographic distribution by age, race, sex, weight, body mass index, and height by treatment groups are summarized in Table 3.

Table 3. Demographic Characteristics

	CP-690,550		
	5 mg BID (N = 381)	10 mg BID (N = 105)	Total (N = 486)
Age (years): n (%)			
<18	0	0	0
18-44	81 (21.3)	35 (33.3)	116 (23.9)
45-64	233 (61.2)	62 (59.0)	295 (60.7)
≥65	67 (17.6)	8 (7.6)	75 (15.4)
Mean	53.5	49.3	52.6
SD	11.2	11.7	11.4
Range	23-74	20-70	20-74
Race: n (%)			
Asian	381 (100.0)	105 (100.0)	486 (100.0)
Sex: n (%)			
Male	63 (16.5)	19 (18.1)	82 (16.9)
Female	318 (83.5)	86 (81.9)	404 (83.1)
Weight (kg)			
Mean	54.4	55.4	54.6
SD	9.6	10.5	9.8
Range	31.4-95.0	34.3-83.6	31.4-95.0
Body mass index (kg/m^2)			
Mean	21.9	22.1	21.9
SD	3.5	3.4	3.5
Range	15.5-38.5	16.2-31.4	15.5-38.5
Height (cm)			
Mean	157.5	157.9	157.6
SD	7.4	7.4	7.4
Range	139.8-181.0	142.7-177.0	139.8-181.0

Body mass index was calculated as $Weight/(Height/100)^2$.
BID = twice daily, SD = standard deviation.

The primary diagnoses and durations by treatment groups are summarized in Table 4.

Table 4. Primary Diagnoses and Durations

	CP-690,550		
	5 mg BID (N = 381)	10 mg BID (N = 105)	Total (N = 486)
Rheumatoid arthritis			
Number of subjects	381	105	486
Duration since first diagnosis (years)			
Mean	7.8	6.1	7.4
Range	0.4-38.0	0.4-45.0	0.4-45.0

Duration (years) is defined from first diagnosis to Day 1 of qualifying study, any time in the qualifying study to the first day in the long-term safety study is not accounted for.
BID = twice daily.

The median duration of treatment in this study (excluding the treatment duration in the qualifying study) was 1185.0 days; duration of exposure ranged from 5 to 2016 days for all CP-690,550 treated subjects. The median duration of treatment in this study was 1813.0 days (approx. 5.0 years; range: 5 to 2016 days), 1228.0 days (approx. 3.4 years; range: 8 to 1497 days), and 620.5 days (approx. 1.7 years; range: 12 to 847 days) for subjects from Studies A3921039, A3921040, and A3921044, respectively.

Other baseline characteristics are summarized in Table 5. The qualifying study baseline data were used as baseline data.

Table 5. Other Baseline Characteristics

	CP-690,550		
	5 mg BID (N = 381)	10 mg BID (N = 105)	Total (N = 486)
HAQ-DI			
Mean	1.23	1.22	1.23
SD	0.66	0.64	0.66
ESR (mm/hr)			
Mean	50.72	47.65	50.05
SD	27.00	27.52	27.12
CRP (mg/L)			
Mean	24.14	27.43	24.85
SD	25.47	29.59	26.41
Patient Global Assessment of Arthritis (mm)			
Mean	59.19	60.30	59.43
SD	22.90	21.05	22.50
Physician Global Assessment of Arthritis (mm)			
Mean	61.64	65.54	62.48
SD	18.17	16.92	17.96
Patient Assessment of Arthritis Pain (mm)			
Mean	58.33	61.23	58.96
SD	23.76	20.51	23.11
Tender Joint Count			
Mean	16.10	17.01	16.29
SD	9.75	10.27	9.86
Swollen Joint Count			
Mean	13.42	14.30	13.61
SD	7.98	8.55	8.11
DAS28-4 (ESR)			
Mean	6.03	6.06	6.04
SD	0.93	1.02	0.95
DAS28-3 (CRP)			
Mean	5.04	5.17	5.07
SD	0.87	1.03	0.91

The qualifying study baseline data were used as baseline data.
BID = twice daily, CRP = C-reactive protein, DAS = disease activity score, ESR = erythrocyte sedimentation rate, HAQ-DI = Health Assessment Questionnaire-Disability Index, SD = standard deviation.

Efficacy Results: The ACR20, ACR50, and ACR70 response rates are shown in Table 6.

Table 6. ACR20, ACR 50, and ACR70 Response Rates

	CP-690,550								
	5 mg BID			10 mg BID			Total		
	N	n	%	N	n	%	N	n	%
ACR20									
Week 2	378	303	80.2	105	72	68.6	483	375	77.6
Week 4	373	325	87.1	105	74	70.5	478	399	83.5
Week 8	371	334	90.0	105	76	72.4	476	410	86.1
Week 12	370	340	91.9	105	81	77.1	475	421	88.6
Week 24	357	324	90.8	104	89	85.6	461	413	89.6
Week 36	339	319	94.1	102	89	87.3	441	408	92.5
Week 48	331	310	93.7	102	90	88.2	433	400	92.4
Week 60	323	298	92.3	102	92	90.2	425	390	91.8
Week 72	315	291	92.4	99	86	86.9	414	377	91.1
Week 84	309	288	93.2	92	80	87.0	401	368	91.8
Week 96	281	259	92.2	87	80	92.0	368	339	92.1
Week 108	259	238	91.9	84	73	86.9	343	311	90.7
Week 120	242	221	91.3	80	71	88.8	322	292	90.7
Week 132	232	214	92.2	79	67	84.8	311	281	90.4
Week 144	224	201	89.7	76	66	86.8	300	267	89.0
Week 156	219	200	91.3	73	62	84.9	292	262	89.7
Week 168	213	197	92.5	70	58	82.9	283	255	90.1
Week 180	180	167	92.8	57	49	86.0	237	216	91.1
Week 192	138	128	92.8	42	36	85.7	180	164	91.1
Week 204	109	101	92.7	30	27	90.0	139	128	92.1
Week 216	76	73	96.1	13	11	84.6	89	84	94.4
Week 228	68	62	91.2	5	4	80.0	73	66	90.4
Week 240	65	61	93.8	5	4	80.0	70	65	92.9
Week 252	65	60	92.3	5	4	80.0	70	64	91.4
Week 264	59	53	89.8	5	4	80.0	64	57	89.1
Week 276	22	21	95.5	1	1	100.0	23	22	95.7
Week 288	3	3	100.0	0	0	-	3	3	100.0
ACR50									
Week 2	378	225	59.5	105	38	36.2	483	263	54.5
Week 4	373	238	63.8	105	37	35.2	478	275	57.5
Week 8	371	261	70.4	105	50	47.6	476	311	65.3
Week 12	370	262	70.8	105	49	46.7	475	311	65.5
Week 24	357	272	76.2	104	65	62.5	461	337	73.1
Week 36	339	262	77.3	102	58	56.9	441	320	72.6
Week 48	331	256	77.3	102	61	59.8	433	317	73.2
Week 60	323	249	77.1	102	68	66.7	425	317	74.6
Week 72	315	245	77.8	99	74	74.7	414	319	77.1
Week 84	309	243	78.6	92	59	64.1	401	302	75.3
Week 96	281	220	78.3	87	53	60.9	368	273	74.2
Week 108	259	207	79.9	84	61	72.6	343	268	78.1
Week 120	242	185	76.4	80	55	68.8	322	240	74.5
Week 132	232	179	77.2	79	57	72.2	311	236	75.9
Week 144	224	175	78.1	76	53	69.7	300	228	76.0
Week 156	219	174	79.5	73	48	65.8	292	222	76.0
Week 168	213	169	79.3	70	47	67.1	283	216	76.3
Week 180	180	148	82.2	57	41	71.9	237	189	79.7
Week 192	138	110	79.7	42	26	61.9	180	136	75.6
Week 204	109	92	84.4	30	24	80.0	139	116	83.5
Week 216	76	66	86.8	13	7	53.8	89	73	82.0

Table 6. ACR20, ACR 50, and ACR70 Response Rates

	CP-690,550								
	5 mg BID			10 mg BID			Total		
	N	n	%	N	n	%	N	n	%
Week 228	68	52	76.5	5	4	80.0	73	56	76.7
Week 240	65	54	83.1	5	2	40.0	70	56	80.0
Week 252	65	56	86.2	5	2	40.0	70	58	82.9
Week 264	59	50	84.7	5	2	40.0	64	52	81.3
Week 276	22	18	81.8	1	1	100.0	23	19	82.6
Week 288	3	3	100.0	0	0	-	3	3	100.0
ACR70									
Week 2	378	140	37.0	105	20	19.0	483	160	33.1
Week 4	373	167	44.8	105	21	20.0	478	188	39.3
Week 8	371	177	47.7	105	22	21.0	476	199	41.8
Week 12	370	185	50.0	105	17	16.2	475	202	42.5
Week 24	357	193	54.1	104	29	27.9	461	222	48.2
Week 36	339	192	56.6	102	25	24.5	441	217	49.2
Week 48	331	198	59.8	102	35	34.3	433	233	53.8
Week 60	323	191	59.1	102	38	37.3	425	229	53.9
Week 72	315	195	61.9	99	38	38.4	414	233	56.3
Week 84	309	186	60.2	92	33	35.9	401	219	54.6
Week 96	281	167	59.4	87	37	42.5	368	204	55.4
Week 108	259	157	60.6	84	36	42.9	343	193	56.3
Week 120	242	150	62.0	80	30	37.5	322	180	55.9
Week 132	232	141	60.8	79	32	40.5	311	173	55.6
Week 144	224	137	61.2	76	27	35.5	300	164	54.7
Week 156	219	135	61.6	73	30	41.1	292	165	56.5
Week 168	213	134	62.9	70	29	41.4	283	163	57.6
Week 180	180	115	63.9	57	27	47.4	237	142	59.9
Week 192	138	88	63.8	42	18	42.9	180	106	58.9
Week 204	109	68	62.4	30	17	56.7	139	85	61.2
Week 216	76	53	69.7	13	4	30.8	89	57	64.0
Week 228	68	43	63.2	5	1	20.0	73	44	60.3
Week 240	65	45	69.2	5	1	20.0	70	46	65.7
Week 252	65	48	73.8	5	1	20.0	70	49	70.0
Week 264	59	42	71.2	5	1	20.0	64	43	67.2
Week 276	22	15	68.2	1	0	-	23	15	65.2
Week 288	3	2	66.7	0	0	-	3	2	66.7

ACR = American College of Rheumatology, BID = twice daily.

The mean changes from baseline in HAQ-DI are presented in Table 7.

Table 7. Mean Change From Baseline in HAQ-DI

	CP-690,550								
	5 mg BID			10 mg BID			Total		
	N	Mean	SE	N	Mean	SE	N	Mean	SE
Week 2	378	-0.55	0.03	105	-0.44	0.05	483	-0.53	0.03
Week 4	372	-0.61	0.03	105	-0.45	0.05	477	-0.57	0.03
Week 8	371	-0.66	0.03	105	-0.49	0.05	476	-0.62	0.03
Week 12	370	-0.66	0.03	105	-0.51	0.05	475	-0.63	0.03
Week 24	357	-0.69	0.03	104	-0.55	0.05	461	-0.65	0.03
Week 36	339	-0.70	0.03	102	-0.54	0.05	441	-0.66	0.03
Week 48	331	-0.70	0.03	102	-0.62	0.05	433	-0.68	0.03
Week 60	323	-0.71	0.03	102	-0.57	0.05	425	-0.67	0.03
Week 72	315	-0.72	0.03	99	-0.60	0.05	414	-0.69	0.03
Week 84	309	-0.72	0.04	92	-0.61	0.05	401	-0.69	0.03
Week 96	281	-0.72	0.04	87	-0.61	0.06	368	-0.69	0.03
Week 108	259	-0.70	0.04	84	-0.64	0.06	343	-0.69	0.03
Week 120	242	-0.70	0.04	80	-0.63	0.06	322	-0.68	0.03
Week 132	232	-0.70	0.04	79	-0.64	0.06	311	-0.68	0.03
Week 144	224	-0.67	0.04	76	-0.59	0.07	300	-0.65	0.04
Week 156	219	-0.68	0.04	72	-0.62	0.06	291	-0.66	0.03
Week 168	213	-0.68	0.04	70	-0.57	0.07	283	-0.65	0.04
Week 180	180	-0.70	0.05	57	-0.63	0.08	237	-0.68	0.04
Week 192	138	-0.69	0.05	42	-0.61	0.09	180	-0.67	0.05
Week 204	109	-0.67	0.06	30	-0.67	0.09	139	-0.67	0.05
Week 216	76	-0.62	0.06	13	-0.42	0.09	89	-0.59	0.05
Week 228	68	-0.62	0.06	5	-0.25	0.10	73	-0.59	0.06
Week 240	65	-0.66	0.06	5	-0.33	0.14	70	-0.64	0.06
Week 252	65	-0.68	0.07	5	-0.25	0.12	70	-0.65	0.06
Week 264	59	-0.65	0.07	5	-0.23	0.07	64	-0.62	0.07
Week 276	22	-0.83	0.11	1	-0.63	-	23	-0.82	0.11
Week 288	3	-0.96	0.37	0	-	-	3	-0.96	0.37

The qualifying study baseline data were used as baseline data.
BID = twice daily, HAQ-DI = Health Assessment Questionnaire-Disability Index, SE = standard error.

The mean changes from baseline in DAS28-4 (ESR) are presented in Table 8.

Table 8. Mean Change From Baseline in DAS28-4 (ESR)

	CP-690,550								
	5 mg BID			10 mg BID			Total		
	N	Mean	SE	N	Mean	SE	N	Mean	SE
Week 2	378	-2.60	0.07	105	-1.94	0.13	483	-2.45	0.06
Week 4	372	-2.77	0.07	105	-1.95	0.13	477	-2.59	0.06
Week 8	371	-2.95	0.06	104	-2.14	0.12	475	-2.77	0.06
Week 12	370	-3.01	0.06	105	-2.08	0.12	475	-2.81	0.06
Week 24	357	-3.12	0.06	104	-2.42	0.12	461	-2.96	0.06
Week 36	339	-3.18	0.07	102	-2.54	0.13	441	-3.03	0.06
Week 48	331	-3.20	0.07	102	-2.72	0.13	433	-3.08	0.06
Week 60	323	-3.25	0.07	101	-2.80	0.12	424	-3.15	0.06
Week 72	315	-3.20	0.07	99	-2.83	0.12	414	-3.11	0.06
Week 84	309	-3.26	0.07	92	-2.86	0.14	401	-3.17	0.06
Week 96	281	-3.21	0.07	87	-2.87	0.14	368	-3.13	0.07
Week 108	259	-3.22	0.08	83	-2.83	0.15	342	-3.12	0.07
Week 120	242	-3.24	0.08	79	-2.78	0.14	321	-3.12	0.07
Week 132	232	-3.14	0.08	79	-2.84	0.15	311	-3.07	0.07
Week 144	224	-3.17	0.09	76	-2.84	0.16	300	-3.09	0.08
Week 156	218	-3.08	0.09	72	-2.84	0.16	290	-3.02	0.08
Week 168	213	-3.16	0.09	70	-2.87	0.17	283	-3.09	0.08
Week 180	178	-3.21	0.10	56	-3.06	0.19	234	-3.18	0.09
Week 192	138	-3.17	0.11	42	-3.07	0.19	180	-3.15	0.09
Week 204	109	-3.24	0.12	30	-3.35	0.25	139	-3.26	0.11
Week 216	76	-3.20	0.13	13	-2.44	0.44	89	-3.09	0.13
Week 228	68	-3.08	0.17	5	-2.25	0.58	73	-3.02	0.16
Week 240	65	-3.22	0.15	5	-2.61	0.70	70	-3.17	0.14
Week 252	65	-3.33	0.15	5	-1.81	0.51	70	-3.23	0.15
Week 264	59	-3.32	0.15	5	-2.09	0.45	64	-3.23	0.14
Week 276	21	-3.34	0.25	1	-2.15	-	22	-3.29	1.15
Week 288	3	-2.95	0.51	0	-	-	3	-2.95	0.51

The qualifying study baseline data were used as baseline data.
BID = twice daily, DAS = disease activity score, ESR = erythrocyte sedimentation rate, SE = standard error.

The mean changes from baseline in DAS28-3 (CRP) are presented in Table 9.

Table 9. Mean Change From Baseline in DAS28-3 (CRP)

	CP-690,550								
	5 mg BID			10 mg BID			Total		
	N	Mean	SE	N	Mean	SE	N	Mean	SE
Week 2	378	-2.44	0.06	105	-1.90	0.12	483	-2.32	0.06
Week 4	372	-2.55	0.06	105	-1.90	0.12	477	-2.41	0.06
Week 8	371	-2.68	0.06	105	-2.06	0.11	476	-2.55	0.05
Week 12	370	-2.75	0.06	105	-1.97	0.11	475	-2.57	0.05
Week 24	357	-2.85	0.06	104	-2.29	0.11	461	-2.72	0.05
Week 36	337	-2.92	0.06	102	-2.45	0.11	439	-2.81	0.05
Week 48	331	-2.92	0.06	102	-2.58	0.12	433	-2.84	0.05
Week 60	322	-2.92	0.06	102	-2.60	0.11	424	-2.85	0.05
Week 72	315	-2.93	0.06	99	-2.61	0.11	414	-2.86	0.05
Week 84	309	-2.98	0.06	92	-2.70	0.12	401	-2.92	0.06
Week 96	281	-2.95	0.07	87	-2.69	0.13	368	-2.88	0.06
Week 108	259	-2.93	0.07	83	-2.64	0.13	342	-2.86	0.06
Week 120	242	-2.97	0.07	80	-2.60	0.13	322	-2.88	0.06
Week 132	231	-2.89	0.07	79	-2.66	0.13	310	-2.83	0.06
Week 144	224	-2.90	0.08	76	-2.68	0.14	300	-2.85	0.07
Week 156	219	-2.84	0.08	72	-2.70	0.14	291	-2.81	0.07
Week 168	213	-2.90	0.08	70	-2.68	0.15	283	-2.84	0.07
Week 180	180	-2.92	0.09	57	-2.80	0.17	237	-2.89	0.08
Week 192	138	-2.93	0.09	42	-2.84	0.16	180	-2.91	0.08
Week 204	109	-2.95	0.11	30	-3.05	0.22	139	-2.97	0.10
Week 216	76	-2.94	0.12	13	-2.46	0.34	89	-2.87	0.12
Week 228	68	-2.84	0.17	5	-2.38	0.44	73	-2.81	0.16
Week 240	65	-2.97	0.13	5	-2.36	0.57	70	-2.92	0.13
Week 252	65	-3.09	0.14	5	-1.89	0.42	70	-3.00	0.14
Week 264	58	-3.13	0.15	5	-1.86	0.30	63	-3.03	0.14
Week 276	22	-3.24	0.24	1	-1.50	-	23	-3.16	0.24
Week 288	3	-2.67	0.27	0	-	-	3	-2.67	0.27

The qualifying study baseline data were used as baseline data.
BID = twice daily, CRP = C-reactive protein, DAS = disease activity score, SE = standard error.

The proportion of the subjects with DAS28-4 (ESR) score ≤3.2 at Week 12 was 52.4% in the total study group; that increased with treatment duration although evaluable subjects decreased at later time points. The proportion of the subjects with DAS28-4 (ESR) score <2.6 at Week 12 was 33.7% in the total study group; that was increased with treatment duration although evaluable subjects decreased at later time points. Similar trend was observed in DAS28-3 (CRP) as well as DAS28-4 (ESR).

The mean changes from baseline in the patient global assessment of arthritis are presented in Table 10.

Table 10. Mean Change From Baseline in Patient Global Assessment of Arthritis (mm)

	CP-690,550								
	5 mg BID			10 mg BID			Total		
	N	Mean	SE	N	Mean	SE	N	Mean	SE
Week 2	378	-34.52	1.38	105	-25.38	2.43	483	-32.54	1.21
Week 4	372	-37.81	1.36	105	-25.34	2.61	477	-35.06	1.23
Week 8	371	-39.61	1.35	105	-28.86	2.31	476	-37.24	1.19
Week 12	370	-39.31	1.38	105	-27.33	2.23	475	-36.67	1.20
Week 24	357	-40.67	1.39	104	-30.75	2.53	461	-38.43	1.24
Week 36	339	-41.70	1.42	102	-29.95	2.63	441	-38.98	1.27
Week 48	331	-41.03	1.46	102	-32.48	2.56	433	-39.02	1.28
Week 60	323	-41.79	1.44	102	-34.33	2.42	425	-40.00	1.25
Week 72	315	-41.30	1.53	99	-35.38	2.31	414	-39.88	1.29
Week 84	309	-42.29	1.53	92	-35.12	2.63	401	-40.65	1.33
Week 96	281	-41.90	1.62	87	-34.98	2.88	368	-40.27	1.42
Week 108	259	-42.47	1.67	84	-34.95	2.98	343	-40.63	1.46
Week 120	242	-42.97	1.71	80	-35.00	3.05	322	-40.99	1.50
Week 132	232	-42.87	1.73	79	-35.05	3.13	311	-40.88	1.52
Week 144	224	-42.48	1.77	76	-33.78	3.22	300	-40.27	1.57
Week 156	219	-42.72	1.71	72	-32.64	3.13	291	-40.22	1.52
Week 168	213	-43.00	1.72	70	-33.61	3.22	283	-40.67	1.53
Week 180	180	-43.22	1.91	57	-36.14	3.72	237	-41.52	1.71
Week 192	138	-42.05	2.10	42	-34.40	3.95	180	-40.27	1.86
Week 204	109	-42.44	2.36	30	-35.73	5.31	139	-40.99	2.18
Week 216	76	-42.04	2.87	13	-23.92	9.22	89	-39.39	2.86
Week 228	68	-37.09	2.96	5	-17.60	10.66	73	-35.75	2.89
Week 240	65	-38.91	2.98	5	-18.20	8.36	70	-37.43	2.89
Week 252	65	-40.37	2.92	5	-7.60	9.17	70	-38.03	2.95
Week 264	59	-37.32	3.69	5	-16.20	9.01	64	-35.67	3.54
Week 276	21	-35.62	6.09	1	-10.00	-	22	-34.45	5.92
Week 288	3	-41.67	7.31	0	-	-	3	-41.67	7.31

The qualifying study baseline data were used as baseline data.
BID = twice daily, SE = standard error.

The mean changes from baseline in the physician global assessment of arthritis are presented in Table 11.

Table 11. Mean Change From Baseline in Physician Global Assessment of Arthritis (mm)

	CP-690,550								
	5 mg BID			10 mg BID			Total		
	N	Mean	SE	N	Mean	SE	N	Mean	SE
Week 2	378	-42.80	1.13	105	-33.49	2.01	483	-40.78	1.00
Week 4	372	-46.06	1.08	105	-34.91	2.20	477	-43.60	0.99
Week 8	371	-47.34	1.06	105	-37.15	2.00	476	-45.09	0.95
Week 12	370	-47.78	1.09	105	-36.56	2.23	475	-45.30	1.00
Week 24	357	-48.29	1.07	104	-41.26	2.01	461	-46.70	0.95
Week 36	339	-49.28	1.09	102	-41.92	2.01	441	-47.58	0.97
Week 48	331	-49.96	1.13	102	-45.28	2.08	433	-48.86	1.00
Week 60	323	-49.89	1.14	102	-47.01	2.05	425	-49.20	1.00
Week 72	315	-50.03	1.14	99	-45.70	1.95	414	-48.99	0.99
Week 84	309	-50.61	1.16	92	-46.89	2.17	401	-49.75	1.02
Week 96	281	-49.99	1.28	87	-48.16	2.23	368	-49.55	1.11
Week 108	259	-49.62	1.33	83	-47.99	2.56	342	-49.22	1.18
Week 120	242	-49.42	1.47	80	-47.76	2.39	322	-49.01	1.26
Week 132	231	-49.99	1.41	78	-50.19	2.33	309	-50.04	1.20
Week 144	224	-50.80	1.46	76	-49.55	2.44	300	-50.49	1.25
Week 156	219	-50.68	1.39	72	-49.78	2.58	291	-50.46	1.23
Week 168	213	-51.52	1.45	70	-46.33	2.60	283	-50.23	1.27
Week 180	180	-52.20	1.51	57	-50.33	2.84	237	-51.75	1.33
Week 192	138	-51.41	1.72	42	-50.43	2.98	180	-51.18	1.49
Week 204	109	-51.10	1.73	30	-50.97	4.12	139	-51.07	1.61
Week 216	76	-50.91	2.01	13	-42.77	6.37	89	-49.72	1.96
Week 228	67	-49.57	2.37	5	-33.60	8.88	72	-48.46	2.33
Week 240	65	-49.94	2.25	5	-34.40	10.30	70	-48.83	2.25
Week 252	65	-51.78	2.17	5	-31.60	7.92	70	-50.34	2.17
Week 264	58	-52.62	2.36	5	-33.80	9.49	63	-51.13	2.36
Week 276	21	-53.05	3.92	1	-7.00	-	22	-50.95	4.29
Week 288	3	-37.67	1.33	0	-	-	3	-37.67	1.33

The qualifying study baseline data were used as baseline data.
BID = twice daily, SE = standard error.

The mean changes from baseline in patient assessment of arthritis pain are presented in Table 12.

Table 12. Mean Change From Baseline in Patient Assessment of Arthritis Pain (mm)

	CP-690,550								
	5 mg BID			10 mg BID			Total		
	N	Mean	SE	N	Mean	SE	N	Mean	SE
Week 2	378	-34.23	1.40	105	-27.98	2.39	483	-32.87	1.22
Week 4	372	-37.32	1.38	105	-27.70	2.61	477	-35.20	1.23
Week 8	371	-39.54	1.34	105	-30.69	2.32	476	-37.59	1.17
Week 12	370	-39.34	1.36	105	-29.03	2.25	475	-37.06	1.18
Week 24	357	-40.70	1.42	104	-33.60	2.50	461	-39.10	1.24
Week 36	339	-41.70	1.45	102	-32.71	2.56	441	-39.62	1.27
Week 48	331	-41.98	1.41	102	-34.39	2.52	433	-40.19	1.24
Week 60	323	-42.37	1.44	102	-36.65	2.36	425	-41.00	1.24
Week 72	315	-41.84	1.51	99	-37.41	2.28	414	-40.79	1.28
Week 84	309	-42.49	1.53	92	-37.65	2.55	401	-41.38	1.32
Week 96	281	-42.21	1.63	87	-38.21	2.87	368	-41.27	1.42
Week 108	259	-42.61	1.68	84	-37.99	2.87	343	-41.48	1.45
Week 120	242	-42.44	1.74	80	-37.45	2.92	322	-41.20	1.50
Week 132	232	-42.52	1.78	79	-37.86	3.04	311	-41.33	1.54
Week 144	224	-42.05	1.81	76	-37.07	3.09	300	-40.79	1.56
Week 156	219	-43.77	1.75	72	-36.39	2.89	291	-41.94	1.51
Week 168	213	-43.87	1.73	70	-37.96	3.24	283	-42.41	1.54
Week 180	180	-43.85	1.92	57	-40.21	3.51	237	-42.97	1.68
Week 192	138	-42.64	2.22	42	-36.67	3.93	180	-41.24	1.94
Week 204	109	-41.11	2.59	30	-38.70	5.25	139	-40.59	2.32
Week 216	76	-41.61	2.90	13	-30.38	9.30	89	-39.97	2.84
Week 228	68	-37.19	2.96	5	-28.40	12.48	73	-36.59	2.87
Week 240	65	-36.72	3.08	5	-21.20	7.85	70	-35.61	2.94
Week 252	65	-38.54	3.19	5	-21.20	10.56	70	-37.30	3.08
Week 264	59	-36.80	3.72	5	-16.60	11.91	64	-35.22	3.60
Week 276	21	-40.19	5.00	1	-44.00	-	22	-40.36	4.77
Week 288	3	-34.67	9.82	0	-	-	3	-34.67	9.82

The qualifying study baseline data were used as baseline data.
BID = twice daily, SE = standard error.

The mean changes from baseline in tender joint counts are presented in Table 13.

Table 13. Mean Change From Baseline in Tender Joint Counts

	CP-690,550								
	5 mg BID			10 mg BID			Total		
	N	Mean	SE	N	Mean	SE	N	Mean	SE
Week 2	378	-11.88	0.48	105	-10.17	0.95	483	-11.51	0.43
Week 4	373	-12.13	0.51	105	-10.46	0.90	478	-11.77	0.45
Week 8	371	-13.06	0.47	105	-10.75	0.96	476	-12.55	0.43
Week 12	370	-13.41	0.47	105	-10.74	0.97	475	-12.82	0.43
Week 24	357	-14.02	0.50	104	-12.62	0.89	461	-13.70	0.44
Week 36	339	-14.32	0.53	102	-13.05	0.94	441	-14.03	0.46
Week 48	331	-14.23	0.53	102	-13.43	0.99	433	-14.04	0.47
Week 60	323	-14.23	0.55	102	-13.67	0.94	425	-14.09	0.48
Week 72	315	-14.45	0.56	99	-14.00	0.96	414	-14.34	0.48
Week 84	309	-14.39	0.56	92	-14.04	1.11	401	-14.31	0.50
Week 96	281	-14.44	0.60	87	-13.92	1.03	368	-14.32	0.52
Week 108	259	-14.46	0.61	83	-13.66	1.14	342	-14.26	0.54
Week 120	242	-14.67	0.65	80	-13.69	1.07	322	-14.42	0.55
Week 132	232	-14.01	0.73	79	-13.30	1.33	311	-13.83	0.64
Week 144	224	-14.45	0.68	76	-13.83	1.18	300	-14.29	0.59
Week 156	219	-14.24	0.70	72	-14.15	1.20	291	-14.22	0.61
Week 168	213	-14.41	0.73	70	-14.06	1.25	283	-14.33	0.63
Week 180	180	-14.78	0.79	57	-15.18	1.46	237	-14.87	0.70
Week 192	138	-15.01	0.87	42	-14.57	1.42	180	-14.91	0.74
Week 204	109	-14.79	0.94	30	-15.67	1.93	139	-14.98	0.84
Week 216	76	-14.42	1.04	13	-11.38	2.64	89	-13.98	0.97
Week 228	68	-13.78	1.56	5	-11.60	5.46	73	-13.63	1.49
Week 240	65	-15.11	1.15	5	-10.80	4.92	70	-14.80	1.12
Week 252	65	-15.34	1.17	5	-9.60	4.55	70	-14.93	1.14
Week 264	59	-15.54	1.27	5	-9.80	3.95	64	-15.09	1.22
Week 276	22	-17.55	2.55	1	-4.00	-	23	-16.96	2.51
Week 288	3	-8.67	1.20	0	-	-	3	-8.67	1.20

The qualifying study baseline data were used as baseline data.
BID = twice daily, SE = standard error.

The mean changes from baseline in swollen joint counts are presented in Table 14.

Table 14. Mean Change From Baseline in Swollen Joint Counts

	CP-690,550								
	5 mg BID			10 mg BID			Total		
	N	Mean	SE	N	Mean	SE	N	Mean	SE
Week 2	378	-9.67	0.38	105	-8.69	0.74	483	-9.46	0.34
Week 4	373	-10.12	0.42	105	-8.54	0.75	478	-9.78	0.37
Week 8	371	-10.90	0.39	105	-9.31	0.73	476	-10.55	0.35
Week 12	370	-11.18	0.40	105	-9.21	0.67	475	-10.74	0.35
Week 24	357	-11.33	0.40	104	-10.46	0.72	461	-11.13	0.35
Week 36	339	-11.62	0.43	102	-10.75	0.73	441	-11.41	0.37
Week 48	331	-11.76	0.44	102	-11.11	0.74	433	-11.61	0.38
Week 60	323	-11.83	0.44	102	-10.97	0.76	425	-11.62	0.38
Week 72	315	-12.00	0.46	99	-11.38	0.80	414	-11.85	0.40
Week 84	309	-12.08	0.47	92	-11.72	0.88	401	-12.00	0.41
Week 96	281	-11.97	0.50	87	-11.54	0.84	368	-11.87	0.43
Week 108	259	-11.94	0.52	83	-11.60	0.91	342	-11.86	0.45
Week 120	242	-12.09	0.56	80	-11.24	0.87	322	-11.88	0.47
Week 132	232	-11.69	0.64	79	-11.15	1.16	311	-11.55	0.56
Week 144	224	-11.90	0.61	76	-11.74	0.94	300	-11.86	0.51
Week 156	219	-12.07	0.61	72	-11.86	1.04	291	-12.02	0.52
Week 168	213	-12.17	0.62	70	-11.67	1.05	283	-12.05	0.54
Week 180	180	-12.43	0.70	57	-12.26	1.24	237	-12.39	0.61
Week 192	138	-12.36	0.79	42	-12.48	1.47	180	-12.38	0.69
Week 204	109	-12.35	0.82	30	-12.50	1.89	139	-12.38	0.76
Week 216	76	-12.34	0.99	13	-9.00	2.35	89	-11.85	0.91
Week 228	68	-11.74	1.47	5	-11.00	5.09	73	-11.68	1.41
Week 240	65	-13.09	1.12	5	-11.40	5.48	70	-12.97	1.10
Week 252	65	-13.20	1.15	5	-10.60	4.70	70	-13.01	1.11
Week 264	59	-13.58	1.24	5	-10.00	4.11	64	-13.30	1.19
Week 276	22	-15.32	2.53	1	-6.00	-	23	-14.91	2.46
Week 288	3	-8.33	0.88	0	-	-	3	-8.33	0.88

The qualifying study baseline data were used as baseline data.
BID = twice daily, SE = standard error.

The mean changes from baseline in SF-36 health survey domain scores (physical function, role physical, bodily pain, general health, vitality, social function, role emotional, and mental health) are presented in Table 15. Scores can range from 0 to 100, with higher scores indicating better outcomes.

Table 15. Mean Change From Baseline in SF-36 Domain Scores

	CP-690,550								
	5 mg BID			10 mg BID			Total		
	N	Mean	SE	N	Mean	SE	N	Mean	SE
Physical Functioning									
Week 12	370	7.87	0.45	105	5.94	0.76	475	7.45	0.39
Week 24	357	8.67	0.46	104	6.12	1.01	461	8.10	0.42
Week 48	331	9.06	0.48	102	6.84	1.05	433	8.54	0.45
Week 72	315	9.10	0.51	99	7.61	0.93	414	8.74	0.45
Week 96	281	9.11	0.55	87	8.26	0.88	368	8.91	0.47
Week 120	242	9.12	0.57	80	8.34	1.09	322	8.92	0.51
Week 144	224	8.85	0.66	76	7.57	1.18	300	8.53	0.57
Week 168	213	9.01	0.68	70	7.16	1.36	283	8.55	0.61
Week 192	138	9.43	0.78	42	8.09	1.25	180	9.12	0.66
Week 216	76	8.78	0.98	13	5.04	2.27	89	8.23	0.91
Week 240	65	8.91	1.00	5	3.27	1.90	70	8.51	0.95
Week 264	59	8.85	1.08	5	1.64	1.98	64	8.28	1.03
Week 288	3	10.23	1.18	0	-	-	3	10.23	1.18
Role Physical									
Week 12	370	7.31	0.57	105	5.48	1.00	475	6.90	0.50
Week 24	357	8.21	0.59	104	6.29	1.06	461	7.77	0.51
Week 48	331	8.38	0.64	102	7.77	0.92	433	8.23	0.53
Week 72	315	7.23	0.67	99	7.47	1.08	414	7.29	0.57
Week 96	281	7.24	0.70	87	8.15	1.16	368	7.46	0.60
Week 120	242	7.69	0.75	80	6.77	1.10	322	7.46	0.63
Week 144	224	7.21	0.80	76	6.56	1.23	300	7.05	0.67
Week 168	213	7.38	0.77	70	5.42	1.41	283	6.90	0.68
Week 192	138	6.59	1.01	42	6.70	1.57	180	6.61	0.86
Week 216	76	6.53	1.37	13	4.59	2.53	89	6.25	1.22
Week 240	65	6.13	1.56	5	-0.48	2.86	70	5.66	1.48
Week 264	59	6.15	1.58	5	0.95	2.68	64	5.74	1.48
Week 288	3	22.27	5.22	0	-	-	3	22.27	5.22
Bodily Pain									
Week 12	370	11.04	0.48	105	8.13	0.77	475	10.40	0.41
Week 24	357	11.87	0.50	104	9.63	0.79	461	11.36	0.43
Week 48	331	12.19	0.53	102	10.65	0.75	433	11.83	0.44
Week 72	315	11.96	0.56	99	9.92	0.81	414	11.47	0.47
Week 96	281	11.35	0.59	87	11.60	1.04	368	11.41	0.51
Week 120	242	11.98	0.62	80	10.42	1.08	322	11.60	0.54
Week 144	224	11.51	0.68	76	11.15	1.04	300	11.42	0.57
Week 168	213	11.82	0.65	70	11.07	1.11	283	11.63	0.56
Week 192	138	11.19	0.85	42	11.43	1.57	180	11.25	0.75
Week 216	76	12.43	1.03	13	8.52	2.37	89	11.86	0.95
Week 240	65	11.34	1.04	5	5.25	2.63	70	10.90	0.99
Week 264	59	11.27	1.28	5	4.50	2.87	64	10.74	1.22
Week 288	3	7.08	5.60	0	-	-	3	7.08	5.60
General Health									
Week 12	370	6.07	0.38	105	4.24	0.70	475	5.67	0.34
Week 24	357	6.38	0.39	104	5.00	0.58	461	6.07	0.33
Week 48	331	6.40	0.40	102	5.20	0.67	433	6.12	0.34
Week 72	315	6.29	0.42	99	5.35	0.63	414	6.06	0.35
Week 96	281	6.00	0.45	87	4.82	0.73	368	5.72	0.38
Week 120	242	5.86	0.49	80	5.36	0.82	322	5.74	0.42
Week 144	224	5.37	0.54	76	4.38	0.94	300	5.12	0.47

Table 15. Mean Change From Baseline in SF-36 Domain Scores

	CP-690,550								
	5 mg BID			10 mg BID			Total		
	N	Mean	SE	N	Mean	SE	N	Mean	SE
Week 168	213	5.82	0.53	70	3.93	0.87	283	5.35	0.46
Week 192	138	4.72	0.61	42	4.10	1.05	180	4.57	0.53
Week 216	76	3.73	0.87	13	1.59	1.31	89	3.42	0.77
Week 240	65	4.39	0.96	5	-1.50	1.90	70	3.97	0.92
Week 264	59	4.12	1.01	5	-1.03	2.17	64	3.72	0.96
Week 288	3	-0.94	4.23	0	-	-	3	-0.94	4.23
Vitality									
Week 12	370	7.37	0.59	105	6.61	0.90	475	7.20	0.50
Week 24	357	7.24	0.58	104	6.25	0.97	461	7.02	0.50
Week 48	331	6.83	0.58	102	7.22	0.89	433	6.92	0.49
Week 72	315	7.02	0.61	99	6.44	0.98	414	6.88	0.52
Week 96	281	6.78	0.61	87	6.19	1.11	368	6.64	0.54
Week 120	242	6.49	0.70	80	6.96	1.26	322	6.61	0.61
Week 144	224	6.27	0.75	76	5.51	1.15	300	6.08	0.63
Week 168	213	6.58	0.72	70	4.75	1.27	283	6.12	0.63
Week 192	138	5.40	0.92	42	5.70	1.62	180	5.47	0.80
Week 216	76	5.04	1.18	13	5.30	2.47	89	5.08	1.07
Week 240	65	5.11	1.21	5	-0.60	3.05	70	4.70	1.15
Week 264	59	4.72	1.17	5	-1.80	3.36	64	4.21	1.13
Week 288	3	14.97	8.64	0	-	-	3	14.97	8.64
Social Functioning									
Week 12	370	4.99	0.60	105	5.17	1.09	475	5.03	0.52
Week 24	357	5.57	0.62	104	4.96	1.25	461	5.44	0.56
Week 48	331	5.28	0.64	102	5.27	1.14	433	5.28	0.55
Week 72	315	4.81	0.64	99	4.78	1.31	414	4.81	0.58
Week 96	281	4.88	0.67	87	6.43	1.19	368	5.25	0.58
Week 120	242	5.20	0.76	80	5.98	1.11	322	5.39	0.63
Week 144	224	5.23	0.77	76	3.33	1.39	300	4.75	0.67
Week 168	213	4.72	0.79	70	3.84	1.43	283	4.50	0.69
Week 192	138	4.56	0.96	42	5.63	1.36	180	4.81	0.80
Week 216	76	4.53	1.23	13	3.31	2.48	89	4.35	1.10
Week 240	65	4.88	1.41	5	0.00	0.00	70	4.53	1.32
Week 264	59	4.47	1.45	5	-2.15	2.15	64	3.95	1.37
Week 288	3	14.34	9.49	0	-	-	3	14.34	9.49
Role Emotional									
Week 12	370	6.65	0.65	105	4.98	1.19	475	6.28	0.57
Week 24	357	6.88	0.73	104	4.40	1.41	461	6.32	0.65
Week 48	331	7.26	0.75	102	5.49	1.29	433	6.85	0.65
Week 72	315	6.02	0.78	99	5.54	1.28	414	5.91	0.67
Week 96	281	6.04	0.79	87	5.96	1.43	368	6.02	0.69
Week 120	242	5.68	0.90	80	3.98	1.40	322	5.26	0.76
Week 144	224	5.39	0.96	76	3.74	1.56	300	4.97	0.82
Week 168	213	5.90	0.89	70	4.43	1.49	283	5.54	0.76
Week 192	138	4.31	1.23	42	4.42	1.91	180	4.33	1.04
Week 216	76	4.33	1.55	13	3.49	2.76	89	4.21	1.38
Week 240	65	4.72	1.66	5	-0.76	4.22	70	4.33	1.58
Week 264	59	5.07	1.74	5	-0.76	4.22	64	4.61	1.64
Week 288	3	22.71	5.78	0	-	-	3	22.71	5.78
Mental									
Week 12	370	6.27	0.63	105	5.38	1.04	475	6.08	0.54

Table 15. Mean Change From Baseline in SF-36 Domain Scores

	CP-690,550								
	5 mg BID			10 mg BID			Total		
	N	Mean	SE	N	Mean	SE	N	Mean	SE
Week 24	357	6.22	0.65	104	3.84	1.17	461	5.69	0.57
Week 48	331	5.73	0.64	102	5.35	1.02	433	5.64	0.54
Week 72	315	4.77	0.70	99	5.48	1.04	414	4.94	0.59
Week 96	281	5.23	0.68	87	5.89	1.14	368	5.38	0.59
Week 120	242	5.56	0.77	80	5.26	1.31	322	5.49	0.67
Week 144	224	5.10	0.84	76	4.37	1.34	300	4.91	0.71
Week 168	213	5.12	0.76	70	3.76	1.29	283	4.79	0.66
Week 192	138	3.77	0.93	42	5.21	1.75	180	4.11	0.82
Week 216	76	2.66	1.21	13	4.26	3.04	89	2.89	1.12
Week 240	65	3.75	1.20	5	3.32	2.04	70	3.72	1.12
Week 264	59	4.18	1.34	5	0.00	1.75	64	3.85	1.25
Week 288	3	14.78	7.56	0	-	-	3	14.78	7.56

The qualifying study baseline data were used as baseline data.
BID = twice daily, SE = standard error, SF-36 = Short Form-36.

The mean changes from baseline in SF-36 health survey component scores (physical and mental) are presented in Table 16.

Table 16. Mean Change From Baseline in SF-36 Component Scores

	CP-690,550								
	5 mg BID			10 mg BID			Total		
	N	Mean	SE	N	Mean	SE	N	Mean	SE
Physical									
Week 12	370	8.44	0.39	105	6.09	0.68	475	7.92	0.34
Week 24	357	9.39	0.38	104	7.56	0.70	461	8.98	0.34
Week 48	331	9.75	0.43	102	8.24	0.72	433	9.39	0.37
Week 72	315	9.72	0.43	99	8.21	0.76	414	9.36	0.37
Week 96	281	9.35	0.48	87	8.93	0.77	368	9.25	0.41
Week 120	242	9.66	0.49	80	8.79	0.92	322	9.45	0.43
Week 144	224	9.26	0.54	76	8.60	0.92	300	9.09	0.47
Week 168	213	9.51	0.54	70	7.86	1.03	283	9.10	0.48
Week 192	138	9.51	0.65	42	8.56	1.18	180	9.29	0.57
Week 216	76	9.59	0.88	13	5.37	1.93	89	8.97	0.82
Week 240	65	9.00	0.93	5	1.91	2.87	70	8.49	0.91
Week 264	59	8.72	1.03	5	2.31	2.27	64	8.22	0.99
Week 288	3	6.87	1.88	0	-	-	3	6.87	1.88
Mental									
Week 12	370	5.13	0.63	105	4.82	1.01	475	5.06	0.54
Week 24	357	4.95	0.67	104	3.38	1.26	461	4.60	0.59
Week 48	331	4.56	0.66	102	4.45	1.06	433	4.54	0.56
Week 72	315	3.63	0.69	99	4.15	1.14	414	3.75	0.59
Week 96	281	3.88	0.68	87	4.53	1.25	368	4.03	0.60
Week 120	242	3.79	0.80	80	3.68	1.37	322	3.76	0.69
Week 144	224	3.57	0.84	76	2.24	1.40	300	3.23	0.72
Week 168	213	3.64	0.80	70	2.45	1.41	283	3.35	0.70
Week 192	138	2.05	0.99	42	3.44	1.80	180	2.38	0.86
Week 216	76	1.49	1.29	13	3.14	3.04	89	1.73	1.18
Week 240	65	2.41	1.27	5	-0.04	1.81	70	2.23	1.19
Week 264	59	2.59	1.42	5	-2.25	1.41	64	2.21	1.32
Week 288	3	18.64	4.01	0	-	-	3	18.64	4.01

The qualifying study baseline data were used as baseline data.
BID = twice daily, SE = standard error, SF-36 = Short Form-36.

The mean changes from Month 24 (the final visit) in A3921044 in modified total Sharp scores are presented in Table 17.

Table 17. Change From Month 24 in Study A3921044 in mTSS

Study	Visit	CP-690,550											
		5 mg BID				10 mg BID				Total			
		N	Mean	SE	Median	N	Mean	SE	Median	N	Mean	SE	Median
A3921041	Week 24	69	0.17	0.09	0.00	7	0.50	0.22	0.50	76	0.20	0.08	0.00
	Week 48	64	0.27	0.17	0.00	7	1.75	1.16	0.50	71	0.41	0.19	0.00
	Week 96	39	0.40	0.21	0.00	1	1.00	-	1.00	40	0.42	0.20	0.00

BID = twice daily, mTSS = modified Total Sharp Score, SE = standard error.

The rates of "not progressing" in modified total Sharp scores from Month 24 in Study A3921044 are presented in Table 18.

Table 18. Proportion of "Not Progressing" in mTSS from Month 24 in Study A3921044

Study	Visit	CP-690,550								
		5 mg BID			10 mg BID			Total		
		N	n	%	N	n	%	N	n	%
A3921041	Week 24	69	62	89.86	7	5	71.43	76	67	88.16
	Week 48	64	58	90.63	7	5	71.43	71	63	88.73
	Week 96	39	32	82.05	1	0	0.00	40	32	80.00

No radiographic progression was defined as an increase from Month 24 of 0.5 unit or less in mTSS.
BID = twice daily, mTSS = modified Total Sharp Score.

The mean changes from Month 24 in Study A3921044 in erosion scores are presented in Table 19.

Table 19. Mean Change From Month 24 in Study A3921044 in Erosion Scores

Study	Visit	CP-690,550											
		5 mg BID				10 mg BID				Total			
		N	Mean	SE	Median	N	Mean	SE	Median	N	Mean	SE	Median
A3921041	Week 24	69	0.03	0.04	0.00	7	0.36	0.24	0.00	76	0.06	0.05	0.00
	Week 48	64	-0.04	0.05	0.00	7	0.96	0.96	0.00	71	0.06	0.10	0.00
	Week 96	39	0.05	0.08	0.00	1	0.00	-	0.00	40	0.05	0.07	0.00

BID = twice daily, SE = standard error.

The mean changes from Month 24 in Study A3921044 in joint space narrowing (JSN) are presented in Table 20.

Table 20. Mean Change From Month 24 in Study A3921044 in JSN

Study	Visit	CP-690,550											
		5 mg BID				10 mg BID				Total			
		N	Mean	SE	Median	N	Mean	SE	Median	N	Mean	SE	Median
A3921041	Week 24	69	0.14	0.07	0.00	7	0.14	0.09	0.00	76	0.14	0.07	0.00
	Week 48	64	0.30	0.15	0.00	7	0.79	0.42	0.50	71	0.35	0.14	0.00
	Week 96	39	0.35	0.16	0.00	1	1.00	-	1.00	40	0.37	0.16	0.00

BID = twice daily, JSN = joint space narrowing, SE = standard error.

Safety Results:

Treatment-emergent all causality and treatment related adverse events (not including serious adverse events) by system organ class (SOC) and preferred term that occurred in ≥5% of subjects in any treatment group are summarized in Table 21.

Table 21. Treatment-Emergent All Causality and Treatment Related Adverse Events (not Including Serious Adverse Events) Occurring at an Incidence of 5% or Greater in Any Treatment Group by Preferred Term

	CP-690,550					
	All Causalities			Treatment Related		
	5 mg BID n (%)	10 mg BID n (%)	Total n (%)	5 mg BID n (%)	10 mg BID n (%)	Total n (%)
Number (%) of subjects:						
Evaluable for adverse events	381	105	486	381	105	486
With adverse events occurring at an incidence of 5% or greater in any treatment group	345 (90.6)	101 (96.2)	446 (91.8)	315 (82.7)	97 (92.4)	412 (84.8)
System Organ Class and Preferred Term (MedDRA v.16.1)						
Blood and lymphatic system disorders						
Anaemia	14 (3.7)	11 (10.5)	25 (5.1)	11 (2.9)	9 (8.6)	20 (4.1)
Eye disorders						
Conjunctivitis	17 (4.5)	6 (5.7)	23 (4.7)	-	-	-
Gastrointestinal disorders						
Abdominal pain upper	13 (3.4)	6 (5.7)	19 (3.9)	-	-	-
Constipation	34 (8.9)	9 (8.6)	43 (8.8)	19 (5.0)	7 (6.7)	26 (5.3)
Dental caries	39 (10.2)	15 (14.3)	54 (11.1)	24 (6.3)	10 (9.5)	34 (7.0)
Diarrhoea	28 (7.3)	5 (4.8)	33 (6.8)	21 (5.5)	4 (3.8)	25 (5.1)
Gastritis	22 (5.8)	4 (3.8)	26 (5.3)	-	-	-
Stomatitis	25 (6.6)	7 (6.7)	32 (6.6)	20 (5.2)	3 (2.9)	23 (4.7)
General disorders and administration site conditions						
Pyrexia	15 (3.9)	9 (8.6)	24 (4.9)	12 (3.1)	7 (6.7)	19 (3.9)
Infections and infestations						
Bronchitis	45 (11.8)	5 (4.8)	50 (10.3)	44 (11.5)	5 (4.8)	49 (10.1)
Cystitis	39 (10.2)	7 (6.7)	46 (9.5)	37 (9.7)	7 (6.7)	44 (9.1)
Gastroenteritis	34 (8.9)	11 (10.5)	45 (9.3)	26 (6.8)	9 (8.6)	35 (7.2)
Gingivitis	10 (2.6)	7 (6.7)	17 (3.5)	6 (1.6)	7 (6.7)	13 (2.7)
Herpes zoster	59 (15.5)	22 (21.0)	81 (16.7)	59 (15.5)	22 (21.0)	81 (16.7)
Influenza	37 (9.7)	11 (10.5)	48 (9.9)	32 (8.4)	9 (8.6)	41 (8.4)
Nasopharyngitis	221 (58.0)	72 (68.6)	293 (60.3)	202 (53.0)	67 (63.8)	269 (55.3)
Oral herpes	26 (6.8)	7 (6.7)	33 (6.8)	26 (6.8)	7 (6.7)	33 (6.8)
Periodontitis	20 (5.2)	3 (2.9)	23 (4.7)	-	-	-
Pharyngitis	36 (9.4)	10 (9.5)	46 (9.5)	35 (9.2)	10 (9.5)	45 (9.3)
Tinea pedis	31 (8.1)	3 (2.9)	34 (7.0)	29 (7.6)	2 (1.9)	31 (6.4)
Upper respiratory tract infection	40 (10.5)	8 (7.6)	48 (9.9)	38 (10.0)	7 (6.7)	45 (9.3)
Injury, poisoning and procedural complications						
Contusion	36 (9.4)	12 (11.4)	48 (9.9)	-	-	-
Fall	51 (13.4)	20 (19.0)	71 (14.6)	-	-	-
Ligament sprain	11 (2.9)	9 (8.6)	20 (4.1)	-	-	-
Road traffic accident	9 (2.4)	8 (7.6)	17 (3.5)	-	-	-
Investigations						
Alanine aminotransferase increased	25 (6.6)	1 (1.0)	26 (5.3)	-	-	-
Aspartate aminotransferase increased	22 (5.8)	1 (1.0)	23 (4.7)	-	-	-
Blood cholesterol increased	9 (2.4)	6 (5.7)	15 (3.1)	8 (2.1)	6 (5.7)	14 (2.9)
Low density lipoprotein increased	17 (4.5)	6 (5.7)	23 (4.7)	16 (4.2)	6 (5.7)	22 (4.5)
Lymphocyte count decreased	29 (7.6)	9 (8.6)	38 (7.8)	28 (7.3)	9 (8.6)	37 (7.6)
White blood cell count decreased	17 (4.5)	10 (9.5)	27 (5.6)	16 (4.2)	10 (9.5)	26 (5.3)
Metabolism and nutrition disorders						
Hypercholesterolaemia	13 (3.4)	6 (5.7)	19 (3.9)	-	-	-
Hyperlipidaemia	36 (9.4)	20 (19.0)	56 (11.5)	32 (8.4)	19 (18.1)	51 (10.5)

Table 21. Treatment-Emergent All Causality and Treatment Related Adverse Events (not Including Serious Adverse Events) Occurring at an Incidence of 5% or Greater in Any Treatment Group by Preferred Term

	CP-690,550					
	All Causalities			Treatment Related		
	5 mg BID n (%)	10 mg BID n (%)	Total n (%)	5 mg BID n (%)	10 mg BID n (%)	Total n (%)
Musculoskeletal and connective tissue disorders						
Back pain	43 (11.3)	3 (2.9)	46 (9.5)	-	-	-
Rheumatoid arthritis	6 (1.6)	7 (6.7)	13 (2.7)	-	-	-
Nervous system disorders						
Headache	38 (10.0)	10 (9.5)	48 (9.9)	28 (7.3)	7 (6.7)	35 (7.2)
Respiratory, thoracic and mediastinal disorders						
Cough	24 (6.3)	9 (8.6)	33 (6.8)	18 (4.7)	6 (5.7)	24 (4.9)
Oropharyngeal pain	19 (5.0)	4 (3.8)	23 (4.7)	-	-	-
Upper respiratory tract inflammation	25 (6.6)	9 (8.6)	34 (7.0)	24 (6.3)	8 (7.6)	32 (6.6)
Skin and subcutaneous tissue disorders						
Eczema	25 (6.6)	2 (1.9)	27 (5.6)	-	-	-
Rash	17 (4.5)	6 (5.7)	23 (4.7)	-	-	-
Vascular disorders						
Hypertension	40 (10.5)	15 (14.3)	55 (11.3)	29 (7.6)	13 (12.4)	42 (8.6)

BID = twice daily, MedDRA = Medical Dictionary for Regulatory Activities.
-: <5% of subjects

A summary table of all causality and treatment related serious adverse events are presented in Table 22.

Table 22. All Causality and Treatment Related Serious Adverse Events

	CP-690,550					
	All Causalities			Treatment Related		
	5 mg BID n (%)	10 mg BID n (%)	Total n (%)	5 mg BID n (%)	10 mg BID n (%)	Total n (%)
Number (%) of Subjects:						
Evaluable for adverse events	381	105	486	381	105	486
With serious adverse events	111 (29.1)	28 (26.7)	139 (28.6)	78 (20.5)	17 (16.2)	95 (19.5)
System Organ Class and Preferred Term (MedDRA v.16.1)						
Blood and lymphatic system disorders						
Anaemia	1 (0.3)	0	1 (0.2)	1 (0.3)	0	1 (0.2)
Disseminated intravascular coagulation	1 (0.3)	0	1 (0.2)	1 (0.3)	0	1 (0.2)
Thrombotic thrombocytopenic purpura	1 (0.3)	0	1 (0.2)	1 (0.3)	0	1 (0.2)
Cardiac disorders						
Acute coronary syndrome	1 (0.3)	0	1 (0.2)	-	-	-
Angina pectoris	1 (0.3)	0	1 (0.2)	-	-	-
Prinzmetal angina	1 (0.3)	0	1 (0.2)	1 (0.3)	0	1 (0.2)
Ventricular fibrillation	1 (0.3)	0	1 (0.2)	1 (0.3)	0	1 (0.2)
Ear and labyrinth disorders						
Vertigo	1 (0.3)	0	1 (0.2)	1 (0.3)	0	1 (0.2)
Vertigo positional	1 (0.3)	0	1 (0.2)	-	-	-
Endocrine disorders						
Hyperparathyroidism primary	1 (0.3)	0	1 (0.2)	1 (0.3)	0	1 (0.2)
Eye disorders						
Cataract	2 (0.5)	1 (1.0)	3 (0.6)	-	-	-
Dacryostenosis acquired	1 (0.3)	0	1 (0.2)	-	-	-
Retinal artery occlusion	0	1 (1.0)	1 (0.2)	-	-	-
Retinal detachment	1 (0.3)	0	1 (0.2)	-	-	-
Gastrointestinal disorders						
Colitis ischaemic	1 (0.3)	0	1 (0.2)	1 (0.3)	0	1 (0.2)
Gastric polyps	1 (0.3)	0	1 (0.2)	-	-	-
Gastric ulcer haemorrhage	1 (0.3)	0	1 (0.2)	-	-	-
Ileus	0	1 (1.0)	1 (0.2)	0	1 (1.0)	1 (0.2)
Inguinal hernia	0	1 (1.0)	1 (0.2)	0	1 (1.0)	1 (0.2)
Large intestine polyp	3 (0.8)	0	3 (0.6)	-	-	-
Radicular cyst	1 (0.3)	0	1 (0.2)	1 (0.3)	0	1 (0.2)
General disorders and administration site conditions						
Chest pain	1 (0.3)	0	1 (0.2)	1 (0.3)	0	1 (0.2)
Device material issue	1 (0.3)	0	1 (0.2)	-	-	-
Submandibular mass	0	1 (1.0)	1 (0.2)	0	1 (1.0)	1 (0.2)
Hepatobiliary disorders						
Cholecystitis chronic	1 (0.3)	0	1 (0.2)	1 (0.3)	0	1 (0.2)
Cholelithiasis	1 (0.3)	0	1 (0.2)	-	-	-
Liver disorder	1 (0.3)	0	1 (0.2)	1 (0.3)	0	1 (0.2)
Infections and infestations						
Appendicitis	0	1 (1.0)	1 (0.2)	0	1 (1.0)	1 (0.2)
Bronchitis	1 (0.3)	0	1 (0.2)	1 (0.3)	0	1 (0.2)
Cellulitis	3 (0.8)	1 (1.0)	4 (0.8)	3 (0.8)	1 (1.0)	4 (0.8)
Chronic sinusitis	0	1 (1.0)	1 (0.2)	0	1 (1.0)	1 (0.2)
Diverticulitis	1 (0.3)	0	1 (0.2)	1 (0.3)	0	1 (0.2)
Enteritis infectious	1 (0.3)	0	1 (0.2)	1 (0.3)	0	1 (0.2)
Enterocolitis infectious	1 (0.3)	0	1 (0.2)	1 (0.3)	0	1 (0.2)
Enterocolitis viral	1 (0.3)	0	1 (0.2)	1 (0.3)	0	1 (0.2)
Gastroenteritis	2 (0.5)	1 (1.0)	3 (0.6)	2 (0.5)	1 (1.0)	3 (0.6)
Herpes zoster	11 (2.9)	2 (1.9)	13 (2.7)	11 (2.9)	2 (1.9)	13 (2.7)
Herpes zoster disseminated	0	1 (1.0)	1 (0.2)	0	1 (1.0)	1 (0.2)

Table 22. All Causality and Treatment Related Serious Adverse Events

	CP-690,550					
	All Causalities			Treatment Related		
	5 mg BID n (%)	10 mg BID n (%)	Total n (%)	5 mg BID n (%)	10 mg BID n (%)	Total n (%)
Mycobacterium avium complex infection	0	1 (1.0)	1 (0.2)	0	1 (1.0)	1 (0.2)
Nasopharyngitis	1 (0.3)	0	1 (0.2)	1 (0.3)	0	1 (0.2)
Pneumocystis jirovecii pneumonia	2 (0.5)	0	2 (0.4)	2 (0.5)	0	2 (0.4)
Pneumonia	6 (1.6)	1 (1.0)	7 (1.4)	6 (1.6)	1 (1.0)	7 (1.4)
Pneumonia bacterial	1 (0.3)	0	1 (0.2)	1 (0.3)	0	1 (0.2)
Pneumonia haemophilus	2 (0.5)	0	2 (0.4)	2 (0.5)	0	2 (0.4)
Pneumonia mycoplasmal	1 (0.3)	0	1 (0.2)	1 (0.3)	0	1 (0.2)
Pulmonary tuberculosis	0	1 (1.0)	1 (0.2)	0	1 (1.0)	1 (0.2)
Pyelonephritis	3 (0.8)	2 (1.9)	5 (1.0)	3 (0.8)	1 (1.0)	4 (0.8)
Sepsis	1 (0.3)	0	1 (0.2)	1 (0.3)	0	1 (0.2)
Septic shock	0	1 (1.0)	1 (0.2)	0	1 (1.0)	1 (0.2)
Urinary tract infection	2 (0.5)	0	2 (0.4)	2 (0.5)	0	2 (0.4)
Injury, poisoning and procedural complications						
Ankle fracture	1 (0.3)	0	1 (0.2)	-	-	-
Compression fracture	1 (0.3)	0	1 (0.2)	-	-	-
Contusion	3 (0.8)	0	3 (0.6)	-	-	-
Femoral neck fracture	2 (0.5)	0	2 (0.4)	-	-	-
Femur fracture	0	1 (1.0)	1 (0.2)	-	-	-
Hand fracture	1 (0.3)	0	1 (0.2)	-	-	-
Humerus fracture	1 (0.3)	0	1 (0.2)	-	-	-
Joint dislocation	2 (0.5)	0	2 (0.4)	-	-	-
Patella fracture	1 (0.3)	0	1 (0.2)	-	-	-
Post procedural haemorrhage	1 (0.3)	0	1 (0.2)	-	-	-
Pubis fracture	1 (0.3)	0	1 (0.2)	-	-	-
Radius fracture	1 (0.3)	0	1 (0.2)	-	-	-
Tendon rupture	9 (2.4)	0	9 (1.9)	2 (0.5)	0	2 (0.4)
Tibia fracture	1 (0.3)	0	1 (0.2)	-	-	-
Ulna fracture	1 (0.3)	0	1 (0.2)	-	-	-
Upper limb fracture	1 (0.3)	0	1 (0.2)	-	-	-
Investigations						
Alanine aminotransferase increased	1 (0.3)	0	1 (0.2)	1 (0.3)	0	1 (0.2)
Computerised tomogram thorax abnormal	1 (0.3)	0	1 (0.2)	1 (0.3)	0	1 (0.2)
Metabolism and nutrition disorders						
Decreased appetite	1 (0.3)	0	1 (0.2)	1 (0.3)	0	1 (0.2)
Hypokalaemia	1 (0.3)	0	1 (0.2)	1 (0.3)	0	1 (0.2)
Musculoskeletal and connective tissue disorders						
Arthropathy	1 (0.3)	0	1 (0.2)	-	-	-
Foot deformity	1 (0.3)	1 (1.0)	2 (0.4)	-	-	-
Intervertebral disc protrusion	1 (0.3)	0	1 (0.2)	-	-	-
Joint destruction	2 (0.5)	0	2 (0.4)	1 (0.3)	0	1 (0.2)
Kyphosis	1 (0.3)	0	1 (0.2)	1 (0.3)	0	1 (0.2)
Lumbar spinal stenosis	0	4 (3.8)	4 (0.8)	-	-	-
Neck pain	0	1 (1.0)	1 (0.2)	-	-	-
Osteoarthritis	2 (0.5)	1 (1.0)	3 (0.6)	0	1 (1.0)	1 (0.2)
Osteonecrosis	0	1 (1.0)	1 (0.2)	0	1 (1.0)	1 (0.2)
Periostitis	1 (0.3)	0	1 (0.2)	1 (0.3)	0	1 (0.2)
Rheumatoid arthritis	3 (0.8)	1 (1.0)	4 (0.8)	1 (0.3)	0	1 (0.2)
Spinal column stenosis	3 (0.8)	0	3 (0.6)	-	-	-
Spondylolisthesis	0	1 (1.0)	1 (0.2)	-	-	-

Table 22. All Causality and Treatment Related Serious Adverse Events

	CP-690,550					
	All Causalities			Treatment Related		
	5 mg BID n (%)	10 mg BID n (%)	Total n (%)	5 mg BID n (%)	10 mg BID n (%)	Total n (%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)						
Acute myeloid leukaemia	1 (0.3)	0	1 (0.2)	1 (0.3)	0	1 (0.2)
Adenocarcinoma gastric	1 (0.3)	0	1 (0.2)	1 (0.3)	0	1 (0.2)
Breast cancer	2 (0.5)	0	2 (0.4)	2 (0.5)	0	2 (0.4)
Colon adenoma	1 (0.3)	0	1 (0.2)	1 (0.3)	0	1 (0.2)
Colon cancer	1 (0.3)	0	1 (0.2)	1 (0.3)	0	1 (0.2)
Colorectal adenocarcinoma	1 (0.3)	0	1 (0.2)	1 (0.3)	0	1 (0.2)
Fallopian tube cancer	1 (0.3)	0	1 (0.2)	1 (0.3)	0	1 (0.2)
Gastric cancer	2 (0.5)	0	2 (0.4)	2 (0.5)	0	2 (0.4)
Haemangioma	1 (0.3)	0	1 (0.2)	-	-	-
Liposarcoma	1 (0.3)	0	1 (0.2)	1 (0.3)	0	1 (0.2)
Lymphoproliferative disorder	1 (0.3)	0	1 (0.2)	1 (0.3)	0	1 (0.2)
Malignant ascites	1 (0.3)	0	1 (0.2)	1 (0.3)	0	1 (0.2)
Malignant pleural effusion	1 (0.3)	0	1 (0.2)	1 (0.3)	0	1 (0.2)
Metastases to liver	1 (0.3)	0	1 (0.2)	1 (0.3)	0	1 (0.2)
Metastases to lung	1 (0.3)	0	1 (0.2)	1 (0.3)	0	1 (0.2)
Metastases to lymph nodes	3 (0.8)	0	3 (0.6)	3 (0.8)	0	3 (0.6)
Metastases to peritoneum	2 (0.5)	0	2 (0.4)	1 (0.3)	0	1 (0.2)
Neuroendocrine carcinoma of the skin	1 (0.3)	0	1 (0.2)	1 (0.3)	0	1 (0.2)
Oesophageal carcinoma	1 (0.3)	0	1 (0.2)	1 (0.3)	0	1 (0.2)
Ovarian cancer	1 (0.3)	0	1 (0.2)	1 (0.3)	0	1 (0.2)
Ovarian cancer metastatic	1 (0.3)	0	1 (0.2)	1 (0.3)	0	1 (0.2)
Ovarian germ cell teratoma benign	0	1 (1.0)	1 (0.2)	0	1 (1.0)	1 (0.2)
Paget's disease of nipple	0	1 (1.0)	1 (0.2)	0	1 (1.0)	1 (0.2)
Peritoneal neoplasm	1 (0.3)	0	1 (0.2)	1 (0.3)	0	1 (0.2)
Small cell lung cancer	1 (0.3)	0	1 (0.2)	1 (0.3)	0	1 (0.2)
Squamous cell carcinoma of lung	1 (0.3)	0	1 (0.2)	1 (0.3)	0	1 (0.2)
Transitional cell carcinoma	1 (0.3)	0	1 (0.2)	1 (0.3)	0	1 (0.2)
Uterine leiomyoma	2 (0.5)	0	2 (0.4)	2 (0.5)	0	2 (0.4)
Nervous system disorders						
Carpal tunnel syndrome	1 (0.3)	0	1 (0.2)	-	-	-
Cerebral haemorrhage	1 (0.3)	0	1 (0.2)	1 (0.3)	0	1 (0.2)
Cerebral infarction	1 (0.3)	0	1 (0.2)	1 (0.3)	0	1 (0.2)
Cerebral thrombosis	1 (0.3)	0	1 (0.2)	1 (0.3)	0	1 (0.2)
Convulsion	1 (0.3)	0	1 (0.2)	1 (0.3)	0	1 (0.2)
Cubital tunnel syndrome	1 (0.3)	0	1 (0.2)	1 (0.3)	0	1 (0.2)
IIIrd nerve paralysis	1 (0.3)	0	1 (0.2)	1 (0.3)	0	1 (0.2)
Lacunar infarction	0	1 (1.0)	1 (0.2)	-	-	-
Loss of consciousness	1 (0.3)	0	1 (0.2)	1 (0.3)	0	1 (0.2)
Spondylitic myelopathy	1 (0.3)	0	1 (0.2)	1 (0.3)	0	1 (0.2)
Temporal lobe epilepsy	1 (0.3)	0	1 (0.2)	1 (0.3)	0	1 (0.2)
Transient global amnesia	1 (0.3)	0	1 (0.2)	-	-	-
Renal and urinary disorders						
Calculus ureteric	1 (0.3)	1 (1.0)	2 (0.4)	1 (0.3)	0	1 (0.2)
Glomerulonephritis membranous	1 (0.3)	0	1 (0.2)	1 (0.3)	0	1 (0.2)
Reproductive system and breast disorders						
Uterine polyp	1 (0.3)	0	1 (0.2)	-	-	-
Respiratory, thoracic and mediastinal disorders						
Chronic obstructive pulmonary disease	1 (0.3)	0	1 (0.2)	1 (0.3)	0	1 (0.2)
Interstitial lung disease	1 (0.3)	0	1 (0.2)	1 (0.3)	0	1 (0.2)
Organising pneumonia	1 (0.3)	0	1 (0.2)	1 (0.3)	0	1 (0.2)
Pleurisy	1 (0.3)	0	1 (0.2)	1 (0.3)	0	1 (0.2)

Table 22. All Causality and Treatment Related Serious Adverse Events

	CP-690,550					
	All Causalities			Treatment Related		
	5 mg BID n (%)	10 mg BID n (%)	Total n (%)	5 mg BID n (%)	10 mg BID n (%)	Total n (%)
Skin and subcutaneous tissue disorders						
Skin ulcer	0	1 (1.0)	1 (0.2)	0	1 (1.0)	1 (0.2)

BID = twice daily, MedDRA = Medical Dictionary for Regulatory Activities.

A summary of all withdrawals due to adverse events, regardless of causality is presented in Table 23.

Table 23. All Withdrawals Due to Adverse Events (All Causality)

	CP-690,550		
	5 mg BID n (%)	10 mg BID n (%)	Total n (%)
Number (%) of subjects:			
Evaluable for adverse events	381	105	486
With adverse events leading to withdrawal	94 (24.7)	24 (22.9)	118 (24.3)
System Organ Class and Preferred Term (MedDRA v.16.1)			
Blood and lymphatic system disorders			
Anaemia	2 (0.5)	0	2 (0.4)
Leukopenia	1 (0.3)	0	1 (0.2)
Lymphopenia	0	2 (1.9)	2 (0.4)
Cardiac disorders			
Prinzmetal angina	1 (0.3)	0	1 (0.2)
Congenital, familial and genetic disorders			
Epidermolysis bullosa	0	1 (1.0)	1 (0.2)
Ear and labyrinth disorders			
Vertigo	1 (0.3)	0	1 (0.2)
Gastrointestinal disorders			
Abdominal pain upper	1 (0.3)	0	1 (0.2)
Ileus	0	1 (1.0)	1 (0.2)
Stomatitis	0	1 (1.0)	1 (0.2)
Hepatobiliary disorders			
Cholecystitis chronic	1 (0.3)	0	1 (0.2)
Hepatic function abnormal	1 (0.3)	0	1 (0.2)
Infections and infestations			
Acarodermatitis	1 (0.3)	0	1 (0.2)
Appendicitis	0	1 (1.0)	1 (0.2)
Atypical mycobacterial infection	2 (0.5)	0	2 (0.4)
Cellulitis	3 (0.8)	1 (1.0)	4 (0.8)
Chronic sinusitis	0	1 (1.0)	1 (0.2)
Diverticulitis	1 (0.3)	0	1 (0.2)
Herpes zoster	11 (2.9)	1 (1.0)	12 (2.5)
Herpes zoster disseminated	0	1 (1.0)	1 (0.2)
Mycobacterium avium complex infection	0	1 (1.0)	1 (0.2)
Pericoronitis	1 (0.3)	0	1 (0.2)
Pharyngitis	0	1 (1.0)	1 (0.2)
Pneumocystis jirovecii pneumonia	1 (0.3)	0	1 (0.2)
Pneumonia	6 (1.6)	3 (2.9)	9 (1.9)
Pneumonia bacterial	1 (0.3)	0	1 (0.2)
Pneumonia haemophilus	2 (0.5)	0	2 (0.4)
Pneumonia mycoplasmal	1 (0.3)	0	1 (0.2)
Pulmonary tuberculosis	0	1 (1.0)	1 (0.2)
Pyelonephritis	4 (1.0)	1 (1.0)	5 (1.0)
Sepsis	1 (0.3)	0	1 (0.2)
Septic shock	0	1 (1.0)	1 (0.2)
Tonsillitis	1 (0.3)	0	1 (0.2)
Tooth abscess	0	1 (1.0)	1 (0.2)
Upper respiratory tract infection	1 (0.3)	0	1 (0.2)
Urinary tract infection	2 (0.5)	0	2 (0.4)
Injury, poisoning and procedural complications			
Femoral neck fracture	1 (0.3)	0	1 (0.2)
Joint dislocation	1 (0.3)	0	1 (0.2)
Tendon rupture	1 (0.3)	0	1 (0.2)
Investigations			
Alanine aminotransferase increased	4 (1.0)	0	4 (0.8)
Aspartate aminotransferase increased	2 (0.5)	0	2 (0.4)
Blood creatine phosphokinase increased	1 (0.3)	0	1 (0.2)
Blood creatinine increased	5 (1.3)	1 (1.0)	6 (1.2)

Table 23. All Withdrawals Due to Adverse Events (All Causality)

	CP-690,550		
	5 mg BID n (%)	10 mg BID n (%)	Total n (%)
Blood triglycerides increased	1 (0.3)	0	1 (0.2)
Haemoglobin decreased	2 (0.5)	0	2 (0.4)
Hepatitis B core antibody positive	0	1 (1.0)	1 (0.2)
Lymphocyte count decreased	6 (1.6)	1 (1.0)	7 (1.4)
Musculoskeletal and connective tissue disorders			
Joint destruction	2 (0.5)	0	2 (0.4)
Lumbar spinal stenosis	0	1 (1.0)	1 (0.2)
Osteoarthritis	1 (0.3)	1 (1.0)	2 (0.4)
Osteonecrosis	1 (0.3)	0	1 (0.2)
Spinal column stenosis	1 (0.3)	0	1 (0.2)
Spondylolisthesis	0	1 (1.0)	1 (0.2)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute myeloid leukaemia	1 (0.3)	0	1 (0.2)
Adenocarcinoma gastric	1 (0.3)	0	1 (0.2)
Breast cancer	2 (0.5)	0	2 (0.4)
Colon cancer	1 (0.3)	0	1 (0.2)
Colorectal adenocarcinoma	1 (0.3)	0	1 (0.2)
Fallopian tube cancer	1 (0.3)	0	1 (0.2)
Gastric cancer	2 (0.5)	0	2 (0.4)
Liposarcoma	1 (0.3)	0	1 (0.2)
Lymphoproliferative disorder	1 (0.3)	0	1 (0.2)
Malignant ascites	1 (0.3)	0	1 (0.2)
Malignant pleural effusion	1 (0.3)	0	1 (0.2)
Metastases to liver	1 (0.3)	0	1 (0.2)
Metastases to lung	1 (0.3)	0	1 (0.2)
Metastases to lymph nodes	3 (0.8)	0	3 (0.6)
Metastases to peritoneum	1 (0.3)	0	1 (0.2)
Neuroendocrine carcinoma of the skin	1 (0.3)	0	1 (0.2)
Oesophageal carcinoma	1 (0.3)	0	1 (0.2)
Ovarian cancer	1 (0.3)	0	1 (0.2)
Ovarian cancer metastatic	1 (0.3)	0	1 (0.2)
Paget's disease of nipple	0	1 (1.0)	1 (0.2)
Peritoneal neoplasm	1 (0.3)	0	1 (0.2)
Squamous cell carcinoma of lung	1 (0.3)	0	1 (0.2)
Transitional cell carcinoma	1 (0.3)	0	1 (0.2)
Uterine leiomyoma	1 (0.3)	0	1 (0.2)
Nervous system disorders			
Cerebral haemorrhage	1 (0.3)	0	1 (0.2)
Convulsion	1 (0.3)	0	1 (0.2)
IIIrd nerve paralysis	1 (0.3)	0	1 (0.2)
Loss of consciousness	1 (0.3)	0	1 (0.2)
Post herpetic neuralgia	1 (0.3)	0	1 (0.2)
Temporal lobe epilepsy	1 (0.3)	0	1 (0.2)
Renal and urinary disorders			
Glomerulonephritis membranous	1 (0.3)	0	1 (0.2)
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease	1 (0.3)	0	1 (0.2)
Interstitial lung disease	1 (0.3)	0	1 (0.2)
Skin and subcutaneous tissue disorders			
Rash	1 (0.3)	0	1 (0.2)
Skin ulcer	0	1 (1.0)	1 (0.2)
Toxic skin eruption	1 (0.3)	0	1 (0.2)

BID = twice daily, MedDRA = Medical Dictionary for Regulatory Activities.

Deaths which occurred in this study are presented in Table 24. A total of 7 deaths (all from the 5 mg BID group) were reported.

Table 24. Deaths (As of 28 April 2014)

Subject Number	Race	Sex	Age	Dose at Onset [a] (mg/day)	Action Taken	Day of Death	Event with Fatal Outcome MedDRA Preferred Term (version 16.1)	Cause of Death MedDRA Preferred Term (version 16.1)
5 mg BID group								
10061003	Asian	F	58	10	Permanently withdrawn [b]	913	Malignant ascites	Ovarian cancer Metastases to lymph nodes
				10	Permanently withdrawn [b]		Malignant pleural effusion	Cachexia Ovarian cancer recurrent
				10	Permanently withdrawn [b]		Mesenteric neoplasm	Sepsis Pneumonia
				10	Permanently withdrawn [b]		Metastases to lymph nodes	Malignant pleural effusion Malignant ascites
				10	Permanently withdrawn [b]		Ovarian cancer	Mesenteric neoplasm
10061036	Asian	F	61	20	Permanently withdrawn [c]	796	Liposarcoma	Liposarcoma
10031002	Asian	M	54	10	Permanently withdrawn [d]	1313	Small cell lung cancer metastatic	Small cell lung cancer metastatic
10211003	Asian	F	59	10	Permanently withdrawn [e]	230	Thrombotic thrombocytopenic purpura	Multi-organ failure Thrombotic thrombocytopenic purpura
10271005	Asian	F	57	10	Permanently withdrawn [f]	831	Adenocarcinoma gastric	Metastases to peritoneum Adenocarcinoma gastric
				10	Permanently withdrawn [f]		Metastases to peritoneum	
10461008	Asian	M	60	10	Permanently withdrawn [g]	1081	Colorectal adenocarcinoma	Metastases to peritoneum Metastases to liver
				10	Permanently withdrawn [g]		Metastases to liver	Metastases to lung Metastases to lymph nodes
				10	Permanently withdrawn [g]		Metastases to lung	Colorectal adenocarcinoma
				10	Permanently withdrawn [g]		Metastases to lymph nodes	
				10	Permanently withdrawn [g]		Metastases to peritoneum	
10551002	Asian	M	66	10	Post-therapy [h]	1274	Acute respiratory distress syndrome	Acute respiratory distress syndrome
				10	Post-therapy [h]		Pulmonary alveolar haemorrhage	Pulmonary alveolar haemorrhage

BID = twice daily, F = Female, M = Male, MedDRA = Medical Dictionary for Regulatory Activities.
[a] Dose for CP-690,550 treatment at the earliest onset date. [b] CP-690,550 was permanently discontinued on Day 586 due to malignant ascites, malignant pleural effusion, mesenteric neoplasm, metastases to lymph nodes and ovarian cancer. [c] CP-690,550 was permanently discontinued on Day 108 due to liposarcoma.
[d] CP-690,550 was permanently discontinued on Day 1099 due to small cell lung cancer metastatic and glomerulonephritis membranous. [e] CP-690,550 was permanently discontinued on Day 161 due to interstitial lung disease. [f] CP-690,550 was permanently discontinued on Day 200 due to adenocarcinoma gastric and metastases to peritoneum. [g] CP-690,550 was permanently discontinued on Day 755 due to metastases to liver, metastases to lung, metastases to lymph nodes, metastases to peritoneum and colorectal adenocarcinoma.
[h] CP-690,550 was permanently discontinued the CP-690,550 on Day 1195 due to herpes zoster.

The decreases in neutrophils (range of mean change: −3.62 to −1.47 × 10^3/mm^3) and platelet counts (range of mean change: −61.67 to −31.51 × 10^3/mm^3), increases in hemoglobin (range

of mean change: 0.28 to 1.47 g/dL), high-density lipoprotein (HDL) cholesterol (range of mean change: 14.17% to 26.79%), low-density lipoprotein (LDL) cholesterol (range of mean change: 12.18% to 25.26%), total cholesterol (range of mean change: 18.24% to 29.05%), and serum creatinine (range of mean change: 0.03 to 0.10 mg/dL) were observed in the total study group from either Week 2 or Week 12 to Week 288.

Mean changes from baseline in diastolic and systolic blood pressures were generally small in the total study group (from Week 2 to Week 264, mean change from baseline ranged from -0.26 to 1.70 mmHg for diastolic blood pressure, and from -0.69 to 1.64 mmHg for systolic blood pressure). No clinically significant change was observed in diastolic or systolic blood pressure during study.

There were 3 subjects who showed a QTc value corrected for Bazett (QTcB) interval that was 500 msec or greater and 5 subjects indicated a QTcB value that increased 60 msec or greater from baseline. None of these changes were reported as an adverse event.

CONCLUSION(S):

This was a Phase 3, multi-center, open-label, non-comparative, long-term study. A total of 486 subjects who had completed qualifying controlled CP-690,550 RA study in Japan were assigned to study treatment and all of them were treated.

A total of 308 (63.4%) subjects completed the study, and 178 (36.6%) subjects were discontinued from the study. The primary reason of study discontinuation was adverse events regardless of whether or not they were treatment emergent. The median duration of treatment in this study (excluding the treatment duration in the qualifying study) was 1185.0 days in this study.

In this study (A3921041), CP-690,550 5 mg BID and 10 mg BID provided: maintenance of improvement in signs and symptoms as measured by ACR20/50/70 response rates, DAS28-4 (ESR), DAS28-3 (CRP); maintenance of improvement in physical function measured by HAQ-DI; and maintenance of structural preservation measured by mTSS throughout the long-term treatment period.

The incidences of all causality and treatment related adverse events (not including serious adverse events) (occurring at an incidence of 5% or greater in any treatment group) were 91.8% (446/486 subjects) and 84.8% (412/486 subjects), respectively. The most commonly experienced all causality adverse events were nasopharyngitis, herpes zoster, fall, hyperlipidaemia, hypertension and dental caries.

Although 118 subjects permanently discontinued study treatment as a result of treatment-emergent all causality adverse events, overall, CP-690,550 at doses of 5 mg BID and 10 mg BID was safe and well tolerated in this study.

A total of 7 deaths were reported. All causality serious adverse events were reported in 139 (28.6%) subjects and were considered treatment related in 95 (19.5%) subjects. Most of the serious adverse events were resolved after the discontinuation of the study treatment.

Decreases in neutrophils and platelet counts, increases in hemoglobin, serum lipids (HDL cholesterol, LDL cholesterol and total cholesterol), and serum creatinine observed in the qualifying studies were not found significant change during this study.