2.0 Synopsis

Abbott Laboratories	**Individual Study Table Referring to Part of Dossier:**	**(For National Authority Use Only)**
Name of Study Drug: Adalimumab	**Volume:**	
Name of Active Ingredient: Adalimumab	**Page:**	

Title of Study:

Phase 2 Extension Study of Two Dosing Schedules of Adalimumab in Subjects with Moderate to Severe Chronic Plaque Psoriasis

Investigator:

Coordinating Investigator: Mark Lebwohl, M.D., Mount Sinai School of Medicine, 5 East 98th Street, 12th Floor, Box 1048, New York, New York 10029

Study Sites:

Multicenter (14 study sites in the United States (US) [11 sites] and Canada [3 sites]).

Publications:

None.

Studied Period (Years):	**Phase of Development:** 2
First Subject's Screening Visit: 04 Nov 2003 Last Subject's Last Study Visit: 02 Sep 2004	

Objectives:

The objectives of this study were to evaluate the safety and efficacy of retreatment upon relapse in subjects with moderate to severe chronic plaque psoriasis entering from Study M02-538.

Methodology:

This was a 24-week, Phase 2, multi-center, efficacy and safety study to evaluate clinical response following retreatment with adalimumab in subjects with moderate to severe chronic plaque psoriasis who discontinued from the lead-in Study M02-538 due to relapse by Week 24 (< PASI 50 response after open-label adalimumab (loading dose of 80 mg at Week 0 and 1 followed by 10 weeks of treatment with adalimumab 40 mg weekly). The lead-in study, Study M02-538, was a 76−week, Phase 2, multi-center, exploratory efficacy and safety study to evaluate the time to relapse after adalimumab 40 mg weekly withdrawal (placebo treatment) or dose decrease (adalimumab 40 mg every other week [eow] treatment) in subjects with moderate to severe chronic plaque psoriasis following the receipt of open-label adalimumab. The lead-in study included a 12−week open-label treatment period, and a 12-week double blind treatment period. Subjects who relapsed on or before Week 24 in the lead-in study were eligible for enrollment in this study, Study M03−596, in which they received retreatment with adalimumab. Any of the 136 subjects who were randomized into Study M02-538 and had < PASI 50 response (relapse) after Week 12 and on or before Week 24 of Study M02-538, and met all inclusion and none of the exclusion criteria, may have enrolled in this study.

All Study M03-596 study weeks were given the 'x' designation to differentiate the visits in this continuation study from the 12 visits that occurred in Study M02-538. Study M03-596 consisted of two study periods, an open-label period (Week 0x to Week 11x) and a double-blind period (Week 12x to Week 24x).

In Study M03-596, all subjects were to receive retreatment with open-label 80 mg adalimumab at Week 0x (study entry) and at Week 1x followed by adalimumab 40 mg weekly from Week 2x to Week 11x (open-label period). Subjects with ≥ PASI 50 response (relative to Study M02-538 Week 0) at Week 12x (start of the double-blind period) were to continue in a double-blind manner in their assigned treatment arm from Study M02-538: 40 mg adalimumab eow or placebo eow. Subjects who relapsed (< PASI 50 response after Week 12x, but before Week 24x) were to be discontinued from the study. Likewise, subjects who experienced rebound (PASI score ≥125% of the Week 0 PASI score in Study M02-538) or new generalized pustular or erythrodermic psoriasis after Week 12x were to be discontinued from the study.

Number of Subjects (Planned and Analyzed):

Planned: 145 subjects

Analyzed: Open-label period (Week 0x to Week 11x): 32 subjects in the Full Analysis Set (subjects who received at least one dose of study medication in that study period) for efficacy and 32 subjects were analyzed for safety. 24 subjects completed the open-label period.

Double-blind period (Week 12x to Week 24x): 24 subjects in the Full Analysis Set (subjects who received at least one dose of study medication in that study period) were analyzed for efficacy and 24 subjects were analyzed for safety. 15 subjects completed the double-blind period of the study.

Diagnosis and Main Criteria for Inclusion:

Eligible subjects were subjects who were randomized and relapsed on or before Week 24 of the lead-in study, Study M02-538. Subjects were males and females ≥ 18 years of age with moderate to severe chronic plaque psoriasis (at entry into the lead-in study: psoriasis history for 1 year, psoriasis involving at least 5% of total body surface area (BSA) for at least 2 months before Screening and Baseline [Week 0], and minimum PASI score ≥ 8 at Screening and at Week 0). Subjects with erythrodermic psoriasis, generalized pustular psoriasis, or medication induced or exacerbated psoriasis were excluded. Subjects had active disease despite topical therapy, and had not previously received treatment with anti-TNF therapy. Topical psoriasis therapies, phototherapy, and excessive sun exposure or tanning booth use were discontinued for 2 weeks prior to entry of the lead-in study and throughout the continuation study. Non-biologic systemic psoriasis therapies were discontinued 4 weeks prior to the lead-in study entry, etanercept and efalizumab were discontinued at least 6 weeks before the lead-in study entry, infliximab, alefacept, and other biologic agents not mentioned were discontinued at least 12 weeks before entry into the lead-in study. Investigative chemical agents were discontinued at least 30 days or five half-lives prior to entry of the lead-in study. Subjects did not have other active skin diseases or skin infections that would have interfered with the evaluation of psoriasis. Subjects did not have history of neurologic symptoms suggestive of central nervous system demyelinating disease, history of active untreated tuberculosis or listeriosis, or persistent chronic or active infections requiring hospitalization with intravenous antibiotics, antivirals, or antifungals within 30 days or oral antibiotics within 14 days prior to entry of the lead-in study. Subject did not have poorly controlled medical conditions, including but not limited to unstable cardiovascular disease, active inflammatory bowel disease, recent stroke (within three months), advanced or poorly controlled diabetes, or documented history of recurrent

infections. Subjects previously treated with adalimumab or who previously participated in an adalimumab clinical study were excluded from participation in this study.

Test Product, Dose/Strength/Concentration, Mode of Administration and Lot Number:

Adalimumab 40 mg/0.8 mL sc - Lot number: 90-015HK

Duration of Treatment:

Subjects in the adalimumab 40 mg weekly/adalimumab 40 mg eow treatment group received treatment with adalimumab for up to 24 weeks in this study. Subjects in the adalimumab 40 mg weekly/placebo treatment group received adalimumab for up to 12 weeks.

Reference Therapy, Dose/Strength/Concentration and Mode of Administration and Lot Number:

Placebo 0.8 mL sc - Lot number: 90-014HK

Criteria for Evaluation

Efficacy:

The primary efficacy analysis was a comparison between treatment groups of the proportion of subjects with clinical response, defined as ≥ PASI 50 response relative to the Week 0 PASI in the lead-in study, Study M02-538, following 12 weeks (Week 12x) of re-treatment with open-label adalimumab.

Secondary efficacy variables included those to assess relapse and clinical response:

For those subjects with ≥ PASI 50 at Week 12x, the following secondary efficacy variables were analyzed in the double-blind period to assess relapse:

- The proportion of subjects who relapsed (loss of ≥ PASI 50 response) after Week 12x.
- The time to relapse after Week 12x through Week 24x.
- The proportion of subjects with a ≥ PASI 50/75/90 response at Week 12x.
- The proportion of subjects with a PGA of clear/almost clear at Week 12x.
- The proportion of subjects with ≥ PASI 50/75/90 at any time from Week 0x to Week 12x.
- Time to ≥ PASI 50/75 response up to Week 12x.

Double-blind Period (only those subjects who were PASI 50 responders at Week 12x)

- The proportion of subjects with a ≥ PASI 50/75/90 response at Week 24x.
- The proportion of subjects with a PGA of clear/almost clear at Week 24x.
- The change from the lowest PASI score during the first 12 weeks of the study to the subject's final visit

Comparative analyses of within-arm (the same arm) and between-arm in Studies M02-538 and M03-596:

- The proportion of subjects who achieved the same or better PASI response in Study M03−596 compared to Study M02-538 (last evaluable response in the open-label periods).
- The proportion of subjects in each PASI response category (< 50, ≥ 50 to < 75, ≥ 75) at Week 12 of Study M02-538 and at Week 12x of Study M03-596.
- The time to relapse in the double-blind periods of Studies M02-538 and M03-596 were compared.

Safety:

Adverse events (AEs) were monitored throughout the study. Standard laboratory evaluations, vital signs determinations, and physical examinations were performed at specified timepoints throughout the study. Electrocardiogram, chest x-ray, and tuberculin (purified protein derivative) test were performed at Screening.

Statistical Methods

All statistical tests were two-sided and conducted at an $\alpha = 0.05$ level. Descriptive statistics (frequency and percentage, mean, 95% confidence interval, standard deviation, minimum, 1st quartile, median, 3rd quartile and maximum) were used to describe all data.

Efficacy:

The primary efficacy endpoint was the proportion of subjects with clinical response, defined as ≥ PASI 50 response relative to the Week 0 PASI in the lead-in study, Study M02-538, following 12 weeks (Week 12x) of re-treatment with open-label adalimumab. The p-value was from Fisher's Exact Test to compare the adalimumab weekly/placebo and adalimumab weekly/adalimumab eow treatment groups. Subjects with missing PASI scores were counted as non-responders.

For time to relapse, the risk ratio of adalimumab 40 mg eow and placebo after Week 24 was computed. A 95% confidence interval for the risk ratio and a p-value using the Cox Proportional Hazards model with treatment group were provided.

For the clinical response endpoints, the Fisher Exact Test was used to compare the treatment groups. The change from the lowest PASI score in the open-label period to the last visit in the randomized period was analyzed using an ANCOVA model. The median time to clinical response was calculated using the Kaplan-Meier Method.

Safety:

Treatment emergent AEs and serious adverse events (SAEs) were summarized by system organ class (SOC) and preferred term (PT) according to the Medical Dictionary for Regulatory Activities (MedDRA) AE coding dictionary (version 4.0). A summary of AEs by severity and relationship to study drug was performed. Changes in laboratory data were described using statistical characteristics and shift tables were provided.

Summary/Conclusions

Key demographic and disease characteristics are presented below:

Demographic data at Screening:

	Adalimumab weekly/ placebo[a] N=21	**Adalimumab weekly/ adalimumab eow[a] N=11**	**Total N=32**	**Subjects Who Discontinued in the Open-label Period[b] N=8**
Age (years)				
Mean ± SD	46.86 ± 11.01	49.36 ± 13.89	47.72 ± 11.91	51.38 ± 13.22
Median (range)	49 (19-66)	54 (26-64)	50.5 (19-66)	55.5 (32-66)
Gender, n (%)				
Male	16 (76.2)	4 (36.4)	20 (62.5)	5 (62.5)
Female	5 (23.8)	7 (63.6)	12 (37.5)	3 (37.5)
Race, n (%)				
White	21 (100.0)	10 (90.9)	31 (96.9)	7 (87.5)
Black	0	1 (9.1)	1 (3.1)	1 (12.5)
Asian	0	0	0	0
Hispanic, n (%)	0	0	0	0

eow: every other week

Note: Subjects are presented by their randomized treatment assignment in Study M02-538.

a. In Study M03-596, all subjects received 12-weeks of treatment with open-label adalimumab (loading doses of adalimumab 80 mg at Week 0x and at Week 1x followed by adalimumab 40 mg weekly from Week 2x to Week 11x). Subjects who were PASI 50 responders at Week 12x were to have received adalimumab 40 mg eow or placebo from Week 12x to Week 24x. Subjects were to have received open-label adalimumab followed by either placebo or adalimumab 40 mg eow for 12 weeks in the lead-in study, Study M02-538.

b. Subjects who discontinued in the open-label period are counted separately in the column titled "Subjects Who Discontinued in the Open-label Period," but are also counted in the column of the treatment group they discontinued from and in the total column.

Disease Characteristics at Study Entry:

Disease Characteristic	Adalimumab weekly/ placebo[a] N=21	Adalimumab weekly/ adalimumab eow[a] N=11	Total N=32	Subjects Who Discontinued in the Open-label Period[b] N=8
Psoriasis duration (years), mean ± SD	18.95 ± 9.40	19.42 ± 15.02	19.11 ± 11.39	16.29 ± 8.34
Baseline PASI				
Mean	16.6	14.9	16.0	14.4
(95% CI)	(12.8, 20.4)	(10.1, 19.7)	(13.2, 18.9)	(9.46-19.4)
Baseline PASI Score, n (%)				
< 12	9 (42.9)	5 (45.5)	14 (43.8)	3 (37.5)
12-20	7 (33.3)	4 (36.4)	11 (34.4)	4 (50.0)
> 20	5 (23.8)	2 (18.2)	7 (21.9)	1 (12.5)
Baseline BSA, mean ± SD	25.9 ± 25.07	26.09 ± 21.73	25.97 ± 23.62	21.63 ± 14.56

BSA: body surface area; eow: every other week; PASI: Psoriasis Area and Severity Index

Note: Subjects are presented by their randomized treatment assignment in Study M02-538.

a. In Study M03-596, all subjects received 12-weeks of treatment with open-label adalimumab (loading doses of adalimumab 80 mg at Week 0x and at Week 1x followed by adalimumab 40 mg weekly from Week 2x to Week 11x). Subjects who were PASI 50 responders at Week 12x were to have received adalimumab 40 mg eow or placebo from Week 12x to Week 24x. Subjects were to have received open-label adalimumab followed by either placebo or adalimumab 40 mg eow for 12 weeks in the lead-in study, Study M02-538.

b. Subjects who discontinued in the open-label period are counted separately in the column titled "Subjects Who Discontinued in the Open-label Period," but are also counted in the column of the treatment group they discontinued from and in the total column.

Efficacy Results:

The results of this study demonstrated that retreatment with open-label adalimumab in subjects who relapsed (< PASI 50 response) during dose reduction or dose withdrawal can be effective in restoring response.

Primary efficacy: Re-treatment with open-label adalimumab for 12 weeks in subjects who relapsed (< PASI 50 response) following adalimumab dose decrease or withdrawal resulted in regain of ≥ PASI 50 response for 81.3% of subjects. Furthermore, a greater proportion of subjects in the previously treated with adalimumab eow achieved a ≥ PASI 50 response compared to subjects previously treated with placebo ($p = 0.637$).

Secondary efficacy:

Relapse

In terms of relapse, subjects who were successfully retreated using open-label adalimumab were less likely to relapse following dose decrease to adalimumab 40 mg eow than with dose withdrawal (placebo). Subjects in the adalimumab weekly/adalimumab eow treatment group had a 57% reduction in

the risk of relapse after Week 12x through Week 24x compared to subjects in the adalimumab weekly/placebo treatment group (37.5% *vs.* 50.0%; risk ratio 0.43; p = 0.2858; 95% CI: 0.09, 2.05). Efficacy results for relapse are presented in tabular form below:

	Adalimumab weekly/ placebo[a] N=16	Adalimumab weekly/ adalimumab eow[a] N=8	p-value
Relapse Rate After Week 12x (n, %)[b]			
Week 15x	2 (12.5)	0	0.536[c]
Week 18x	5 (31.3)	2 (25.0)	1.000[c]
Week 21x	7 (43.8)	2 (25.0)	0.657[c]
Week 24x	7 (43.8)	3 (37.5)	1.000[c]
Week 24x (LOCF)	7 (43.8)[d]	3 (37.5)	1.000[c]
Time to Relapse After Week 12x through Week 24x			
Number of relapsers	8 (50.0)[d]	3 (37.5)	0.2858[e]
Risk Ratio (95% CI)[f]		0.43 (0.09, 2.05)	

eow: every other week

Note: Subjects are presented by their randomized treatment assignment in Study M02-538.

a. In Study M03-596, all subjects received 12-weeks of treatment with open-label adalimumab (loading doses of adalimumab 80 mg at Week 0x and at Week 1x followed by adalimumab 40 mg weekly from Week 2x to Week 11x). Subjects who were PASI 50 responders at Week 12x were to have received adalimumab 40 mg eow or placebo from Week 12x to Week 24x. Subjects were to have received open-label adalimumab followed by either placebo or adalimumab 40 mg eow for 12 weeks in the lead-in study, Study M02-538.

b. Subjects with missing PASI scores were counted as relapsers, except for LOCF.

c. The p-value is from Fisher's Exact Test to compare the adalimumab weekly/placebo and adalimumab weekly/adalimumab eow treatment groups.

d. Explanation for the 7 relapsed placebo subjects for analysis of relapse rate *vs.* the 8 placebo relapsed subjects for analysis of time to relapse: Time to relapse analysis used the number of the first relapser at any time after Week 12x. Subject #36-06 relapsed at Week 18x, but continued in the study and regained PASI 50 response at Week 21x and 24x. This subject was counted as a relapse in the analysis of time to relapse, but counted as no-relapse at Week 24x in the relapse rate.

e. The p-value is from Cox Proportional Hazards model.

f. Risk of adalimumab weekly/adalimumab eow *vs.* adalimumab weekly/placebo.

Clinical Response

Open-label Period

Subjects who were previously treated with open-label adalimumab followed by eow dosing did better following retreatment with open-label adalimumab than subjects who previously received open-label adalimumab followed by placebo (dose withdrawal).

Retreatment for 12 weeks with open-label adalimumab resulted in half of all subjects achieving a ≥ PASI 75 response at Week 12x, and 84.4% and 53.1% of all retreated subjects achieving a ≥ PASI 50 and ≥

PASI 75 response, respectively, at some time between Weeks 0x and 12x. After re-treatment with open-label adalimumab, subjects previously treated with adalimumab eow required less time to achieve response: a statistically significantly difference in favor of subjects previously treated with adalimumab weekly/eow for ≥ PASI 75 response was observed (57 days *vs.* 86 days, respectively; p = 0.0494). In other words, subjects who received continuous treatment with adalimumab in both Study M02-538 and this study, had a shorter response time than subjects who took placebo. A total of 25.0% of retreated subjects achieved PGA of clear/almost clear. These results indicate that retreatment with open-label adalimumab is effective in restoring clinical response. Furthermore, subjects who received open-label adalimumab followed by eow therapy in Study M02-538 achieved ≥ PASI 50/75/90 responses and PGA of clear/almost clear in greater proportions than subjects who were treated with open-label adalimumab followed by placebo in Study M02-538. Efficacy results for clinical response in the open-label period are presented in tabular form below:

Clinical Response for Subjects With a ≥ PASI 50 at Week 12x

≥ PASI 50/75/90 and PGA clear/almost clear at Week 12x

	Adalimumab weekly/ placebo N=21	**Adalimumab weekly/ adalimumab eow N=11**	**Total N=32**	**Subjects Who Discontinued in the Open-label Period N=8**	**p-value[a]**
Assessment	**n (%)**				
≥ PASI 50	16 (76.2)	10 (90.9)	26 (81.3)	2 (25.0)	0.637
≥ PASI 75	8 (38.1)	8 (72.7)	16 (50.0)	1 (12.5)	0.135
≥ PASI 90	3 (14.3)	2 (18.2)	5 (15.6)	0	1.00
PGA clear/ almost clear	3 (14.3)	5 (45.5)	8 (25.0)	0	0.088
≥ PASI 50/75/90 at any time up to Week 12x					
≥ PASI 50	17 (81.0)	10 (90.9)	27 (84.4)	3 (37.5)	0.637
≥ PASI 75	9 (42.9)	8 (72.7)	17 (53.1)	1 (12.5)	0.147
≥ PASI 90	3 (14.3)	3 (27.3)	6 (18.8)	0	0.390

Time to ≥ PASI 50/75 response up to Week 12x

	Adalimumab weekly/ placebo N=21	**Adalimumab weekly/ adalimumab eow N=11**	**p-value[b]**
	Median (days)		
Time to ≥ PASI 50 response	29	16	0.2876
Time to ≥ PASI 75 response	86	57	0.0494

a. The p-value is from Fisher's Exact test to compare the adalimumab weekly/placebo and adalimumab weekly/adalimumab 40 mg eow treatment groups. Subjects with missing scores were counted as non-responders.

b. The p-value is from Log Rank test to compare the adalimumab weekly/placebo and adalimumab weekly/adalimumab 40 mg eow treatment groups.

Double-blind Period

At Week 24x, a greater proportion of subjects who received adalimumab in both Studies M02-538 and M03-596 were able to achieve a ≥ PASI 50 response than subjects who took placebo, indicating that subjects who were retreated using open-label adalimumab did better in terms of ≥ PASI 50 response following dose decrease to adalimumab 40 mg eow than with dose withdrawal (placebo). Efficacy results for clinical response in the double-blind period are presented in tabular form below:

Clinical Response - Double-blind Period

≥ PASI 50/75/90 and PGA clear/almost clear at Week 24x

	Adalimumab weekly/ placebo N=16	**Adalimumab weekly/ adalimumab eow N=8**	**p-value[a]**
Assessment	**n (%)**		
≥ PASI 50	9 (56.3)	5 (62.5)	1.000
≥ PASI 75	4 (25.0)	1 (12.5)	0.631
≥ PASI 90	2 (12.5)	0	0.536
PGA clear/almost clear	3 (18.8)	1 (12.5)	1.000

a. The p-value is from Fisher's Exact test to compare the adalimumab weekly/placebo and adalimumab weekly/adalimumab 40 mg eow treatment groups.

Change in the Lowest PASI Score During the First 12 Weeks of the Study to the Subject's Final Visit

	Adalimumab weekly/ placebo N=16	**Adalimumab weekly/ adalimumab eow N=8**	**Difference (%) (95% CI for Difference)**	**p-value[b]**
	Mean ± SD			
Lowest PASI Score in Open-label Period	3.72 ± 2.73	2.96 ± 4.39	-0.756 (-3.761, 2.248)	0.6069
Last Visit in Randomized Period	7.71 ± 5.06	6.54 ± 4.14	-1.17 (-5.467, 3.129)	0.5785
Change from Lowest PASI Score to Last Visit	3.99 ± 4.63	3.58 ± 2.22	-0.413 (-4.028, 3.203)	0.8152

a. The p-value is from Fisher's Exact test to compare the adalimumab weekly/placebo and adalimumab weekly/adalimumab 40 mg eow treatment groups. Subjects with missing scores were counted as non-responders.

b. The p-value is from ANOVA to compare the adalimumab weekly/placebo and adalimumab weekly/adalimumab 40 mg eow treatment groups.

Within-arm and Between-arm Comparative Analyses

After re-treatment with open-label adalimumab, over 36% of subjects from both previously adalimumab−treated groups achieved the same or better PASI response compared to results at the end of the previous 12 weeks of open-label adalimumab treatment in Study M02-538, regardless of a subject's previous treatment in Study M02−538. More subjects in the group previously treated with adalimumab eow in study M02-538 shifted to a better PASI response category than did subjects who received placebo. Time to relapse in the double-blind period of Study M02-538 compared to Study M03-596 demonstrated that subjects who were randomized to placebo relapsed sooner in Study M03-596 (45 days) than in Study M02-538 (64 days) than did subjects randomized to adalimumab eow (91 days *vs.* 64 days, respectively; log-rank test p-values 0.2725 and 0.8850, respectively) indicating that subjects who received continuous treatment with adalimumab, even at a lower dose frequency, maintained their response longer than subjects who received placebo.

In summary, within-arm and between-arm analyses indicate that subjects who were previously treated with adalimumab eow had a better clinical response following retreatment with adalimumab 40 mg weekly than subjects who received placebo (dose withdrawal). The proportions of subjects with the same or better PASI response in Study M03-596 as in Study M02-538 are presented below:

	Adalimumab weekly/ placebo N=21	**Adalimumab weekly/ adalimumab eow N=11**	**Total N=32**	**p-value[a]**
		n (%)		
Week 12 (LOCF)				1.000
Yes	8 (38.1)	4 (36.4)	12 (37.5)	
No	12 (57.1)	7 (63.6)	19 (59.4)	

a. The p-value is from Fisher's Exact Test to compare the adalimumab weekly/placebo and adalimumab weekly/adalimumab 40 mg eow treatment groups.

Safety Results:

Retreatment with open-label adalimumab for 12 weeks in subjects who relapsed (< PASI 50 response) following previous adalimumab dose decrease or withdrawal was well-tolerated as evidenced by the assessment of AEs and SAEs, laboratory assessments, and other safety assessments.

No deaths occurred during the study and the number of subjects who reported treatment-emergent SAEs was few (2 subjects). None were definitively attributed to study drug.

Treatment-emergent AEs most commonly reported were few. Most treatment-emergent AEs were probably not or not related to study drug according to the Investigator, and most events were mild to moderate in severity. Treatment-emergent AEs experienced by more than 1 subject irrespective of treatment group are presented below by MedDRA System Organ Class and Preferred Term for both study periods:

Open-label Period (Week 0x to Week 11x)	Adalimumab weekly/ placebo N=21	Adalimumab weekly/ adalimumab eow N=11	Total N=32	Subjects who Discontinued in the Open-label Period N=8
MedDRA Preferred Term[a]		**n (%)**		
Total subjects with at least one AE	13 (61.9)	9 (81.8)	22 (68.8)	7 (87.5)
Upper respiratory infection	2 (9.5)	1 (9.1)	3 (9.4)	0
Headache NOS	3 (14.3)	0	3 (9.4)	0
Conjunctivitis NOS	2 (9.5)	0	2 (6.3)	1 (12.5)
Injection site reaction NOS	1 (4.8)	1 (9.1)	2 (6.3)	0
Sinusitis NOS	1 (4.8)	1 (9.1)	2 (6.3)	2 (25.0)
Nasopharyngitis	2 (9.5)	0	2 (6.3)	0
Muscle strain	1 (4.8)	1 (9.1)	2 (6.3)	0
Double-blind Period (Week 12x to Week 24x)	**N=16**	**N=8**	**N=24**	
MedDRA Preferred Term[a]		**n (%)**		
Total subjects with at least one AE	11 (68.8)	5 (62.5)	16 (66.7)	
Seasonal Allergy	1 (6.3)	1 (12.5)	2 (8.3)	

a. Subjects with one or more events.

No clinically meaningful changes in mean laboratory values were observed. Shifts to high or low were generally infrequent and were similar between treatment groups during the double blind period of the study. Changes in vital signs were clinically unremarkable.

Conclusions:

The results of this study demonstrate that adalimumab is effective in subjects with moderate to severe chronic plaque psoriasis who were retreated with open-label adalimumab after loss of clinical response (< PASI 50 response) following adalimumab dose decrease or withdrawal. Furthermore, continuous dosing with adalimumab (open-label adalimumab followed by dose decrease) was more effective than open-label treatment followed by placebo in terms of maintenance or regain of treatment response. Additionally, the results of this study demonstrated that treatment with open-label adalimumab (loading dose of 80 mg at Week 0x and 1x followed by 40 mg weekly) followed by 40 mg eow is generally well tolerated in the treatment of adult subjects with moderate to severe chronic plaque psoriasis.

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