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

Investigator:

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Study Sites:

Multicenter (16 study sites in the United States (US) [12 sites] and Canada [4 sites]).

Publications:

Blum R, Lebwohl M, Wong V, Gottlieb A, Luo A, Hoffman R. Durability of treatment response in patients with moderate to severe psoriasis following withdrawal from or a dose reduction in adalimumab therapy. Presented at the AAD Annual Meeting, 2005.

Studied Period (Years): First Subject's Screening Visit: 19 Jun 2003 Last Subject's Last Visit: 10 Mar 2005	**Phase of Development:** 2

Objective:

The objective of this study was to investigate the time to relapse after either withdrawal of adalimumab therapy or dose decrease in subjects with moderate to severe chronic plaque psoriasis who achieved a PASI response of at least 50% after 12 weeks of open-label weekly adalimumab therapy. Time to relapse was defined as the time when the PASI response fell below 50% from the Week 0 PASI score relative to the randomization visit.

Methodology:

This 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 12 weeks of adalimumab 40 mg weekly therapy (open-label treatment). The study included a 12−week open-label treatment period, a 12-week double blind treatment period, and a 30-, 90-, 180-, 270-, and 360-day follow-up period until relapse or Week 76, whichever came first, for those subjects who did not relapse previously during the study. For those subjects who terminated from the study early for reasons other than relapse, follow-up visits were to be conducted at 30 and 90 days after the subject's final dose of study medication.

At Week 0 and Week 1 all subjects were to receive loading doses of open-label adalimumab 80 mg followed by adalimumab 40 mg weekly from Week 2 through Week 11. At Week 12, subjects who were responders, defined as ≥ PASI 50, were to be randomized to one of two treatment arms: adalimumab 40 mg eow or placebo eow. The randomization was stratified by Week 12 PASI category (< PASI 75 and ≥ PASI 75). Subjects received either adalimumab 40 mg eow or placebo from Week 12 through Week 24. If at any time after Week 12 a subject experienced relapse, defined as loss of PASI 50 response, the subject was to have been discontinued from the study. Rebounders, defined as subjects who developed a PASI score ≥ 125% of the Week 0 PASI score, or those that develop new generalized pustular or erythrodermic psoriasis within 90 days after randomization (Week 12), were to be discontinued from the study. During the follow-up period (Week 25 through Week 76), no study drug was administered.

Treatment regimens were blinded beginning at the Week 12 visit (randomization) as assigned by ClinPhone. Subjects who relapsed on or before Week 24 were eligible for enrollment in Study M03−596, in which they received retreatment with adalimumab. Subjects who relapsed after Week 24 and on or before Week 76 were eligible for immediate enrollment in Study M03-658. Study M03-658 was an open-label continuation study for subjects who previously participated in an adalimumab psoriasis trial.

Number of Subjects (Planned and Analyzed):

Planned: 145 subjects

Analyzed: Open-label period (Week 0 to Week 11): 148 subjects in the Full Analysis Set (subjects who received at least one dose of study medication in that study period) and 130 subjects in the Per-protocol Analysis Set (subjects in the Full Analysis Set who did not violate predetermined criteria) for efficacy and 148 subjects were analyzed for safety. 163 subjects completed the open-label period.

Double-blind period (Week 12 to Week 24): 136 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 148 subjects were analyzed for safety. 96 subjects completed the double-blind period of the study.

Follow-up period: 96 subjects for efficacy and 148 subjects for safety

Diagnosis and Main Criteria for Inclusion:

Eligible subjects were subjects who were males and females ≥ 18 years of age with moderate to severe chronic plaque psoriasis (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 study and throughout the study. Non-biologic systemic psoriasis therapies were discontinued 4 weeks prior to study entry, etanercept and efalizumab were discontinued at least 6 weeks before study entry, infliximab, alefacept, and other biologic agents not mentioned were discontinued at least 12 weeks before study entry. Investigative chemical agents were discontinued at least 30 days or five half-lives prior to entry of the 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 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: 128004 (open-label period) and 90-015HK (double-blind period)

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 endpoint was the time to relapse after Week 12 through Week 24 for subjects who had achieved a Week 12 ≥ PASI 50 response relative to the Week 0 score. Relapse was defined as < PASI 50 response relative to the Week 0 PASI score after randomization (Week 12).

Secondary efficacy variables:

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

Randomized Subjects

Relapse

For all subjects randomized at Week 12, secondary efficacy endpoints to assess relapse included:

- The proportion of subjects who relapsed after Week 12
- The time to relapse from Week 24 through the 360-day post last dose follow-up visit for non-relapsers at Week 24

Clinical Response

For all subjects randomized at Week 12, secondary efficacy endpoints to assess clinical response were:

- The proportion of subjects with ≥ PASI 75 response at Week 12 and Week 24, and at the 30-, 90-, 180-, 270-, and 360-day post last dose follow-up visits
- The proportion of subjects with ≥ PASI 50 response at Week 12 and Week 24 and at the 30-, 90-, 180-, 270-, and 360-day post last dose follow-up visits
- The proportion of subjects with ≥ PASI 90 response at Week 12 and Week 24 and at the 30-, 90−, 180-, 270-, and 360-day post last dose follow-up visits
- The proportion of subjects achieving ≥ PASI 50 response, ≥ PASI 75, and ≥ 90 response from Week 0 to Week 12

- The change from the maximum PASI response in the open-label period to the last visit in the double blind period
- The proportion of subjects with a PGA of "*clear*" or "*almost clear*" at Week 12, Week 24, at the 30-, 90-, 180-, 270-, and 360-day post last dose follow-up visits

Rebound

- The proportion of subjects in the adalimumab 40 mg eow treatment group who had rebound (PASI score ≥ 125% of the Week 0 PASI score, or development of new generalized pustular or erythrodermic psoriasis 90 days post last dose of study drug) within 90 days of the last adalimumab dose

Non-randomized Subjects

For all subjects enrolled in the study (non-randomized), secondary efficacy endpoints to assess clinical response were:

- The proportion of subjects with ≥ PASI 75 at all visits in the open-label period
- The proportion of subjects with a PGA of "*clear*"/"*almost clear*" at all visits in the open-label period

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. A supportive analysis of the primary variable was performed using the Last Observation Carried Forward (LOCF) approach to impute missing values.

Efficacy:

The primary efficacy endpoint was the time to relapse after Week 12 through Week 24 for subjects who had achieved a Week 12 ≥ PASI 50 response relative to the Week 0 score. Relapse was defined as < PASI 50 response after randomization (Week 12). The aim of the primary efficacy analysis was to determine if subjects withdrawn from adalimumab have a higher risk of relapse than subjects who undergo adalimumab dose decrease. The primary efficacy variable was analyzed for the Full Analysis Set (main analysis) as well as for the Per-protocol Analysis Set with discontinued subjects counted as relapsers. The p-value was from the Cox Proportional Hazards model with treatment group and Week 12 PASI strata (< PASI 75 and ≥ PASI 75).

For the secondary efficacy analyses of relapse, the risk ratio of relapse between adalimumab 40 mg eow and placebo after Week 24, and the proportion of relapse from Week 12 to Week 24 were computed. A 95% confidence interval was provided for the difference between treatment groups and a p-value using the Cox Proportional Hazards model with treatment group and PASI strata and Fisher's Exact test were provided. For the proportion of subjects who relapsed after Week 12, a p-value from the CMH Test adjusted for Week 12 PASI strata for results up to Week 24 was provided.

For the secondary clinical response endpoints, the difference between treatment groups and the 95% CI was provided along with a p-value from the CMH test adjusted to PASI strata with the exception of the change from the lowest PASI score in the open-label period to the last visit in the randomized period, which used an ANCOVA model adjusting for PASI strata.

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:

	Randomized from Adalimumab Weekly		**Not Randomized**		
	Placebo[a]	**Adalimumab eow[b]**		**All Subjects Total**	
	N=68	**N=68**	**N=12**	**N=148**	**p-value[c]**
Age (years)					0.261
Mean ± SD	45.1 ± 10.6	43.0 ± 11.3	38.5 ± 11.8	43.6 ± 11.1	
Gender (n, %)					0.218
Male	45 (66.2)	38 (55.9)	10 (83.3)	93 (62.8)	
Female	23 (33.8)	30 (44.1)	2 (16.7)	55 (37.2)	
Race (n, %)					0.530
White	65 (95.6)	62 (91.2)	12 (100.0)	139 (93.9)	
Asian	2 (2.9)	3 (4.4)	0	5 (3.4)	
Black	1 (1.5)	3 (4.4)	0	4 (2.7)	
Hispanic (n, %)	0	0	2 (16.7)	2 (1.4)	

Disease Characteristics at Study Entry:

	Randomized from Adalimumab Weekly		Not Randomized	
	Placebo[a]	Adalimumab eow[b]		All Subjects Total
Disease Characteristic	**N=68**	**N=68**	**N=12**	**N=148**
Psoriasis duration (years), mean ± SD	20.2 ± 10.8	20.6 ± 11.9	13.3 ± 11.7	19.9 ± 11.5
Baseline PASI, mean (95% CI)	16.3 (14.5, 18.1)	16.4 (14.4, 18.4)	16.6 (11.7, 21.5)	16.4 (15.1, 17.7)
Baseline PASI, n (%)				
< 12	27 (39.7)	24 (35.3)	2 (16.7)	53 (35.8)
12-20	25 (36.8)	29 (42.6)	7 (58.3)	61 (41.2)
> 20	16 (23.5)	15 (22.2)	3 (25.0)	34 (23.0)
% BSA psoriasis, mean ± SD	25.0 ± 20.5	25.3 ± 20.5	22.8 ± 18.4	25.0 ± 20.2

a. 40 mg adalimumab weekly Week 0 to Week 11, placebo Week 12 to Week 24

b. 40 mg adalimumab weekly Week 0 to Week 11, adalimumab 40 mg eow Week 12 to Week 24

c. For categorical data, the p-value is from a Chi-square test to compare the adalimumab weekly/placebo treatment group with the adalimumab weekly/adalimumab eow treatment group. For continuous data, the p-value is from an ANCOVA model to compare the adalimumab weekly/placebo treatment group with the adalimumab weekly/adalimumab eow treatment group.

Efficacy Results:

The efficacy of adalimumab was evaluated by assessing relapse (< PASI 50 response) following 12 weeks of weekly open-label treatment with adalimumab 40 mg, in subjects who adalimumab dose decreased compared to subjects who were withdrawn from adalimumab.

The results of this study demonstrated that subjects administered adalimumab 40 mg eow following previous treatment with adalimumab 40 mg weekly for 12 weeks have less risk of relapse and are better able to maintain clinical response than subjects who are withdrawn from adalimumab.

Relapse

Primary: Subjects who underwent adalimumab dose decrease had a lower risk of relapse (approximately a 50% reduction) during the double blind period (Week 12 through Week 24) than subjects who were withdrawn from adalimumab (risk ratio 0.48; 16.2% *vs.* 30.9%). While clinically significant, this result was not statistically significant (p = 0.060; 95% CI: 0.23-1.03). The median time to relapse, defined as since Week 12 for placebo subjects and since Week 24 for adalimumab subjects, was 172 and 190 days, respectively.

Secondary: Similarly, subjects who underwent adalimumab dose decrease had a statistically significantly lower risk of relapse during the follow-up period (from Week 24 through the 360-day follow-up visit) than subjects who were withdrawn from adalimumab (risk ratio 0.493; p = 0.016; 45.1% *vs.* 64.4%). In general, a smaller proportion of subjects who underwent adalimumab dose

decrease experienced relapse after Week 12 compared to subjects who were withdrawn from adalimumab therapy. Even though adalimumab eow-treated subjects stopped receiving adalimumab at Week 24, they continued to demonstrate relapse in smaller proportions up to the 180-day follow-up visit in comparison to subjects who were withdrawn from adalimumab.

Clinical Response

Open-label period: Following open-label treatment with adalimumab, the majority of subjects had a ≥ PASI 50 response (91.9%) and ≥ PASI 75 response (76.4%) and were "clear" or "almost clear" by PGA (72.1%). Almost half (47.3%) of subjects had achieved a ≥ PASI 90 response.

Double Blind and Follow-up Periods: The majority of subjects achieved a ≥ PASI 50 response (91.9%) following 12 weeks of open-label treatment with adalimumab 40 mg weekly. In subjects who underwent adalimumab dose decrease, 77.9% of subjects had a ≥ PASI 50 response at Week 24. Relapse was higher among subjects who were withdrawn from adalimumab, with 66.2% of placebo-treated subjects having a PASI 50 response at Week 24 *vs.* 77.9% of adalimumab-treated subjects, indicating that subjects treated with an additional 12 weeks of adalimumab have an advantage over subjects who are withdrawn from adalimumab.

The majority of subjects (76.4%) achieved a ≥ PASI 75 response and almost half (47.3%) achieved a ≥ PASI 90 response following 12 weeks of open-label treatment with adalimumab 40 mg weekly. The durability of treatment response in subjects treated with adalimumab was demonstrated by the maintenance of a ≥ PASI 75/90 response at Week 24 in a statistically significantly greater proportion of subjects who underwent adalimumab dose decrease compared to subjects who were withdrawn from adalimumab therapy (67.6% *vs.* 48.5%; respectively, p=0.032 and 47.1% *vs.* 27.9%, respectively; p=0.028, respectively). This trend continued and remained statistically significant at the 30-day and 90−day follow-up visits for PASI 75 response and at the 30-day follow-up visit for PASI 90 response indicating that subjects treated with an additional 12 weeks of adalimumab have an advantage over subjects who are withdrawn from adalimumab.

The majority of subjects (66.2%) were "clear" or "almost clear" by PGA following 12 weeks of open-label treatment with adalimumab 40 mg weekly. Subjects who underwent adalimumab dose decrease had a status of "clear" or "almost clear" by PGA at Week 24 in greater proportions than subjects who were withdrawn from adalimumab (54.4% *vs.* 39.7%, respectively; p=0.069). This trend continued through the 30− and 90−day follow-up visits, indicating that subjects treated with an additional 12 weeks of adalimumab have an advantage over subjects who are withdrawn from adalimumab.

Finally, a statistically significant difference in the change in the maximum PASI response (lowest PASI score) from the open-label period to the last visit in the double-blind period was observed between the adalimumab 40 mg eow treatment group and the placebo treatment group (1.04 *vs.* 3.34, respectively; p = 0.0014). Although on average, the PASI score deteriorated after the adalimumab dose was withdrawn or decreased, subjects who underwent adalimumab dose decrease demonstrated a better clinical response during the double-blind period than subjects who were withdrawn from adalimumab.

Non-randomized subjects: Per the protocol, 12 subjects were not randomized due to lack of a ≥ PASI 50 response at Week 12. Of these, one achieved a ≥ PASI 75 response while 6 achieved a ≥ PASI 50 at some time during the open-label period. None of the non-randomized subjects were assessed by PGA as clear/almost clear at Week 12.

Rebound: Rebound was defined as PASI score ≥ 125% of the Week 0 PASI score, or development of new generalized pustular or erythrodermic psoriasis 90 days post last dose of study drug. One subject who received adalimumab 40 mg eow and two subjects who received placebo had rebound within 90 days of the last dose of study drug. One placebo treatment group subject had a PASI score ≥ 125% of their Week 0 PASI score and the other two subjects experienced an aggravation of their psoriasis (AE: psoriasis aggravated).

Efficacy results are presented in tabular form below:

RELAPSE

	Randomized from Adalimumab weekly	
	Placebo[a]	**Adalimumab 40 mg eow[b]**
Number of Relapsers (Week 12 through Week 24), n (%)[c]	21 (30.9)	11 (16.2)
Risk Ratio[c] (95% CI); p-value[d]	0.481 (0.23, 1.03); 0.060	
Number of Relapsers (Week 24 through the 360-day Follow-up visit), n (%)[d]	29 (64.4)	23 (45.1)
Risk Ratio[c] (95% CI); p-value[d]	0.493 (0.28, 0.88); 0.016	

Number (%) of Subjects Who Relapsed After Week 12

	Week[e]				Follow-Up Visits[f]				
	15	**18**	**21**	**24**	**30-day**	**90-day**	**180-day**	**270-day**	**360-day**
					%				
Plac[a]	2.9	13.2	26.5	33.8	20.0	48.9	62.2	64.4	64.4
Adal[b]	0	4.4	17.6	22.1	5.9	21.6	37.3	45.1	45.1
p-value[g]	0.178	0.094	0.297	0.173	0.126	0.011	0.274	0.830	1.000

CLINICAL RESPONSE

>= PASI 75 Response (%)

	Week[e]		Follow-Up Visits[f]				
	12	**24**	**30-day**	**90-day**	**180-day**	**270-day**	**360-day**
Plac[a]	80.9	48.5	55.6	20.0	8.9	0	2.2
Adal[b]	85.3	67.6	80.4	52.9	11.8	2.0	0
p-value[g]	-	0.032	0.015	0.001	0.746	1.000	0.469
>= PASI 50 Response (%)							
Plac[a]	100.0	66.2	80.0	48.9	20.0	4.4	2.2
Adal[b]	100.0	77.9	92.2	72.5	25.5	5.9	2.0
p-value[g]	-	0.173	0.133	0.022	0.629	1.000	1.000

	Week[c]		Follow-Up Visits[d]				
	12	**24**	**30-day**	**90-day**	**180-day**	**270-day**	**360-day**
>= PASI 90 Response (%)							
Plac[a]	45.6	27.9	24.4	11.1	2.2	0	0
Adal[b]	57.4	47.1	58.8	23.5	2.0	0	0
p-value[g]	0.236	0.028	0.001	0.179	1.000	-	-
"*Clear*"/ "*Almost Clear*" by PGA for Psoriasis (%)							
Plac[a]	72.1	39.7	44.4	15.6	4.4	0	0
Adal[b]	72.1	54.4	68.6	31.4	3.9	0	0
p-value[g]	0.942	0.069	0.023	0.094	1.000	-	-

Change from the Lowest PASI Score in the Open-label Period to the Last Visit in the Double-blind Period – Randomized Subjects

	Placebo[a,c]	Adalimumab eow[b,c]	
	Mean ± SD		**p-value[h]**
Lowest PASI Score in Open-label Period	2.1 ± 2.13	1.88 ± 2.20	0.8428
Last Visit in Double-blind Period	5.43 ± 5.55	2.92 ± 3.63	0.0028
Change from the Lowest PASI Score to the Last Visit	3.34 ± 4.41	1.04 ± 3.72	0.0014

eow: every other week

a. 40 mg adalimumab weekly Week 0 to Week 11, placebo Week 12 to Week 24

b. 40 mg adalimumab weekly Week 0 to Week 11, adalimumab 40 mg eow Week 12 to Week 24

c. Risk of adalimumab 40 mg eow over placebo.

d. The p-value is from the Cox Proportional Hazards model stratified by Week 12 PASI strata.

e. N=68 for both treatment groups.

f. N=45 for the placebo treatment group and N=51 for the adalimumab 40 mg treatment group.

g. The p-value is from the CMH Test adjusted for Week 12 PASI strata for results up to Week 24. Fisher's Exact Test was used for the p-value for the Follow-up Period.

h. The p-value is from ANCOVA to compare the placebo and adalimumab 40 mg eow treatment groups.

Safety Results:

The results of this study demonstrated that treatment with adalimumab 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.

No deaths occurred during the study and the number of subjects who reported treatment-emergent SAEs was few (4 subjects). None were definitively attributed to study drug.

Treatment-emergent AEs most commonly reported were few, mild to moderate in severity, and infrequently considered probably or possibly related to study treatment. By MedDRA SOC, AEs were

most often reported in the category of infections and infestations. Nasopharyngitis and upper respiratory infection NOS, two of the six most frequently (≥ 5%) reported treatment-emergent AEs in any period (nasopharyngitis, upper respiratory tract infection NOS, injection site reaction NOS, arthralgia, psoriatic arthropathy, and headache NOS) by MedDRA PT, were reported across all three periods (open-label, double-blind, and follow-up):

	Randomized from Adalimumab weekly			Not Randomized	
MedDRA PT	**Placebo[a]**	**Adalimumab eow[b]**	**Total**		**All Subjects Total**
	N=68	**N=68**	**N=136**	**N=12**	**N=148**
			n (%)		
Open-label Period					
Injection site reaction NOS	7 (10.3)	8 (11.8)	15 (11.0)	2 (16.7)	17 (11.5)
Nasopharyngitis	4 (5.9)	7 (10.3)	11 (8.1)	0	11 (7.4)
Headache NOS	4 (5.9)	5 (7.4)	9 (6.6)	2 (16.7)	11 (7.4)
Upper respiratory tract infection NOS	6 (8.8)	1 (1.5)	7 (5.1)	2 (16.7)	9 (6.1)
Double-blind Period					
Upper respiratory tract infection NOS	6 (8.8)	10 (14.7)	16 (11.8)	-	-
Nasopharyngitis	7 (10.3)	3 (4.4)	10 (7.4)	-	-
Injection site reaction NOS	1 (1.5)	4 (5.9)	5 (3.7)	-	-
Arthralgia	0	5 (7.4)	5 (3.7)	-	-
Follow-up Period					
Psoriatic arthropathy aggravated	2 (4.4)	5 (9.8)	7 (7.3)	-	-
Nasopharyngitis	4 (8.9)	3 (5.9)	7 (7.3)	-	-
Upper respiratory tract infection NOS	4 (8.9)	2 (3.9)	6 (6.3)	-	-
Arthralgia	3 (6.7)	1 (2.0)	4 (4.2)	-	-

eow: every other week; PT: preferred term

Note: Frequently reported events for the open-label period of the study were events that occurred in ≥5% of all subjects. Frequently reported events for the double-blind and follow-up periods were events that occurred in ≥ 5% of subjects in any treatment group.

a. 40 mg adalimumab weekly Week 0 to Week 11, placebo Week 12 to Week 24

b. 40 mg adalimumab weekly Week 0 to Week 11, adalimumab 40 mg eow Week 12 to Week 24

Because the mechanism of action of anti-TNF antagonists, including adalimumab, is inhibition of an immunologically active cytokine, episodes of infection and malignancy were of particular interest. Serious treatment-emergent infectious AEs were infrequently reported during the study. Identical proportions of subjects in the adalimumab eow and placebo treatment groups experienced non-serious infectious treatment-emergent AEs during the double blind period; these proportions were similar to the proportion of subjects who reported these types of events during open-label treatment with adalimumab (31.3%). One subject reported a non-melanoma skin cancer. No reports of melanoma or malignant neoplasm were reported during the study.

Treatment-emergent AEs leading to study discontinuation (3 subjects) and drug hypersensitivity reactions (3 subjects) were few. Injection site reactions were common during the study, but were predominantly mild and occurred during the treatment period as expected.

No events of lymphoma, tuberculosis infection, demyelination, or drug-induced lupus were observed during the study. There was one case of herpes simplex considered probably not related to study drug.

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 demonstrated that subjects administered adalimumab 40 mg eow following previous treatment with adalimumab 40 mg weekly for 12 weeks have a lower risk of relapse and are better able to maintain clinical response than subjects who are withdrawn from adalimumab. Additionally, the results of this study demonstrated that treatment with adalimumab 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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