



## 2.0 Synopsis

<b>Abbott Laboratories</b>	<b>Individual Study Table Referring to Part of Dossier:</b>  <b>Volume:</b>  <b>Page:</b>	<b>(For National Authority Use Only)</b>
<b>Name of Study Drug:</b> Humira 40 mg / 0.8 mL		
<b>Name of Active Ingredient:</b> Adalimumab		
<b>Title of Study:</b> A Multi-Center, Open-Label Efficacy, Safety, and Pharmacokinetic Study of Adalimumab in Japanese Subjects with Active Ankylosing Spondylitis		
<b>Investigator:</b> [REDACTED]		
<b>Study Sites:</b> [REDACTED]		
<b>Publications:</b> None		
<b>Studied Period (Years):</b> First Subject First Visit: 17 March 2008 (Subject 001601) Last Subject Completed 60-week: 21 Nov. 2009 (Subject 000704)	<b>Phase of Development: III</b>	
<b>Objectives:</b> The objective of this study was to evaluate the efficacy, safety and pharmacokinetics of adalimumab given every other week (eow) subcutaneously (sc) in Japanese subjects with active AS. The secondary objective of this study was to confirm the similarity between the data obtained from this study and those from Study [REDACTED] in Western subjects with active AS.		
<b>Methodology:</b> This was a phase 3, open-label, multi-center study to evaluate efficacy, safety and pharmacokinetics of adalimumab in Japanese subjects with active AS who had an inadequate response to, or who were intolerant to, treatment with one or more NSAIDs. Subjects also had a lack of efficacy, or intolerance to one or more disease modifying ant-rheumatic drugs (DMARDs). The subjects were assessed for eligibility of all inclusion and exclusion criteria in the 2-week screening period. The treatment with study drug was to be continued until the approval of adalimumab for the AS indication in Japan. The subjects who met all the inclusion criteria and none of the exclusion criteria at Screening were eligible for participation in the study. All subjects received 40 mg of adalimumab sc eow at Baseline. Efficacy and safety were to be assessed at Baseline, Weeks 2, 4, 8, 12, 16, 20, 24, at every 12 weeks after Week 24, and at study completion (or at early termination (ET)). Blood samples for evaluation of serum adalimumab and anti-adalimumab antibody (AAA) concentration were to be collected at Baseline, Weeks 2, 4, 8, 12, 16, 20, 24, at every 12 weeks after Week 24, at study completion (or at ET), and the Follow-up visit if applicable. The primary efficacy objective was ASAS 20 response rate at Week 12. The		



subjects who completed 16 weeks of therapy and who failed to achieve ASAS 20 response on or after Week 16, could increase the dose of adalimumab to 80 mg eow. Subjects, who wanted to conduct self-injection, had an option for self-injection of the study drug at home by themselves or by his/her family members, after the informed consent for the conduct of self-injection in written form was obtained and the sufficient education and training of treatment procedure were performed. Once the investigator judges that the administrator performed the sc injection adequately according to the procedure of self-injection, the subject and /or his /her family members could perform the self-injection at home. Subjects who completed the study or who prematurely terminated from the study were to have a 28-day follow-up after the completion or discontinuation from the study, and 70-day follow-up after the last dose of adalimumab administration to evaluate safety.

**Number of Subjects (Planned and Analyzed):**

Planned: 30; Obtained informed consent: 49; Entered: 41; Completed Week 60: 37

All 41 subjects who entered the study were evaluated for efficacy, safety and PK variables at Week 60.

**Diagnosis and Main Criteria for Inclusion:**

<Inclusion criteria>

1. Subject was age 15 or older at the time of informed consent.
2. Subject met the definition of AS based on the Modified New York Criteria.
3. Subject had a diagnosis of active ankylosing spondylitis, as defined by fulfillment of at least two of the following 3 conditions:
  - BASDAI 19 score  $\geq$  40 mm
  - Visual analog scale (VAS) for total back pain VAS  $\geq$  40 mm
  - Morning stiffness  $\geq$  1 hr
4. Subjects had an inadequate response to or intolerance to one or more NSAIDs as defined by the investigator
5. Subject might also had failed one or more DMARDs.
6. Subject with total spinal ankylosis (bamboo spine) could be included in this study
7. If female, subject was either not of child bearing potential, defined as postmenopausal for at least 1 year, surgically sterile (bilateral tubal ligation, bilateral oophorectomy or hysterectomy), or was of childbearing potential and practicing one of the following methods of birth control during the study and for 150 days after last dose of study medication.
  - Condoms, sponge, foam, jellies, diaphragm or intrauterine device (IUD)
  - Oral or contraceptives from 90 days prior to study drug administration until 150 days after the last administration of the study drug.
  - A vasectomized partner
8. If female of child bearing potential, the result of a urine pregnancy test performed at the screening and Week 0 were negative.
9. In the case of subject who had one or more of the following conditions: psoriasis, uveitis, inflammatory bowel disease (i.e. ulcerative colitis, Crohn's disease), and reactive arthritis, these conditions were stable and well controlled, as defined by the investigator's best clinical judgment, for at least 4 weeks prior to the start of screening.



10. Subject was able and willing to give written informed consent and to comply with the requirements of this study protocol. If the subject was < 20 years old, a subject's parent or legal guardian was willing to give written informed consent.

<Exclusion criteria>

1. Subject had a history of cancer, lymphoma, leukemia or lymphoproliferative disease, other than a successfully treated non-metastatic cutaneous squamous cell or basal cell carcinoma and/or localized carcinoma in situ of the cervix for 5 years.
2. Subject was known to have immune deficiency or a history of HIV, was immunocompromised or immunosuppressed or could not discontinue alkylating agents, e.g. cyclophosphamide or, anti-cancer alkaloids, e.g. vindesine sulfate for at least 6 months prior to the baseline visit and during the study.
3. Subject had a history of listeriosis, histoplasmosis, active TB, persistent chronic infections, or recent active infections requiring hospitalization or treatment with intravenous (iv) anti-infectives within 28 days or oral anti-infectives within 14 days prior to the screening evaluation.
4. Subject had a history of neurologic symptoms suggestive of central nervous system (CNS) demyelinating disease.
5. Subject with a history of clinically significant drug or alcohol abuse.
6. Subject had a poorly controlled medical condition such as follows and any other condition which, in the opinion of the investigator, would put the subject at risk by participation in the study;
  - Uncontrolled diabetes
  - Unstable ischemic heart disease, congestive heart failure
  - Recent cerebrovascular accidents, recent stroke (within 1 year prior to the screening evaluation)
7. Subjects with clinically significant abnormalities found during the electrocardiogram (ECG) evaluation at the screening visit.
8. Subject had positive serology for anti-HIV antibody (HIV Ab), Hepatitis B surface antigen (HBs Ag), anti-hepatitis C antibody (HCV Ab), in screening laboratory analysis.
9. Screening laboratory analysis showed any of the following abnormal results:
  - Hemoglobin < 9.0 g/dL for male, or < 8.5 g/dL for female;
  - Total white blood cell (WBC) count < 3,000/mm<sup>3</sup>;
  - Platelet count < 100,000/mm<sup>3</sup>;
  - Aspartate transaminase (AST) or alanine transaminase (ALT) > 2 x the upper limit of the reference range;
  - Total bilirubin > 3 mg/dL;
  - Serum creatinine > 1.5 mg/dL
10. Subjects who revealed any findings, which showed a history of TB infection (calcified nodules or granulomas and/or fibrotic scar, apical or basilar thickening) by chest X-ray examination at the screening evaluation.
11. Subjects judged as "strongly positive" or PPD  $\geq$  5 mm of induration in a purified protein derivative (PPD) skin test for the detection of latent TB infection at the screening evaluation.
  - "Strongly positive" was defined as induration and erythema ( $\geq$ 10 mm of diameter) with either bulla, necrosis or double redness.



- Subjects who demonstrated evidence of latent TB infection (either PPD  $\geq$  5 mm of induration, irrespective of BCG vaccination status, and negative CXR findings for active TB) but not be evaluated as "strongly positive" were included to participate in the study under the condition that the prophylactic treatment (isoniazid 300 mg/day for 9 months) for latent TB was initiated 21 days prior to administration of study drug, however the course of prophylaxis did not have to be completed prior to the onset of study drug (screening period was to be extended to 5 weeks in subjects who receive a TB prophylaxis). The liver enzymes (ALT and AST) were measured 1 week prior to study drug administration in each clinical site and the subject discontinued from the study as defined by laboratory abnormal results ( $> 2 \times$  the upper limit of the reference range and/or the investigator's best clinical judgment). Subject who had documented and completed prophylactic treatment for TB did not have to repeat this treatment.
12. Previous treatment with adalimumab, previous participation in an adalimumab clinical study, or a history of an allergic reaction or significant sensitivity to constituents of study drug.
  13. Subject had previously received anti-TNF therapy.
  14. Subject had received any investigational chemical agent in the past 28 days or 5 half-lives prior to Baseline (whichever is longer).
  15. Subject had received any other biological or investigational biological agents in the past 6 months or 5 half-lives prior to Baseline (whichever is longer).
  16. Subject was administered a live vaccine within 12 weeks prior to screening or planned to receive a live vaccine during the study.
  17. Subject had received DMARDs (except MTX and/or SSZ) or any immunosuppressants within 28 days prior to Baseline.
  18. Subject had received intra-articular joint injection(s) with corticosteroids or hyaluronate sodium within 28 days prior to Baseline.
  19. Subject had received spinal surgery or joint surgery involving joints to be assessed within 2 months prior to the screening.
  20. Female subject who was pregnant or breast-feeding or considering becoming pregnant during the study or for 150 days after the last dose of study medication.
  21. Subject was considered by the investigator, for any reason, to be an unsuitable candidate for the study.

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

Study Drug: Injection form packaged in pre-filled syringes containing 40 mg adalimumab/0.8 mL

Dose/Strength/Concentration: Adalimumab 40 mg

Mode of Administration: Subcutaneous

Study Drug	Lot No. / Product No.	Production No.	Adalimumab concentration	Manufacturing Date	Expiry Date
Adalimumab 40 mg	07-011196/17102472	RUZA	50 mg/mL	Mar. 2007	Sep. 2009
	07-014216/17102473	RVYA	50 mg/mL	Nov. 2007	May 2010



**Duration of Treatment:**

Until the approval of adalimumab for the AS indication in Japan. 60 weeks of treatment is presented in this clinical study report.

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

None.

**Criteria for Evaluation**

**Efficacy:**

**Primary variable:**

ASAS 20 response rate at Week 12.

**Secondary variables:**

**Reduction of Signs and Symptoms:**

- The ASAS 20 response at Weeks 2, 4, 8, 16, 20,24 and at every 12 weeks after Week 24.
- The ASAS 40/50/70 responses at Weeks 2, 4, 8 12, 16, 20,24 and at every 12 weeks after Week 24.
- The BASDAI 50 response at Weeks 2, 4, 8 12, 16, 20,24, and at every 12 weeks after Week 24
- Change in Patient's global assessment of disease activity at Weeks 2, 4, 8 12, 16, 20, 24 and at every 12 weeks after Week 24.
- Change in total back pain (VAS score) at Weeks 2, 4, 8 12, 16, 20 24 and at every 12 weeks after Week 24.
- Change in the BASFI at Weeks 2, 4, 8 12, 16, 20, 24 and at every 12 weeks after Week 24.
- Change in CRP at Weeks 2, 4, 8 12, 16, 20, 24 and at every 12 weeks after Week 24.
  
- ASAS 5/6 criteria response at every Week 12.
- The ASAS 40 responses at Weeks 2, 4, 8 12, 16, 20, 24 and at every 12 weeks after Week 24.
- Partial remission at Weeks 12, 16, 20, 24 and at every 12 weeks after Week 24.
  
- Change in the BASMI at every 12 weeks.
- Change in chest expansion at every 12 weeks.
- Change in the MASES at every 12 weeks.
- Change in nocturnal pain (VAS score) at Weeks 2, 4, 8 12, 16, 20, 24 and at every 12 weeks after Week 24.
- Changes in the swollen joint index (44 joints) at every 12 weeks.
- Changes in the tender joint index (46 joints) at every 12 weeks.

**Patient-Reported Outcomes:**

- Change in the SF-36 Health Survey Index (the physical component summary and mental component summary) at every 12 weeks.

**Pharmacokinetic:**

Serum adalimumab concentration and serum AAA concentration were measured at Baseline, Weeks 2, 4, 8,



12, 16, 20, 24, at every 12 weeks after Week 24, at study completion (or at ET) and follow-up visit.

**Safety:**

Adverse events, vital signs and laboratory values.

**Statistical Methods**

The analysis population was described below. Because of the open-label study, additional analysis was not performed on the per-protocol set (PPS) population, which excluded all subjects with major protocol deviation.

- Full analysis set (FAS): FAS population was defined as all subjects who received at least one injection of study drug.
- Safety analysis set: The safety analysis set population was defined as all subjects who received at least one injection of study drug (Same as FAS).
- Self-injection set: The self-injection set was defined as all subjects with self-injection.

The self-injection set was used only for safety analysis.

**Demographic:**

Demographic and baseline characteristics (age, gender, body weight etc.) and clinical laboratory parameters (HLA-B27 etc.) were summarized. Summary statistics for continuous variables included the number of observations, mean, standard deviation, median, minimum, and maximum. Categorical variables were summarized by frequencies counts and percentages.

**Efficacy:**

The efficacy analysis was performed for FAS. Only summary statistics were presented. No inferential analyses were performed. The analysis was not stratified by study site because of a small sample size in each investigation site.

Primary Efficacy Variables:

The primary efficacy analysis was summarized in the frequency, % of subjects achieving a clinical response and 95% confidence interval as defined by ASAS 20 response at Week 12. The criteria of the efficacy as defined by ASAS 20 response rate at Week 12 in this study was established to be 40% based on the lower limit of the 95 % confidence interval of normal approximation.

Secondary Efficacy Variables:

The secondary efficacy analysis was summarized. Summary statistics for continuous variables included the number of observations, mean, standard deviation, 1st quartile, median, 3rd quartile, minimum, and maximum. Discrete variables were summarized by frequencies and relative frequencies (percent).

To evaluate the impact of subjects who discontinued from the study in the primary analysis; ASAS 20 response rate at Week 12, the last observation carried forward (LOCF) approach was performed to impute missing values.

The similarity between the data obtained from this study and those from Study M03-607 and M03-606 in Western subjects with active AS was compared visually.

**Pharmacokinetic:**

Adalimumab concentrations were summarized at each time point using descriptive statistics including



number of subjects, number of non-missing observations ( $n_{\text{nmis}}$ ), mean, median, standard deviation, coefficient of variation, minimum and maximum. Individual subject concentration vs time plots and mean concentration vs time plots were provided. Population pharmacokinetics analysis was performed to estimate adalimumab apparent clearance (CL/F) and apparent volume of distribution (V/F) in subjects with AS. Serum AAA concentrations were listed at each collection time.

**Safety:**

Adverse Events:

A TEAE was defined as an event with onset or worsening after the first study drug injection and within 70 days after the last study drug injection. Pre-treatment serious adverse events (SAEs) occurred from informed consent until the first study drug administration were summarized as well. The number and percentages of subjects experiencing treatment emergent adverse event were tabulated by Medical Dictionary for Drug Regulatory Affairs (MedDRA) system organ class and MedDRA preferred term. The version 11.0 of MedDRA was used. In addition, a summary of adverse events by severity and relationship to study drug were presented. Treatment-emergent adverse events that were judged by the investigator to be probably or possibly related and probably, possibly or probably not related to study drug were also tabulated. A summary of serious and severe adverse events, deaths, and adverse events leading to discontinuation were also provided.

Laboratory Data and Vital Signs:

Mean change in laboratories variable and vital signs variables at each visit were summarized for safety analysis population. The last evaluation prior to the first dose of study drug was used as baseline for all analyses.

**Summary/Conclusions**

**Efficacy Results:**

- The primary efficacy variable; ASAS 20 response rate at Week 12 was 73.2% (30 of 41 subjects) and it was higher than the criteria of efficacy (40%) defined in the protocol. These results demonstrated that adalimumab was effective in reducing the signs and symptoms in Japanese subjects with active AS. (Please refer 24W interim report, R&D/09/012).

Reduction of Signs and Symptoms:

- Following initiation of adalimumab therapy, ASAS 20, ASAS 50, ASAS 70 response rates, BASDAI 50 response rates, and the mean changes from Baseline in Patient's Global Assessment of Disease Activity, Total Back Pain, BASFI, CRP improved over time through Week 12. These improvement observed at Week 12 were sustained from Week 16 up to Week 24, and furthermore maintained up to Week 60. These results demonstrated that adalimumab was effective in reducing the signs and symptoms in Japanese subjects with active AS, and these improvements were subsequently maintained up to 60 weeks.
- Other secondary efficacy endpoints such as the mean changes from Baseline in BASMI, Chest Expansion, MASES, Nocturnal Pain and SJC 44 improved at Week 12. These improvements were sustained at Week 24, and furthermore maintained up to Week 60. These results demonstrated that adalimumab was effective in reducing the signs and symptoms in Japanese subjects with active AS, and these improvements were subsequently maintained up to 60 weeks.

Disease Controlling Clinical Response:

- Following initiation of adalimumab therapy, ASAS 5/6 criteria response rates, ASAS 40 response



rates, and partial remission response rates improved at 12 weeks. These improvements were sustained at Week 24, and furthermore maintained up to Week 60. These results demonstrated that adalimumab was effective in establishing a disease controlling clinical response in Japanese subjects with active AS, and these improvements were subsequently maintained up to 60 weeks.

**Patient-Reported Outcomes:**

- The mean changes from Baseline in SF-36 PCS and MCS improved at Week 12, and were clinically meaningful (i.e.,  $\geq 3.0$  points). These improvements were sustained at Week 24, and furthermore maintained up to Week 60. These results demonstrated that adalimumab was effective in improving QOL in Japanese subjects with active AS, and these improvements were subsequently maintained up to 60 weeks.
- Six (6) subjects increased the dose of adalimumab to 80 mg eow by Week 60. Two (2) of 6 subjects maintained ASAS 20 after dose escalation by Week 60.
- In subgroup analysis, differences of ASAS 20 response rates at Week 12 were observed in the subgroups of sex (male vs female) and CRP (normal at baseline vs abnormal). However, any conclusion could not be made based on these analyses because the number of subjects of each subgroup was small. There was no significant difference in ASAS 20 response at Week 12 between the subgroups of weight (< 40 kg), total spinal ankylosis, HLA-B27 status and DMARDs use at Baseline.

These results demonstrated that adalimumab was effective in reducing the signs and symptoms and improving QOL in Japanese subjects with active AS, and these improvements were subsequently maintained up to 60 weeks.

**Pharmacokinetic Results:**

Mean concentrations for subjects on 40 mg eow monotherapy/with MTX(N=16) remained relatively constant through Week 36 to Week 60 (10.84 – 11.36  $\mu\text{g/mL}$ ). Serum mean concentrations were higher in subjects with MTX (N=15, 11.05-11.96  $\mu\text{g/mL}$ ) compared to subjects who remained on 40 mg eow monotherapy for the study duration.

No new subjects became AAA+ during Week 36 through Week 60

Pharmacokinetic results through Week 24 were shown in 24W interim report, R&D/09/012.

**Safety Results:**

- The overall incidence of AEs was 100% (41/41 subjects), and the number of AEs overall per 100 patient year (PYs) was 568.2 events/100PYs. Treatment-emergent AEs occurred in were nasopharyngitis (31.1%, 13 subjects), diarrhoea (19.5%, 8 subjects), hepatic function abnormal (19.5%, 8 subjects), injection site erythema (14.6%, 6 subjects), upper respiratory tract infection (14.6%, 6 subjects) and upper respiratory tract inflammation (14.6%, 6 subjects).
- More than half (177/250 events) of the AEs were considered not related or probably not related to the study drug. Most of AEs were mild.
- The incidence of total adverse events did not differ between the self-injection group (100%, 22/22) and the non-self injection group (100%, 19/19). A similar trend was also noted in the incidence of individual adverse events. In addition, the incidence of injection site reaction AEs in self-injection group was 18.2% and that in non-self injection group was 26.3%. No adverse event posing a significant problem was noted after the start of self-injection. These results indicated that there was no





safety concern in administering the study drug by medical professionals and self-injection by subjects.

- Among the 6 subjects where dose was increased and evaluation was possible, the incidence of adverse events was 100% both before and after dose increase. All of the adverse events (13 events) developing after dose increase was insignificant, with severity rated as mild for 10 events and moderate for 3 events. Causal relationship to the test drug was rated as “not related” for all of the 3 moderate adverse events. Although dose increase was implemented only in a small number of subjects, the data collected during period until Week 60 suggested no safety problem with dose increase.
- In the subgroup analysis of AEs, there was no significant difference in overall incidence of AEs between subgroups by sex and body weight (only  $\leq 40$  kg vs  $> 40$  kg). Subgroup analysis by age was not performed because there was no subject aged over 65. In subgroup analysis by body weight, the group with body weight less than 40 kg was not analyzed because there was no subject with body weight less than 40 kg.
- No subject was died during the study through Week 60.
- Seven (7) SAEs was reported for 4 subjects (9.8%), including 3 infectious AEs. 5 SAEs were severe, and 20 SAEs were moderate. Two SAEs were considered possibly or probably related to the study drug. Of 7 SAEs, four events (Subject [REDACTED]: thrombocytopenia and adenomyosis, [REDACTED]: breast cancer and pneumonia) was resolved by Week 60, however, two events ([REDACTED] intervertebral discitis and osteomyelitis) were significant and required discontinuation of test drug treatment. Both events remained to be seen as of November 9, 2009. One event ([REDACTED]: periodontitis) remained to be seen at Week 60.
- Three treatment-emergent AEs leading to discontinuation were reported for 2 subjects (4.9%). Subject [REDACTED] experienced breast cancer and Subject [REDACTED] experienced intervertebral discitis and osteomyelitis. Causal relationship to the test drug was rated as “probably not related” for breast cancer and “probably related” for intervertebral discitis and osteomyelitis. All of these events were severe and reported as significant adverse events.
- Infectious AEs were reported for 61.0% (25/41) of the subjects (51 events). Three (3) events of them were reported as SAEs (Subject [REDACTED] intervertebral discitis and osteomyelitis, Subject [REDACTED]; pneumonia). Of all infectious AEs, 2 AEs were severe (Subject [REDACTED]; intervertebral discitis, osteomyelitis), 5 AEs were moderate (Subject [REDACTED]; gastroenteritis, Subject [REDACTED]; bronchitis, Subject [REDACTED] pneumonia, and Subject [REDACTED]; hordeolum and cytomegalovirus infection) and 21 AEs were mild. Twenty five (25) infectious AEs were considered possibly or probably related to the study drug. Of these 25 events, 6 events (Subject [REDACTED]; gastroenteritis, Subject [REDACTED]; intervertebral discitis, osteomyelitis, Subject [REDACTED]; bronchitis, and Subject [REDACTED]; hordeolum and cytomegalovirus infection) were moderate or severe, however, the others were mild and could be treated with medication, etc. Of these 25 events with at least possibly related to the study drug, 2 events (Subject [REDACTED]; intervertebral discitis, osteomyelitis) were continued but all the other events were resolved.
- Cytomegalovirus infection occurred in 1 subject (1 event) as an opportunistic infection (not including tuberculosis).
- Hepatic events were reported for 31.7% (13/41) of the subjects (15 events). Three (3) events were moderate and 12 events were mild. Four (4) hepatic events were considered possibly or probably related to the study drug. Of these 4 events, 2 events were moderate (both are abnormal liver function), and one had not resolved and continued as of Week 60.
- Injection site reaction AEs were reported for 22.0% (9/41) of the subjects (19 events). All of these



events except for one were considered possibly or probably related to the study drug, and the severity was mild. Of all 14 injection site reaction AEs, only one subject required treatment for injection site reaction AE, and the remaining 18 AEs were resolved with no treatment. All injection site reaction AEs reported through Week 60 were resolved by Week 60.

- One (1) malignant (breast cancer) was reported for one subject (2.4%) (Subject [REDACTED] probably not related to the study drug, severe). It was reported as a SAE, and the subject was discontinued from the study due to breast cancer.
- Two (2) hematological events were reported for 2 subjects (4.9%). One of them (Subject [REDACTED] thrombocytopenia, probably not related to the study drug, severe) was reported as a SAE. The other event (leucopenia) was mild and considered possibly related to the study drug.
- There was no adverse event whose incidence increased as the dosing period became longer.
- There was no TB, congestive heart failure related AE, demyelinating disease related AE, allergic reaction or Lupus-like syndrome AE.
- There was no clinically significant change in laboratory values, physical findings and vital signs.
- Between Week 24 and Week 60, no event posing a safety problem developed.

The results demonstrated that adalimumab 40 mg eow was generally safe and well tolerated in Japanese patients with active AS.

**Conclusions:**

In the study M10-239, adalimumab 40 mg eow was effective up to Week 60 in reducing the signs and symptoms in Japanese subjects with active AS, generally safe and well tolerated.