



2.0 Synopsis

Abbott Laboratories	Individual Study Table Referring to Part of Dossier:	(For National Authority Use Only)
Name of Study Drug: Humira	Volume:	
Name of Active Ingredient: Adalimumab	Page:	
Title of Study: Evaluation of Quality of Life Changes in Puerto Rican Subjects with Active Rheumatoid Arthritis Treated with Humira as their First Anti-TNF Monoclonal Antibody (VIVIR).		
Investigator: Multicenter study		
Study Sites: [REDACTED]		
Publications: N/A		
Studied Period (Years): First Subject First Visit: 30/NOV/06 Last Subject Last Visit: 27/AUG/08	Phase of Development: IV	
Objectives: Primary: To evaluate quality of life changes in Puerto Rican subjects with Rheumatoid Arthritis treated with Humira (Adalimumab) as their first Anti-TNF Monoclonal Antibody. Quality of life will be evaluated using the Health Survey Questionnaire, Version 2 (SF-36 v2) and Modified Health Assessment Questionnaire (mHAQ). Secondary: To evaluate changes in the American College of Rheumatology Response Criteria for RA in these subjects in 24 weeks of treatment.		



Methodology:

W06-407 was an open-label, multicenter trial. All subjects received Humira for 24 weeks.

Subjects went to a screening visit, in which laboratory tests were drawn, and a Medical History was documented. Between screening and baseline, CXRays and PPD tests were performed.

After the baseline visit, subjects returned to the sites at week 2, and thereafter every four weeks up to the end of the study. Laboratories were drawn at baseline and weeks 2, 4, 8, 16 and 24.

Adverse events assessment and concomitant medications were assessed at all study visits.

Number of Subjects (Planned and Analyzed): The planned enrollment was 50 subjects. The final enrollment was 14 subjects. Seven subjects of fourteen completed the treatment period (24weeks).



Diagnosis and Main Criteria for Inclusion:

Diagnosis: RA subjects naïve to biologics.

- Subject has voluntarily signed and dated an informed consent form, approved by an Institutional Review Board (IRB)/Independent Ethics Committee (IEC), prior to any study-specific procedures.
- Subject is 18 years of age or older.
- If female, subject is either not of childbearing potential, defined as postmenopausal for at least 1 year or surgically sterile (bilateral tubal ligation, bilateral oophorectomy or hysterectomy), or is of childbearing potential and practicing one of the following methods of birth control:
 - condoms, sponge, foams, jellies, diaphragm or intrauterine device (IUD).
 - contraceptives (oral or parenteral) for three months prior to study drug administration).
 - a vasectomized partner.
 - total abstinence from sexual intercourse.
- If female, the results of a serum pregnancy test performed at Screening, prior to the first dose of Humira (Adalimumab) must be negative.
- Subject has confirmed diagnosis of active rheumatoid arthritis as defined by ≥ 6 swollen joints and ≥ 9 tender joints.
- Subject has an Erythrocyte Sedimentation Rate (ESR) of >20 mm/hr. ESR will be measured using the Westergreen method.
- Subject meets the ACR criteria for diagnosis of RA for at least 3 months prior to enrollment and requires to be started in a biologic containing treatment for the first time, and the investigator chooses Humira (Adalimumab).
- Subject has had unsatisfactory response or intolerance to one or more prior DMARDs (e.g. hydroxychloroquine, leflunomide, methotrexate, parenteral gold, sulfasalazine, azathioprine or any combination of those).
- Subject will have an evaluation for latent tuberculosis with a tuberculosis skin test done in the screening visit. Subjects who have evidence of prior TB infection should be given prophylaxis in accordance with CDC guidelines. The prophylaxis will start at least 30 days before Humira (Adalimumab) is administered, but the course of the prophylaxis need not be completed.



Test Product, Dose/Strength/Concentration, Mode of Administration and Lot Number: Humira (Adalimumab) 40 mg SC EOW.

Duration of Treatment: 24 weeks

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

Criteria for Evaluation

Efficacy: The primary endpoint was to evaluate quality of life changes in Puerto Rican subjects with Rheumatoid Arthritis treated with Humira (Adalimumab) as their first Anti-TNF Monoclonal Antibody. Quality of life will be evaluated using the Health Survey Questionnaire, Version 2 (SF-36 v2) and Modified Health Assessment Questionnaire (mHAQ). The secondary endpoint was to evaluate changes in American College of Rheumatology Response Criteria for RA in these subjects in 24 weeks of treatment.

Pharmacokinetic: N/A

Safety: Laboratory evaluations (hematology, chemistries, Hepatitis B and C tests, CRP, ESR, RF, ANA Test and Anti-DS DNA) were performed at screening. Hematology, chemistries and ESR were performed at baseline, ESR was performed at study weeks 2, 4, 8 and 16; and hematology, chemistries, CRP, ESR, RF ANA Test and Anti-DS DNA were performed at week 24/ET. Physical exams were performed at screening, baseline and week 24/ET visits. Adverse events assessments were performed at all study visits.



Statistical Methods

Efficacy: Descriptive statistics was made. Continuous variables were summarized by the number of observations, mean, median, minimum, and maximum; discrete variables were summarized by counts and percentages. Discrete variables will be summarized by counts and frequency distribution.

The DAS 28 was also evaluated in visits week 2, 4, 8, 16, and 24. % of change was evaluated compared to baseline.

Pharmacokinetic: N/A

Safety: Serious adverse events that began after the informed consent process and within 70 days after the last dose of study medication were considered.

Non-serious adverse events were collected from the time of the first dose.

Summary/Conclusions

Efficacy Results: Percent of reduction of DAS-28 compared to baseline in the different study weeks is as follows: 25.70%, 25.92%, 28.63%, 37.19% and 31.36% on weeks 2, 4, 8, 16 and 24/ET respectively.

The mean percent of change in the first set of questions of the Health Assessment Questionnaire from baseline to week 24 was 59% (17 vs 6.6).

The mean change in question 1 of SF-36 questionnaire (general health status) from baseline to week 24 was 16.7% (23 vs 19). In question 2 (general health now vs one year ago), the mean percent of change was 40.5% (23 vs 13). In terms of functionality questions, the mean change from baseline to week 24 was 20.3%. In the set of questions that asked about the general status during the last 4 weeks, the mean change from baseline to week 24 was 42.9%.

Pharmacokinetic Results: N/A

Safety Results: There were no safety concerns during the study. There were only 2 SAEs reported in the study. One of them was at the screening period (no drug received) and other was an hospitalization due to a fall, not-related to study drug.



Conclusions: There were 14 subjects enrolled into the study and 7 that completed it. Among the ones that completed the study, there was a reduction in the DAS-28 score as well as an increase in the QOL assessments. There were few cases to establish statistical significance among the results.