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:

An Open-Label, Prospective, Multicenter Study to Assess the Safety and Efficacy of Adalimumab (HUMIRA®) When Added to Inadequate Standard Anti-Rheumatic Therapy in Patients with Active Rheumatoid Arthritis

Coordinating Investigator: [redacted] redacted information 14Nov2014

Study Sites: 5 sites in the Russian Federation

Publications: None

Studied Period (Years):	**Phase of Development:** 3b
First Subject First Visit: 20 December 2007	
Last Subject Last Visit: 25 February 2010	

Objectives: The objectives of the study were to demonstrate the safety of adalimumab in subjects receiving concomitant anti-rheumatic therapy and the effectiveness of adalimumab when added to preexisting inadequate standard anti-rheumatic therapy in subjects with moderately to severely active rheumatoid arthritis (RA).

Methodology: This was an open-label, multicenter study. It consisted of a screening period, a study treatment period (Baseline [Day 0] through Week 24 with the last injection performed at Week 22), and a safety follow-up period of 70 days after the last dose of adalimumab.

Number of Subjects (Planned and Analyzed): 100

Diagnosis and Main Criteria for Inclusion: Subjects were males and females ≥ 18 years of age. Subjects were to have American College of Rheumatology (ACR) criteria for diagnosis of RA for at least 6 months, disease activity score (28 joints) (DAS28) ≥ 3.2 (at Baseline only), at least 6 swollen joints out of the 66 assessed, and at least 8 tender joints out of the 68 assessed. Subjects were to have a C-reactive protein (CRP) ≥ 1.5 mg/dL or erythrocyte sedimentation rate (ESR) ≥ 28 mm/1h at Screening and were to have had an unsatisfactory response or intolerance to prior DMARDs (must have failed at least 1 DMARD). Subjects were not to have had prior treatment with alkylating agents such as cyclophosphamide or chlorambucil within at least 5 years before enrollment; prior treatment with intravenous immunoglobulin or any investigational agent "chemical" in nature within 30 days, or 5 half-lives of the product, whichever was longer; prior treatment with cyclosporine within the last 6 months; or prior treatment with investigational biologic therapy (e.g., anti CD4). Subject was not to have had chronic arthritis diagnosis before the age of 17 years.

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

Adalimumab 40 mg/0.8 mL, subcutaneous injection

[redacted] (bulk lot number); [redacted] (commercial lot numbers)

Duration of Treatment: 24 weeks

Reference Therapy, Dose/Strength/Concentration and Mode of Administration and Lot Number: None

Criteria for Evaluation

Efficacy: Effectiveness variables included DAS28, ACR20/50/70 and their components, and the Health Assessment Questionnaire (HAQ). Exploratory variables included rheumatoid factor (RF), Anti-cyclic citrullinated peptide (anti-CCP), [redacted] Anti-CCP, [redacted]
redacted information 14Nov2014

Safety: Adverse events (AEs) and changes in laboratory and vital signs parameters were collected.

Statistical Methods

Efficacy: The efficacy analysis was descriptive. For continuous data, n, mean, standard deviation, minimum, 1st quartile, median, 3rd quartile, and maximum were presented, for categorical data, absolute and relative frequencies were calculated.

Safety: Treatment-emergent AEs (TEAEs) were summarized. TEAEs were defined as AEs with an onset date after the first adalimumab injection and until 70 days after the last adalimumab injection. AEs that started more than 70 days after the last adalimumab injection were considered as post-treatment AEs. In case of increasing severity of an existing AE, the worsening was considered as a new AE with a new onset date. Other safety variables, such as laboratory data, were analyzed descriptively. Tables and listings were provided for abnormal values, whereby the normal range of the analyzing laboratory was used.

Summary/Conclusions

Efficacy Results: Adalimumab was shown to be effective when added to preexisting inadequate standard anti-rheumatic therapy in subjects with moderately to severely active RA:

Improvement in DAS28 score was observed from Baseline to Week 24/Early termination (ET) (mean decrease of –2.75).

The proportions of subjects who achieved DAS ≤ 2.6 and DAS ≤ 3.2 increased over time. A total of 24.7% and 37.1% of subjects achieved DAS ≤ 2.6 and DAS ≤ 3.2, respectively, at Week 24/ET.

The proportions of subjects with ACR20/50/70 responses increased over time (Week 2 34.3%/6.1%/2.0%; Week 24/ET 87.9%/66.7%/26.3%).

Improvements from baseline to Week 24/ET were seen in ACR core set components.

Improvement from baseline (mean 1.861) was observed at each visit for the HAQ. At Week 24, subjects had a mean HAQ score of 1.042.

Improvement from baseline was observed at each visit for ESR and CRP.

Improvement from baseline was observed at Week 24/ET for RF, anti-CCP, [redacted] redacted information 14Nov2014

Safety Results: No deaths were reported during the study. One subject reported a serious TEAE (pyogenic arthritis; possibly related per the investigator). Thirty-eight subjects reported at least 1 TEAE. The most frequently reported TEAEs (4 subjects each) by MedDRA PT were nasopharyngitis and respiratory disorder. All but 1 subject reported events that were mild or moderate; 1 subject reported a severe TEAE (angioedema). Twenty-four subjects experienced TEAEs that were at least possibly related to study drug. Nasopharyngitis was the most frequently reported at least possibly related TEAE. Three subjects experienced at least 1 TEAE that led to premature discontinuation; all were nonserious. Changes in laboratory parameters and vital signs were unremarkable.

Conclusions: In this study, adalimumab was effective when added to preexisting inadequate standard anti-rheumatic therapy in subjects with moderately to severely active RA and was well tolerated in subjects with moderately to severely active RA who received concomitant anti-rheumatic therapy.