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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: Multicenter Early Access Program (EAP) of the Safety of Human Anti-TNF Monoclonal Antibody Adalimumab in Subjects with Active Rheumatoid Arthritis		
Investigator: Multicenter Program (investigator information on file at Abbott Laboratórios do Brasil)		
Study Sites: 18 sites in Brazil		
Publications: None		
Studied Period (Years): 1 year 2 months First Subject First Visit: 15 July 2003 Last Subject Last Visit: 29 September 2004	**Phase of Development:** 3b	
Objectives: The primary objective of this early access program (EAP) was to evaluate the safety of adalimumab, by collecting serious adverse events, in subjects with moderately to severely active rheumatoid arthritis who have failed one or more prior DMARDs. The secondary objective was to obtain efficacy data on these subjects.		

Methodology: Subjects with confirmed diagnosis of active rheumatoid arthritis, as defined by ≥ 6 swollen joints and ≥ 9 tender joints, could enter this access protocol upon enrollment by the treating physician who has registered for the program. The decision to adalimumab for treatment of the subject was based on the EAP-specific inclusion and exclusion criteria. Subjects were administered adalimumab 40 mg subcutaneously every other week and returned to assessment periodically. Safety was assessed by serious adverse events report. Physical examination and changes in disease activity score, as well as laboratory tests, were used as efficacy parameters. The statistical analyses were conducted in the intent-to-treat population (ITT). Continuous variables were summarized by the number of observations, mean, standard deviation, 1st quartile, median, 3rd quartile, minimum, and maximum; discrete variables were summarized by counts and percentages.

Number of Subjects (Planned and Analyzed): 200 patients planned, 62 patients analyzed

Diagnosis and Main Criteria for Inclusion:

1. Male or female ≥ 18 years old.
2. 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 drug administration)
   - A vasectomized partner
   - Total abstinence from sexual intercourse
3. If female, the results of a serum pregnancy test performed at Screening, prior to the first dose of adalimumab must be negative.
4. Confirmed diagnosis of active rheumatoid arthritis as defined by ≥ 6 swollen joints and ≥ 9 tender joints.
5. Subject meets the ACR criteria for diagnosis of RA for at least 3 months
6. Subject has active RA as defined by DAS28 ≥ 3.2 at entry.
7. 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).
8. Subject will have an evaluation for latent tuberculosis. Subjects who have evidence of prior TB infection should be given prophylaxis in accordance with CDC guidelines. The prophylaxis will start before adalimumab is administered, but the course of the prophylaxis need not be completed.
9. For those subjects using Prednisone, dose must be ≤ 10 mg/day.
10. Subject has voluntarily signed and dated an informed consent form, approved by local Health Authorities, prior to any EAP-specific procedures.
11. Subject agrees to the guidelines on prior and concomitant therapy as listed in Sections 5.2.3, *Prior and Concomitant Therapy* and 5.2.3.1, *Concomitant Therapy* **of the protocol.**
12. Subject will meet ACR Functional Class I, II or III (1992 criteria). See Appendix K of the protcol M03-583)

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

Adalimumab in prefilled syringes containing 40 mg adalimumab in 0.8 mL injection solution packed in a two-syringe-carton for subcutaneous usage.

Duration of Treatment: 1 (one) year

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

This was an open label study, with no comparative therapy.

Criteria for Evaluation

Efficacy: Response was evaluated by change in disease activity score (resulting from 28 swollen and tender joint count, ESR and VAS) at visit Week 12 as compared to baseline. These parameters were used to calculate the Patient General Health section of the DAS 28, which consisted on this program efficacy assessment.

Pharmacokinetic: No pharmacokinetic evaluation was conducted in this study.

Safety: Serious adverse events were collected and assessed throughout the early access program (EAP).

Statistical Methods

Efficacy: The primary objective of this Early Access Program was to evaluate safety. The efficcacy analyses were conducted in the intent-to-treat population (ITT), which is defined as all randomized subjects who received at least one dose of study drug.

Safety: Treatment-emergent SAEs were summarized and reported. The number and percentage of subjects experiencing SAEs were tabulated by body system and MedDRA preferred term. Baseline laboratory data were summarized using descriptive statistics.

Summary/Conclusions

Efficacy Results: Adalimumab significantly decreased DAS 28 from baseline to week 12.

Safety Results: Adalimumab was safe and well tolerated. Ten SAEs were reported, being 50% considered probably or possibly related to adalimumab, and 50% considered as probably not related or not related to adalimumab.

Conclusions: Adalimumab was safe and well tolerated in patients with active RA who failed to respond to previous treatment with DMARDs