2.0 Synopsis

<table>
<tr><td>Abbott Laboratories</td><td>Individual Study Table Referring to Part of Dossier:</td><td>(For National Authority Use Only)</td></tr>
<tr><td>Name of Study Drug:
Adalimumab</td><td>Volume:</td><td rowspan="2"></td></tr>
<tr><td>Name of Active Ingredient:
Adalimumab</td><td>Page:</td></tr>
<tr><td colspan="3">Title of Study:
Trial of Usability in Clinical Settings of the Humira Autoinjector vs. Pre-filled Syringe (TOUCH)</td></tr>
<tr><td colspan="3">Coordinating Investigator:
Alan Kivitz, MD CCI</td></tr>
<tr><td colspan="3">Study Sites:
Multicenter; six study sites in the United States enrolled subjects.</td></tr>
<tr><td colspan="3">Publications:
None</td></tr>
<tr><td colspan="2">Studied Period (Years):
First Subject First Visit: 29 Dec 2005
Last Subject Last Visit: 04 May 2006</td><td>Phase of Development: 2</td></tr>
<tr><td colspan="3">Objectives:
The objective of this study was to assess subject preference of the subcutaneous (sc) delivery administration of adalimumab via the autoinjector (Pen) vs. the pre-filled syringe. Additionally, this study compared injection site pain from sc administration of adalimumab via the Pen vs. the pre-filled syringe.</td></tr>
<tr><td colspan="3">Methodology:
Study M05-770 was a Phase 2, multicenter, non-randomized, open-label, single arm study. All subjects received three self-administered injections of adalimumab during the course of this study. The first dose was self-administered via the pre-filled syringe. The second and third doses were self-administered via the Pen. The approved adalimumab dose of 40 mg every other week (eow) was administered sc.
At Baseline, subjects were administered a questionnaire designed to assess the subject's overall HUMIRA® experience, or impression (e.g., How long have you been injecting, how long does it take, what is your overall impression of injecting HUMIRA with a syringe...). At subsequent visits, as described below, subjects were administered questionnaires to assess injection delivery method in terms of impression and preference as well as in terms of injection site pain.
At Visit 1, subjects self-administered an sc 40 mg dose of adalimumab via a pre-filled syringe at a 45° angle under supervision of study personnel. Subjects completed questionnaires at two time points post-injection: immediately post-injection and between 15-30 minutes post-injection.</td></tr>
</table>

At Visit 2, study personnel instructed the subjects on the proper administration of adalimumab (40 mg) *via* the Pen. A written brochure, instructional video, and an exact replica of the Pen were used in the instruction process. The subject self-administered the sc 40 mg dose of adalimumab injection *via* the Pen at a 90° angle at Visits 2 and 3 under supervision of study personnel. At both visits, subjects completed questionnaires immediately post-injection and between 15-30 minutes post-injection for each injection. Site assessments at Visit 2 and 3 were based on the observation of subject compliance following subject training.

A 70-day follow-up phone call was made to collect adverse event (AE) data.

Number of Subjects (Planned and Analyzed):

Planned: 50 subjects; Analyzed for efficacy and safety: 52 subjects

Diagnosis and Main Criteria for Inclusion:

Subjects must have fulfilled the American College of Rheumatology criteria for rheumatoid arthritis (RA) and must have been self-administering sc adalimumab for treatment of RA at a dose of 40 mg eow *via* a pre-filled syringe for at least 3 months prior to Screening.

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

Adalimumab, 40 mg/0.8 mL, sc

Bulk Drug Product Lot Number: 05-002299

Duration of Treatment:

Visit 1 to the 70-day phone call was 112 days. All subjects received three injections of adalimumab 40 mg over the duration of the study.

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

None.

Criteria for Evaluation

Efficacy:

This study was not designed to assess the efficacy of adalimumab, rather it was designed to assess preference for, and pain related to, two different sc adalimumab delivery devices. No differentiation is made between primary and secondary variables. Questionnaires were used for assessment.

Safety:

Safety was assessed by the assessment of AEs and vital signs.

Statistical Methods

Efficacy:

All subjects who received one injection using the adalimumab pre-filled syringe and at least one injection using the Pen were analyzed for subject preference and injection site pain.

Subject preference was summarized using counts and percentages to describe the number of subjects who preferred the adalimumab pre-filled syringe, the number who preferred the adalimumab Pen, and the number who had no preference. In addition, exact 95% confidence intervals were computed for the percentage of subjects who either preferred the Pen or had no preference compared to those who preferred the adalimumab pre-filled syringe.

The mean change from Visit 1 (adalimumab pre-filled syringe) to each subsequent study visit (Pen) with respect to injection site pain was analyzed using paired t-tests. In addition, 95% confidence intervals for the mean change from Visit 1 were computed to assess the clinical equivalence of injection site pain using the adalimumab pre-filled syringe and the Pen.

Safety:

All subjects who received at least one injection of study drug were included in the safety analyses. A summary of the number of days to which subjects were exposed to study drug was provided. Adverse events were summarized by counts and percentages.

Summary/Conclusions

Efficacy Results:

This study demonstrated subject preference of the Pen for the sc delivery of adalimumab and demonstrated that injection site pain was statistically significantly reduced when the Pen was used:

- A total of 88.5% of subjects reported an overall preference to the Pen over the pre-filled syringe (5.8%). Subject preference based on ease of use convenience, time it took to complete the injection, safety, and the occurrence of less pain was also in favor of the Pen.
- Subjects demonstrated statistically significant reductions in injection site pain immediately post-injection when comparing the syringe at Visit 1 and the Pen at Visits 2 and 3 (−1.4 and −1.6, respectively, in an 11-point scale) and 15 to 30 minutes post-injection (–0.6 and –0.6).

Furthermore, almost all subjects (94.2%) reported that they would be likely to use the Pen in the future if it was available at the same cost as the syringe, and would recommend it to other patients. The majority of subjects (90.4%) reported that the instructional video and written brochure prepared them to use the Pen.

Assessment performed by site personnel demonstrated high compliance in use of the Pen. This high level of compliance indicates that the Pen is relatively easy to use once subjects are trained.

Safety Results:

No new safety signals were observed during this study. Adalimumab was demonstrated to be safe and well-tolerated irrespective of syringe or Pen delivery. No statistically significant difference was observed between AEs reported during syringe use *vs.* Pen use either in terms of overall AEs or by individual Medical Dictionary for Drug Regulatory Activities (MedDRA) preferred term. One subject reported an AE that was considered at least possibly related to adalimumab while using the syringe (pneumonia probably related) and two while using the Pen (pneumonia, empyema, pneumothorax possibly related for one subject and cough probably related for the other subject). Two subjects had a SAE while using the Pen. Of these, one subject reported an SAE that was severe (cardiac failure congestive), and the other reported empyema, pneumonia and pneumothorax. No deaths were reported. No subjects discontinued from the study in response to a treatment-emergent AE. Three infections and one drug hypersensitivity reaction were reported. No other TNF inhibitor events of interest, including malignancies, demyelinating events (including multiple sclerosis), or lupus-like reactions, were reported during this study.

Conclusions:

This study demonstrated subject preference of the Pen for the sc delivery of adalimumab and demonstrated that injection site pain was statistically significantly reduced when the Pen was used. No new safety signals were observed during this study. Adalimumab was demonstrated to be safe and well-tolerated irrespective of syringe or Pen delivery.

Date of Report: 14Aug2006