



2.0 Synopsis

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| Abbott Laboratories | Individual Study Table Referring to Part of Dossier: Volume: Page: | (For National Authority Use Only) |
| Name of Study Drug: Adalimumab | | |
| Name of Active Ingredient: Adalimumab | | |
| Title of Study: A Multicenter, Randomized, Open-Label Study of the Injection Time and Usability of the Physiolis Syringe and Autoinjector in Injection-Experienced Rheumatoid Arthritis Patients | | |
| Coordinating Investigator: [REDACTED] MD, [REDACTED] | | |
| Study Sites: 10 sites in the United States [REDACTED] redacted information 23Sep2014 | | |
| Publications: none | | |
| Studied Period (Years): First Subject First Visit: 12 May 2010 Last Subject Last Visit: 01 Nov 2010 | Phase of Development: 2 | |
| Objectives: The primary objectives of this study were to assess the subject's overall satisfaction of the drug administration experience with the Physiolis prefilled glass syringe and autoinjector, to determine the difference in injection time for the current autoinjector configuration compared to the Physiolis autoinjector when injected in vitro (i.e., into a test tube) and in vivo, and to determine if there is a statistically significant difference in injection time when each delivery device is administered at room temperature compared to administration at 2° to 8°C. | | |
| Methodology: This was a Phase 2, open-label study consisting of 2 study phases with a total of 3 study visits, each visit occurring 2 weeks apart from each other. Phase A (User Experience) was a randomized, 2-period, cross-over phase in which single subcutaneous (SC) dose injections were administered using either the Physiolis autoinjector and current autoinjector or the Physiolis syringe and current syringe in a 1:1 ratio. Subjects re-randomized for Phase B. Phase B (Injection Time) was a randomized, single-visit, parallel-arm study, with an in vitro injection followed by a single in vivo SC injection of the Physiolis autoinjector or current autoinjector administered at 2 different temperature ranges (2° to 8°C and 20° to 27°C [room temperature]). If a subject only completed Visit 1 and Visit 2, then the subject was to be replaced for Visit 3. If the subject only completed Visit 1, the subject was to be replaced for all study visits. | | |
| Number of Subjects (Planned and Analyzed): Planned: 80 subjects Analyzed: 84 subjects in Phase A, 81 subjects in Phase B | | |
| Diagnosis and Main Criteria for Inclusion: Adult subjects with rheumatoid arthritis (RA) who have been self-injecting adalimumab 40 mg subcutaneously (SC) every other week (eow) without interruption for at least 3 months prior to screening. | | |



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| <p>Test Product, Dose/Strength/Concentration, Mode of Administration and Lot Number: Adalimumab supplied in prefilled syringes and autoinjectors, 40 mg/0.8 mL, SC injection Bulk Product Lot Numbers [REDACTED] redacted information 23Sep2014</p> |
| <p>Duration of Treatment: This study consisted of 3 different visits, each occurring 2 weeks apart from each other. Each subject was to receive 3 adalimumab 40 mg SC injections over a period of approximately 4 weeks.</p> |
| <p>Reference Therapy, Dose/Strength/Concentration and Mode of Administration and Lot Number: None</p> |
| <p>Criteria for Evaluation</p> <p>Efficacy: Efficacy data were not collected in this study.</p> <p><u>Primary Response Variables:</u></p> <ol style="list-style-type: none">1. To assess the subjects' overall satisfaction with the drug administration experience using the Physiolis prefilled syringe (Physiolis syringe) in comparison to the current prefilled syringe (current syringe) in a syringe user group.2. To assess the subjects' overall satisfaction with the drug administration experience using the Physiolis prefilled autoinjector (Physiolis autoinjector) in comparison to the current prefilled autoinjector (current autoinjector) in an autoinjector user group.3. To compare the injection time for the Physiolis autoinjector when administered at room temperature (20° to 27°C) to the administration time of not more than 10 seconds as specified in the current autoinjector ejection time specification (data on file at Abbott).4. To compare the injection time for the Physiolis autoinjector when administered at the storage temperature (2° to 8°C) to the administration time of not more than 10 seconds as specified in the current autoinjector ejection time specification (data on file at Abbott). <p><u>Secondary Response Variables:</u></p> <ol style="list-style-type: none">1. To determine the difference in injection time for the current autoinjector compared to the Physiolis autoinjector when injected in vivo (human).2. To compare the injection times for the current autoinjector injected in vivo (human) when administered at room temperature versus the storage temperature (2° to 8°C). <p>[REDACTED]</p> <p>[REDACTED]</p> <p>[REDACTED]</p> |
| <p>Safety: Adverse events, physical examination, vital signs, and laboratory data were assessed throughout the study.</p> |

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Statistical Methods

Efficacy: Efficacy data were not collected in this study.

The four primary hypotheses for usability evaluations and injection time measurements were tested at $\alpha = 0.10$ in hierarchical order using a fixed step-down method to adjust for multiplicity (i.e., a later hypothesis was to be tested only if the previous hypothesis was rejected). The first 2 hypotheses were tested for equivalence of user impression scores between current and Physiolis configurations with equivalence intervals of $(-1, 1)$ and $(-1.6, 1.6)$, respectively. The third and the fourth hypotheses were tested using a 2-sided alternative hypothesis ($\alpha = 0.10$) that the injection times differ at 2 temperatures for current autoinjector user and Physiolis autoinjector user. Descriptive summaries were provided for all questionnaire data collected. The primary efficacy population was the Intent-to-Treat population, which included all subjects who received at least 1 dose of study drug.

Safety: Treatment-emergent adverse events, laboratory parameters, and vital signs measurements were summarized.

Summary/Conclusions

This Phase 2, multicenter, randomized, open-label study had 2 periods: a cross-over phase consisting of 2 visits (Phase A) followed by re-randomization into a parallel-arm phase consisting of 1 visit (Phase B). A total of 84 RA subjects (42 current autoinjector users and 42 current syringe users) already on adalimumab treatment who fulfilled the study eligibility criteria were randomly assigned to the autoinjector or syringe arms (depending on whether they were current autoinjector or syringe users). For Visits 1 and 2, study drug was self-administered SC in either the abdomen or thigh. For Visit 3, investigator staff administered either the current or Physiolis autoinjector into the abdomen at either the storage temperature (2° to 8°C) or at room temperature (20° to 27°C). All randomized subjects who received at least 1 dose of study drug were included in the efficacy analyses (ITT population).

The study population was similar across treatment groups in both Phase A and Phase B, with no significant differences in demographics, medical history, baseline disease and other characteristics, and prior and concomitant medications observed between treatment groups. Approximately 80% of subjects were female, and 87% were white. Mean age was 56.5 years. Mean duration of RA was 11.3 years, and mean duration of adalimumab use was 3.5 years.

Efficacy Results: No efficacy data were collected in this study. Results of the primary and secondary response variables are as follows:

- For both the Physiolis syringe and the Physiolis autoinjector, the 90% CIs for the Subject Overall Satisfaction VAS were within their respective equivalence intervals, demonstrating that the Physiolis was equivalent to the current configuration in user overall satisfaction with the injection.
- The injection duration for the Physiolis autoinjector when injected either at room temperature (20° to 27°C) or at refrigeration temperature (2° to 8°C) was not more than 10 seconds ($P < 0.001$).



Efficacy Results (Continued):

- The difference in injection duration (in vivo) at room temperature (20° to 27°C) for the Physiolis autoinjector compared to the current autoinjector was not statistically significant (6.66 seconds versus 6.32 seconds, $P = 0.924$).
- The difference in injection duration (in vivo) for the current autoinjector at room temperature (20° to 27°C) compared to storage temperature (2° to 8°C) was not statistically significant (6.32 seconds versus 7.29 seconds, $P = 0.376$).

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Efficacy Results (Continued):

- [Redacted]
- [Redacted]

Safety Results: Adalimumab was well tolerated among this RA population of commercial adalimumab users, with no differences observed in the safety profile across the different injector types, needle types, and temperatures used in the study.

No deaths or other SAEs were reported. One subject had an AE after completing Phase A that led to study drug discontinuation (subject withdrew consent and did not enter Phase B).

During Phase A, 9 subjects (10.7%) reported 1 or more AEs. Events in 2 subjects (edema and swelling in 1 subject, and injection site reaction in 1 subject) were assessed by the investigator as probably related to study drug; all other events were assessed as probably not or not related. During Phase B, 1 subject (1.2%) reported 2 AEs, both of which were assessed by the investigator as not related to study drug. With the exception of moderate abdominal pain in 1 subject, all AEs were mild in severity.

No clinically meaningful differences were noted among the treatment groups in hematology, clinical chemistry, or urinalysis parameters, or in vital signs measures or body weight.

Conclusions: The results of this Phase 2, open-label study of injector usability in RA subjects who were experienced adalimumab users successfully demonstrated the equivalence of the Physiolis prefilled syringe and autoinjector to the current prefilled syringe and autoinjector, respectively, for subject overall satisfaction with the drug administration experience.

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