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: A Canadian open-label access program to evaluate the safety and the effectiveness of adalimumab when added to inadequate therapy for the treatment of psoriasis (PRIDE)

Investigator: [redacted] MD, PhD, FRCPC redacted information 10Nov2014

Study Site(s): 27 sites in Canada

Publications: 0

Studied Period (Years):	**Phase of Development:** 3b
First Subject First Visit: 19 September 2007 Last Subject Last Visit: 04 September 2008	

Objectives: The objectives of this study were to evaluate the safety profile, effectiveness, and economic impact of adalimumab when used for the treatment of subjects with active plaque psoriasis who have not adequately responded to prior psoriasis therapy.

Methodology: This was an open-label, multicenter Early Access Program, designed to further assess the safety and effectiveness of adalimumab in the treatment of subjects with active plaque psoriasis who had failed prior psoriasis treatment.

Number of Subjects (Planned and Analyzed): 250 planned, 203 enrolled and analyzed

Diagnosis and Main Criteria for Inclusion: Adult males and females with stable, moderately to severely active plaque psoriasis who had failed to respond to, or were intolerant to, topical agents, phototherapy, cyclosporine A, methotrexate, and oral retinoid. Subjects could have received prior systemic therapies, including biologics, regardless of their response to those therapies.

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

Adalimumab (40 mg/0.8 mL) was administered via subcutaneous injection using a pre-filled syringe housed in a pen device. Subjects received a loading dose of 80 mg adalimumab at Baseline, 40 mg adalimumab at Week 1, and 40 mg adalimumab every other week (eow) thereafter.

Lot number: [redacted] redacted information 10Nov2014

Duration of Treatment: 24 weeks

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

None

Criteria for Evaluation

Efficacy: The primary efficacy variable was PASI 75 response (75% reduction in the Psoriasis Area and Severity Index) at Week 16. Secondary efficacy variables included PASI 50/90/100, change and percent change from Baseline in PASI, Physician's Global Assessment of Psoriasis (PGA), Physician Global Assessment of Arthritic Disease Activity, swollen and tender joint count (SJC/TJC), patient global assessment of joint pain, Dermatology Life Quality Index (DLQI), Beck Depression Inventory-II (BDI-II).

Safety: Safety was assessed throughout the study by AE reporting, laboratory data, physical examinations, and assessment of vital signs.

Statistical Methods

Efficacy: Descriptive statistics were presented for all effectiveness variables. Counts and percentages were provided for categorical variables. Changes and percent changes from Baseline in continuous variables were summarized by number of subjects with both Baseline and visit values, Baseline mean, visit mean, and mean, standard deviation, median for change (percent change) from Baseline. Summaries were also provided for subgroups of subjects treated with topical or systemic therapies or phototherapy in combination with adalimumab, those treated with adalimumab monotherapy, as well as for subjects with and without prior exposure to other biologics. Comparisons between these subject subgroups were based on the appropriate statistical tests that included Analysis of Variance for continuous scale variables and the Fisher's Exact test for categorical variables.

Safety: Descriptive statistics were presented for adverse event, laboratory, and vital signs data.

Summary/Conclusions

Efficacy Results:

This open-label study evaluated the effectiveness of adalimumab when used for the treatment of subjects with active plaque psoriasis who had not adequately responded to prior psoriasis therapy.

Subjects enrolled in this study were predominantly male, White, and under 65 years of age. The mean duration of disease was 22.2 years, and 55.7% of subjects had > 20% BSA involvement. The majority of subjects had received phototherapy, systemic non-biologics, or topical treatments prior to enrollment in this study. Seventy-eight subjects (38.4%) had received prior biologic therapies and discontinued those therapies due to lack of efficacy (n = 25, 12.3%) or the termination of the clinical study/investigation in which the biologic had been administered (n = 29, 14.3%).

Mean compliance was 99.3% by Week 16 and 98.8% by Week 24.

The primary endpoint in this study was PASI 75 response at Week 16; this was achieved by 75.4% of subjects. Additionally, 76.5% of subjects achieved PASI 75 response at Week 24 (secondary endpoint). PASI 75 response rates were generally similar across subgroups with the exception that slightly higher response rates were observed among subjects who were < 40 years of age, male, or had no prior exposure to biologics.

Efficacy Results (Continued):

Consistent improvements were observed for the secondary and tertiary endpoints:

- PASI 50/90/100 responses were achieved at Week 16 in 88.5%/52.4%/25.7% of subjects, respectively; these response rates were maintained at Week 24. The mean percent PASI score decreased from Baseline by 81.5% and 83.0% at Weeks 16 and 24, respectively.
- The Physician's Global Assessment for Psoriasis tended to improve consistently over time. "Clear or Minimal" was achieved by 58.1% and 66.1% of subjects, and "Clear" was achieved by 27.7% and 32.2% of subjects at Weeks 16 and 24, respectively. Improvements were noted at Week 4 in 80.6% of subjects. No subjects were assessed as having Very Severe psoriasis from Week 12 onward.
- The mean Physician's Global Assessment of Arthritic Disease Activity score decreased from 27.4 at Baseline to 8.7 at Week 16 among subjects with non-zero activity at Baseline; this improvement was maintained at Week 24.
- Among subjects with non-zero activity at Baseline, the mean number of tender joints decreased from 14.9 at Baseline to 6.3 at Week 16; the mean number of swollen joints decreased from 6.4 to 1.7 during the same period. Both improvements were maintained at Week 24.
- The mean Patient's Global Assessment of Joint Pain was reduced by approximately 50% at Week 16 and was maintained at Week 24.
- A DLQI score of 0 (indicating total lack of impairment) was achieved by 35.1% and 45.6% of subjects at Weeks 16 and 24, respectively. An approximately 10-point mean improvement in DLQI was observed at Weeks 16 and 24 (a 2.3- to 5.7-point change is the minimum clinically important difference).
- The mean Beck Depression Index-II score was 9.2 at Baseline and decreased to 5.1 at Week 16 and to 5.0 at Week 24.
- The mean mPGA score improved from 39.3 at Baseline to 8.4 at Week 16 and from 39.2 at Baseline to 8.0 at Week 24. More than 97% of subjects showed mPGA improvements at each time point.

Safety Results:

In this study, the mean duration of adalimumab exposure was 167.3 days. Adverse events were reported for 145/203 subjects (71.4%). The majority of events was mild to moderate in severity and were not considered by the investigator to be possibly or probably related to study drug.

Nine subjects experienced SAEs, four of which were considered by the investigator to be possibly or probably related to adalimumab: one case each of basal cell carcinoma, renal vasculitis, Stevens-Johnson syndrome, and pneumonia. The subjects with renal vasculitis and Stevens-Johnson syndrome were discontinued from the study. Seven other subjects discontinued due to AEs that were not considered related to adalimumab.

Safety Results (Continued):

There were two deaths during the course of this study. Neither was considered by the investigator to be related to adalimumab.

Infections occurred in 40.9% of subjects in this study; however, nasopharyngitis and upper respiratory tract infection were the only events to occur in ≥ 5% of subjects. This is consistent with the known safety profile of adalimumab. There were two serious infections: pneumonia (possibly related to adalimumab) and appendicitis (not related to adalimumab).

No cases of demyelinating disorders, lupus-like syndrome, or congestive heart failure were observed during the study.

Laboratory and vital signs findings were unremarkable and no clinically meaningful trends were observed. There were 14 subjects with LFTs meeting potentially clinically significant criteria; however, the majority of abnormal values were transient and resolved by the end of the study.

These results suggest that adalimumab was safe and well-tolerated in these subjects with active plaque psoriasis who had not adequately responded to prior psoriasis therapy.

Conclusions:

Taken together, these results indicate that 16 weeks of treatment with adalimumab was safe, well tolerated, and effective in the treatment of subjects with active plaque psoriasis who had not adequately responded to prior psoriasis therapy, including with biologics. The overall responses observed after 16 weeks were maintained or improved after 24 weeks of treatment.