2.0 Synopsis

AbbVie Inc.	**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:

An Open-Label, Prospective Study to Assess the Safety and Effectiveness of Adalimumab (Humira®) in Patients with Moderate to Severe Plaque Psoriasis in the Russian Federation

Investigator:

[redacted] Moscow, [redacted]
Russian Federation

Study Sites:

7 study sites in the Russian Federation, though only 6 enrolled patients.

Publications:

None

Studied Period (Years):	**Phase of Development:**
First Subject First Visit: 23 May 2012 Last Subject Last Visit: 09 September 2013	

Objective:

This was an open-label study designed to establish the safety and effectiveness of adalimumab in the treatment of moderate to severe plaque psoriasis (Ps) after 24 weeks of treatment in the Russian Federation.

Methodology:

The study consisted of a 2- to 31-day screening period, a 24-week study treatment period, and a follow-up phone call 70 days after the last dose of study drug administration. Subjects were evaluated for response at each visit in the study treatment period.

All subjects received adalimumab in this open-label study. During the treatment period, subjects received an initial adalimumab 80 mg subcutaneous (SC) dose, followed by adalimumab 40 mg SC every other week, starting 1 week after the initial dose. No study drug was to be administered or injected at the final visit.

Number of Subjects (Planned and Analyzed):

Planned: 50 subjects

Analyzed: 50 subjects

Diagnosis and Main Criteria for Inclusion:

Subjects were to have a clinical diagnosis of Ps for at least 6 months as determined by subject interview of his or her medical history and confirmation of diagnosis through physical examination by the investigator, stable plaque Ps for at least 2 months before Screening and Baseline visits as determined by subject interview of his or her medical history, and moderate to severe plaque Ps (defined by ≥ 10% Body Surface Area (BSA) involvement and Physician's Global Assessment of Ps (PGA) score of 'Moderate' at the Baseline visit). Subjects were also to have a Ps Area and Severity Index (PASI) score of ≥ 10 at the Baseline visit. Subjects must have had a negative tuberculosis (TB) screening assessment (including a QuantiFERON-TB Gold test and negative chest x-ray (posterior-anterior and lateral views) at Screening. If the subject had evidence of a latent TB infection; the subject must have initiated and completed a minimum of 3 months of anti-TB therapy or have documented completion of a course of anti-TB therapy, prior to baseline.

Subjects with diagnoses of of erythrodermic Ps, pustular Ps, medication-induced or medication-exacerbated Ps or new onset of guttate Ps were excluded, as were subjects who had a diagnosis of other active skin diseases or skin infections (bacterial, fungal, or viral) that may have interfered with the evaluation of Ps or subjects who could not discontinue topical therapies for the treatment of Ps.

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

Adalimumab 40 mg/0.8 mL SC injection [redacted]

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 the proportion of subjects achieving at least a 75% improvement in the PASI (i.e., PASI 75) at Week 24 compared with baseline.

Secondary efficacy variables were:

- Proportion of subjects achieving PGA 0, achieving PGA 0/1, and achieving at least 1 grade improvement.
- The proportion of subjects achieving at least 50%, 75%, 90% and 100% improvement in the PASI (i.e., PASI 50, PASI 75, PASI 90, and PASI 100) compared with baseline.
- Change and percentage change in PASI from baseline.
- Changes in Dermatology Life Quality Index (DLQI) total score from baseline.
- Percent change in target fingernail Nail Psoriasis Severity Index (NAPSI) score from baseline.

Safety:

Adverse events (AEs), laboratory data, physical examinations, and vital signs were assessed throughout the study.

Statistical Methods

Efficacy:

Descriptive statistics were provided for effectiveness endpoints. Counts, percentages and 95% exact confidence intervals were provided for categorical variables. Mean, standard deviation, median, minimum, maximum and 95% confidence interval for mean were provided for continuous variables.

Safety:

The number and percent of subjects experiencing treatment-emergent AEs was tabulated using the Medical Dictionary for Drug Regulatory Activities (MedDRA®) system organ class and preferred term. In addition, summary of AEs by severity and relationship to study drug were presented. Summaries (including percentage and event per 100 patient-years) of serious AEs (SAEs), deaths, AEs leading to discontinuation from the study, and pre-specified AEs of special interest were provided as well.

Mean change from baseline in laboratory variables and vital sign variables at each visit were summarized. For selected parameters, a listing of all subjects with any laboratory determination meeting Common Toxicity Criteria (CTC) version 3.0 of Grade 3 or higher were provided. Shift tables for changes from baseline according to the normal range were also provided.

Summary/Conclusions

Efficacy Results:

At Week 24, a significant majority of subjects achieved PASI 75 response: among the 50 subjects treated in this study, 82% were responders. Similarly positive results were observed in all secondary efficacy endpoints:

- At Week 24, 35 subjects (70.0%) achieved a PGA value of 'clear' and 40 subjects (80.0%) achieved a PGA value of either 'clear' or 'minimal.' Almost all subjects (96.0%) experienced improvement (i.e., a shift from baseline to a less severe category) in PGA from baseline.
- Improvement in PASI continued from baseline until end of treatment at Week 24 (percent change: –91.18). Over 75% of subjects achieved PASI 75 response by Week 12.
- Improvement in DLQI continued from baseline until end of treatment at Week 24 (mean change: –11.0).
- Improvement in target fingernail NAPSI score continued from baseline until end of treatment at Week 24 (percent change: –68.06).

Safety Results:

Adalimumab was generally safe and well tolerated as evaluated by TEAEs, laboratory values, and vital signs values.

Fourteen (28%) subjects experienced at least 1 TEAE. The most frequently reported TEAE was latent TB (4 [8%] subjects). According to the study protocol, all subjects were required to have a QuantiFERON TB-Gold test performed at Week 24 or Premature Discontinuation. All 4 subjects with latent tuberculosis were asymptomatic with no abnormal findings on chest-x-rays, and all were directed to consult with a TB specialist.

All TEAEs were nonserious and mild or moderate in severity; no subjects experienced a severe TEAE. Most subjects' events were assessed by the investigator to be possibly (n = 7) or probably (n = 2) related to adalimumab.

There were no deaths or SAEs in this study. There were also no AEs leading to discontinuation of study drug.

Seven (14%) subjects experienced at least 1 treatment-emergent infection. Six of these treatment-emergent infections were considered by the investigator to be possibly (n = 4) or probably (n = 2) related to adalimumab. No opportunistic infections were reported.

One subject reported an event of urticaria during the study. This event was mild in severity and was considered by the investigator to be probably not related to adalimumab.

One subject reported TEAEs of alanine and aspartate aminotransferase increased, both of which resolved in 15 days and did not require a change in adalimumab therapy. These events were mild in severity and considered possibly related to study drug by the investigator.

No cases of lymphoma, NMSC, demyelinating disease, or hematologic events (serious or leading to permanent discontinuation) occurred during the study.

No clinically significant changes in mean laboratory values were observed. Shifts to high or low were generally infrequent. Changes in vital signs and urinalysis were clinically unremarkable.

Conclusions:

Adalimumab was efficacious, safe and well-tolerated in this study of 24 weeks of open-label adalimumab therapy in subjects with moderate to severe plaque Ps in the Russian Federation. The majority of subjects in this study met the primary endpoint of PASI 75 response at Week 24. Considerable efficacy was also observed in all secondary efficacy endpoints. The safety profile of 24 weeks of adalimumab treatment in this study is consistent with the experience in other adalimumab clinical trials in subjects with Ps.