2.0 Synopsis

Sponsor/Company:
Abbott Laboratories de México S.A. de C.V.

Name of finished product:
Humira.

Name of active ingredient:
Adalimumab.

Title of Study:
Immediate response with Adalimumab and its impact on quality of life and other comorbidity factors in patients with moderate to severe plaque psoriasis.

Investigators:
[redacted]

Study centre (s):
8 centres.

Studied period:
Date of first enrolment: 27.10.2010
Date of last completed: 03.02.2012

Phase of development:
Phase 4.

Objectives:
Primary study objectives

- To evaluate immediate response (Week-4) of Adalimumab in patients with moderate to severe plaque psoriasis naïve to systemic therapy or with an inadequate response to conventional systemic therapy or other biologic agents.

- To evaluate the impact of the treatment with Adalimumab on Quality of Life on weeks 4 and 16.

Secondary study objectives

- To evaluate the response to Adalimumab in patients with moderate to severe plaque psoriasis with an inadequate response to other biologic agents, including infliximab, etanercept, efalizumab and alefacept.
- To evaluate the effect of Adalimumab on other co-morbid factors, including body mass index, waist-hip ratio and its relation to treatment response.
- To determine whether cardiovascular risk factors (ie cholesterol, HDL, VLDL, LDL, triglycerides, CRP, homocysteine) are modified at Week-16.
- To evaluate the change in serum folate levels with therapy with Adalimumab at Week-16.

Methodology:

150 subjects having a diagnosis of active plaque psoriasis and fulfilling the study eligibility criteria were enrolled. Adalimumab was administered as follows: 80 mg at baseline, followed by 40 eow (stating at week 1 until week 15). Safety and efficacy measures were performed throughout the study.

Number of patients (planned and analyzed):
150 subjects planned and analyzed.

Diagnosis and main criteria for inclusion:

- Able and willing to give written informed consent prior to any study related procedure and to comply with the requirements of the study protocol.
- Male and female subjects between 18 and 75 years old.
- Diagnosis of moderate to severe plaque psoriasis with at least 6 months of duration.
- Documented moderate to severe plaque psoriasis based on Psoriasis Area and Severity Index (PASI) score >10.
- Subjects naïve to Adalimumab therapy.
- Negative active and latent tuberculosis (TB) infection evaluated by using a Purified Protein Derivative (PPD) skin test, chest x-Ray and a detailed review of subject´s medical history.
- A negative pregnancy test for women of childbearing potential prior to start of study treatment.
- Able and willing to self-administer subcutaneous injections or have available a suitable person.

- Subject is judged to be in generally good health as determined by the Investigator.

Test product, dose and mode of administration:

All participants received one dose of 80 mg of Adalimumab subcutaneous (SC) baseline followed by 40 mg eow (week 1 to week 15).

Duration of treatment:
15 weeks.

Reference therapy:
NA

Criteria for evaluation:

Efficacy:

- Percentage of patients with Psoriasis Area and Severity Index (PASI) 75 on Week-4 and Week-16.
- Percentage of patients with a Dermatology Life Quality Index (DLQI) <6 on Week-4 and Week-16.
- Mean change in DLQI score on Week-4 and Week-16.
- DLQI Week-4 and Week-16.
- Percentage of patients with Physician´s Global Assessment (PGA) of "almost clear" or "clear" on Week-16.
- Percentage of patients with PASI-50, 90, 100 in patients naïve to systemic therapy or with an inadequate response to conventional systemic therapy or other biologic agents on Week-4 and Week-16.
- Change in lipid profile, C-Reactive Protein (CRP), homocysteine serum levels from baseline to Week-16.
- Response to treatment in patients with obesity *vs*. patients without obesity.
- Change in serum levels of folic acid and vitamin B on Week-4 and Week-16.

Safety:

- Adverse events.
- Laboratory results.
- Vital signs.

Statistical methods:

Descriptive statistics for demographic and baseline variables was done. For continuous data, the number of valid observations, mean, standard deviation, minimum, first quartile, median, third quartile and maximum are presented. For categorical data, absolute and relative frequencies were calculated. Descriptive statistics for all variables of efficacy and some of safety (laboratory data). For categorical variables, number and percentage of each category, for continuous variables mean, standard deviation, minimum, first quartile, median, third quartile and maximum value. For clinical outcomes were described baseline and changes from baseline at weeks 4 and 16. Comparisons of means Week-0 and Week-4 and/or Week-16 were made with the dependent t test for paired samples and Wilcoxon Rank Test. The comparison of two proportions was performed using the Chi^2 test. For the analysis of observations at weeks 0, 4 and 16 was used the Friedman test.

Summary - conclusions:

Efficacy results:

- Response to Adalimumab was observed from the first weeks of administration, at Week-4, 31% of patients achieved PASI-75 and at Week-16 the percentage of subjects was increased to 85%.
- The effect of psoriasis on quality of life decreased throughout the study, at Week-4 65% of subjects reported a DLQI <6, at 16 weeks 86% of patients had a total score <6.
- The quality of life was significantly improved during treatment. The DLQI mean decreased from 11.7 (very large effect on quality of life) at baseline to 5.2 (small effect on quality of life) at Week-4, and 1.8 (no effect on quality of life) at Week-16.
- The percentage of patients with DLQI that showed a very large effect (Total Score 11-20) and extremely large effect (Total Score 21-30) in their lives was reduced from 56% at baseline to 14% at Week-4, and to only 4% at Week-16.
- The percentage of patients achieving improvement with Adalimumab treatment was observed from the first 4 weeks: 59% of patients achieved PASI-50, 11% PASI-90 and 2% PASI-100. The response was much better at Week-16 when it was observed 93% of patients

PASI-50, 73% PASI-90 and 49% PASI-100.

- The severity of the disease decreased with the treatment. At week 16, 76% of patients had a Physician's Global Assessment "clear" or "almost clear".
- Response was also found in nail psoriasis, 56% of patients achieved NAPSI-50, 42% NAPSI-75 and 29% NAPSI-90 at week 16.
- A different response was observed between obese and non-obese patients: 76% of obese subjects achieved PASI-75 compared to 92% of non-obese subjects.
- Response in quality of life was similar in obese and non-obese patients.
- At Week-16 there were no significant differences in the mean values of total cholesterol, HDL, VLDL, LDL and triglycerides, but there was a significant decrease in the mean values of C-Reactive Protein and homocysteine.
- There was a significant decrease in the values of folic acid and vitamins B6 and B12 at 16 weeks compared to Week-0.

Safety Results:

- None of the patients experienced serious adverse events or death during the study.
- 85% of adverse events that occurred were graded as mild, and only 17.4% were classified as possibly or probably related to Adalimumab.
- The most common adverse event related to the administration of Adalimumab was pain and pruritus at site injection, which was occurred in 12 occasions in seven patients.

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