1.0 Abstract

Title

Prevalence and Incidence of Articular Symptoms and Signs Related to Psoriatic Arthritis in Patients with Psoriasis Severe or Moderate with Adalimumab Treatment (TOGETHER).

Keywords

Psoriasis, Incidence, Quality of Life, Psoriatic Arthritis, Prevalence

Rationale and Background

Psoriasis (Ps) is a chronic inflammatory disease affecting 1% to 3% of the population worldwide. A significant portion (5% – 40%) of patients with Ps develop psoriatic arthritis (PsA), a chronic inflammatory arthritis that causes progressive joint damage, reduced functionality and increased mortality risk. Skin disease typically manifests before arthritis in more than 80% of PsA patients, and psoriasis symptoms usually precede joint symptoms by an average of 10 years. Patients with Ps who have comorbid PsA incur substantially increased cost of care and experience greater impairment of physical functioning and quality of life compared with patients with psoriasis alone.

Given the significant disease and economic burden of PsA, it is important to describe the prevalence of articular signs and symptoms among patients with moderate to severe Ps in Colombia and to assess the effectiveness and safety of adalimumab treatment in treating these conditions in a real-world Colombian clinical setting.

Research Question and Objectives

The overall objective of this study is to describe the profile of patients with severe or moderate Ps in Colombia and to assess the effectiveness and safety of adalimumab treatment.

Primary objective: To describe the effect of adalimumab treatment in patients with active moderate to severe Ps regarding PsA symptoms.

Secondary objectives:

- To determine the time between Ps diagnosis and time of onset of PsA symptoms or signs.
- To describe the demographic characteristics of this population.
- To evaluate the improvement of skin symptoms in patients with moderate to severe chronic plaque Ps treated with adalimumab.
- To evaluate the safety profile of adalimumab.
- To establish the most frequent co-morbidities related to Ps and PsA.
- To assess the impact of adalimumab treatment on health-related QoL.
- To measure the proportion of Ps patients with articular symptoms and signs.
- To determine the prevalence and incidence of PsA in patients with Ps diagnosis during their first year of treatment with adalimumab.

Study Design

Transversal, descriptive, prospective, open label, single cohort, postmarketing observational study.

Setting

Ps patients treated with adalimumab were followed by their treating physician for a maximum period of 1 year. The investigational sites consisted of 33 private practices of dermatologists with experience in the treatment of Ps patients and rheumatologists with experience in PsA. All treatments and patient management were as per routine care with suggested assessments at Months 2, 6 and 12. Additional assessments could also occur as per the judgment of the treating physicians.

Subjects and Study Size, Including Dropouts

Based on practical considerations, namely the study duration and the population size constraints in Colombia, a sample size of 142 evaluable patients was planned to be enrolled. Assuming a 20% attrition rate for loss to follow-up the final sample size requirement was established at 177 patients. At the time of study discontinuation, 52 patients had been enrolled in the study.

Variables and Data Sources

Examinations, diagnostic measures, findings and observations routinely performed in patients were entered by the investigator or staff according to the protocol in the case report forms (CRF) provided.

Patient-reported outcomes included QoL as assessed by the SF-36 questionnaire and pain evaluated using a VAS scale. Physician assessments included the PASI questionnaire (dermatologists) and the CASPAR criteria (rheumatologists) to evaluate skin symptoms and PsA symptoms and signs, respectively, assessment of joint symptoms and extra-articular manifestations, the number of joint tenderness and swelling, as well as physician global assessment of disease activity on a VAS scale (rheumatologists). Safety was assessed with the incidence of treatment-emergent adverse events (AEs).

Results

The mean (SD) age at baseline was 48.85 (14.66) years and 59.6% were male. Overall, among the 52 patients with psoriasis enrolled in the study, 19 (36.5%) developed PsA, as per the two protocol-specified definitions, during the course of the study. The crude incidence rate (95% CI) of PsA since the diagnosis of psoriasis was 2.66 (1.70 – 4.14) per 100 person-years. The proportion of patients with one or more inflamed joints or a CASPAR score of ≥3 decreased from 17.3% at baseline to 10.3% and 3.6% after 6 and 12 months of treatment with adalimumab, respectively. Furthermore, the proportion of patients who met at least one of the two protocol-specified definitions of PsA significantly decreased from 46.2% at 6 months to 35.7% after 12 months of treatment with

adalimumab, respectively ($p < 0.001$). Finally, the proportion of patients with self-reported or physician-reported (inflamed joints) articular signs or symptoms decreased from 61.2% at baseline to 33.3% ($p = 0.002$) and to 25.0% ($p = 0.112$) after 6 and 12 months of treatment with adalimumab, respectively; the mean (95% CI) time from psoriasis diagnosis to first occurrence of articular signs or symptoms was 23.17 (16.33 – 30.01) years.

Statistically significant (significantly different than zero) within group improvements over time were observed from baseline in PASI with a mean (SD) decrease of –11.56 (11.96) ($p < 0.001$) at Visit 2, –13.12 (12.69) ($p < 0.001$) at Visit 3, and –15.17 (12.69) ($p < 0.001$) at Visit 4. The comorbid profiles of patients who developed PsA and those who did not were similar and not significantly different. The general health and social functioning SF-36 scales showed a statistically significant increase (improvement) in scores from baseline to Visit 3 and Visit 4. Statistically significant within group differences were observed for the change in general health and social functioning with a mean (SD) increase of 8.24 (28.3) ($p = 0.026$) and 13.56 (29.24) ($p = 0.006$) at Visit 3, and 12.95 (31.45) ($p = 0.006$) and 13.39 (36.98) ($p = 0.014$) at Visit 3, respectively. The change in role-emotional showed the highest increases in scores at Visit 4 with a mean (SD) of 15.67 (34.05) ($p = 0.003$). The proportion of patients with a CASPAR score ≥ 3 significantly decreased from 67.3% at baseline to 64.1% after 6 months of treatment ($p = 0.009$). The proportion of patients with SJC = 0 significantly increased from 75.5% at baseline to 92.9% ($p = 0.043$) at Visit 4. Similarly, the proportion of patients with TJC = 0 significantly increased from 63.3% at baseline to 85.7% ($p = 0.007$) at Visit 4. The proportion of patients reporting joint symptoms significantly decreased from 61.2% at baseline to 30.8% ($p = 0.004$) at Visit 3 and to 25.5% ($p < 0.001$) at Visit 4. The proportion of patients with peripheral arthritis decreased from 32.7% at baseline to 17.9% at Visit 4, while the proportion of patients with morning stiffness (peripheral) decreased from 24.5% at baseline to 11.1% at Visit 4. The majority of the patients were compliant with treatment. There were 86.3%, 77.1% and 75.6% of the patients who had taken $\geq 80\%$ of their study medication. Adalimumab was well tolerated during the course of the study. A total of 65 adverse events (including non-SAEs and SAEs) were experienced by

19 patients. Of the total AEs reported, 28 (43.1%) were considered to be possibly or probably related to study medication. Forty-nine of the 65 adverse events experienced by 16 patients met at least one of the SAE criteria and were therefore considered as SAEs. The most frequently reported SAEs by preferred term were: transaminases increased (3.8%), neck pain (3.8%) psoriatic arthropathy (3.8%), blister (3.8%), psoriasis (3.8%), and rash generalized (3.8%). No deaths were reported during the course of the study. A total of 16 non-SAEs were experienced by 8 patients. None of the SAEs were experienced by ≥ 5% of the study population whereas among the non-SAEs only influenza like illness (9.6% of patients) met this criterion.

Discussion

The results of the current study have shown that the crude incidence rate (95% CI) of PsA since the diagnosis of psoriasis was 2.66 (1.70 – 4.14) per 100 person-years. Twelve-month treatment with adalimumab was associated with a decrease in the proportion of patients with ≥ 1 inflamed joint or a CASPAR score of ≥ 3 as well as in the proportion of patients with articular signs or symptoms. Furthermore, treatment with adalimumab improved health-related quality of life and decreased disease activity during the course of the study. No new safety signal or trend is identified during this trial. These findings should be interpreted with caution due to the small sample size of the study.