1.0 Abstract

Title

Canadian Humira Post Marketing Observational Epidemiological Study: Assessing Effectiveness in Psoriasis (Complete - Psoriasis)

Keywords

Humira, psoriasis, effectiveness, real-world

Rationale and Background

For moderate to severe psoriasis that does not respond to topical agents or phototherapy, systemic treatments are used, either in monotherapy or in combination therapy with topical agents. These include traditional and biologic disease modifying agents. Adalimumab (Humira®), one such biologic, is a fully human anti-TNF-α monoclonal antibody which, in inhibiting the action of TNF-α, halts the inflammatory processes characteristic of psoriasis.

Complete is a three-part Canadian observational research study program aimed at assessing the real-life effectiveness of adalimumab in the management of psoriasis, psoriatic arthritis and ankylosing spondylitis. More specifically, the aim of the current study was to assess clinical and patient reported outcomes that are relevant in the management of moderate-to-severe psoriasis and its impact on the patient's quality of life and societal burden of illness. The results of this study will also add to the existing evidence on long term safety of adalimumab.

Research Question and Objectives

The primary objective of this study was to compare the real – life effectiveness of adalimumab to topical and traditional systemic agents in the management of moderate to severe plaque psoriasis in Canada.

Secondary objectives included assessment of articular and extra-articular manifestations of psoriasis; description of the profile and regional variation of Canadian psoriasis patients in terms of demographics, disease parameters, flare – up trigger, comorbidities and concomitant medication use; and assessment of the impact of treatment on psoriasis-related burden of illness, incorporating health care utilization and costs, quality of life, psychological impact, and work productivity.

Ongoing safety and tolerability of adalimumab, and of systemic and topical agents, was also ascertained.

Study Design

This was a Canadian post-marketing observational study (PMOS) utilizing a prospective cohort design. Patients were entered into one of two study cohorts (adalimumab cohort or topical/traditional systemic cohort) at the time of change of their psoriasis treatment for any reason and were followed for a maximum of 24 months with recommended assessments at 3, 6, 12, 18 and 24 months after baseline.

Setting

Patients were enrolled from the offices of community dermatologists across Canada treating patients with psoriasis.

Subjects and Study Size, Including Dropouts

A total of 662 patients were enrolled in the study, of which 658 were included in the safety population, and 595 were included in the ITT. Overall, 244 patients did not complete the study, with reasons primarily lost to follow up (n = 122).

Variables and Data Sources

The primary outcome measure was the percent of patients with a physician global assessment (PGA) score of ≤ 1.0 at 6 months of treatment.

Secondary effectiveness outcomes included:

- Time to PGA ≤ 1 over 24 months of follow-up
- Percent of patients with PGA ≤ 1.0 at 3, 12, 18 and 24 months
- Change in the Psoriasis and Arthritis Screening Questionnaire (PASQ) at 3, 6, 12, 18 and 24 months
- Change in Body Surface Are (BSA) at 6, 12, 18 and 24 months
- Change in the Dermatology Quality of Life Index (DLQI) at 3, 6, 12, 18 and 24 months
- Proportion of patients achieving and time to DLQI ≤ 1 through 24 months
- Change in Beck Depression Inventory (BDI) at 6, 12 and 24 months
- Change in Medical Outcome Study Short Form 12 (SF-12) at 6, 12 and 24 months
- Change in Working Limitations Questionnaire (WLQ) at 6, 12 and 24 months
- Health Care Utilization (HCU) and Health Economics Questionnaire through the 24 months of treatment
- Compliance with treatment over 24 months

Safety was assessed with the incidence of treatment-emergent adverse events (AEs) as recorded by the treating physician through the spontaneously reported events during the 24 months of treatment.

Results

The proportion of patients achieving a PGA ≤ 1 at Month 6, was reported by 56.3% (n = 139/293) of the adalimumab cohort and 31.4% (n = 70/302) for patients initiated on a topical/traditional systemic agent ($P < 0.001$). Logistic regression models identified adalimumab treatment to be a significant positive predictor of PGA ≤ 1 at Month 6, with

these odds 3.1 (95% CI: 2.4, 4.1) times higher than the topical/traditional systemic agent cohort in the bivariate model, and 2.4 (1.3, 4.3) times higher in the adjusted multivariable analysis. Odds for the achievement of DLQI ≤ 1 over 24 months, adjusting for baseline DLQI, indicated a 2-times higher chance for adalimumab patients to achieve DLQI ≤ 1 at any time point during the study, compared to patients initiated on topical/traditional systemic agents.

Analysis of time-to PGA ≤ 1 and DLQI ≤ 1 achievement also confirmed significantly (P < 0.05) more rapid achievement of both endpoints for the adalimumab vs. topical/traditional systemic agent cohort [median (95% CI) for PGA ≤ 1: 5.7 (4.4, 6.0) vs. 13.3 (11.8, 22.0) months; DLQI ≤ 1: 8.2 (6.3, 12.0) vs.17.7 (11.5, NE) months].

No notable between-cohort differences in unadjusted BDI-II (depression), SF-12 (quality of life) or WLQ scores (work limitation and productivity) were observed at any follow-up visits. Statistically higher unadjusted PASQ scores observed for adalimumab-initiated patients at baseline [6.6 (4.4) vs. 8.3 (4.8); P < 0.001], Visit 2 [6.3 (4.3) vs. 7.6 (4.5); P = 0.003], and Visit 3 [6.3 (4.4 vs. 7.5 (4.5); P = 0.016], with statistical trends for higher PASQ in the adalimumab cohort identified up to Visit 5 (P < 0.150).

Health care utilization was also not found, in general, to differ between treatment cohorts at any study visit. However, for the ITT population, the proportion of patients reporting HCU in the 4 weeks preceding the visit in question, decreased steadily over time from 65.2% (n =388/595) at baseline to 38.5% (n = 181/470) at Visit 3, 39.3% (n = 170/433) at Visit 4, and 30.9% (n = 112/362) at Visit 6.

Statistically significant (P < 0.050) regional differences were observed in patient profiles (race, smoking habits, alcohol consumption and employment status), as well as in psoriasis history, psoriasis medication profiles and in PGA of disease activity. No significant regional difference was observed in CRP, ESR, BSA and rheumatology consults at baseline.

With respect to safety, the number and proportion of patients reporting AEs and SAEs was considerably greater in the adalimumab cohort compared to the topical/traditional

systemic agent cohort [AEs: 10.1% (n = 33) vs 0.6% (n=2)]); SAEs: 7.0% (n = 23) vs. 0.6% (n =2), respectively].

Discussion

The results of this study indicate that treatment with adalimumab was effective in reducing disease activity and improving quality of life outcomes in people living with moderate-to-severe plaque psoriasis in Canada. In addition, effectiveness was found to be significantly greater for adalimumab-treated patients compared to those initiated on a topical/traditional systemic agent. Rapid improvements in disease activity and in PROs were also observed, which were sustained to the end of the follow-up period. Although treatment with adalimumab resulted in a greater number of AEs relative to treatment with tropical/traditional systemic agent, including higher rates of cancer and infections, adalimumab still demonstrated a tolerable and consistent with known safety profile of adalimumab.

Conclusion

These findings have important implications for both physicians and patients, indicating that adalimumab is more effective than traditional topical or systemic therapies in the management of moderate-to-severe psoriasis in routine clinical care, and that it is relatively safe and tolerable. Additional research is warranted to further characterize the regional variation observed with respect to baseline patient and disease profile.

Marketing Authorisation Holder(s)

AbbVie Corporation

Names and Affiliations of Principal Investigators

Please refer to Annex 1. List of Investigators