

1.0 Abstract

Title

Canadian Humira Post Marketing Observational Epidemiological Study: Assessing Effectiveness in Psoriatic Arthritis (COMPLETE – PsA)

Keywords

Adalimumab; Effectiveness; Psoriatic Arthritis; Post-Marketing Observational Study

Rationale and Background

Adalimumab (ADA) has been approved in Canada for the treatment of moderate to severe PsA among patients who did not respond or were intolerant to traditional disease modifying anti-rheumatic drugs (DMARDs). Complete-PsA was an observational study among biologic-naïve Canadian adults with active PsA who were treated with ADA or DMARDs. The study aimed to assess the real-life effectiveness of ADA in the management of PsA compared to DMARDs.

Research Question and Objectives

The primary objective was to compare the real-life effectiveness of adalimumab to traditional non-biologic DMARDs in the management of articular and dermatological manifestations of moderate to severe PsA.

The secondary objectives were:

1. to describe the profile and regional variation in terms of demographics, disease parameters, comorbidities, concomitant medication use and management by dermatologists and rheumatologists of Canadian patients with PsA;
2. to describe the population-based burden of illness of PsA in Canada in terms of quality of life, health care utilization, work productivity, health care costs, depression and psychological impairment;
3. to compare the effect of non-biologic DMARDs and adalimumab on PsA related burden of illness in terms of quality of life, health care utilization, work productivity, health care costs, depression and psychological impairment in Canada;
4. and to provide an ongoing assessment of the real – life safety and tolerability of adalimumab and non-biologic DMARDs used under routine care in Canada.

Study Design

This was an observational study utilizing a prospective cohort design. Patients were enrolled at the time their PsA treatment was changed for any reason and followed up for 24 months with recommended visits occurring at 3, 6, 12, 18, and 24 months after baseline visit.

Setting

Patients were enrolled from rheumatologist and dermatologist practices across Canada. Selection of physicians was done so that they were a random representation of the Canadian population and reflected the distribution of rheumatologists/dermatologist. A total of 40 sites were included from British Columbia, Manitoba, Ontario, Quebec, Nova Scotia, and Newfoundland and Labrador.

Subjects and Study Size, Including Dropouts

A total of 486 patients were enrolled in the study, specifically 185 (38.1%) in the DMARD treatment group and 301 (61.9%) in the ADA treatment group. The safety population, defined as all patients who received at least one dose of study medication, consisted of 484 patients (185 [100.0%] and 299 [99.3%] in each treatment group, respectively). The ITT population, defined as all patients who received at least one dose of study medication and met all inclusion/exclusion criteria, consisted of 425 patients (148 [80.0%] and 277 [92.0%], respectively). Overall, 316 (74.4%) patients completed the study. These results were similar across treatment groups, with a total of 71.6% of DMARD-treated patients completing the study compared to 75.8% of ADA-treated patients.

Variables and Data Sources

Variables assessed in this study included Health Assessment Questionnaire Disability Index (HAQ-DI), Patient's Global Assessment of Disease Activity (SGA), Patient Assessment of Pain, Dermatology Life Quality Index (DLQI), Psoriasis and Arthritis Screening Questionnaire (PASQ), Medical Outcome Study Short Form 12 (SF-12), Health Care Utilization and Health Economics Questionnaire, Working Limitations Questionnaire (WLQ), and Beck's Depression Inventory (BDI), Tender (TJC) and Swollen (SJC) Joint Counts based on 28 joints, enthesitis (Achilles Tendon and Plantar Fascia) and dactylitis, Physician's Global Assessment of Disease Activity (PGA), duration of morning stiffness, and body surface area affected by psoriasis (BSA)

Results

Over the course of the study, ADA-treated patients experienced significantly greater reductions in DAS-28 scores compared to DMARD-treated patients, with baseline-adjusted DAS-28 scores being consistently higher in DMARD- vs. ADA-treated patients up until 12 months, inclusively. Specifically, the least square means (LSM) in DMARD- vs. ADA-treated patients were 3.9 vs. 2.9 ($p<0.001$) at 3 months, 3.6 vs. 2.7 ($p<0.001$) at 6 months, and 3.4 vs. 2.6 ($p<0.001$) at 12 months.

Furthermore, ADA-treated patients showed a greater response to treatment in terms of other disease outcomes/PROs particularly early on during treatment. At month 3, the baseline-adjusted TJC (DMARD- vs. ADA-treated patients: 6.2 vs. 3.8; $p<0.001$), SJC (4.4 vs. 2.6; $p<0.001$), and PGA (38.5 vs. 25.5; $p<0.001$) scores were significantly lower in ADA-treated patients. These differences also continued up to 6 months for PGA and up to 12 months for SJC, inclusively. DLQI and SF-12 PCS were only assessed at month 6 for a first follow-up visit, and also showed significantly higher improvement early on among ADA-treated patients; specifically, at 6 months, the mean baseline-adjusted DLQI score in DMARD- vs. ADA-treated patients was 4.0 vs. 2.5 ($p=0.032$) while the mean baseline-adjusted SF-12 PCS score was 35.2 vs. 42.8 ($p<0.001$), respectively. For the remaining treatment periods, outcomes were statistically comparable between treatment groups.

ADA-treated patients were more likely to achieve therapeutic thresholds, specifically with HRs (95% CI) as follows: 2.4 (1.7-3.4) for ACR20, 2.4 (1.6-3.6) for ACR50, 2.8 (1.7-4.5) for ACR70, 2.1 (1.5-2.9) for PsARC, 2.4 (1.7-3.5) for DAS-28 remission, and 1.7 (1.2-2.5) for modified MDA.

Regarding safety/tolerability, AEs and SAEs were mostly comparable between groups, however DMARD-treated patients had lower rates, specifically 1.6% vs. 10.7% and 1.6% vs. 8.0%, respectively for DMARD- vs. ADA-treated patients. Among ADA-treated patients, the most commonly reported AE relationship to study drug was not related (4.0% of patients) compared to possibly related (2.7%), probably not related (1.3%), or probably related (1.0%). The number of deaths was comparable, whereby there were 0 among DMARD-treated patients compared to 2 among ADA-treated patients.

Discussion

Patients with PsA who are treated with ADA have greater response to treatment compared to DMARD-treated patients and are more likely to achieve therapeutic targets including thresholds for disease activity. Furthermore, ADA is well tolerated and demonstrates a similar safety profile to DMARDs.

Marketing Authorisation Holder(s)

AbbVie Corporation

Names and Affiliations of Principal Investigators

A list of principal investigators and affiliations are presented in Appendix- Annex 3.