Enhanced Effectiveness of Adalimumab Compared to Topical/Traditional Systemic Agents in the Treatment of Moderate to Severe Plaque Psoriasis: Results from a Canadian Observational Epidemiologic Study (COMPLETE-PS)

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ABSTRACT

Introduction: Real-world evidence is important for post-marketing evaluation. Data comparing adalimumab's effectiveness and safety with traditional therapies in clinical settings are currently lacking. The aim of this study was to compare real-world effectiveness of adalimumab versus topical/traditional systemic agents for management of moderate to severe plaque psoriasis

Methods: Patients requiring change in treatment were enrolled between 2011 and 2016 and followed per routine care for up to 24 months. Achievement of Physician Global Assessment (PGA) ≤ 1.0 at 6 months was assessed with logistic regression; time to achievement was assessed using Cox regression. Additional outcomes were assessed using repeated measures mixed models.

Results: Patients receiving adalimumab ($n = 293$) versus topical/traditional systemic agents ($n = 302$) were more likely to achieve PGA ≤ 1.0 at 6 months (odds ratio 2.37, 95% confidence interval [CI] 1.31–4.30) in a shorter time (hazard ratio 2.14, 95% CI 1.53–3.00), reporting both lower body surface area and improved quality of life and work productivity.

Conclusion: In this real-world study, adalimumab was more effective than topical/traditional systemic agents at reducing disease activity and improving quality of life outcomes among Canadians with moderate to severe plaque psoriasis. (NCT00799877).

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Key Summary Points

Why carry out this study?

There is currently a paucity of real-world studies evaluating the comparative effectiveness of psoriasis treatment regimens.

The study focuses on the real-world assessment of the impact of adalimumab when compared to topical/traditional systemic agents for management of moderate to severe plaque psoriasis.

What was learned from the study?

Adalimumab was more effective in real-world than topical/traditional systemic agents at reducing disease activity and improving quality of life outcomes among Canadians with moderate to severe plaque psoriasis.

Results are in line with those reported in randomized controlled trials of adalimumab and could therefore inform decision-making in the management of patients with plaque psoriasis.

INTRODUCTION

Psoriasis is an immune-mediated illness characterized by chronic non-contagious skin manifestations [1] caused by an immunologically accelerated cell turnover [2], with plaque psoriasis being the most common type. The global prevalence of psoriasis has increased over the last three decades, rising from 758 cases per 100,000 in 1990 to 812 cases per 100,000 in 2017 [3]. According to the Canadian Dermatology Association, it is estimated that psoriasis will affect 1 million Canadians in 2021 [4]. In the USA, prevalence of psoriasis is also high, affecting more than 7.4 million adults [5]. New incidence of psoriasis in Canada has increased from 0.09% in 2000 to 0.15% in 2015 [6].

For moderate to severe psoriasis, topical first-line drugs are recommended as adjuncts alongside additional treatments, including phototherapy or systemic therapy, which consist of traditional (i.e. methotrexate and cyclosporine) and biological agents. At the time of study enrollment, Canadian guidelines in effect were those published in 2009 [7]; these have remained the same with the exception of an addendum in 2016 to include new treatment options [8].

Early in the biologic treatment landscape, four such treatments had US Food and Drug Administration and Health Canada approval for treatment of moderate to severe psoriasis, all of which were tumour necrosis factor-alpha inhibitors [9, 10]. Today, more than 20 types of biologic treatments, including biosimilars, are approved in the USA, while 12 biologic/biosimilars are currently available in Canada [11]. Adalimumab was one of the earliest biologics to be approved for the treatment of plaque psoriasis and has been investigated in several key clinical trials; with more than 15 years of clinical experience underlying its use, adalimumab remains an important treatment option in moderate to severe psoriasis [12].

Real-world evidence is important for monitoring the post-marketing safety and effectiveness of treatments and is often used to support clinical decisions. While several studies have evaluated adalimumab in a real-world setting, there is very limited information comparing adalimumab's effectiveness and safety with traditional therapies. The aim of this study was to compare the real-world effectiveness of adalimumab with topical/traditional systemic agents in the management of moderate to severe plaque psoriasis in Canadian routine care.

METHODS

Study Design

COMPLETE-PS was a prospective Canadian post-marketing observational study among patients with plaque psoriasis across 43 community dermatologist sites. Patients were

followed up to 2 years, and visits were according to routine care, with a recommendation for visits at 3, 6, 12, 18, and 24 months after treatment initiation, if considered acceptable practice. All clinical decisions, including the initiation of adalimumab, were based on the physician's judgment, regional regulations, and the Canadian product monograph [8, 13].

Ethics approval was obtained from central and local research ethics boards, as required. Prior to inclusion in the study, all patients signed a written informed consent agreeing to allow use of their data in the study. The study was performed in accordance with the Helsinki Declaration of 1964, and its later amendments.

Analysis Population

Eligible patients were aged ≥ 18 years with active moderate to severe plaque psoriasis who required a change or addition of treatment as per judgment of the treating physician independently of being enrolled in the study. Patients were excluded if they were participating in another prospective study with similar objectives, did not sign the informed consent, or had a condition as per the physician that prohibited them from participating or obscured assessment of the treatment. All patients were enrolled between August 2011 and June 2016.

Outcome Measures

Disease severity was assessed using the Physician Global Assessment (PGA) of psoriasis; this is a 6-point scale measuring the severity of disease, ranging from 'clear' (0) to 'very severe' (5) [14]. The primary effectiveness endpoint was achievement of PGA of ≤ 1 at 6 months of treatment, indicating clear or almost clear skin.

Secondary effectiveness endpoints included time to achieving PGA ≤ 1 over 24 months, achievement of PGA ≤ 1 at all visits, baseline-adjusted scores of PGA and Dermatology Quality of Life Index (DLQI) at all visits, and baseline-adjusted scores of psoriasis body surface area (BSA) and Work Limitations Questionnaire (WLQ) score at 6, 12, and 24 months. Safety was

ascertained through the incidence of treatment-emergent serious adverse events (SAEs).

Statistical Analyses

Patients who signed the informed consent and received at least one dose of the study drug were included in the safety population. All effectiveness outcomes were assessed in the intent-to-treat (ITT) population, a subset of the safety population. Patients were excluded from the ITT population due to one or more of the following reasons: ineligibility based on entry criteria; absence of a study medication start date; initiation of a biologic other than adalimumab; initiation of phototherapy without concomitant administration of other topical/systemic agents; or study medication start date > 30 days before baseline. Baseline patient demographics and characteristics were assessed using summary statistics, while differences between treatment groups were assessed for statistical significance using the independent-samples t-test for continuous parameters and the Chi-square test or Fisher's exact test, as appropriate, for categorical variables.

Between-group differences for achievement of PGA ≤ 1 at 6 months was assessed with univariate logistic regression; multivariate logistic regression adjusted for potential confounders (baseline variables showing a statistical trend, specifically $P < 0.10$, in the between-group comparison). The time to achievement of PGA ≤ 1 over time was assessed using a multivariate Cox proportional hazard model, adjusting for potential confounders as described above. Between-group differences for achievement of PGA ≤ 1 over 24 months of treatment was assessed using a generalized estimating equation regression model. Differences between treatment groups in baseline-adjusted scores over time for psoriasis BSA, PGA, DLQI, and WLQ were assessed using mixed effects models with repeated measures.

Treatment switch, defined as initiation of a different biologic treatment in the adalimumab group and initiation of any biologic treatment in the topical/traditional systemic agents group, was assessed with descriptive statistics and Cox

regression. Treatment-emergent SAEs were coded using Medical Dictionary for Regulatory Activities version 13.1 and were described by system organ class (SOC) and preferred term (PT). Statistical analyses were conducted using SAS software, version 9.4 (SAS Institute, Cary, NC, USA). For between-group comparisons, statistical significance was defined as $P \leq 0.05$.

RESULTS

A total of 293 patients initiated on adalimumab and 302 initiated on topical/traditional systemic agents were included in the ITT analysis. Compared with patients treated with topical/traditional systemic agents, at baseline, patients treated with adalimumab were comparable in age; had significantly ($P < 0.05$) longer duration of psoriasis; and were more likely to be employed, have severe to very severe psoriasis flare-ups (48.8% vs. 36.1%), have concomitant psoriatic arthritis, be evaluated by a rheumatologist, and have a PGA score of severe to very severe (31.7% vs. 20.5%) (Table 1). The most common concomitant medications at baseline were corticosteroids, calcipotriene-betamethasone, and methotrexate among patients treated with either adalimumab or topical/traditional systemic agents.

At baseline, a comparable percentage of patients were evaluated at PGA ≤ 1 in the adalimumab and topical/traditional systemic agents groups (2.9% vs. 1.4%, respectively) (Fig. 1). Over the course of treatment, however, the percentage of patients achieving PGA ≤ 1 was significantly higher ($P < 0.001$) among patients treated with adalimumab for 3 months (49.6% vs. 19.5%), 6 months (58.4% vs. 33.0%), 12 months (61.3% vs. 38.0%), 18 months (65.6% vs. 38.9%), and 24 months (60.8% vs. 40.1%). Time to achieve PGA ≤ 1 was also significantly shorter in the adalimumab group, with a hazard ratio (HR) of 2.14 (95% confidence interval[CI] 1.53–3.00) upon adjusting for potential confounders (Table 2). Similarly, the odds of achieving PGA ≤ 1 at 6 months were twofold greater for patients treated with adalimumab compared with patients treated with topical/traditional systemic agents (odds ratio

2.37, 95% CI 1.31–4.30) after adjusting for potential confounders (Table 3).

Baseline-adjusted scores for psoriasis BSA, PGA, DLQI, and WLQ are presented in Electronic Supplementary Material (ESM) Fig. S1. For all outcomes, patients treated with adalimumab reported lower scores at each study visit compared with patients treated with topical/traditional systemic agents, with overall treatment effect significantly ($P < 0.05$) in favor of adalimumab. These differences were observed as early as 3 months after treatment initiation and were maintained up until 24 months.

Overall, 35.5% of patients treated with adalimumab and 46.4% of those treated with topical/traditional systemic agents discontinued the study prematurely ($P = 0.005$). In terms of treatment switch, no significant differences were observed, with 18.4% of patients treated with adalimumab initiating a different biologic versus 17.5% of patients treated with topical/traditional initiating any biologic; time to switch was also comparable between groups (HR 0.95, 95% CI 0.65–1.39).

A total of 328 patients treated with adalimumab and 330 patients treated with topical/traditional systemic agents were included in the safety analysis; SAEs were experienced by 7.0% versus 0.6% of patients, respectively, over the course of the study. The most common SAEs observed in patients treated with adalimumab by SOC were 'general disorders and administration site conditions' (9 events/5 patients: 1.5%), 'infections and infestations' (8 events/4 patients; 1.2%), and 'neoplasms benign, malignant, and unspecified' (11 events/8 patients: 2.4%). SAEs by PT are summarized in ESM Table S1.

DISCUSSION

The results of this real-world observational study support the existing body of evidence regarding the effectiveness and safety of adalimumab for the treatment of moderate to severe plaque psoriasis. Results of an interim analysis of ESPRIT [15], a 10-year international prospective registry study evaluating adalimumab in the treatment of moderate to severe

Table 1 Participant characteristics and medication use at baseline

Patient characteristics or medication use	Treatment groups		P value
	Adalimumab (*n* = 293)	**Topical/traditional systemic agent** (*n* = 302)	
Age, years, mean (SD)	48.2 (13.6)	50.3 (15.1)	0.082
Sex, male, %	60.4	58.6	0.655
Race, %			0.293
White	87.0	86.8	
Asian	8.9	7.6	
Other	4.1	5.5	
Employed,[a] %	71.0	60.6	0.006*
Unemployed,[a] %	28.7	39.4	
Due to disability	14.3	3.4	–
Age at diagnosis, years, mean (SD)	29.7 (15.6)	34.3 (17.5)	0.001*
PS duration, years, mean (SD)	19.3 (14.2)	16.6 (14.0)	0.021*
Number of PS flare-ups in previous 12 months, mean (SD)	3.8 (7.8)	3.2 (6.1)	0.348
Severity of PS flare-ups[a], %			
Mild	4.1	4.6	0.006*
Moderate	28.7	37.7	
Severe	39.9	32.5	
Very severe	8.9	3.6	
Family history of PS, %	54.9	49.3	0.094
Rheumatoid factor, %	2.0	1.7	0.552
Concomitant PsA[a], %	34.5	11.6	< 0.001*
Rheumatology consult, %	17.1	8.6	0.002*
Current PS medication use, %			
Systemic treatments	10.8	62.6	NA
Methotrexate	8.5	38.4	
Cyclosporine	0.0	5.0	
Retinoids	1.7	16.9	
Phosphodiesterase-4 inhibitor	0.0	2.0	
Topical	47.9	81.1	
Corticosteroids	31.1	65.2	
Calcipotriene-betamethasone	23.2	29.5	

Table 1 continued

Patient characteristics or medication use	Treatment groups		P value
	Adalimumab (*n* = 293)	Topical/traditional systemic agent (*n* = 302)	
Vitamin D analogues	7.8	10.3	
Coal tar	2.4	11.3	
Calcineurin inhibitors	4.1	9.3	
Antifungal agents	2.4	3.6	
Salicylic acid	0.3	2.6	
Photography	3.1	15.9	
Other	2.8	12.6	
CRP, mg/L, mean (SD)	7.8 (16.2)	6.4 (7.4)	0.078
ESR, mm/h, mean (SD)	12.8 (14.5)	15.1 (13.6)	0.236
BSA, %, mean (SD)	19.2 (15.3)	16.0 (12.8)	0.007*
PGA, %			
Clear	1.4	1.0	0.002*
Minimal	1.4	0.3	
Mild	0.0	1.7	
Moderate	58.7	71.5	
Severe	27.6	18.2	
Very severe	4.1	2.3	

BSA Body surface area, *CRP* C-reactive protein, *ESR* erythrocyte sedimentation rate, *NA* not applicable, *PGA* Physician Global Assessment, *PsA* psoriatic arthritis, *PS* psoriasis, *SD* standard deviation

*Statistical difference between groups at $P < 0.05$

[a]Among patients receiving adalimumab vs. topical/traditional systemic agents: patients with missing information for employment status were $n = 1$ and $n = 0$ severity, respectively; for PS flare-ups, $n = 54$ (18.4%) and $n = 65$ (21.6%), respectively; for concomitant psoriatic arthritis, $n = 44$ (15.0%) and $n = 76$ (25.2%), respectively; and for PGA, $n = 20$ (6.8%) and $n = 15$ (5.0%), respectively

psoriasis, showed that the effectiveness of adalimumab was maintained through 84 months of treatment exposure. Specifically, month 24 results for the percentage of patients achieving PGA ≤ 1 was 55.4% in patients who were adalimumab-naive at baseline and is comparable with the 60.8% of patients treated with adalimumab reporting this endpoint at month 24 in our study.

In addition, patients enrolled in ESPRIT reported a significant positive impact on quality of life, as well as on work productivity, as assessed with the DLQI and the Work Productivity and Activity Impairment (WPAI) questionnaire, respectively, with reductions in both
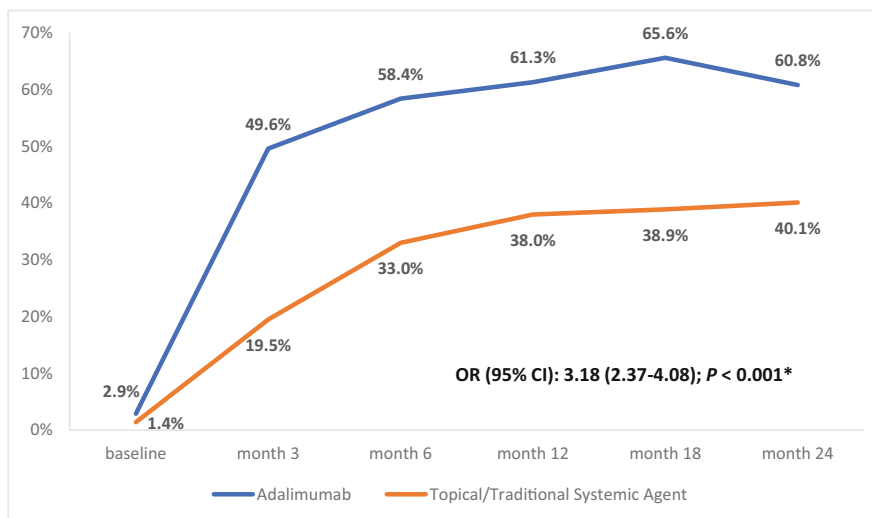
Fig. 1 Percentages of patients with moderate to severe plaque psoriasis achieving Physician Global Assessment ≤ 1.0 over time. Asterisk (*)Calculated based on a generalized estimating equation regression model. Percentages are based on patients with available information. *CI* Confidence interval, *OR* odds ratio

Table 2 Cox proportional hazard model for time to achieving PGA ≤ 1.0 over 24 months

Covariate[a]	Reference	HR	95% CI	*P* value
Age, years	NA	0.96	0.55–1.67	0.871
Age at diagnosis, years	NA	1.05	0.60–1.83	0.873
Time since diagnosis, years	NA	1.05	0.60–1.83	0.862
Psoriasis BSA	NA	1.00	0.98–1.01	0.481
PGA at baseline	NA	0.87	0.62–1.23	0.431
Treatment group	Adalimumab vs. topical/traditional systemic agent	2.14	1.53–3.00	< 0.001*
Employment status	Yes vs. no	1.08	0.74–1.58	0.679
Family history of PS	Yes vs. no	0.85	0.60–1.19	0.339
Severity of flare-ups	Severe/very severe vs. mild/moderate	1.41	1.00–2.00	0.050*
Concomitant psoriatic arthritis	Yes vs. no	0.92	0.61–1.40	0.694
Rheumatology consult	Yes vs. no	1.18	0.73–1.92	0.503

CI Confidence interval, *HR* hazard ratio

*Statistical difference between groups at $P < 0.05$

[a]Baseline patient and disease characteristics with $P < 0.10$ for treatment group comparison were considered as potential confounders in the multivariate model. Bold text denotes statistical significance ($P < 0.05$)

DLQI and WPAI observed and maintained throughout yearly follow-up visits. These results are also in line with the results reported in our study, whereby patients treated with adalimumab experienced rapid and sustained improvements in DLQI and WLQ.

Table 3 Multivariate logistic regression for achievement of PGA $\leq$ 1.0 at 6 months

Covariate[a]	Reference	OR	95% CI	*P* value
Age at baseline, years	NA	0.51	0.20–1.30	0.158
Age at diagnosis, years	NA	1.97	0.77–5.08	0.159
Time since diagnosis, years	NA	1.99	0.77–5.11	0.153
Psoriasis BSA	NA	1.00	0.98–1.02	0.914
PGA at baseline	NA	0.82	0.52–1.30	0.394
Treatment group	Adalimumab vs. topical/traditional systemic agent	**2.37**	**1.31–4.30**	**0.005**
Employment status	Yes vs. no	0.95	0.50–1.80	0.880
Family history of PS	Yes vs. no	0.78	0.44–1.39	0.401
Severity of flare-ups	Severe/very severe vs. mild/moderate	**2.43**	**1.35–4.40**	**0.003**
Concomitant psoriatic arthritis	Yes vs. no	0.88	0.45–1.71	0.705
Rheumatology consult	Yes vs. no	0.80	0.37–1.73	0.565

[a]Baseline patient and disease characteristics with $P < 0.10$ for treatment group comparison were considered as potential confounders in the multivariate model. Bold test denotes statistical significance

Despite the generalizability of our study to routine clinical practice, there is currently a paucity in the literature surrounding the real-world safety and effectiveness of adalimumab compared with topical/traditional systemic agents. In this study, we directly compared adalimumab with traditional psoriasis treatments and found that adalimumab had a superior effectiveness in terms of disease activity (PGA and BSA) and patient-reported outcomes (DLQI and WLQ) that were observed early on and maintained throughout treatment.

With respect to safety, the results of this study showed that patients treated with adalimumab had a higher incidence of SAEs compared with traditional treatments; however, this was expected as per the safety profile of adalimumab [13, 15]. While safety may be slightly less favorable than traditional therapy or certain other biologics, adalimumab remains suitable for long-term use, with an established safety profile and between 50 and 80% drug survival rates after 1–2 years of treatment [12]. A recent systematic review and meta-analysis based on 20 randomized controlled trial (RCTs) [16] further established that there is no association between adalimumab therapy and SAEs,

serious infections, or discontinuations due AEs, reconfirming its well-established safety and tolerability profile.

Following the real-world setting of the current study, assessment of the Psoriasis Area and Severity Index (PASI), a common clinical trial endpoint, was not included as a study outcome. As PGA is a rapid and convenient psoriasis disease severity measure prevalent in daily clinical practice, the relationship between PGA and PASI has been assessed in two recent publications. Using data from the British Association of Dermatologists Biologic and Immunomodulators Register, including more than 23,000 longitudinal PASI and PGA scores, Mahil et al. [17] determined that PASI 90 response ($\geq$ 90% improvement from baseline) was concordant with an absolute PASI score $\leq$ 2; correlating absolute PASI with PGA, an agreement between absolute PASI $\leq$ 2 and PGA clear was observed in 90% of cases assessed. A literature review by Wu et al. [18] evaluated phase 2 and 3 randomized clinical trials for which the proportions of patients achieving PASI 90/100 and PGA 0/1 were primary endpoints. Although 73% of studies assessed showed a $\geq$ 10% difference in the proportion of the respective

endpoints, three of the four adalimumab studies included reported results for PASI 100 and PGA 0 that varied by < 5%.

Taken together, the above reports suggest that patients in the current study with PGA ≤ 1 may be considered as PASI 90 responders. In RCTs of adalimumab in moderate to severe psoriasis, achievement of PASI 90 after 16 weeks of treatment was reported by 45.0% and 51.9% of patients in the REVEAL [19] and CHAMPION [14] studies, respectively. In addition, in an open-label extension of the REVEAL study, whereby adalimumab responders (PASI ≥ 75) were eligible to receive adalimumab up to 3 years after study start, PASI 90 was reported by 59% of patients after 100 weeks of continuous treatment [19, 20]. Considering that in the current study, 60.8% of patients treated with adalimumab reported a PGA ≤ 1, or PASI 90, at month 24 (approximately 100 weeks), this study not only shows a response rate similar to those reported in clinical trials but also establishes that this response can be sustained up to 24 months in a real-word population of patients with psoriasis.

A potential limitation of this study was that due to the observational study design, systematic collection of AEs was not mandated by the study protocol. However, the current report focused on the incidence of SAEs. As the safety profile of adalimumab is well documented and the SAEs reported herein are in line with the current knowledge base, as discussed above, there is no concern regarding new or un-established safety signals.

An additional limitation of our study relates primarily to the potential for a channeling bias, whereby patients with more severe disease may have been selected for adalimumab treatment; however, this type of bias is inherent to observational studies. To address this bias, multivariable analyses adjusting for potential confounders, defined as baseline characteristics differing between treatment groups, were used in the assessment of achievement and time to PGA ≤ 1. A further limitation is centered on the ITT approach used in the current analysis, whereby patients in the adalimumab group switching to another biologic and patients in the topical/traditional systemic agents group changing regimen or initiating a biologic were not assessed as separate groups, which may have confounded observed treatment effects. However, as the percentage of biologic switch/initiation was comparable between groups, taking the ITT approach is not expected to have major implications on the results reported herein.

Finally, due to the nature of observational studies, treatment with adalimumab was left to the judgment of the treating physician. We therefore report baseline combination therapy in patients treated with adalimumab, specifically methotrexate and retinoids; however, the proportions were substantially lower than patients treated with topical/traditional systemic agents. It is notable that the results reported herein are reflective of routine clinical practice and therefore support the generalizability of our findings to real-world clinical settings.

CONCLUSIONS

In this real-world study, adalimumab was more effective than topical/traditional systemic agents at reducing disease activity and improving quality-of-life outcomes among Canadians with moderate to severe plaque psoriasis. Results of this study are in line with those reported in RCTs.

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REFERENCES

1. Sivamani RK, Correa G, Ono Y, Bowen MP, Raychaudhuri SP, Maverakis E. Biological therapy of psoriasis. Indian J Dermatol. 2010;55(2):161–70.

2. MedlinePlus. Psoriasis, http://www.nlm.nih.gov/medlineplus/psoriasis.html. Accessed 5 Oct 2021.

3. AlQassimi S, AlBrashdi S, Galadari H, Hashim MJ. Global burden of psoriasis—comparison of regional and global epidemiology, 1990 to 2017. Int J Dermatol. 2020;59(5):566–71.

4. Canadian Dermatology Association. Psoriasis. 2021. https://dermatology.ca/public-patients/skin/psoriasis/. Accessed 5 Oct 2021.

5. Rachakonda TD, Schupp CW, Armstrong AW. Psoriasis prevalence among adults in the United States. J Am Acad Dermatol. 2014;70(3):512–6.

6. Eder L, Widdifield J, Rosen CF et al. Trends in the prevalence and incidence of psoriasis and psoriatic arthritis in Ontario, Canada: a population-based study. Arthritis Care Res (Hoboken). 2019;71(8):1084–91.

7. Canadian Psoriasis Guidelines Committee. Canadian guidelines for the management of plaque psoriasis. 2009. https://www.dermatology.ca/wp-content/uploads/2012/01/cdnpsoriasisguidelines.pdf. Accessed 5 Oct 2021.

8. Canadian Psoriasis Guidelines Addendum, C. 2016 Addendum to the Canadian guidelines for the management of plaque psoriasis 2009. J Cutan Med Surg. 2016;20(5):375–431.

9. Caiazzo G, Fabbrocini G, Di Caprio R et al. Psoriasis, cardiovascular events, and biologics: lights and shadows. Front Immunol. 2018;9:1668.

10. Freiman A, Barankin B. Psoriasis. CMAJ. 2013;185(3):E174.

11. Canadian Psoriasis Network. Biologics and Biosimilars. 2020. https://www.canadianpsoriasisnetwork.com/psoriasis-treatment/biologics/. Accessed 24 Feb 2021.

12. Sator P. Safety and tolerability of adalimumab for the treatment of psoriasis: a review summarizing 15 years of real-life experience. Ther Adv Chronic Dis. 2018;9(8):147–58.

13. AbbVie Corporation. Product monograph. Humira (Adalimumab). https://www.abbvie.ca/content/dam/abbvie-dotcom/ca/en/documents/products/HUMIRA_PM_EN.pdf. Appearance to 21 April 2021. Accessed 5 Oct 2021.

14. Saurat J-H, Stingl G, Dubertret L et al. Efficacy and safety results from the randomized controlled comparative study of adalimumab vs. methotrexate vs. placebo in patients with psoriasis (CHAMPION). Br J Dermatol. 2008;158(3):558–66.

15. Menter A, Thaçi D, Wu JJ et al. Long-term safety and effectiveness of adalimumab for moderate to severe psoriasis: results from 7-year interim analysis of the ESPRIT registry. Dermatol Ther (Heidelb). 2017;7(3):365–81.

16. Guan X, Zhang CL. An update on clinical safety of adalimumab in treating psoriasis: a systematic review and meta-analysis based on 20 randomized controlled trials. J Cosmet Dermatol. 2019;18:1550–9.

17. Mahil SK, Wilson N, Dandet N. Psoriasis treat to target: defining outcomes in psoriasis using data from a real-world, population-based cohort study (the British Association of Dermatologists Biologics and Immunomodulators Register, BADBIR). Br J Dermatol. 2020;182(5):1158–66.

18. Wu AG, Conway J, Barazani L, Roy B, Cline A, Pereira F. Is clear always clear? Comparison of Psoriasis Area and Severity Index (PASI) and the Physician's Global Assessment (PGA) in psoriasis clearance. Dermatol Ther (Heidelb). 2020;10(5):1155–63.

19. Gordon K, Papp K, Poulin Y, Gu Y, Rozzo S, Sasso EH. Long-term efficacy and safety of adalimumab in patients with moderate to severe psoriasis treated continuously over 3 years: results from an open-label extension study for patients from REVEAL. J Am Acad Dermatol. 2012;66(2):241–51.

20. Papp KA, Armstrong AW, Reich K, Karunaratne M, Valdecantos W. Adalimumab efficacy in patients with psoriasis who received or did not respond to prior systemic therapy: a pooled post hoc analysis of results from three double-blind, placebo-controlled clinical trials. Am J Clin Dermatol. 2016;17(1):79–86.