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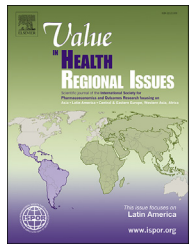

Economic Evaluation

Cost-Effectiveness of Secukinumab Versus Other Biologics in the Treatment of Psoriatic Arthritis: An Argentinean Perspective

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ABSTRACT

Objective: Psoriatic arthritis (PsA) is a chronic, systemic inflammatory disease. This study assessed the cost-effectiveness of secukinumab, an interleukin-17A inhibitor, versus other biologics in PsA from the Argentinean social security perspective. **Methods:** A semi-Markov model evaluated subcutaneous (sc) treatment with secukinumab 150 mg and 300 mg against other sc treatments such as adalimumab, certolizumab pegol, etanercept, golimumab, ustekinumab, and intravenous treatment infliximab in biologic-naïve (with or without moderate to severe psoriasis) and biologic-experienced PsA patients over a lifetime horizon. Response to treatments was determined using the PsA Response Criteria (PsARC) at 12 weeks. Model inputs were derived from randomized controlled trials, network meta-analyses, published literature, and other Argentinean sources. Model outcomes included quality-adjusted life years (QALYs) gained and incremental cost-effectiveness ratios. Sensitivity analyses and alternative scenarios with a higher cost option were also conducted. **Results:** Among biologic-naïve PsA patients without psoriasis, secukinumab 150 mg provided the highest QALYs (7.18) versus all sc biologics at the lowest cost ($3 755 678 Argentine peso), thus dominating them. Among biologic-naïve PsA patients with psoriasis and biologic-experienced PsA patients, secukinumab 300 mg provided highest QALYs (6.99 and 7.53, respectively), dominated infliximab, and was cost-effective versus other sc biologics. Deterministic sensitivity analyses indicated sensitivity of results to variation in PsARC rates, drug acquisition costs, Health Assessment Questionnaire change, and utilities. A probabilistic sensitivity analysis showed maximum net monetary benefits with both secukinumab doses. Results from an alternative scenario analysis were similar to base-case analysis. **Conclusions:** For both biologic-naïve and experienced PsA patients, secukinumab is either a dominant or cost-effective treatment option compared with other biologics in Argentina.

Keywords: secukinumab, psoriatic arthritis, cost-effectiveness, Argentina, interleukin-17A inhibitor, tumor necrosis factor inhibitors, incremental cost-effectiveness ratio, quality-adjusted life year.

Introduction

Psoriatic arthritis (PsA) is a chronic, progressive inflammatory disease associated with psoriasis.[1-3] It primarily affects the peripheral joints, connective tissues, and axial skeleton, with patients experiencing joint pain, swelling, stiffness, and skin lesions.[2-6] The major structural changes in PsA are primarily driven by enthesitis.[7] In Argentina, the estimated PsA prevalence was 0.074% based on a health insurance cohort dataset for 2006, and the annual incidence was reported to be 6.3 cases per 100 000 persons for the entire study period (2000-2006).[8,9]

Psoriatic arthritis causes pain, fatigue, and functional disability and affects negatively psychosocial functioning, severely affecting health-related quality of life (HRQoL) even at early stages of the disease.[10,11] Patients with PsA also suffer from comorbidities[12] and have a higher mortality risk compared with the general population.[13] A recent multicenter study conducted in Argentina reported a worsening in HRQoL and work disability among patients with recent onset of PsA (disease duration <3 years). The deterioration of work capacity expressed in lost workdays was associated with functional disability and disease activity parameters.[14]

Conflict of interest: The authors have indicated that they have no conflicts of interest with regard to the content of this article.

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Treatment recommendations from European League against Rheumatism and the Group for Research and Assessment of Psoriasis and Psoriatic Arthritis[15-18] suggest the use of nonsteroidal anti-inflammatory drugs (NSAIDs) for controlling PsA symptoms and conventional synthetic disease-modifying anti-rheumatic drugs (csDMARDs) (eg, methotrexate, sulfasalazine, cyclosporine, and leflunomide) for providing relief in the early stages of disease progression.[16] Biologic treatments including tumor necrosis factor-alpha inhibitors (TNFi) (certolizumab pegol, golimumab, adalimumab, etanercept, infliximab, or their biosimilars), IL-12/IL-23 inhibitor (ustekinumab), and interleukin (IL)-17A inhibitors (secukinumab and ixekizumab) are recommended as a second-line treatment if patients had inadequate response to previous therapies.[16,17] For PsA patients experiencing biologic treatment failures, switching between biologic therapies is recommended.[19] National-level recommendations for treating PsA in Argentina are currently lacking. A recent retrospective study described the PsA treatment patterns among 275 PsA patients, in a hospital setting in Argentina from 2000 to 2017.[20] According to the study results, NSAIDs and csDMARDs were the major first-line therapies.

Secukinumab is a first-in-class, recombinant, high-affinity, fully human monoclonal antibody that selectively targets IL-17A.[6,21] Secukinumab was approved by Argentina's National Administration of Drugs, Food, and Medical Technology in 2016 for the treatment of active PsA.[22] Patients with PsA (biologic-naïve and experienced) treated with secukinumab in placebo-controlled trials have shown significant and sustained improvements in signs and symptoms, HRQoL, and inhibition of structural progression of active PsA up to 5 years.[23-30] Further, published matching-adjusted indirect comparisons have shown better efficacy outcomes with secukinumab compared with adalimumab, infliximab, and etanercept.[31-33] To confirm superiority of secukinumab over adalimumab, a head-to-head trial (Efficacy of Secukinumab Compared to Adalimumab in Patients With Psoriatic Arthritis) is currently under way.[34]

There are no published cost-effectiveness studies of secukinumab for PsA in Argentina. The present analysis reports the findings from a cost-effectiveness study of secukinumab against currently licensed biologics for PsA (certolizumab pegol, etanercept, ustekinumab, adalimumab, golimumab, and infliximab) in Argentina.

Methods

Patient Population and Interventions

Adults (≥18 years) with active PsA, despite treatment with NSAIDs, csDMARDs, or TNFi, were included in the analysis. Subpopulations included (1) biologic-naive patients (without moderate to severe psoriasis), (2) biologic-naïve patients (with moderate to severe psoriasis), and (3) biologic-experienced patients. These subpopulations were analyzed separately because the clinical response to biologic treatments may vary significantly based on previous biologic exposure (biologic-naive and biologic-experienced populations), and secukinumab has been recommended in 2 different doses depending on the patient population. FUTURE 2 trial was the pivotal phase-3 clinical trial for secukinumab in PsA, evaluating both secukinumab 150 mg and 300 mg and including a subcutaneous (sc) loading phase of secukinumab.[23,24,26,27] Thus, the population inputs were taken from the patient baseline characteristics from the FUTURE 2 study (see Appendix Table 1 in Supplemental Materials found at https://doi.org/10.1016/j.vhri.2019.03.002).

The cost-effectiveness of sc secukinumab in PsA was evaluated against currently licensed biologics (sc treatments certolizumab pegol, adalimumab, golimumab, etanercept, and ustekinumab; and intravenous [IV] treatment infliximab) from the Argentinean social security (employment-based health insurance system) perspective. Information related to treatment regimens such as dosing and frequencies are available in the supplementary material (see Appendix Table 2 in Supplemental Materials found at https://doi.org/10.1016/j.vhri.2019.03.002). As per the Argentinean marketing authorization, secukinumab 150 mg was considered for biologic-naïve PsA patients without moderate to severe psoriasis and secukinumab 300 mg was considered for biologic-naïve PsA patients with moderate to severe psoriasis and biologic-experienced PsA patients.[22]

Model Structure

The model used in the present study was based on a semi-Markov model structure[35] (Fig. 1). This model has been adapted from a UK model[36] that assessed the cost-effectiveness of secukinumab compared with other biologics in the treatment of PsA. A first adaptation has been recently published and established the cost-effectiveness of secukinumab versus other biologics in the treatment of PsA from the Canadian healthcare system perspective.[37] The present analysis had the same model structure as the Canadian adaptation and is briefly described below.

As per the model, patients initiated a given treatment and response to the biologic was assessed using the PsA Response Criteria (PsARC) after the induction period of 3 months. Several publications also used the PsARC as the main response criteria, and it has been positively assessed by the National Institute for Health and Care Excellence.[36,38-43] Transitions between different health states occurred at every 3 months considering the PsARC rates, malignancy, infections, withdrawal rates, and death (Fig. 1). All patients transitioning to 'Malignancy' state were assumed to be at higher mortality risk for 5 years into this health state.

Patients switched to alternative subsequent-line biologics upon withdrawing from the initial treatment. Owing to the limited evidence regarding both efficacy and switch patterns, average estimates of efficacy, costs, treatment withdrawal rates, and adverse event (AE) rates were used to model subsequent-line biologic. Once patients dropped out of subsequent-line biologic treatment, they transitioned to standard of care and were not eligible to switch back to biologics at any time-point in the model.

Model Inputs

Clinical inputs

The following clinical inputs were used in the model: PsARC response at 3 months as a measure of anti-inflammatory response (Table 1)[44,45], the Psoriasis Area and Severity Index (PASI) (ie, the skin lesion response of PsA) response distribution at 3 months (see Appendix Table 3 in Supplemental Materials found at https://doi.org/10.1016/j.vhri.2019.03.002), change in the Health Assessment Questionnaire (HAQ) (ie, the functional status [arthritis] component of PsA) at 3 months (see Appendix Table 4 in Supplemental Materials found at https://doi.org/10.1016/j.vhri.2019.03.002), PsARC and PASI correlation (see Appendix Table 5 in Supplemental Materials found at https://doi.org/10.1016/j.vhri.2019.03.002), and the rate of treatment withdrawal (see Appendix Table 6 in Supplemental Materials found at https://doi.org/10.1016/j.vhri.2019.03.002).

Although PsARC was used in the model to measure the initial response for joints, both PASI and HAQ were used to model the disease progression for psoriatic and arthritic components of the disease, respectively. The PsARC and PASI correlation was used to incorporate any correlation between the skin and joint responses because both responses may not be independent. Hence, there

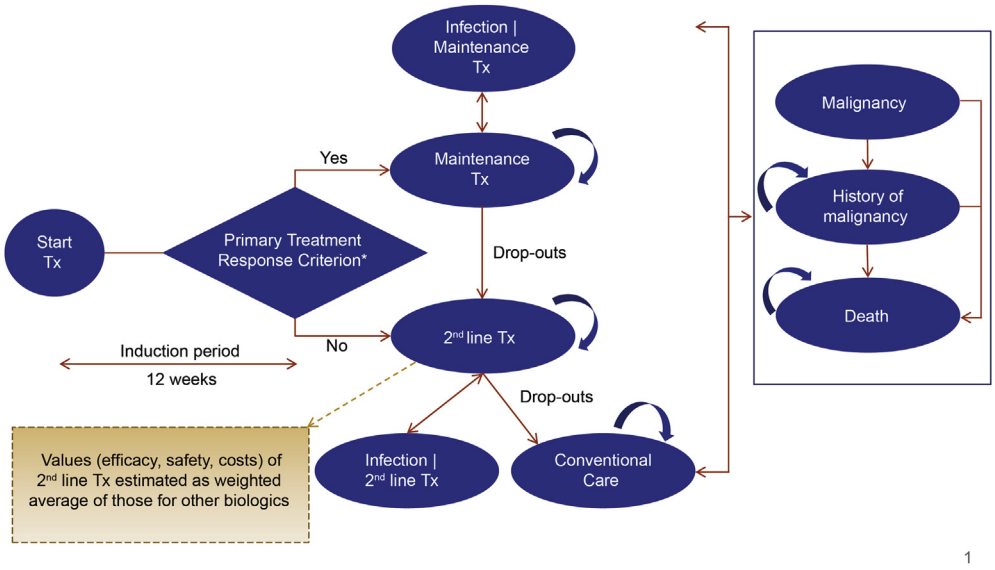

Fig. 1 – Structure of Markov model. *The efficacy parameter depends on the criteria chosen: Psoriatic Arthritis Response Criteria (PsARC) alone, Psoriasis Area and Severity Index (PASI), or a combination of PsARC and PASI. Tx indicates treatment.

was a need to incorporate an estimate of this correlation into the model.

Comparative effectiveness data for biologics were taken from a Bayesian network meta-analysis (NMA)[44] owing to the lack of head-to-head trials between treatments. For treatments with missing clinical inputs, the clinical effectiveness was assumed to be equivalent to the average of other biologics in the NMA.

Cost inputs

Only direct costs were considered in the model, which included drug acquisition costs, disease-related costs, medical support costs, and AE costs. Costs were converted to Argentine pesos (ARS) (1 British pound = 22.19 ARS; exchange rate on July 17, 2017, from www.xe.com). Drug acquisition costs for all the biologic treatments were obtained from the Alfabeta.net[46] website, which is a publicly available source for drug prices in Argentina (Table 2). Disease-related costs for both arthritis and psoriasis components of PsA were obtained from published studies[47-49] and inflated to reflect the costs in 2017 using inflation values from the Unit Costs of Health and Social Care[50] (see Appendix Table 7 in Supplemental Materials found at https://doi.org/10.1016/j.vhri.2019.03.002).

Although arthritis-related costs were modeled using a linear regression based on change in HAQ, psoriasis-related costs were modeled considering PASI response, taking into account costs for uncontrolled psoriasis (PASI <75) and controlled psoriasis

Table 1 – PsARC response inputs at 3 months

Administration	Treatment	Biologic-naïve,[*,†] (%)	Biologic-experienced,[‡,§] (%)
Subcutaneous	Secukinumab 150 mg	59.82	NA
	Secukinumab 300 mg	51.18	82.45
	Adalimumab	62.84	51.72
	Certolizumab pegol	73.61	67.89
	Etanercept	70.91	68.38
	Golimumab	79.96	59.90
	Ustekinumab	73.61	63.52
Intravenous	Infliximab	78.65	67.73

Note. PsARC response data are from Bayesian fixed-effects NMA performed by RTI Health Solutions.[44]
NA indicates not applicable; NMA, network meta-analysis; PsARC, Psoriatic Arthritis Response Criteria.

[*] Secukinumab 150 mg was evaluated in a biologic-naïve population without moderate to severe psoriasis, and secukinumab 300 mg was evaluated in biologic-naïve patients with moderate to severe psoriasis.

[†] Biologic-naive data for certolizumab pegol and ustekinumab were not available and were assumed equivalent to be average of other biologics in the NMA. Trials for 50 mg etanercept once weekly did not link into the network, thus data for 25 mg etanercept twice weekly were used.

[‡] Data for the experienced population was lacking and was computed by applying a reduction to the mixed population. Secukinumab: 0.43% reduction, other tumor necrosis factor-alpha inhibitor: 10.1%. For secukinumab, we have all relevant efficacy data available from the FUTURE 2 trial, hence reductions in secukinumab efficacy for the biologic-experienced population were computed from the trial data. For other treatments (ie, anti-tumor necrosis factor), the reductions were taken from Gladman et al.[45] Hence, 2 different rates have been applied.

[§] Biologic-experienced data for ustekinumab were not available and were assumed equivalent to the average of other biologics in the NMA. Trials for 50 mg etanercept once weekly did not link into the network, thus data for 25 mg etanercept twice weekly were used.

Table 2 – Drug acquisition costs

Administration	Treatment	Dose (per unit)	Cost (per unit) (in ARS)
Subcutaneous	Secukinumab	150 mg/dose	$17 287.54
	Secukinumab	300 mg/dose	$34 575.09
	Adalimumab	40 mg/prefilled syringe	$14 994.52
	Certolizumab pegol	200 mg/ prefilled syringe	$14 137.96
	Etanercept	50 mg/prefilled syringe	$8098.30
	Golimumab	50 mg/prefilled syringe	$33 883.85
	Ustekinumab	45 mg/prefilled syringe	$94 979.42
Intravenous	Infliximab	100 mg/vial	$25 668.28

Note. All the costs were obtained from Alfabeta.net.[46]
ARS indicates Argentine peso.

(PASI ≥75). Tuberculosis incidence rates and associated costs were considered in the analysis (see Appendix Tables 8 and 9 in Supplemental Materials found at https://doi.org/10.1016/j.vhri.2019.03.002). Medical visits and laboratory test costs included in the analysis are presented in supplementary material (see Appendix Tables 10 and 11 in Supplemental Materials found at https://doi.org/10.1016/j.vhri.2019.03.002).

Other Inputs

Utility weight inputs were used in the model to calculate quality-adjusted life years (QALYs) using a regression-based equation based on HAQ and PASI scores (see Appendix Table 12 in Supplemental Materials found at https://doi.org/10.1016/j.vhri.2019.03.002). For base-case analysis, utility inputs obtained from the York model[38] were considered. We assumed the York input to be consistent with other publications,[38-43] so that the results can be compared. Further, as described earlier, the York method had been previously used in many cost-effectiveness publications and National Institute for Health and Care Excellence submissions. All-cause age-related mortality, disease-specific mortality, and AEs-related mortality were also considered (see Appendix Tables 13 and 14 in Supplemental Materials found at https://doi.org/10.1016/j.vhri.2019.03.002).

Base-Case Analysis

The primary effectiveness outcome was QALY. Secukinumab was first evaluated for dominance (ie, secukinumab having higher QALYs at lower cost vs comparator). In case of non-dominance, the incremental cost-effectiveness ratio (ICER) was reported.

Owing to the chronic nature of PsA, the primary analysis was conducted over a lifetime horizon (60 years of disease duration), which led to the extrapolation of response benefits. Future costs and outcomes were discounted with an annual discounting rate of 5%.[51] In the absence of an express cost-effectiveness threshold in Argentina, the willingness-to-pay (WTP) threshold for Argentina was considered to be 3× the Argentinean gross domestic product per capita and set at $1 078 116 ARS. This was based on the recommendations by World Health Organization (WHO).[52]

Sensitivity Analysis

Three different types of sensitivity analyses assessed the impact of variation in input parameters on base-case results.

In one-way deterministic sensitivity analysis, the model input parameters that were expected to have the greatest effect on model results were varied one at a time (see Appendix Table 15 in Supplemental Materials found at https://doi.org/10.1016/j.vhri.2019.03.002).

In probabilistic sensitivity analysis, the impact of variation in input parameters on the base-case results was determined by assigning certain distributions to the input parameters and then randomly sampling all the parameters from the distribution during simulations (see Appendix Table 16 in Supplemental Materials found at https://doi.org/10.1016/j.vhri.2019.03.002). The probabilistic sensitivity analysis results were presented using cost-effectiveness acceptability curves, which were calculated using the net monetary benefit (NMB) statistic for a range of WTP thresholds for each treatment.

Various alternative scenario analyses were also conducted: private payer cost (medical support costs and AE costs for private payers differed from social security system) (see Appendix Tables 10 and 11 in Supplemental Materials found at https://doi.org/10.1016/j.vhri.2019.03.002), using a combination of PsARC and PASI responses as the primary efficacy criteria, varying time horizons to 5 and 10 years, varying discounting rates of 3% and 10% for both costs and outcomes, considering the natural history for the HAQ rebound assumption, applying utility values from the FUTURE 2 trial,[24] and finally applying a disutility value of -0.156 for 1 month in case of any occurrence of tuberculosis infection.[53]

Results

Base-Case Results

Biologic-naive PsA patients without moderate to severe psoriasis

For the lifetime horizon, among all sc biologics, secukinumab 150 mg provided the highest QALYs (7.18) at the lowest costs ($3 755 678 ARS) (Table 3). Thus, secukinumab 150 mg dominated all other sc biologics. Intravenously administered infliximab provided slightly higher QALYs (7.31) than sc secukinumab 150 mg, but at higher costs ($6 543 069 ARS), resulting in a very high ICER compared with secukinumab 150 mg (Table 3). Different components of costs (drug costs, disease-related costs, medical support costs, switching costs, AE-related costs) that contributed to the total costs are presented in the supplementary material (see Appendix Table 17 in Supplemental Materials found at https://doi.org/10.1016/j.vhri.2019.03.002). In summary, secukinumab 150 mg resulted in being the most cost-effective treatment for biologic-naive patients without moderate to severe psoriasis in Argentina.

Biologic-naive PsA patients with moderate to severe psoriasis

Secukinumab 300 mg provided the highest QALYs (6.99) versus all sc and IV biologics over the lifetime horizon (Table 3). Secukinumab dominated IV infliximab and was the most cost-effective option compared with sc biologics at the Argentinean WTP threshold.

Biologic-experienced PsA patients

Secukinumab 300 mg provided the highest QALYs (7.53) versus all biologics. Secukinumab dominated IV infliximab and was the most cost-effective option against all sc biologics at the Argentinean WTP threshold. The QALYs, costs, and ICER values

Table 3 – Direct costs, QALYs, and ICER values for all analyzed patient populations (base-case analysis)

Biologic-naïve (without moderate to severe psoriasis)				
Administration	**Treatment**	**Costs**	**QALYs**	**ICER (secukinumab 150 mg vs comparator)**
Subcutaneous	Secukinumab 150 mg	$3 755 678	7.18	—
	Adalimumab	$4 291 348	6.93	Secukinumab dominates adalimumab
	Certolizumab pegol	$4 214 621	6.83	Secukinumab dominates certolizumab pegol
	Etanercept	$4 422 582	7.11	Secukinumab dominates etanercept
	Golimumab	$4 185 456	6.75	Secukinumab dominates golimumab
	Ustekinumab	$4 524 564	6.92	Secukinumab dominates ustekinumab
Intravenous	Infliximab	$6 543 069	7.31	$20 784 684*
Biologic-naïve (with moderate to severe psoriasis)				
Administration	**Treatment**	**Costs**	**QALYs**	**ICER (secukinumab 300 mg vs comparator)**
Subcutaneous	Secukinumab 300 mg	$4 842 096	6.99	—
	Adalimumab	$4 451 461	6.54	$870 062
	Certolizumab pegol	$4 363 312	6.44	$871 898
	Etanercept	$4 577 794	6.73	$1 008 007
	Golimumab	$4 356 728	6.36	$763 069
	Ustekinumab	$4 672 395	6.54	$376 599
Intravenous	Infliximab	$6 665 734	6.95	Secukinumab dominates infliximab
Biologic-experienced				
Administration	**Treatment**	**Costs**	**QALYs**	**ICER (secukinumab 300 mg vs comparator)**
Subcutaneous	Secukinumab 300 mg	$5 276 941	7.53	—
	Adalimumab	$4 401 093	6.65	$994 155
	Certolizumab pegol	$4 374 946	6.60	$965 461
	Etanercept	$4 596 230	6.89	$1 062 826
	Golimumab	$4 294 288	6.48	$930 708
	Ustekinumab	$4 622 624	6.67	$755 831
Intravenous	Infliximab	$6 366 507	7.01	Secukinumab dominates infliximab

ICER indicates incremental cost-effectiveness ratio; QALY, quality-adjusted life year.
* ICER of infliximab vs secukinumab.

for all treatments and analyzed subpopulations are provided in Table 3.

Sensitivity Analyses

In one-way deterministic sensitivity analysis, PsARC response rates, drug acquisition costs, HAQ change with PsARC response, and utility HAQ coefficients of the York model were the most sensitive parameters affecting model outcomes in all subpopulations (see Appendix Figures 1, 2, and 3 in Supplemental Materials found at https://doi.org/10.1016/j.vhri.2019.03.002).

Results from probabilistic sensitivity analysis (see Appendix Table 18 in Supplemental Materials found at https://doi.org/10.1016/j.vhri.2019.03.002) demonstrated that, in biologic-naïve patients without moderate to severe psoriasis, secukinumab 150 mg was likely to provide the highest NMB in 86% of simulations. Similarly, secukinumab 300 mg was likely to provide the highest NMB in 44% and 51% of simulations for biologic-naïve patients with moderate to severe psoriasis and biologic-experienced patients, respectively. Further, the cost-effectiveness acceptability curves demonstrated that both secukinumab 150 mg and 300 mg had the highest probability of being cost-effective versus other biologics at various WTPs in all the analyzed populations of PsA (Fig. 2).

For the alternative scenario analysis, considering the private payer perspective, results were similar to the base-case analysis for all the subpopulations. The summary of results for all the alternative scenarios analyzed is presented in Table 4.

Discussion

This study evaluated the cost-effectiveness of secukinumab compared with the licensed biologics in patients with active PsA over 60 years of time horizon (lifetime) and was carried out from the perspective of the Argentinean social security healthcare system. The analysis was conducted in biologic-naïve patients without moderate to severe psoriasis, biologic-naïve patients with moderate to severe psoriasis, and biologic-experienced patients as per the marketing authorization of secukinumab in Argentina.

We found that secukinumab was either cost-effective or dominant (provided better outcomes at lower costs) compared with other biologics indicated for PsA. In the biologic-naive population without moderate to severe psoriasis, sc secukinumab 150 mg dominated all other sc biologics, whereas IV infliximab provided slightly higher QALYs (7.31) than secukinumab 150 mg, but at higher costs ($6 543 069 ARS), resulting in a very high ICER compared with secukinumab 150 mg. Thus, based on the considered WTP threshold for Argentina, IV infliximab would not be considered cost-effective. Further, sc administration of secukinumab makes it a more convenient alternative compared with IV infliximab.

In the biologic-naive population with moderate to severe psoriasis and in the biologic-experienced population, sc secukinumab 300 mg was found to be cost-effective compared with all other sc biologics and dominated IV infliximab. Sensitivity analyses confirmed the robustness of the results.

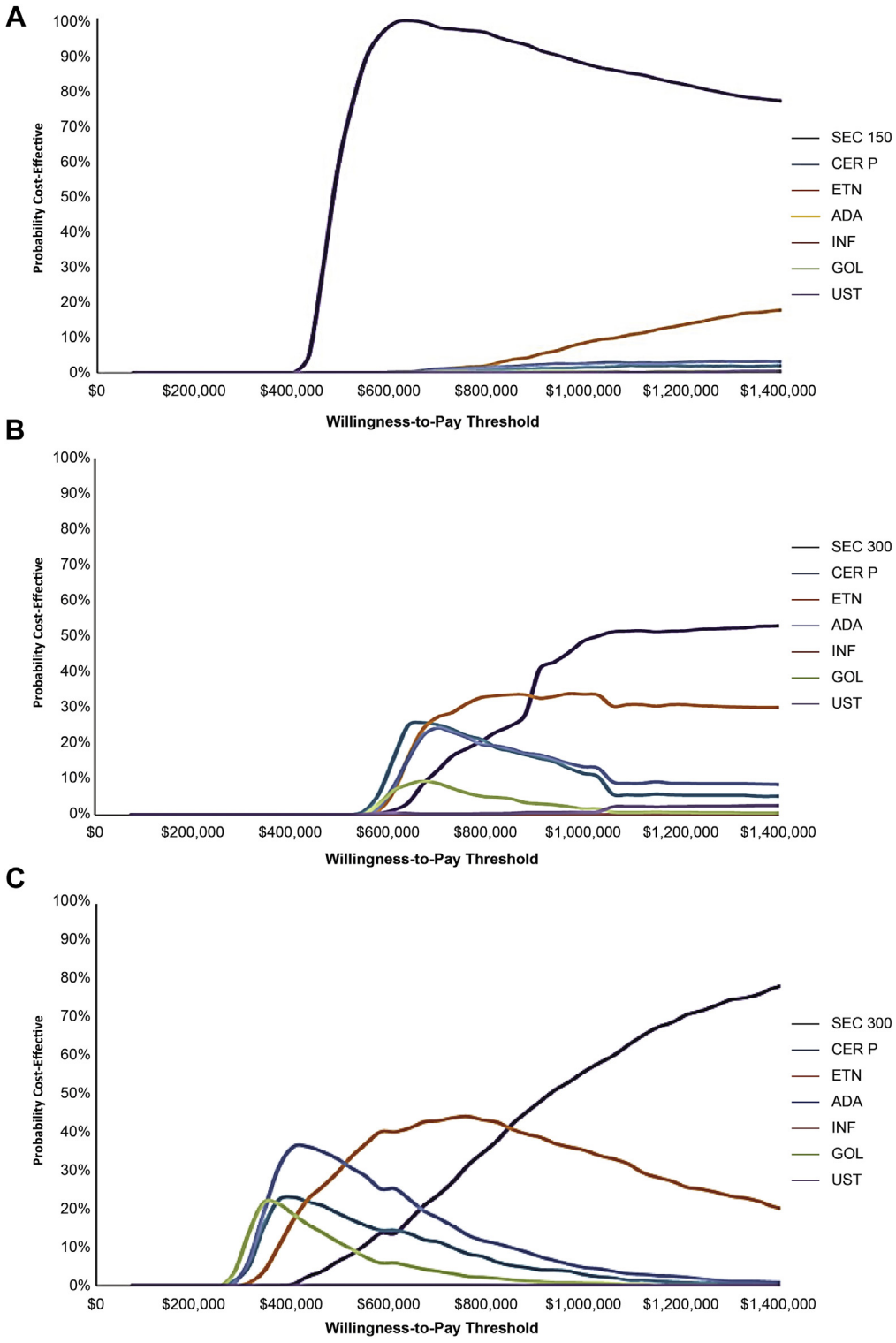

Fig. 2 – Cost-effectiveness acceptability curves. (A) Secukinumab 150 mg (biologic-naive PsA patients without moderate to severe psoriasis). (B) Secukinumab 300 mg (biologic-naive PsA patients with moderate to severe psoriasis). (C) Secukinumab 300 mg (biologic-experienced PsA patients). ADA indicates adalimumab; CER P, certolizumab pegol; ETN, etanercept; GOL, golimumab; INF, infliximab; PsA, psoriatic arthritis; SEC, secukinumab; UST, ustekinumab.

Table 4 – Summary of ICER results for secukinumab versus biologics by varying base-case assumptions

Parameters	Base-case inputs	Alternative scenario inputs	Secukinumab 150 mg (biologic-naive: without moderate to severe psoriasis)	Secukinumab 300 mg (biologic-naive: with moderate to severe psoriasis)	Secukinumab 300 mg (biologic-experienced)
Cost type	Social security	Private plan	Similar to base case*	Similar to base case†	Similar to base case‡
Time horizon	Lifetime (60 years)	5 years and 10 years	Dominates all except for ETN and INF. Both are not cost-effective vs secukinumab.	5 years: only cost-effective vs GOL, UST. INF has slightly higher QALYs. 10 years: cost-effective vs CER P, GOL, UST. INF has slightly higher QALYs.	5 years: only cost-effective vs GOL, UST. INF has slightly higher QALYs. 10 years: dominates INF. Cost-effective vs CER P, GOL, UST.
Discount rates	5%	3% 10%	Similar to base case* Similar to base case*	Similar to base case† Similar to base case†	Similar to base case‡ Dominates INF. Cost-effective vs CER P, GOL, UST.
Efficacy criteria	PsARC	PASI ≥75 PsARC and PASI ≥75	Similar to base case*	Similar to base case† Similar to base case except for INF. INF has higher QALYs.	Similar to base case‡ Similar to base case‡
Utility	From Rodgers et al[37]	From FUTURE 2[24]	Dominates INF. Cost-effective against UST. Slightly higher ICER than the rest of biologics.	Cost-effective against INF	Cost-effective against INF
Disutility	No	Yes	Similar to base case*	Similar to base case†	Similar to base case‡
HAQ rebound assumption	Equal to initial gain	Natural history	Similar to base case*	Similar to base case†	Similar to base case‡

CER P indicates certolizumab pegol; ETN, etanercept; GOL, golimumab; HAQ, Health Assessment Questionnaire; ICER, incremental cost-effectiveness ratio; INF, infliximab; PASI, Psoriasis Area and Severity Index; PsARC, Psoriatic Arthritis Response Criteria; QALY, quality-adjusted life year; UST, ustekinumab.

* Base case for secukinumab 150 mg (naive: no moderate to severe): dominates all biologics except INF. But INF was not cost-effective vs secukinumab 150 mg.

† Base case for secukinumab 300 mg (naive: moderate to severe): cost-effective vs all biologics (dominates INF).

‡ Base case for secukinumab 300 mg (experienced): cost-effective vs all biologics (dominates INF).

Whereas the better outcomes achieved with secukinumab reflect enhanced HRQoL of PsA patients and provide an ideal treatment choice for a rheumatologist, from the payer's perspective, secukinumab is a cost-effectiveness treatment option.

In the past, multiple cost-effectiveness studies have evaluated TNFi adalimumab, golimumab, etanercept, and infliximab in active PsA patients, mainly conducted from the UK perspective.[38-43,54] To our knowledge, this is the first-ever study that assessed the cost-effectiveness of secukinumab in PsA in Argentina. Hence, findings of this study add substantial evidence to the existing literature on economic evaluations of biologic treatments in PsA.

Varied factors contributed to the overall strength of the analysis. The comparative clinical efficacy data for different treatments were robustly grounded and derived from the NMA (based on 20 randomized controlled trials and 6021 patients). Drug acquisition costs, medical support costs, and AE costs used in the present analysis reflect the true economic burden imposed by PsA on a healthcare system. Further, the lifetime horizon considered in the analysis provides a precise estimation of the chronic course of PsA. Finally, the robust model structure and methodology support the study results, which were confirmed by both one-way and probabilistic sensitivity analyses.

The complexity of the disease process and the scarcity of data mean that there are a number of limitations and uncertainties in this kind of cost-effectiveness analysis.

Only short-term comparative effectiveness data (up to week 16) obtained from NMA[44] were available and were extrapolated for the long-term time horizon, which can be considered one of the limitations of the analysis. Extrapolation of treatment effects was performed to assess long-term outcomes, and assumptions were made for long-term HAQ and PASI scores. If the patient decided to continue on a biologic beyond 3 months, it was assumed that they would maintain their initial improvement in HAQ while on therapy. This was based on evidence from an opinion elicitation exercise by clinical experts and supported by data on HAQ and HRQoL from biologic registers.[55,56] It was also assumed that patients would maintain their improvement in PASI while on biologic therapy. Secukinumab has shown sustained clinical response in the long-term clinical trials[30,57,58] and indirect comparison methods.[31-33] Hence, it is likely that long-term benefits from secukinumab treatment may have been underestimated in the current NMA. This analysis could be rerun once long-term clinical efficacy data for all treatments become available. The PsARC had been used as the main response criteria in the present analysis and may be a source of weakness in the

current model because it may not be extensively used in routine clinical practice. Furthermore, data on disease-related costs in Argentina (including cost incurred for unit change in HAQ and cost for controlled [PASI ≥75] and uncontrolled psoriasis [PASI <75]) were lacking, and hence costs were taken from other sources.[47,49] Another limitation was lack of efficacy data for ustekinumab, and hence efficacy estimates for ustekinumab were assumed to be an average of the efficacy of other biologics. Nevertheless, sensitivity and alternate scenario analyses around these parameters showed minimal or no influence on the overall results.

Research has shown that switching between biologic therapies should be considered in patients experiencing treatment failure either owing to primary nonresponse, secondary loss of efficacy or effectiveness, or occurrence of AEs. Unfortunately, there was lack of efficacy data for patients on subsequent-line biologics after withdrawal from primary biologic therapy, given the need to capture switches between multiple different biologics, and necessitating a longer follow-up period. Thus, the base-case analysis assumed that patients on subsequent-line biologics were treated with an average biologic based on all other biologics modeled.

The cost-effectiveness outcomes are sensitive to drug acquisition costs, and any change in drug cost could affect outcomes. Finally, because the analysis was performed from a payer's perspective, societal costs were not considered.

Conclusions

The present cost-effectiveness analysis demonstrated that, from the Argentinean social security healthcare system perspective, secukinumab is either a dominant or cost-effective treatment option compared with other biologics for biologic-naive (without or with moderate to severe psoriasis) and biologic-experienced PsA patients in Argentina and constitutes an important advancement in the treatment of active PsA.

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Supplemental Material

Supplementary data associated with this article can be found in the online version at https://doi.org/10.1016/j.vhri.2019.03.002.

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