VALUE IN HEALTH REGIONAL ISSUES 5C (2014) 65–72

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevier.com/locate/vhri

Cost-Effectiveness of Biologic Agents in the Treatment of Moderate-to-Severe Psoriasis: A Brazilian Public Health Service Perspective

Bruno Salgado Riveros, MSc[1], *Patrícia Klarmann Ziegelmann, PhD*[2], *Cassyano Januário Correr, PhD*[1,*]

[1]*Pharmaceutical Sciences Department, Federal University of Parana, Curitiba, Brazil;* [2]*Department of Statistics, Federal University of Rio Grande do Sul, Porto Alegre, Brazil*

ABSTRACT

Background: Psoriasis is a chronic disease that affects public health and budget payers. In Brazil, biologic therapy for psoriasis is mostly provided by means of lawsuit with no strategy for efficient allocation of resources. **Objective:** This study aimed to identify which of the available biologic alternatives for psoriasis is the most efficient from the perspective of the Brazilian Public Health Service (SUS). **Methods:** Direct costs and efficacy were expressed in Brazilian currency (real [R$]; US $1 = R$1.97) and Psoriasis Area Severity Index 75 (PASI75), respectively. The Markov model process included 12 cycles of 3 months each, comprising 3 years of horizon. Adalimumab (80 mg at week 0 followed by a maintenance dose of 40 mg at week 1 and then every other week), etanercept (50 mg twice weekly for 12 weeks followed by a maintenance dose of 25 mg weekly), infliximab (5 mg/kg at weeks 0, 2, and 6 and then every 8 weeks), and ustekinumab (45 mg at weeks 0 and 4 and then every 12 weeks) were assessed. One-way and horizon sensitivity analyses were performed. Moreover, probabilistic sensitivity analysis was applied to evaluate model robustness. The final result was interpreted as the cost for each patient who achieved and maintained PASI75 for at least 3 years. **Results:** Adalimumab was the most cost-effective biologic therapy (R$120,981.45/PASI75) for moderate-to-severe psoriasis, followed by ustekinumab (R$126,336.67/PASI75), etanercept (R$225,074.71/PASI75), and infliximab (R$377,656.28/PASI75). One-way sensitivity analysis determined that the acquisition cost of biologics was the most sensitive parameter of the model. Horizon analysis suggests that the result was the same when the horizon was varied from 1 year to a lifetime. Probabilistic sensitivity analysis showed that adalimumab has 80% to 10% probability of being the most cost-effective biologic considering a willingness-to-pay value ranging from R$50,000 to R$500,000, whereas ustekinumab presented a probability of 20% to 90% for the same range. **Conclusions:** From the pharmacoeconomics point of view, adalimumab 80 mg at week 0 followed by a maintenance dose of 40 mg at week 1 and then every other week should be the first-line therapy for patients with plaque psoriasis concomitant or not to psoriatic arthritis or nail psoriasis. This study does not have the potential to evaluate the impact of incorporating a specific biologic agent on the final budget. Its goal is to point out which of the technologies is the most efficient, that is, the one that adds more value to the financial resource invested.

Keywords: biological agents, cost effectiveness, drug therapy, pharmacoeconomics, psoriasis.

Introduction

Psoriasis is a chronic autoimmune disease that affects mainly the skin. Its prevalence around the world varies between 0.6% and 4.8% [1]. There are different phenotypes for this disease, with plaque psoriasis (or psoriasis vulgaris) being the most common and affecting 80% of all patients with such a clinical condition [2]. Concomitant phenotypes are possible, such as psoriatic arthritis and plaque psoriasis (40%), with or without nail psoriasis (35%–50%) [3]. Other morphological combinations are less common, but possible as well.

Treatment is based on disease severity (mild, moderate, or severe). There is no consensus in the way to classify it, but most guidelines [4–13] suggest the "rule of 10" as an acceptable tool. The aforementioned clinical approach considers patients with 1) more than 10% of body surface area (BSA) affected by the disease, 2) a score of 10 or more for the Dermatology Life Quality Index (DLQI), or 3) Psoriasis Area Severity Index (PASI) as patients with moderate-to-severe psoriasis. Some authors consider those with a PASI value of 20 as suffering from a clinically severe condition [7]. In cases of mild psoriasis, topic treatment is generally effective [14]. In cases of moderate-to-severe psoriasis, systemic treatment is based on phototherapy, methotrexate, acytretin, or cyclosporine. For patients who do not respond to any of these therapeutic options or develop adverse reactions, biologic agents are an option [15].

In the Brazilian Public Health System (SUS), the clinical protocol for psoriasis does not indicate the best approach regarding the use of biologics. One of the reasons for this might be that there is a lack of economic evaluations that consider the SUS

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

* *Address correspondence to:* Cassyano Januário Correr, nº 632, Pref. Lothario Meissner Avenue, Curitiba 81540050, Brazil.

E-mail: cassyano.correr@gmail.com

2212-1099$36.00 – see front matter

http://dx.doi.org/10.1016/j.vhri.2014.09.002

perspective [7]. Moreover, biologics for the treatment of psoriasis remain unavailable in the SUS [16], making lawsuit the only way for patients to access such expensive treatment.

Therefore, we aimed to identify the most cost-effective biologic agent for moderate-to-severe psoriasis according to the perspective of the SUS.

Methods

This is a cost-effectiveness analysis in which costs were expressed in real (R$, Brazilian currency) and efficacy in PASI75 response (PASI75). The exchange rate between real and US dollar was US$ 1 = R$1.97 at the time of the study. This outcome corresponds to an improvement of 75% to 100% in the basal PASI score. Because the chosen outcome corresponds to efficacy and not effectiveness, it is important to highlight that data extracted from clinical trials were obtained in a controlled environment and not in a real-world scenario.

The result was interpreted as the amount of money spent for a patient who achieve and maintain PASI75 for at least 3 years. The adopted perspective is that of the SUS. A Markov model process with 12 cycles of 3 months each was built to assess the scenario of patients with moderate-to-severe psoriasis, eligible for treatment based on biologics, following Brazilian Consensus of Psoriasis [6].

This pharmacoeconomic study is part of a broader project that involved systematic reviews of clinical efficacy and safety [17] and patient-related outcomes. Moreover, a mixed treatment comparison for these three outcomes and a benefit-risk multicriteria decision analysis were carried out. These studies are under review in scientific journals.

Population

Patients with moderate-to-severe psoriasis treated within the SUS who had an indication to start a biologic agent were our targeted population. Efficacy data of each biologic agent were obtained from the literature [18–22]. Thus, our results are applicable to patients with characteristics described in Table 1, which corresponds to the weighted average of the population evaluated in each clinical trial.

Technologies Assessed

The evaluated biologic agents were the ones approved by the National Health Surveillance Agency (ANVISA) for marketing up to the end of 2012, and selected dosages were the ones indicated by Brazilian Consensus of Psoriasis [6]. Thus, adalimumab (80 mg at week 0 followed by a maintenance dose of 40 mg at week 1 and then every other week), etanercept (50 mg twice weekly for 12 weeks followed by a maintenance dose of 25 mg weekly), infliximab (5 mg/kg at weeks 0, 2, and 6 and then every 8 weeks), and ustekinumab (45 mg at weeks 0 and 4 and then every 12 weeks) were assessed.

Table 1 – Characteristics of the population with psoriasis from which data about efficacy were extracted.

Characteristic	Mean ± SD
Age (y)	44.8 ± 1.31
Men (%)	67.8 ± 2.14
Patients with PsA (%)	29.7 ± 3.54
Disease duration (y)	19.5 ± 1.18
PASI score	19.6 ± 1.9
DLQI score	11.7 ± 0.66

DLQI, Dermatology Life Quality Index; PASI, Psoriasis Area Severity Index; PsA, psoriatic arthritis.

Markov Model

The proposed model, which consisted of four health states, was based on Woolacott et al. [23]: (Fig. 1):

- PASI75—patients who achieved an improvement of 75% to 100% in their basal PASI score.
- PASI50-75—patients who achieved an improvement of 50% to 75% in their basal PASI score.
- Failure—patients who did not achieve an improvement of 50% to 75% in their basal PASI score nor achieved better scores, patients who achieved an improvement of 50% to 75% in their basal PASI score but after 12 weeks did not improve their response to PASI75, or patients who developed an adverse event preventing the maintenance of biologic therapy.
- Death—includes all death cases regardless of cause.

Each Markov cycle corresponds to 12 weeks, and the study time horizon was 3 years. Discounting of 5% [24] was applied following Brazilian statements. The outcome was assessed considering the number of patients with PASI75 health state at the end of the model.

The first 12 weeks of treatment is not shown in the model. It was, however, represented in cycle 0, and costs were expressed as *initial costs*. Thus, *_stage=0* corresponds to a period between 12 and 24 weeks after treatment initiation.

Because all models are a simplified way to understand a complex situation, all of them have assumptions [25]. The present model assumes the following:

1. After therapeutic failure with any biologic agent, patient did not use any other biologic.
2. Temporary interruptions of biologics were not considered in this model.
3. Patients who achieved PASI75 interrupted biologic therapy only if they
   a. got a clinical response worse than 50% of improvement or
   b. developed adverse reaction or any adverse event that increased the risks over the benefits.
4. Patients with an improvement of 50% to 75% in their basal PASI score for more than 12 weeks had their biologics interrupted.
5. Only the clinical efficacy of biologics was taken into account, regardless of association with topic or systemic drugs or phototherapy treatment.

Probabilities

Data of PASI75 were extracted from the literature to serve as foundations for transition probabilities (Table 2). The selected randomized controlled trials (RCTs) were the ones that 1) assessed the same dose regimen as us, 2) showed low risk of bias by means of Cochrane Collaboration's tool, 3) presented long-term results (at least 1 year of follow-up), and 4) had a number of participants weighing more than 500 lb. Probabilities related to the short-term treatment were retrieved from an network meta-analysis involving the four biologics assessed [18].

From the second year of treatment, efficacy data were extrapolated from the last known result. This assumption was based on literature findings [19,20,22].

Death probability was extracted from the Life Table published by the Brazilian Institute of Geography and Statistics (IBGE) [26].