

Biologic Therapies For Moderate-to-Severe Psoriasis: Cost Per Responder Analysis Considering Private Healthcare System in Brazil

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INTRODUCTION

Psoriasis (PsO) is a chronic painful, inflammatory and debilitating systemic condition, currently considered of public health concern by the World Health Organization (WHO).^{1,2} Psoriasis has a relevant impact on quality of life, due to its high disabling potential given by the involvement of the skin and the consequent isolation and/or social discrimination, as well as by the eventual joint involvement and the high risk of comorbidities.³ The most common PsO type is plaque PsO, usually characterized by well-demarcated red plaques with silvery scales. In the past 15 years, management of plaque psoriasis has evolved towards biologic medications, targeting diverse cytokines involved in PsO pathophysiology such as tumor necrosis factor (TNF), interleukin-12, interleukin-23, and interleukin-17.³ Recently, biologic drug classes as the interleukin 23 (IL-23) antagonists have demonstrated more pronounced reduction in PsO lesions, a critical outcome in PsO trials and an unmet need for patients.⁴ Most of biologics clinical trials adopts Psoriasis Area and Severity Index (PASI) outcomes as primary endpoints. PASI combines both qualitative and quantitative dimensions of PsO manifestations in a single measure. PASI score varies from 0 (no disease) to 72 (maximal disease severity) and clinical trials usually report the reduction in patients' PASI scores from baseline values after treatment – i.e., a clinical improvement of at least 75% (PASI 75), 90% (PASI 90), or 100% (PASI 100).⁵ Regardless of a historically solid presence of PASI 75 as primary endpoint in PsO randomized controlled trials (RCT),⁵ updates in clinical guidelines have reinforced that a PASI 90 response may represent a better efficacy outcome for moderate-to-severe disease, as its achievement is related to higher clinically significant improvements on quality of life.⁶ In this scenario of multiple medication, understanding of comparative efficacy and its association with costs is critical to inform clinical and economic decisions. Cost-per-responder has been widely used for this purpose, both in the scientific literature and on health technology assessments (HTA).⁷

METHODS

The cost-effectiveness of biologic therapies for moderate-to-severe PsO was assessed for the Brazilian private healthcare system (Sistema de Saúde Suplementar) using a cost-per-responder (CpR) analysis based on a network meta-analysis (NMA) previously published.⁸ Adalimumab, etanercept, guselkumab, infliximab, ixekizumab, risankizumab, secukinumab, and ustekinumab (considering marketing authorization in Brazil) were included and placebo was the common comparator for all drugs. NMA included short-term (10-16 weeks) randomized controlled trials and long-term (44-60 weeks) trials, which were identified in a systematic literature review. Trials included were phase II and III clinical trials enrolling adults with moderate-to-severe PsO and the outcomes of interest (PASI 75, 90, and 100) were reported. Long-term analysis was performed in two different perspectives: a base case, that included etanercept, ixekizumab, risankizumab, secukinumab, and ustekinumab, and a sensitivity analysis that comprised only phase III studies found in the systematic review.⁸ For 2-years estimations, response rates of long-term trials (44-60 weeks) were maintained. The cost per patient in each treatment arm was calculated for short (10-16 weeks) and long-term (1 and 2 years) periods, once dosing schedules for some comparators in the primary response period are different from those in the maintenance period. To provide an accurate estimate, the cost calculation considered both first-year and maintenance period costs. The mean weight attributed to patients in the model was 70.0 kg, and the proportion of patients with weight ≤100 kg for ustekinumab cost estimation was assumed as 80.0%.

Unit costs included pharmacy costs only and were sourced from the Brazilian official database (Câmara de Regulação do Mercado de Medicamentos [CMED]), considering the ex-factory price added by 18% of value added tax.⁹ Monitoring costs (laboratory tests, physician visits etc) were not included in the cost estimation, once they are not significantly different between biologic drugs considered in the decision model.

OBJECTIVES

To assess the cost-per-responder of biologic therapies available in Brazil to treat moderate-to-severe plaque psoriasis (PsO) using as outcomes a reduction of 75%, 90%, and 100% in Psoriasis Area and Severity Index (PASI 75/90/100), considering private healthcare system perspective.

RESULTS

In all time frames and PASI response criteria (75, 90 and 100), the lowest CpR observed was for risankizumab and guselkumab in the short-term period and for risankizumab followed by ixekizumab in the long-term periods (Figure 1). Overall, the differences in the mean CpR between risankizumab and other biologic drugs increased with higher PASI reduction. Highest CpR in the short-term was observed for infliximab in PASI 75 response and etanercept in PASI 90 and PASI 100 responses; etanercept presented the highest CpR in the long-term analysis (1- and 2-years), considering all PASI response criteria.

Considering the NMA sensitivity analysis⁸, which analyzed all 8 medications in a long-term perspective (1- and 2-year of treatment), lowest CpR for PASI 75 and PASI 90 were achieved by risankizumab and guselkumab. Risankizumab showed the lowest CpR, for PASI 100, followed by ixekizumab in both periods.

Treatment	Drug costs*	CpR – PASI75**	CpR – PASI90**	CpR – PASI100**
Primary response period				
Adalimumab	40,083	62,434	94,091	244,408
Etanercept	22,121	63,567	131,674	539,540
Guselkumab	33,649	41,338	50,906	94,520
Infliximab	48,136	64,096	85,500	182,335
Ixekizumab	36,902	44,194	52,944	93,660
Risankizumab	33,649	40,106	47,729	83,496
Secukinumab	40,365	51,950	67,052	135,454
Ustekinumab	30,194	46,886	70,547	181,893
First year of treatment				
Etanercept	95,858	178,175	267,015	610,563
Ixekizumab	89,620	107,329	128,395	199,155
Risankizumab	84,123	92,341	103,472	140,909
Secukinumab	107,640	134,383	165,093	269,776
Ustekinumab	75,486	108,146	143,782	269,592
Two years of treatment				
Etanercept	191,717	356,351	534,030	1,221,126
Ixekizumab	158,152	189,404	226,579	351,449
Risankizumab	151,421	166,214	186,250	253,636
Secukinumab	195,098	243,569	299,231	488,968
Ustekinumab	140,907	201,872	268,394	503,238

*Drug acquisition costs within the period expressed in BRL (Brazilian reais); Brazilian official database (Câmara de Regulação do Mercado de Medicamentos [CMED]), considering the ex-factory price added by 18% of value added tax; **BRL.

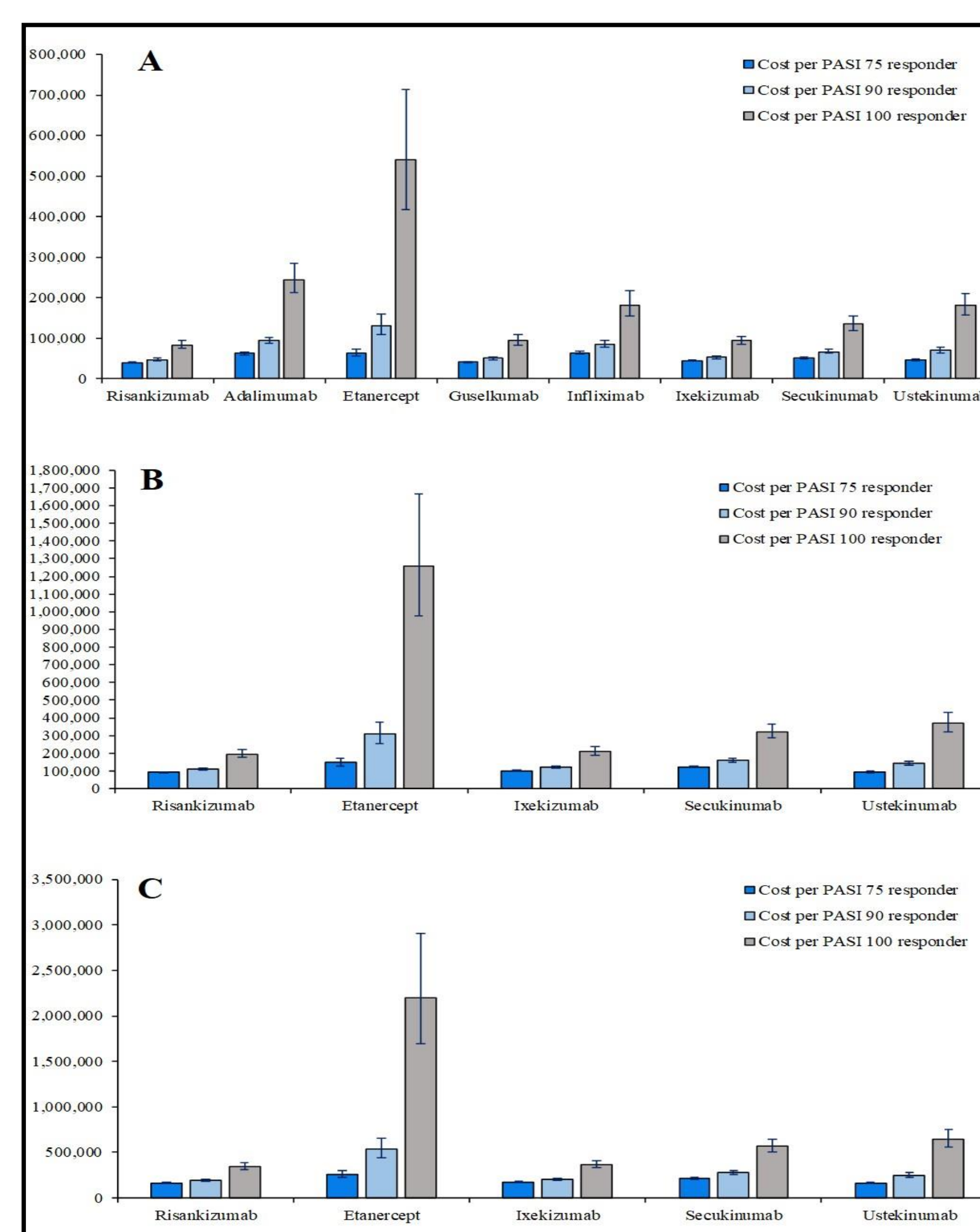


Figure 1. Cost per responder and 95% CI for each biologic using NMA base case results: A) primary response period; B) first year of treatment; C) 2 years of treatment. CI: Confidence Interval.

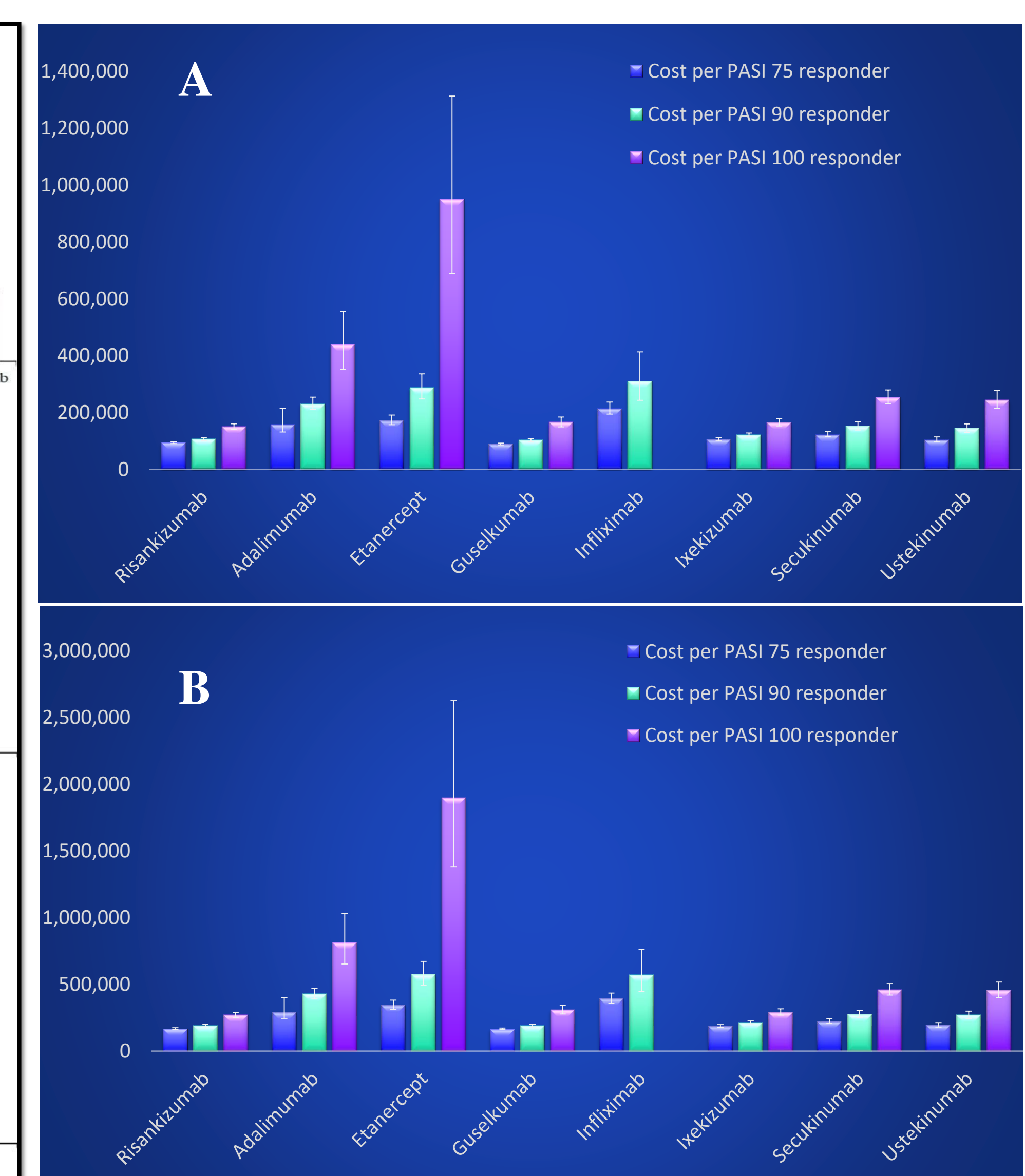


Figure 2. Cost per responder and 95% CI for each biologic considering the sensitivity analysis: A) first year of treatment; B) 2 years of treatment.

DISCUSSION AND CONCLUSIONS

The current CpR analysis adopted a methodologically rigorous NMA of biologic medications for moderate-to-severe PsO to identify effectiveness of each therapeutic option.⁸ Short-term results are consistent with findings from a recent Cochrane NMA¹⁰ comparing drug classes and unique drugs for moderate-to-severe PsO in follow-up durations ranging from 8-24 weeks. Authors identified that the anti-IL23 drugs risankizumab and guselkumab, infliximab and IL17 inhibitors (secukinumab and ixekizumab) were significantly more effective than ustekinumab, adalimumab, certolizumab and etanercept.¹⁰ Given the introduction of novel biologic treatment options for moderate-to-severe PsO in Brazil, this long-term analysis can help guide resource allocation decision-making. Among the evaluated biologic therapies, risankizumab was associated with the lowest CpR in all analyzed PASI outcomes, with more pronounced difference in higher PASI responses, considering Brazilian private healthcare system.

LIMITATIONS

Besides NMA data limitation, inherent to all indirect comparison studies, this study also presents some limitations:

- It was assumed that the results from global clinical trials are valid for the Brazilian population;
- There is no comparative data available for 2-years follow-up period. Therefore, the same response rates of the first year of treatment analysis were maintained for the evaluated therapies;
- One and 2-years CpR for adalimumab, guselkumab and infliximab were performed considering the sensitivity analysis (Figure 2), as they were not included in the NMA base case scenario for long-term response;
- Costs were calculated based on an official database and do not consider possible commercial agreements.

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REFERENCES

- Griffiths CEM, van der Walt JM, Ashcroft DM, et al. The global state of psoriasis disease epidemiology: a workshop report. *Br J Dermatol*. 2017;177(1):e4–e7.
- World Health Organization. Global report on psoriasis. World Health Organization. 2016. Available at: <https://apps.who.int/ris/handle/10665/204417>.
- Menter A, Strober BE, Kaplan DH, et al. Joint AAD-NPF guidelines of care for the management and treatment of psoriasis with biologics. *J Am Acad Dermatol*. 2019;80(4):1029–1072.
- Gordon KB, Strober B, Lebwohl M, et al. Efficacy and safety of risankizumab in moderate-to-severe plaque psoriasis (ULTIMMa-1 and ULTIMMa-2): results from two double-blind, randomised, placebo-controlled and ustekinumab-controlled phase 3 trials. *Lancet*. 2018 Aug 25;392(10148):650–61. Epub 2019 Jun 30.
- Arnone M, Takahashi MDF, Carvalho AVE, et al. Diagnostic and therapeutic guidelines for plaque psoriasis - Brazilian Society of Dermatology. *An Bras Dermatol*. 2019;94(2 Suppl 1):S76–107.
- Puig L. PASI90 response: the new standard in therapeutic efficacy for psoriasis. *J Eur Acad Dermatol Venereol*. 2015;29(4):645–8.
- Brasil. Ministério da Saúde. Adalimumabe, etanercepte, infliximabe, secukinumabe e ustekinumabe para psoríase moderada a grave. Brasília: Ministério da Saúde; 2018.
- Armstrong AW, Puig L, Joshi A, et al. Comparison of Biologics and Oral Treatments for Plaque Psoriasis: A Meta-analysis. *JAMA Dermatol*. 2020; 156(3):258–269.
- Ministério da Saúde. Brasil. Agência Nacional de Vigilância Sanitária. Câmara de Regulação do Mercado de Medicamentos (CMED) [Internet]. 2019 [cited 2019 Nov 28]. Available at: <http://portal.anvisa.gov.br/cmcd>.
- Sbidian E, Chaimani A, Afach S et al. Systemic pharmacological treatments for chronic plaque psoriasis: a network meta-analysis. *Cochrane Database of Systematic Reviews* 2020, Issue 1. Art. No.: CD011535.

DISCLOSURES

de Carvalho, Andre V E has served as advisory board member and speaker for Abbvie, Jansen, Leo Pharma, Novartis, Lilly and UCB; Duarte, G V is a speaker for Abbvie, Janssen, Lilly, Novartis, Pfizer, Biolab, Leo Pharma, Galderma, Bayer and Sanofi-Genzyme; Ianhez, M is speaker for Abbvie, Janssen, Novartis, UCB, Sanofi-Genzyme, Galderma, Leo Pharma, Biolab; and served as advisory board member for Abbvie, Janssen, Novartis and UCB, Sanofi-Genzyme; Silva, Bruno Leonardo; Biella, Carla A; dos Santos, Rafael F: AbbVie employees and may hold AbbVie stocks and/or stock options. The design, study conduct, and financial support for the study were provided by AbbVie. AbbVie participated in the interpretation of data, review, and approval of the publication.