Background

Psoriasis is a chronic, inflammatory disease affecting approximately 1–3% of the population worldwide and is associated with significant morbidity.

Since the introduction of anti-TNF biologic agents more than a decade ago, the management of moderate-to-severe psoriasis has advanced significantly with the modern biologic therapies (IL-17s and IL-23s), enabling millions of people to achieve complete skin clearance.

Despite the clinical benefits associated with these biologic therapies, observational studies have reported high rates of discontinuation for some biologic agents, as well as off-label dose escalation for other biologic agents in clinical practice, suggesting an efficacy-effectiveness gap.

Given the high costs associated with biologic agents, focusing on actual discontinuation and dose adjustment from the real-world setting is central to an accurate assessment of the cost-effectiveness and the true economic impact of these agents.

To compensate for the lower efficacy of certain biologic agents, companies may offer price reductions to make the less effective biologic agents relatively more cost-effective. However, it is unknown how these price reductions affect the cost-effectiveness of the various biologic agents in real life.

Objective

This study seeks to evaluate the cost-effectiveness of biologic agents in plaque psoriasis when taking real-world evidence on discontinuation and dose adjustment into account in Spain.

In addition, the study seeks to assess the impact of price reductions on the cost-effectiveness of biologic agents.

Methods

A cost-per-responder model was developed to evaluate cost-effectiveness of biologic agents, which incorporates the probability of treatment discontinuation and off-label dose adjustment with brodalumab, secukinumab, ustekinumab, adalimumab, etanercept, and infliximab over 2 years.

The probability of discontinuation in each case was calculated every 4 weeks based on a literature review of real-world evidence (RWE).

RWE on treatment discontinuation for infliximab, etanercept, ustekinumab, adalimumab, and secukinumab was included in the literature review (Table 1).

No RWE for brodalumab or ixekizumab was available. Hence, discontinuation rates for brodalumab and ixekizumab were assumed to be 1% per 4 weeks (Table 1). Different levels of discontinuation were tested in a sensitivity analysis.

Off-label dose adjustment was based on a recent large Danish registry study.

For etanercept and infliximab, doses were estimated to be 20% higher than the label from week 13, while a 20% increase in dose was estimated for ustekinumab from week 25. (Table 1)

The efficacy of each biologic agent was determined from the absolute response rates at week 12–16 from a recent network meta-analysis (Table 1).

A reduction of 100% in Psoriasis Area and Severity Index (PASI 100) score was used as a measure of treatment response, indicating complete skin clearance.

As the cost of biologic treatment in plaque psoriasis consists mainly of the drug cost, the analysis was based on direct costs of drug acquisition at public selling prices in Spain (Table 1).

Results

Costs from year 1 to 2 were discounted using an annual discount rate of 3% based on national pharmacoeconomic guidelines.

Cost-effectiveness was assessed by comparing the cost per patient per 4 weeks adjusted for discontinuation relative to achieving a response level of PASI 100.

The impact of reducing the price was assessed in a sensitivity analysis.

For each biologic agent, the price was reduced by 1%.

Subsequently, the cost-effectiveness of this agent was compared to the three most-cost-effective agents (without discount).

The price was reduced by 1% until the agent reached similar levels of cost-effectiveness as the comparators.

The average cost per PASI 100 responder over 2 years of therapy was highest for etanercept at €562,800, followed by ustekinumab (€164,170), adalimumab (€137,511), etanercept (€125,467), secukinumab (€68,467), respectively, and lowest for brodalumab (€62,165).

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When varying discontinuation rates for brodalumab and secukinumab in the sensitivity analysis, brodalumab and secukinumab remained more cost-effective than the other biologic agents.

Sensitivity analyses indicated that price reductions of approximately 83% for etanercept, 43% for ustekinumab, and 36% for adalimumab, and 30% for infliximab, respectively, were necessary in order to achieve similar levels of cost-effectiveness as secukinumab.

Price reductions as high as 88% for etanercept, 40% for ustekinumab, 65% for adalimumab, 50% for infliximab, and were necessary to reach similar levels of cost-effectiveness as adalimumab and brodalumab.

Discussion

Biologic treatments for psoriasis can improve the lives of patients significantly yet can – collectively – become a strain on healthcare budgets. The challenge is how to provide optimal health outcomes for patients with efficient resource prioritization.

The present study indicates that the modern anti-IL-17 biologic therapies are highly cost-effective compared to the anti-TNFs and anti-IL-12/23 in a real-world setting, with brodalumab being the most cost-effective treatment.

In the real-world setting, price reductions may improve the relative cost-effectiveness of anti-TNFs and ustekinumab. However, this study suggests that large price reductions will be necessary for these agents to reach similar cost-effectiveness levels as modern biologic agents, especially brodalumab and ustekinumab.

As the RWE data environment continues to mature rapidly, it is important that health economic experts take advantage of this.

In the present study, a novel approach to cost-effectiveness modelling was adopted with the incorporation of RWE on dosing and discontinuation.

This approach may improve the accuracy of the cost-effectiveness evaluation in clinical practice, which is highly relevant from a health care payers’ perspective.

In the future, a uniform approach to integration of RWE in cost-effectiveness models is warranted.

Conclusions

The present work shows that moderm anti-IL-17s are highly cost-effective compared to anti-TNFs and anti-IL-12/23 over a 2 year treatment period. Overall, brodalumab was the most cost-effective treatment followed by ustekinumab.

Though price reductions would make anti-TNFs and anti-IL-12/23 more cost-effective, the results of this study indicate that very high price reductions would be necessary to achieve this improved efficiency.

References

5. Feldman et al., JMCP 2015 Mar;21(3):201-209.

Table 1: Discontinuation rates per 4 weeks periods, dose escalation, cost per responder, sensitivity analysis of PASI 100 responders for all biologic agents

- Table 1: Drug acquisition at public selling prices in Spain (mainly of the drug cost, the analysis was based on direct costs network-meta analysis)

Figure 1: Average cost per PASI100 responder over 2 years of therapy per biologic agent (EUR)

Figure 2: Price reductions needed for anti-TNFs and ustekinumab to reach similar levels of cost per PASI 100 responder as etanercept, adalimumab & brodalumab, respectively.