6ER-011: MODELLING THE IMPACT OF DISCOUNTS ON THE REAL-LIFE COST-EFFECTIVENESS OF BIOLOGIC THERAPIES IN THE TREATMENT OF MODERATE-TO-SEVERE PLAQUE PSORIASIS IN SPAIN

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Background

- Psoriasis is a chronic, inflammatory disease afflicting approximately 1–5% of the population worldwide and is associated with significant morbidity[1]
- 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 numerous patients to achieve complete skin clearance[1,2,3]
- 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[4,5], suggesting an efficacy-effectiveness gap [6]
- Given the high costs associated with biologic agents, factoring in 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[5,7]
- 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, ixekizumab, 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) [8]
  - RWE on treatment discontinuation for infliximab, etanercept, ustekinumab, adalimumab and secukinumab was included in the literature review [8] (**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 [4]
  - For etanercept and infliximab, doses were estimated to be 20% higher than label from week 13, while a 20% increase in dose was estimated for ustekinumab from week 25 [4] (**Table 1**)
- Treatment efficacy for each biologic agent was determined from the absolute response rates at week 12-16 from a recent network-meta analysis 9 (**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 for 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**)
  - Costs from year 1 to 2 were discounted using an annual discount rate of 3% based on national pharmacoeconomic guidelines [10]
- 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

Table 1: Model input: Discontinuation rates per 4-week periods, dose escalation, cost per syringe, number of syringes per year, and PASI 100 response rates for all treatments

Treatment	Discontinuation rates per 4-week periods	Dose escalation	Cost per syringe (EUR)[e]	Number of syringes per year (1st year)[f]	Number of syringes per year (2nd year)[f]	PASI 100 response rates[h]
Infliximab	1.50%[a]	20%[c]	536	35.7[g]	27.3[g]	26%
Etanercept	1.50%[a]	20%[c]	211	53	52	4%
Adalimumab	1.25%[a]	0%	514	28	26	17%
Ustekinumab	0.80%[a]	20%[d]	2,747	6	4	18%
Secukinumab	2.30%[a]	0%	572	34	26	30%
Ixekizumab	1.00%[b]	0%	1,010	18	13	40%
Brodalumab	1.00%[b]	0%	525	28	26	40%

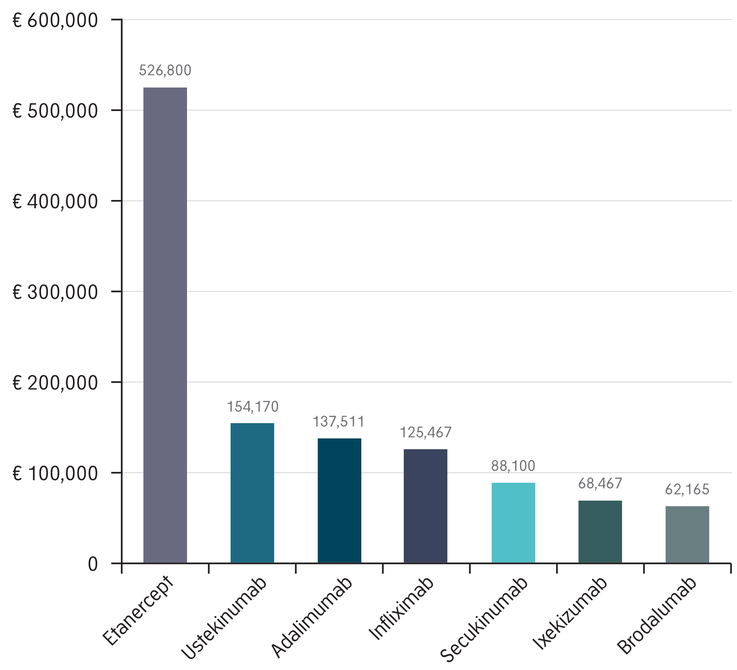
a Estimated based on literature review [8]; b Assumption; c From week 13 – based on supplementary material, Egeberg et al., 2018 [4]; d From week 25– based on supplementary material, Egeberg et al., 2018 [4]; e BotPLUS web database.: Spanish General Council of Official Colleges of Pharmacists. Madrid. Available from: https://botplusweb.portalfarma.com/. Accessed 14.09.2018; f Based on SmPC dosing schedule; g INF dosing based a 83.3 kg and 5 mg/kg = 416.5 mg or 4.2 units per scheduled dose; h Sawyer et al., 2018 [9]

- 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

Results

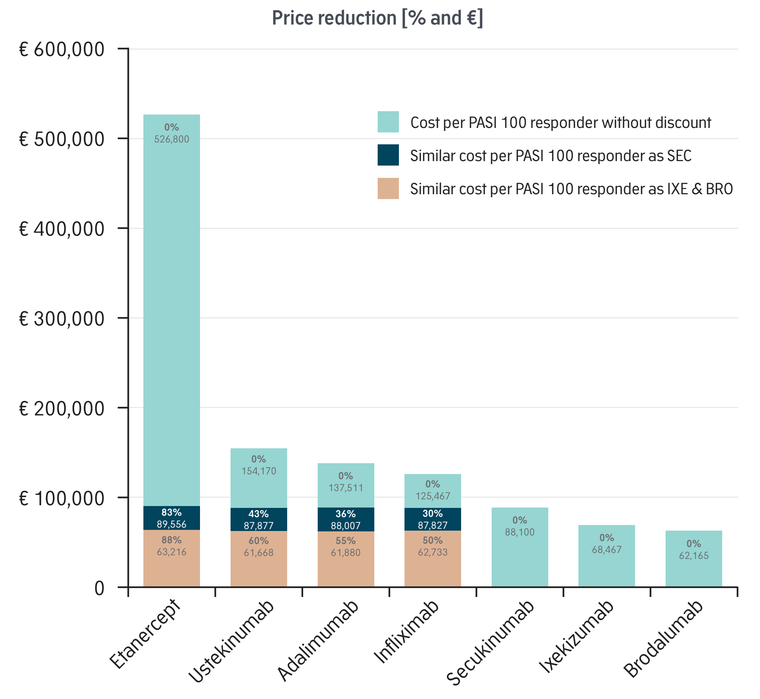
- The average cost per PASI100 responder over 2 years of therapy was highest for etanercept at € 526,800, followed by ustekinumab (€ 154,170), adalimumab (€ 137,511), infliximab (€ 125,467), secukinumab (€ 88,100), ixekizumab (€ 68,467), respectively, and lowest for brodalumab (€ 62,165) (**Figure 1**)

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



- When varying discontinuation rates for brodalumab and ixekizumab in the sensitivity analysis, brodalumab and ixekizumab remained more cost-effective than the other therapies
- Sensitivity analyses indicated that price reductions of approximately 83% for etanercept, 43% for ustekinumab, 36% for adalimumab, and 30% for infliximab, respectively, were necessary in order to achieve similar levels of cost-effectiveness as secukinumab (**Figure 2**)
- Price reductions as high as 88% for etanercept, 60% for ustekinumab, 55% for adalimumab, 50% for infliximab, and were necessary to reach similar levels of cost-effectiveness as ixekizumab and brodalumab (**Figure 2**)

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



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 ixekizumab
- 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 modern 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 ixekizumab
- 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

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