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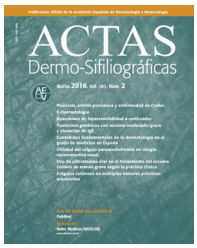

COMMENTARIES

Incremental Cost per Responder (PASI-75, PASI-90 and PASI-100) Based on a Network Meta-Analysis of Biologic Therapies for Psoriasis: Spain 2018☆

Análisis del coste incremental por respondedor (PASI75, PASI90 y PASI100) basado en un metaanálisis en red de tratamientos biológicos para la psoriasis: España 2018

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Incremental Cost per Responder (PASI-75, PASI-90 and PASI-100) Based on a Network Meta-Analysis of Biologic Therapies for Psoriasis: Spain 2018

Network meta-analysis, which now has a well-established methodology, provides information on the relative efficacy of a number of treatments using data from clinical trials that directly compare two or more drugs in addition to indirect comparisons based on data from different trials using the same comparator. Variations between trials are adjusted to the reference arm response rates. Meta-analysis results can be expressed as the differential response compared to placebo (either as a percentage or its corresponding decimal value) or as its inverse—the number needed to treat (NNT), that is, the number of patients that must be treated to achieve a responder. The NNT and the incremental cost per responder—calculated by multiplying the NNT for the drug by the cost for the period considered—provide reliable values that allow us to compare the expected effectiveness of different treatments at various response levels, a datum with important clinical and economic implications for physicians and those responsible for making decisions on treatment funding and reimbursement.

The objective of the study in this issue[1] was to evaluate the cost-effectiveness of ixekizumab as afirst-line biologic for the treatment of psoriasis and to compare it with that of other biologic agents based on data from a recently published network meta-analysis.[2] Employees of the company that markets ixekizumab were involved in carrying out the network meta-analysis. The main interest of the article is that it is the first study to provide data on ixekizumab in Spain. In addition to the information provided by the health technology agencies' assessments, a study similar to this one has recently been published in the United States.[3]

The methodology and results of the study are valid, but the terminology used for the outcome of interest (''cost per NNT'') is debatable: it would probably be preferable to use the expression ''(incremental) cost per successfully treated patient''. The cost per NNT values (cost x NNT) corresponding to each response level are calculated by multiplying the cost of treatment by the respective NNT value (and the 95% credible interval). However, by analogy with widely used concepts such as ''cost per patient'' or ''cost per day'', the term ''cost per NNT'' suggests that the NNT is dividing (cost/NNT) rather than multiplying the cost. The term *incremental* is not relevant in this particular case because the cost of placebo is considered to be zero.

In the analysis by Núñez et al.[1] the population corresponds to the Summaries of Product Characteristics, in each case, and treatment response is expressed as the percentage of reduction in the Psoriasis Area and Severity Index (PASI) with respect to baseline, with 3 different levels of efficacy (PASI 75, PASI 90 and PASI 100). The cost per responder is calculated by multiplying the annual cost (or the cost up to the end of the comparative phase vs placebo, the *endpoint* in the clinical trials) by the NNT. In the meta-analysis, the authors assume that the efficacy at that point is the same as the short-term effectiveness maintained, without loss, for the whole year. The 95% credible interval is not given for most of the results reported in the article. This decision may have been taken to improve readibility, but the use of the "greater than" symbol (>) for comparisons may lead to confusion: although the incremental cost per responder central values differ numerically, one cannot strictly talk about the superiority of one drug over another when their credible intervals overlap.

The model used does not address the response rate achieved by each biologic agent as a rescue treatment or possible differences in the response of patients with a history of prior exposure or treatment failure with other biologic agents (generally unknown or assumed to be similar or inferior in a variable and drug-dependent percentage to the response of patients who have never received biologic therapy). Neither does it take into account drop-out rates, indirect treatment costs, or possible complications.

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The authors could also have included apremilast, which, while not a biologic agent, has a similar acquisition cost.

More complex models have been proposed based on periods of 52 weeks[4] and 2 years.[5] One difference between those 2 studies is the choice of rescue treatment for patients who experience treatment failure (conventional systemic treatment or phototherapy in the German model[4]). In the study that considers the perspective of the Spanish health system,[5] with a 2-year time horizon, indirect costs were not taken into account and assumptions were made regarding the rates of treatment intensification and switches to other biologic treatments as well as the cost-effectiveness of these interventions. The order of efficiency reported in that study differs from that reported in the study in this issue.

Despite its limitations, which actually represent possible alternative approaches, the study is interesting and informative. The methodology is correct (there is always room for debate about whether or not the last dose should be included in the calculation of the interval or apportioned) and the inclusion of a sensitivity analysis based on the results corresponding to the endpoint for each drug (ranging from 10 to 16 weeks) is appropriate, with the limitation of between-trial differences in the duration of that period. The usefulness of this article could be greatly enhanced through the inclusion, as an on-line supplement, of an Excel sheet or a link where the reader could access or download a small Java, Android or Apple application, depending on the platform. This application would enable clinicians or pharmacists to calculate the results for the specific situation of each hospital (given the current highly variable and fluid pricing situation) and to incorporate new drugs as they become available, and even modify the NNT data as new meta-analyses are published.

Conflicts of Interest

L. Puig has received fees as a consultant or lecturer and/or has served as a researcher in clinical trials sponsored by: Abbvie, Almirall, Amgen, Baxalta, Biogen, Boehringer Ingelheim, Celgene, Gebro, Janssen, Leo-Pharma, Lilly, Merck-Serono, MSD, Mylan, Novartis, Pfizer, Regeneron, Roche, Sandoz, Samsung-Bioepis, Sanofi and UCB.

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Patient-Reported Outcomes in Psoriasis Validated in Spain: PROs and Cons☆

Patient reported outcomes en psoriasis validados en España: PROs y contras

This issue of Actas Dermo-Sifiliográficas features a systematic review of studies that have validated or used patient-reported outcome tools in Spanish patients with psoriasis.[1] The review includes 5 tools that have been validated for use in Spain: 2 skin disease–specific quality of life questionnaires (the Dermatology Life Quality Index [DLQI] and Skindex-29), 2 psoriasis-specific questionnaires (the Psoriasis Disability Index [PDI]) and PSO-LIFE, which was developed in Spain), and a treatment satisfaction questionnaire (CESTEP), also developed for psoriasis patients in Spain. The authors are to be commended for their review of PRO tools that have been culturally adapted for use in Spain and for evaluating their characteristics.

Among the notable findings of the review is the weak to moderate—and variable—correlation observed between health-related quality of life (HRQoL) measures and clinical severity measured by the Psoriasis Area and Severity (PASI) index. The nature of this correlation can be explained by the fact that PASI may not capture the effects of lesions in certain areas of the body (hands, arms, genitals, scalp, and nails)[2] or those of certain symptoms and lesion visibility.[3]

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