CASE AND RESEARCH LETTER

[Translated article] The Utility of long-Term Number Needed to Treat to Evaluate Interleukin 17 and 23 Inhibitor Therapies in the Treatment of Moderate to Severe Plaque Psoriasis

La utilidad del número necesario de pacientes a largo plazo a tratar para evaluar las terapias inhibidoras de las interleucinas 17 y 23 en el tratamiento de la psoriasis en placas de moderada a grave

Table 1 Absolute risk reduction (PASI 100) of the biological drug vs placebo on weeks 48 through 52 if the efficacy achieved by placebo on weeks 16 through 24 had been kept in the long term.

	Mean	95% confidence interval
Bimekizumab	65.11	(60.1-72.06)
Brodalumab	36.38	(32.52-40.35)
Guselkumab	46.84	(41.43-52.78)
Ixekizumab	56.09	(51.66-61.35)
Risankizumab	57.86	(53.96-63.26)
Secukinumab	43.57	(41.07-46.16)
Tildrakizumab	31.93	(26.58-37.83)

To the Editor:

One of the useful measures to guide dermatologists and pharmacists is the number needed to treat (NNT), which is the number of patients who need to receive a specific therapy to achieve or prevent a clinical outcome, compared to the number needed to achieve the same outcome with an alternative treatment or placebo.[1] This statistical parameter is an absolute risk measure calculated as the reciprocal of the absolute risk reduction (ARR) and was developed in the context of evidence-based medicine as a useful tool for clinical decision-making. In fact, the Consolidated Standards of Reporting Trials (CONSORT) statement recommends the use of both relative and absolute effect measures in randomized clinical trials (RCT).[2] However, the latter are often underreported, while the former are widely used.

The use of NNT has been increasing in dermatology in recent years, particularly in the management of psoriasis, where very similar efficacy variables are used in various RCT. In fact, recently, the Psoriasis Working Group of the Spanish Academy of Dermatology and Venereology recommended the assessment of parameters such as NNT for efficiency-based prioritization, always using the accepted response objectives of the Psoriasis Area and Severity Index (PASI) (PASI 90, or PASI 100) as a reference.[3] This is consistent with the the latest recommendations from the Permanent Phar-

macy Committee of including the NNT and cost per NNT as efficiency measures in therapeutic positioning reports (TPR).[4]

Therefore, we present an example of how NNT facilitates the interpretation of the effectiveness of different interleukin-17 (anti-IL-17) and IL-23 inhibitors (anti-IL-23p19), and how to use the cost per NNT as an efficiency measure to categorize various treatments based on their level of efficacy.

Based on the long-term efficacy results obtained by anti-IL-17 and anti-IL-23 biological therapies in their RCT, with comparable and consistent baseline patient characteristics, and using complete patient clearance (PASI 100) as a long-term efficacy measure (48 to 52 weeks), we conservatively estimated the ARR of the biological drug vs placebo assuming that the efficacy achieved by placebo on week 16 or 24 would still stands in the long run (Table 1).

The cost per NNT was calculated by multiplying the average annual treatment spending of the 1st and following years by the NNT. Since these are hospital drugs, the costs were calculated using the notified laboratory selling price (LSP) for each pharmaceutical formulation and the deduction established in the Royal Decree-Law (RDL) 8/2010 (Table 2).[5] Unit costs were obtained from the Bot Plus 2.0 database published by the General Council of Official Pharmaceutical Colleges.[6] Annual spending was calculated based on these unit costs and the doses recommended in the technical data sheets of each of the anti-IL drugs under consideration.[7] Since doses are higher within the 1st year of administration, the 1st and following-year averages were used.

Table 2   Costs associated with the assessed therapeutic alternatives.

	LSP/packaging[6]	Deduction RDL 8/2010[5]	Annual spending
Bimekizumab	€2674.00	7.5%	€19 169.24
Brodalumab	€1050.16	7.5%	€13 113.87
Guselkumab	€2536.1	7.5%	€16 421.25
Ixekizumab	€1010	7.5%	€14 480.88
Risankizumab	€3833.49	7.5%	€17 729.89
Secukinumab	€1143.11	7.5%	€14 803.27
Tildrakizumab	€3500	7.5%	€16 187.50

Table 3   NNT and cost (Notified LSP) per NNT of the biological drug vs placebo on weeks 48 through 52 (PASI 100) if the efficacy obtained by placebo on weeks 16 through 24 had been kept in the long term.

	NNT		Cost per NNT	
	Mean	95% confidence interval	Mean	95% confidence interval
Bimekizumab	1.54	(1.66-1.39)	€29 441.31	(€31 895.57 - €26 601.77)
Brodalumab	2.75	(3.08-2.48)	€36 046.93	(€40 325.56 - €32 500.30)
Guselkumab	2.13	(2.41-1.89)	€35 058.17	(€39 636.13 - €31 112.63)
Ixekizumab	1.78	(1.94-1.63)	€25 817.21	(€28 031.12 - €23 603.71)
Risankizumab	1.73	(1.85-1.58)	€30 642.74	(€32 857.47 - €28 027.02)
Secukinumab	2.30	(2.43-2.17)	€33 975.84	(€36 044.01 - €32 069.49)
Tildrakizumab	3.13	(3.76-2.64)	€50 696.84	(€60 901.05 - €42 790.11)

Therefore, if the optimal goal (PASI 100) is applied in the long term, bimekizumab, risankizumab, and ixekizumab achieve response rates higher than other treatments with NNTs of 1.54 (1.66; 1.39), 1.73 (1.85; 1.58), and 1.78 (1.91; 1.63), respectively (Table 3). In terms of efficiency, ixekizumab followed by bimekizumab and risankizumab are the most efficient alternatives of all. However, these results change when confidentially funded LSPs are used, being bimekizumab the most efficient treatment, followed by ixekizumab and risankizumab.

Results suggest that anti-IL-17 and anti-IL-23p19 drugs to treat adult patients with moderate-to-severe plaque psoriasis with higher efficacy (bimekizumab, risankizumab, and ixekizumab) can also have a lower NNT and higher efficiency, being bimekizumab the most efficient treatment when funded LSPs are applied. However, these results are only indicative and do not represent statistically significant differences due to the overlapping confidence intervals reported among some of the treatments.

Our study comes with some limitations too. Firstly, no long-term meta-analysis has been published to this date including all authorized anti-IL-17 and anti-IL-23p19 drugs, nor head-to-head studies among different treatments. Nevertheless, we consider our results to be robust given the homogeneity, comparability, and consistency of the patients' baseline characteristics across the included RCTs. Secondly, we did not use hospital or health service purchase prices, as these are not public.

In conclusion, we would like to mention how these measures can help health care workers and payers alike choose the drugs that should be administered in terms of both efficacy and efficiency for the entire National Health System.

Funding

Conflicts of interest

Acknowledgments

References

1. Laupacis A, Sackett DL, Roberts RS. An assessment of clinically useful measures of the consequences of treatment. N Engl J Med. 1988;318:1728–33.
2. Moher D, Hopewell S, Schulz KF, Montori V, Gotzsche PC, Devereaux PJ, et al. CONSORT 2010 Explanation and Elaboration: Updated guidelines for reporting parallel group randomised trials. BMJ. 2010;340, c869-c869.
3. Carrascosa JM, Puig L, Belinchón Romero I, Salgado-Boquete L, del Alcázar E, Andrés Lencina JJ, et al. Actualización práctica de las recomendaciones del Grupo de Psoriasis de la Academia Española de Dermatología y Venereología (GPS) para el tratamiento de la psoriasis con terapia biológica Parte 1. «Conceptos y manejo general de la psoriasis con terapia biológica». Actas Dermo-Sifiliográficas. 2022;113:261–77. S000173102100380X.
4. REvalMed SNS. Comisión Permanente de Farmacia del Consejo Interterritorial del SNS. Procedimiento normalizado de trabajo de evaluación clínica, evaluación económica y posicionamiento terapéutico para la redacción de Informes de Posicionamiento Terapéutico de medicamentos en el Sistema Nacional de Salud [Internet]. 2020 [consultado 18 Feb 2022]. Disponible en: https://www.sanidad.gob.es/profesionales/farmacia/IPT/docs/20200708.PNT_elaboracion_IPT_CPF8Julio.pdf
5. Ministerio de Sanidad. Listado de Medicamentos afectados por las deducciones del RD 8/2010 [consultado 30 Ene 2022]. Disponible en: http://www.mscbs.gob.es/en/profesionales/farmacia/notasInfor.htm
6. Consejo General de Colegios Farmacéuticos. BOT Plus 2.0. Base de Datos de Medicamentos [Internet] 2022 [consultado 17 Mar 2022]. Disponible en: https://botplusweb.portalfarma.com/
7. CIMA: Centro de información de medicamentos [Internet]. 2021 [consultado 17 Mar 2022]. Disponible en: https://cima.aemps.es/cima/publico/home.html

A. González-Domínguez[a,*], N. García-Agua[b], E. Dauden[c], P. Ventayol-Bosch[d]

[a] Weber, Madrid, Spain
[b] Universidad de Málaga, Málaga, Spain
[c] Servicio de Dermatología, Instituto de Investigación Sanitaria de La Princesa (IIS-IP), Hospital Universitario La Princesa, Madrid, Spain
[d] Servicio de Farmacia Hospitalaria, Hospital Universitario Son Espases, Palma de Mallorca, Spain

[*] Corresponding author.
E-mail address: almudena.gonzalez@weber.org.es (A. González-Domínguez).