Cost analysis in the management of moderate-to-severe psoriasis: comparison between conventional and biological systemic therapies

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Dear Editor,

Psoriasis is a chronic inflammatory skin disease with an estimated worldwide prevalence of 0.5% to 11.4% in adults and up to 1.4% in children.[1]

It is a disease characterized by erythematous, infiltrated, itchy and often painful skin lesions. Recent advances in the scientific community have enabled a greater understanding of the predisposing genetic factors, pathophysiology, comorbidities and treatment of psoriasis. Currently available therapies for moderate-severe psoriasis [Psoriasis Area Severity Index (PASI) greater than 10] include disease-modifying antirheumatic drugs (DMARDs)/conventional systemic drugs [cyclosporine, methotrexate (mtx) and acitretin] and systemic biological drugs, such as tumor necrosis factor (TNF)-α inhibitors and interleukin (IL) inhibitors. According to the Official Bulletin of the Apulia Region - no. 149 of 20-11-2018 about the rationalization of pharmaceutical expenditure, interventions aimed at increasing the prescriptive appropriateness of high-cost systemic immunosuppressive drugs for authorized uses in moderate-to-severe plaque psoriasis were outlined, on the basis of the update guidelines in literature. DMARDS/conventional systemic drugs (cyclosporine, mtx, acitretin) were chosen as first line of treatment, systemic biological TNF-α inhibitors drugs as a second line of treatment, and systemic biological IL inhibitors drugs as a third line.

We performed a cost estimation according to the regional cost list,[2] and we compared the average annual expenditure per patient on conventional DMARDs treatment *vs*. therapy with biosimilar TNF-α inhibitor, considering the costs of outpatient controls, pretreatment and follow-up haematochemical/instrumental examinations, and lost working days compared to the different therapies. In the group of conventional DMARDs, we only considered cyclosporine and mtx. Acitretin, due to its limited therapeutic indications, was not relevant to our study.

We also divided the first 40 consecutive naive patients admitted between January 2021 and January 2022 into 2 groups similar for age (21-73) and gender (M:F). The first group consisted of 20 patients treated with conventional systemic therapy (12 on cyclosporine therapy and 8 on mtx therapy); the second group of 20 patients was treated with biosimilar TNF-α inhibitor, of which 8 were previously treated with conventional DMARDs and 12 naive due to contraindications/intolerance to conventional systemic therapies. Within each group, we analyzed the percentage of 'responders' (patients achieving PASI 75 and PASI 90) and 'non-responders' (patients achieving PASI <75) after one year of treatment. We calculated the 'cost per responder', *i.e.*, the measure of the effectiveness of healthcare technology, by dividing the total expenditure of each drug (cyclosporine, mtx, TNF-α inhibitor) by the percentage number of 'responders' patients.

We also analyzed the number needed to treat (NNT), which is an absolute effect measure representing the number of patients who need to be treated to obtain a therapeutic benefit (responders).

The NNT corresponds to the reciprocal of the absolute risk reduction (ARR), where the ARR coincides with the difference in the incidence of an event between the experimental group (experimental event rate, EER – in our analysis corresponding to the population on treatment with anti-TNF-α biosimilar) and the control group (experimental event rate, clinical evaluation report – in our case represented by the population of patients on DMARDs therapy), as shown in Table 1.

In general, the NNT represents the number of patients who need to be treated with drug A (in our analysis corresponding to anti-TNF-α biosimilar) versus drug B (in our analysis corresponding to DMARDs) in order to achieve a therapeutic benefit (in our

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Table 1. Analysis of the number needed to treat between tumor necrosis factor-α biosimilar inhibitor and disease-modifying antirheumatic drugs.

PASI 75	$NNT = \frac{1}{ARR} = \frac{1}{EER - CER} = \frac{1}{PASI\ 75A - PASI\ 75B}$ $NNT = \frac{1}{PASI\ 75A - PASI\ 75B} = \frac{1}{0.4 - 0.25} = \frac{1}{0.15} = 6.6$
PASI 90	$NNT = \frac{1}{ARR} = \frac{1}{EER - CER} = \frac{1}{PASI\ 90A - PASI\ 90B}$ $NNT = \frac{1}{PASI\ 90A - PASI\ 75B} = \frac{1}{0.45 - 0.15} = \frac{1}{0.3} = 3.3$

PASI, Psoriasis Area Severity Index; NNT, number needed to treat; ARR, absolute risk reduction; CER, experimental event rate; EER, control event rate; A, TNF-α biosimilar inhibitor, B, DMARDs.

Table 2. *Per capita* annual treatment cost per drug.

Drug	Per capita annual treatment cost
Cyclosporine	€ 3,515.35
Metotrexate	€ 1,048.87
TNF-α biosimilar inhibitor	€ 3,030.11

TNF-α, tumor necrosis factor-α.

Table 3. Percentage of responders and non-responders per drug.

Drug (N patients)	PASI 90 (%)	PASI 75 (%)	Non responders (%)
Cyclosporine (12)	8	32	60
Mtx (8)	25	12.5	62.5
TNF-α biosimilar inhibitor (20)	45	40	15
DMARDs (20)	15	25	60

PASI, Psoriasis Area Severity Index; Mtx, Metotrexate; DMARDs, disease-modifying antirheumatic drugs; TNF-α, tumor necrosis factor-α.

analysis: attainment of PASI 75 and PASI 90). It is worth mentioning that the lower the NNT is, the greater the efficacy of the intervention is, compared to the selected comparators.[3]

According to our cost estimate, the annual *per capita* expenditure for treatment with cyclosporin was € 3,515.35; the one for treatment with mtx was € 1,048.87. Annual per capita expenditure for treatment with systemic biological TNF-α biosimilar inhibitor drug was € 3,030.11 (Table 2).

We observed 7 "non-responders" (60%) among the 12 patients treated with cyclosporine, 5 "non-responders" (62.5%) among the 8 patients treated with mtx and 3 "non-responders" (15%) among the 20 patients treated with anti-TNF-α biosimilar. Considering the total of 20 patients treated with DMARDs, the number of 'non-responders' becomes 12 (Table 3). The analysis of "cost per responder" showed a value of € 8,573 for cyclosporine, € 2,834 for mtx and € 3,564 for TNF-α biosimilar inhibitor.

The NNT between TNF-α biosimilar inhibitor and DMARDs showed a value of 6.6 for "responder-PASI 75", while reported a value of 3.3 for "responder-PASI 90" (Table 1).

We conclude that despite conventional DMARDs are among the first-line therapies for moderate-severe psoriasis, mainly because of their economic implications, our cost estimation shows that they have a greater impact on healthcare expenditure than TNF-α biosimilar inhibitors, which are more manageable, more effective and even more cost-effective than their predecessors. The major limitations of this study are the lack of randomization and the small number of patients included. Prospective studies on larger series will be needed in order to validate the results shown in this analysis.

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