Intra-class switch among interleukin-17 inhibitors for the treatment of plaque psoriasis: a single-center experience

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Ethics approval and consent to participate: institutional review board approval was exempted as the study protocol did not deviate from standard clinical practice. The patient received biologics as in good clinical practice, in accordance with European guidelines. All patients had provided written consent for retrospective study of data collected during routine clinical practice (demographics, clinical scores). The study was performed in conformity with the Helsinki Declaration of 1964 and its later amendments. Data collection and handling complied with applicable laws, regulations, and guidance regarding patient protection, including patient privacy.

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Abstract

Psoriasis is a chronic immune-mediated disease primarily affecting the skin. The most common subtype is plaque psoriasis, which can affect any body area, with a predilection for the knees, elbows, scalp, lumbosacral region, and genitalia. The European guidelines adopted in Italy recommend systemic therapies for moderate-to-severe psoriasis, defined by a Psoriasis Area and Severity Index (PASI) ≥10, Dermatology Life Quality Index (DLQI) ≥10, and/or Body Surface Area (BSA) ≥10. Over the past two decades, the development of biological agents has revolutionized psoriasis management, targeting specific cytokines, including tumor necrosis factor (TNF)-α, interleukin (IL)-23, and IL-17. Among these, ixekizumab, secukinumab, brodalumab, and bimekizumab are approved for the treatment of moderate-to-severe plaque psoriasis. However, some patients require switching therapy because of primary/secondary ineffectiveness or side effects.

We retrospectively analyzed 20 patients who had switched from one anti-IL-17 drug to another, assessing both safety and effectiveness. At baseline, the median PASI score was 10 (interquartile range [IQR] 4.5). After 16 weeks, it decreased to 2 (IQR 5.5), and after one year, it decreased further to 1 (IQR 2). Eight (40%) and six patients (30%) achieved PASI 90 and PASI 100 at 16 weeks, respectively. After one year, sustained effectiveness was observed, with PASI 90 (57.1%), PASI 100 (35.7%), and PASI≤2 (78.6%). No serious adverse events (AEs) or discontinuations due to AEs were observed during the study period.

Our study confirms the safety and effectiveness of intra-class switching among IL-17 antagonists within the same class and highlights that switching between different classes of IL-17 inhibitors can be a valid option when patients fail to respond or lose effectiveness with a particular inhibitor. However, a deeper understanding requires further large-scale and long-term studies.

Introduction

Psoriasis is a chronic immune-mediated disease mainly affecting the skin, besides being frequently associated with systemic manifestations. The prevalence in adults is approximately 2-3%. Among the different subtypes, plaque psoriasis is the most common. Theoretically, any area of the body can be affected by psoriasis. Nevertheless, the most frequently involved sites include knees, elbows, scalp, lumbosacral region, and genitalia.[1] According to the Italian adaptation of European Guidelines, systemic therapies are commonly required in case of moderate-to-severe psoriasis, defined by a Psoriasis Area and Severity Index (PASI) ≥10, and/or a Dermatology Life Quality Index (DLQI) ≥10, and/or a Body Surface Area (BSA) ≥10.[2] In the last two decades, the development of several biological agents has revolutionized psoriasis management. When it comes to psoriasis, the targets of this new kind of drug are represented by specific cytokines, such as tumor necrosis factor (TNF)-α, interleukin (IL)-

23, and IL-17.[3] In particular, IL-17 is targeted by different biological agents. Ixekizumab, secukinumab, brodalumab, and bimekizumab are currently approved for the treatment of moderate-to-severe plaque psoriasis after being evaluated in multiple phase-3 clinical trials and real-world experiences.[4-7] Nonetheless, some patients require switching therapy to another drug of the same class due to primary or secondary ineffectiveness or side effects. To date, not much is known about the outcomes in this subgroup of bio-experienced patients.

Materials and Methods

To deepen this topic, we performed a retrospective analysis on 20 patients who had been switched from one anti-IL-17 drug to another, assessing both the safety and the effectiveness of these treatments (Figure 1). Screening for hepatitis B, hepatitis C, tuberculosis, and HIV was performed before patients started their anti-IL-17 treatment. The treatment's effectiveness was evaluated in terms of a 90% or 100% reduction in PASI (PASI 90 or PASI 100, respectively) compared to baseline at weeks 16 and 52. Furthermore, we analyzed the percentages of patients who achieved a PASI≤2 at the same time points.

Patients' demographics and characteristics, including age, gender, Body Mass Index (BMI), cardiovascular comorbidities, concomitant psoriatic arthritis (PsA), and previous exposure to other biological therapies, were collected from electronic medical records.

Institutional review board approval was exempted as the study protocol did not deviate from standard clinical practice. Patients received biologics as in good clinical practice, in accordance with European guidelines, and provided written consent for retrospective study of data collected during routine clinical practice (demographics, clinical scores). The study was performed in conformity with the Helsinki Declaration of 1964 and its later amendments. Data collection and handling complied with applicable laws, regulations, and guidance regarding patient protection, including patient privacy.

Stata/SE 17.0 software was used to perform the statistical analysis. Besides, figures and tables were generated through Microsoft Excel.

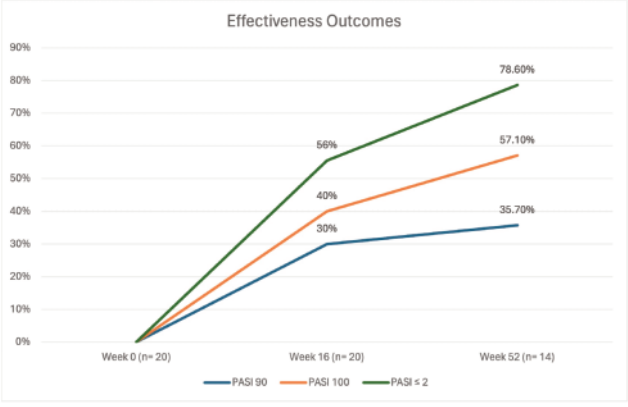

Figure 1. Effectiveness outcomes of patients throughout the study period. PASI, Psoriasis Area and Severity Index.

Results

We enrolled a total of 20 patients with moderate-to-severe plaque psoriasis and a median age of 49.5 years (interquartile range [IQR] 28). Fourteen of them (70%) were males, and the most frequent comorbidity was arterial hypertension (6 patients). Other comorbidities included hypercholesterolemia (3 patients), type II diabetes (1 patient), and obesity (1 patient). Five of our patients had a concomitant diagnosis of psoriatic arthritis. The median BMI was 25.83 kg/m^2 (IQR 4.70), and 1 patient (5%) was obese (BMI≥30 kg/m^2). Before being switched to the current IL-17 inhibitor, 7 patients had failed at least two biologics (comprising an IL-17 antagonist). A loss of effectiveness after more than 6 months was seen in 13 patients (secondary ineffectiveness), whereas the other 7 patients never experienced an improvement with the drug preceding the switch (primary ineffectiveness). Fourteen patients completed at least a year of follow-up, while 2 were lost during follow-up and 4 more are currently still undergoing treatment without having reached the established time limit. Two patients required a switch to bimekizumab (1 from ixekizumab and 1 from brodalumab). Nine patients received brodalumab (6 after failing secukinumab and 3 after ixekizumab), while 9 patients were switched to ixekizumab (all from secukinumab) (Table 1). At baseline, the median PASI (mPASI) in our patients was 10 (IQR 4.5). After 16 weeks, we observed a decrease in mPASI to 2 (IQR 5.5), while the mPASI after one year of treatment was 1 (IQR 2). Eight (40%) and six patients (30%) achieved PASI 90 and PASI 100 at week 16, respectively. At the same time point, 11 patients (55.5%) reached an absolute PASI≤2. After one year, sustained effectiveness was observed in terms of PASI 90 (57.1%), PASI 100 (35.7%), and PASI≤2 (78.6%). Throughout the study period, no adverse events (AEs) leading to discontinuation or serious AEs were observed.

Table 1. Characteristics of our cohort at baseline.

Characteristic	Value
Number of patients	20
Male	14 (70%)
Median (IQR) age, years	49.5 (28)
Median (IQR) BMI	25.83 (4.70)
Patients with obesity	1 (5%)
Median (IQR) disease duration, years	11.1 (18)
Psoriatic arthritis	5 (25%)
Cardiovascular comorbidities	11 (55%)
Multi-failure patients	7
Median (IQR) PASI at baseline	10 (4.5)
Previous anti-IL-17 drug	
Secukinumab	15
Ixekizumab	4
Brodalumab	1
Ongoing anti-IL-17 drug	
Brodalumab	9
Ixekizumab	9
Bimekizumab	2

BMI, Body Mass Index; IQR, interquartile range; PASI, Psoriasis Area and Severity Index; Cardiovascular comorbidities include arterial hypertension, type II diabetes, obesity and hypercholesterolemia.

Discussion and Conclusions

Our study confirms the safety and effectiveness of intra-class switch among IL-17 antagonists, focusing on a cohort that included 7 multi-failure patients (31.81%). Coherently with other real-life studies,[8] our experience shows that an inter-class switch can be a promising and valid option when patients fail to respond or experience a loss of effectiveness to an IL-17 inhibitor. Through our results, we corroborate previous literature[9,10] stating that an inadequate response or secondary inefficacy to a drug does not necessarily imply failure to another molecule of the same class, as also seen with IL-23 antagonists.[11] However, due to its retrospective nature and the exiguous sample size, our experience is limited. Longer and larger studies, possibly with a longitudinal design, are necessary to obtain a deeper comprehension of this topic.

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