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

Gioele Ghezzi,[1,2] Luciano Ibba,[1,2] Luigi Gargiulo,[1,2] Alessandra Narcisi,[1] Antonio Costanzo,[1,2] Mario Valenti[1,2]

[1]Dermatology Unit, IRCCS Humanitas Research Hospital, Rozzano (MI); [2]Department of Biomedical Sciences, Humanitas University, Pieve Emanuele (MI), Italy

Corresponding author: Mario Valenti, MD**,** Department of Biomedical Sciences, Humanitas University, Pieve Emanuele (MI), Italy

Email: mario.valenti@hunimed.eu

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Authors' contributions: GG, LI, collected the clinical data, wrote the draft of the manuscript and reviewed the manuscript; LG, AC, AN, collected the clinical data, and reviewed the manuscript; MV, collected the clinical data and critically reviewed the manuscript.

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. The patient 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.

Conflict of interest: LI, LG have been consultants for Almirall; AN has served on advisory boards, received honoraria for lectures and research grants from Almirall, Abbvie, Leo Pharma, Celgene, Eli Lilly, Janssen, Novartis, Sanofi-Genzyme, Amgen and Boehringer Ingelheim; AC has served as an advisory board member, consultant and has received fees and speaker's honoraria or has participated in clinical trials for Abbvie, Almirall, Biogen, LEO Pharma, Lilly, Janssen, Novartis, Pfizer, Sanofi Genzyme, and UCB-Pharma; MV has been a consultant and/or speaker for Sanofi, Leo Pharma, Eli Lilly, Novartis, Janssen, AbbVie and Boehringer Ingelheim, UCB Pharma; GG has nothing to disclose.

Availability of data and materials: The data used to support the findings of this study are available from the corresponding author upon request.

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 such as TNF-α, 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. 70% of patients was represented by males, with a median age of 49.5 years. The most frequent comorbidities were arterial hypertension and hypercholesterolemia. Effectiveness was evaluated in terms of a 90% (PASI90) and 100% (PASI100) reduction in PASI compared to baseline at 16 and 52 weeks. Before switching to the current IL-17 inhibitor, seven patients had failed at least two biologics. Thirteen patients experienced a loss of effectiveness after more than 6 months (secondary ineffectiveness), whereas the other seven never showed improvement with the previous drug (primary ineffectiveness). Fourteen patients completed at least one year of follow-up. Two patients were lost during the follow-up, while four more are currently still under treatment without having completed the established temporal cut-off. Two patients switched to bimekizumab, nine to brodalumab, and nine to ixekizumab. At baseline, the median PASI was 10 (IQR 4.5). After 16 weeks, the median PASI decreased to 2 (IQR 5.5), and after one year, it was 1 (IQR 2). Eight patients (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 or discontinuations due to adverse events were observed during the study period. Our study confirms the safety and effectiveness of intra-class switching among IL-17 antagonists, highlighting that an inter-class switch can be a valid option when patients fail to respond or lose effectiveness with an IL-17 inhibitor. However, further larger and longer studies are needed for a deeper understanding.

Introduction

Psoriasis is a chronic immune-mediated disease mainly affecting the skin, besides being frequently associated with systemic manifestations.[1] The prevalence in adults is approximately 2-3% [1]. Among the different subtypes, plaque psoriasis is the most common.[1] 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 evalueated 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). Before starting their anti-IL-17 treatment, screening for hepatitis B, hepatitis C, tuberculosis and HIV was performed. The effectiveness was evaluated in terms of a 90% and 100% reduction in PASI (PASI 90 e 100, respectively) compared to baseline at weeks 16 and 52. Furthermore, we analysed 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. The patient received biologics as in good clinical practice, in accordance with European guidelines. The patient 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.

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

Results

We enrolled a total of 20 patients with moderate-to-severe plaque psoriasis with a median age of 49.5 years, with an interquartile range (IQR) of 28. Fourteen of them (70%) were males. The most frequent comorbidity was arterial hypertension (six patients). Other comorbidities included hypercholesterolemia (three patients), type II diabetes (one patient) and obesity (one patient). Five of our patients had a concomitant diagnosis of psoriatic arthritis. The median body mass index (BMI) was 25.83 kg/m^2 (IQR 4.70), and one patient (5%) was obese (BMI $\geq$ 30 kg/m^2). Before being switched to the current IL-17 inhibitor, seven 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. Two were lost during the follow-up, while four more are currently still under treatment without having completed the established temporal cut-off. Two patients required a switch to

bimekizumab (one from ixekizumab and one from brodalumab), nine received brodalumab (six after failing secukinumab, three after ixekizumab), and nine were switched to ixekizumab, all of whom 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 patients (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.

Discussion

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%). Our experience shows, coherently with other real-life studies,[8] 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 one drug does not necessarily imply failure to another molecule of the same class, as also seen with IL-23 antagonists.[11] Because of its retrospective nature and the exiguous sample size, our experience is somehow limited. Further longer and larger studies, possibly with a longitudinal design, are necessary to obtain a deeper comprehension of this topic.

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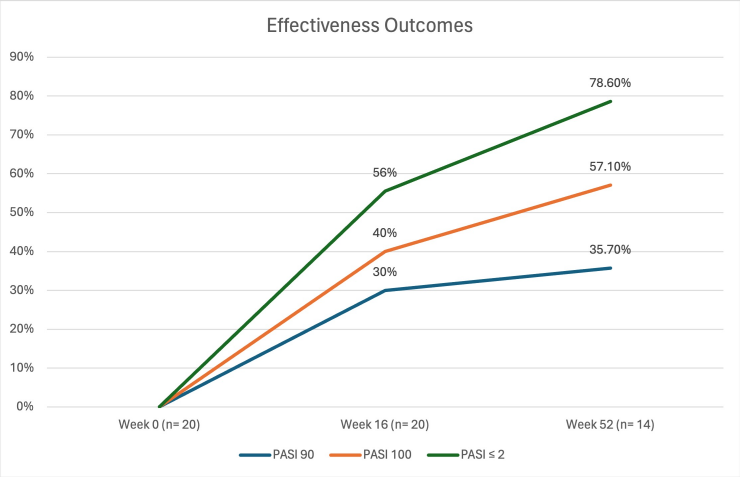

Figure 1: Effectiveness outcomes of our patients throughout the study period.

PASI: Psoriasis Area and Severity Index

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

Table 1: Characteristics of our cohort at baseline.

BMI = Body Mass Index; IQR = InterQuartile Range; PASI = Psoriasis Area and Severity Index. CV comorbidities include arterial hypertension, type II diabetes, obesity and hypercholesterolemia.