Received: 17 January 2024 | Accepted: 19 March 2024

DOI: 10.1111/jdv.20003

JEADV JOURNAL OF THE EUROPEAN ACADEMY OF DERMATOLOGY & VENEREOLOGY

LETTER TO THE EDITOR

Long-term effectiveness and tolerability of apremilast in patients with moderate-to-severe plaque psoriasis: A 5-year multicentre retrospective study—IL PSO (Italian landscape psoriasis)

Dear Editor,

Apremilast is an oral inhibitor of phosphodiesterase (PDE)-4 that has been approved for the treatment of patients with moderate-to-severe plaque psoriasis who have contraindications or inadequate response to conventional systemic treatments.[1,2] It is also indicated for the management of adults with active psoriatic arthritis (PsA) who have failed or are intolerant to other disease-modifying antirheumatic drugs (DMARDs).[1,2] In Italy, apremilast is reimbursed for patients with moderate-to-severe plaque psoriasis in case of inadequate response/intolerance to systemic treatments and those with contraindications to biological drugs.[3] Despite the wide use of apremilast for the treatment of plaque psoriasis, long-term real-world experiences are still limited.[4,5]

We conducted a retrospective study involving 18 Italian Dermatology Units to evaluate the effectiveness and safety of apremilast throughout 5 years of treatment. Apremilast was prescribed according to the Italian Guidelines for plaque psoriasis and its summary of product characteristics.[1,3]

We enrolled 335 patients treated with apremilast for at least 1 year. Demographic characteristics were retrieved from electronic medical records (Table 1).

Notably, 28 (8.36%) of our patients had a personal history of cancer, and 82 (24.48%) were naïve to biological treatments. The mean Psoriasis Area and Severity Index (PASI) at baseline was 12.39, with a standard deviation (SD) of 5.87. A concomitant diagnosis of PsA was made in 136 patients (40.6%).

After 52 weeks, 60.30%, 18.97% and 13.50% of our patients achieved a reduction of 75%, 90% and 100% of PASI compared with baseline (PASI75, PASI90 and PASI100), respectively.

After 4 years, the same endpoints were reached by 79.62%, 52.23% and 28.66% of our population, which included 157 patients.

Finally, at Week 260, among 76 patients, PASI75, PASI90 and PASI100 were achieved by 72.37%, 53.95% and 36.84% of our patients, respectively.

The proportion of those with an absolute PASI ≤2 increased throughout the study, from 49.85% at Week 52 to 73.25% at Week 208 and to 73.25% after 5 years of treatment.

The effectiveness of apremilast throughout the study period is shown in Figure 1.

During the study, 40 patients (11.94%) discontinued apremilast because of loss of effectiveness after 1 year of treatment. No significant safety findings emerged from our study. The most common adverse event (AE) was diarrhoea (19.10%), followed by nausea (14.33%) and headache (11.64%). The occurrence of an AE led to drug discontinuation in 16 patients (4.78%).

This multicentre real-world study supports the effectiveness of apremilast in moderate-to-severe plaque psoriasis with the longest follow-up to date, including patients treated for 5 years.

We found comparable responses with the findings of *Ioannides* et al., who reported PASI 75 in 75.2% and PASI 90 in 39.2% after 1 year of follow-up.[4] Our data are also consistent with those of *Graier* et al., who described a PASI 75 response in 56.4%, 67.3% and 88.9% of patients after 1, 2 and 3 years of treatment, respectively. However, this study included a very small sample size at 3 years of follow-up.[6]

Our study included a significant proportion of patients with cardiometabolic comorbidities, concomitant PsA and a personal history of neoplasm. Despite increasing data available regarding the safety of biological drugs in oncological patients,[7] apremilast is currently recognized as the safest

TABLE 1 Demographic characteristics of our population at baseline.

Patients	**335**
	N **(%)**
Male	188 (56.12)
PsA	136 (40.60)
At least one cardiometabolic comorbidity	83 (24.78%)
Previous history of neoplasm	28 (8.36)
At least one difficult-to-treat area	45 (13.43)
Bio-Naïve	82 (24.48)
	Mean (SD)
Age, years	61.01 (13.69)
BMI, Kg/m^2	25.71 (4.45)
PASI	12.39 (5.87)

Abbreviations: BMI, body mass index; PASI, Psoriasis Area and Severity Index; PsA, psoriatic arthritis; SD, standard deviation.

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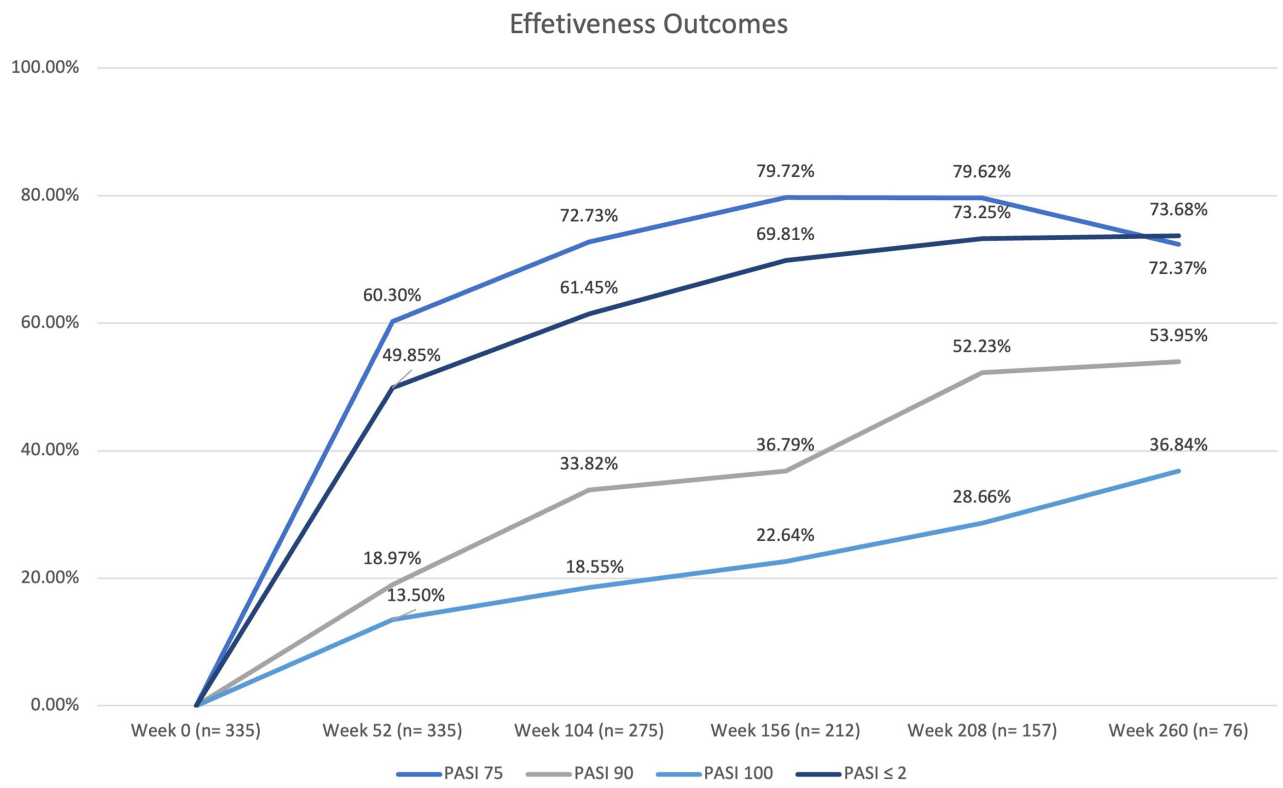

FIGURE 1 Effectiveness of apremilast throughout 5 years of treatment. The effectiveness of apremilast was analysed in terms of PASI 75, PASI 90, PASI 100 and PASI ≤2. The outcomes were reported as observed. PASI, Psoriasis Area and Severity Index.

option among innovative treatments of psoriasis in this subgroup of patients.[8]

The safety profile of apremilast was consistent with both clinical trials and real-world experiences. Most of the AEs were mild-to-moderate and predominantly resolved after the first month of treatment.[4–6,8]

In conclusion, apremilast showed effectiveness and tolerability throughout the 5-year follow-up period in our study. Given its oral administration, favourable risk–benefit profile and good effectiveness, apremilast could represent a useful treatment option for those with contraindications to biological treatments.

FUNDING INFORMATION

None.

CONFLICT OF INTEREST STATEMENT

L. Gargiulo has been a consultant for Almirall. L. Ibba has been a consultant for Almirall. P. Malagoli has been a speaker for AbbVie, Lilly, Novartis, Janssen-Cilag, Celgene, Leo Pharma and Almirall. A. Balato has received honoraria for participation in advisory boards, meetings, or as a speaker for AbbVie, Celgene, Janssen-Cilag, Eli Lilly, Novartis Pharma, Pfizer, Sanofi Genzyme and UCB Pharma. F. Bardazzi has been a consultant advisor and clinical study investigator for Eli Lilly, Abbvie, Novartis, Leo Pharma, Sandoz, Bristol Myers, Abiogen Pharma, Celgene and Janssen. M. Burlando has acted as a speaker and consultant for AbbVie, Janssen, Amgen, Novartis, Eli Lilly and UCB Pharma. C. G. Carrera has served as a board participant or a speaker for Abbvie, Lilly, Janssen, Novartis, Celgene, Almirall and Leo Pharma. P. Dapavo has been a speaker for Novartis, Abbvie, Sanofi, UCB, Janssen, Lilly and Leo Pharma. F. M. Gaiani acted as a speaker or consultant for Novartis, Abbvie, Eli Lilly, Celgene, Leo Pharma and Almirall. G. Girolomoni served as consultant and/or a speaker for AbbVie, Almirall, Amgen, Biogen, Boehringer Ingelheim, Bristol Meyers Squibb, Eli Lilly, Leo Pharma, Novartis, Pfizer, Samsung, Sanofi and UCB. C. Guarneri has been a scientific consultant/speaker/clinical study investigator for Abbvie, Celgene, Janssen, Eli Lilly, Novartis, Pfizer, Sanofi, Almirall and LEO Pharma. C. Lasagni declares a conflict of interest with Abbvie, Novartis, Lilly and Almirall. F. Loconsole served on advisory boards and/or received honoraria for lectures from Abbvie, Janssen-Cilag, Novartis, Lilly and Sanofi. A. V. Marzano reports consultancy/advisory boards disease-relevant honoraria from AbbVie, Boehringer Ingelheim, Novartis, Pfizer, Sanofi and UCB. M. Megna acted as a speaker or consultant for Abbvie, Eli Lilly, Janssen, Leo Pharma, UCB and Novartis. A. Costanzo has served as an advisory board member and 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. A. Narcisi 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. F. Amoruso, V. Dini, M. Maurelli and M. Travaglini have nothing to declare.

DATA AVAILABILITY STATEMENT

Additional data supporting the findings of this manuscript are available on reasonable request to the corresponding author.

ETHICAL APPROVAL

Institutional review board approval was exempted, as the study procedures did not deviate from standard clinical practice. All included patients had provided written informed consent for the retrospective analysis of their clinical data. The study was conducted in accordance with the Helsinki Declaration of 1964 and its later amendments.

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