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Psoriatic patients with a history of cancer: A real-life experience with Apremilast treatment for 104 weeks

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Abstract

Psoriasis is a multifactorial, chronic, auto- inflammatory disease, with a worldwide prevalence of around 2%, subtended by robust genetic predisposition and autoimmune pathogenic traits. The disease, mainly involving the skin and joints, is featured by erythemato-squamous lesions, with a chronic relapsing course and relevant systemic comorbidities. Apremilast is a novel oral agent that has recently been made available to dermatologists for the treatment of moderate-to-severe plaque psoriasis and psoriatic arthritis. Although it is considered as relatively safe molecule with few contraindications, experience with Apremilast in the real-world setting for cancer patients with moderate-to-severe plaque psoriasis is lacking. Hence, we report the real-life experience in patients with psoriasis and a history of cancer who underwent treatment with Apremilast for 104 weeks.

KEYWORDS
Apremilast, oncological disease, psoriasis, psoriatic arthritis, treatment

1 | INTRODUCTION

Psoriasis is a multifactorial, chronic, auto- inflammatory disease, with a worldwide prevalence of around 2%, subtended by robust genetic predisposition and autoimmune pathogenic traits.[1,2]

The disease, mainly involving the skin and joints, is featured by erythemato-squamous lesions, with a chronic relapsing course and relevant systemic comorbidities.[3]

Clinical onset may arise at any age, although basically characterized by two peaks: from 15 to 25 years and from 50 to 60 years of age respectively.[4]

Several recent researches clarified the intricate network of factors and pathways involved in the pathogenesis of psoriasis: immune disorder is the hallmark of psoriasis leading to chronic inflammation, expressed as unregulated proliferation of keratinocytes.[5]

The introduction of biotechnological drugs has significantly improved the management of psoriasis, particularly the moderate/severe forms.

However, some comorbidities, such as infectious or oncological diseases, limit the use of these powerful drugs, that could be further complicated by polypharmacy and possible drug interactions.[6]

Few evidence-based data are available about treatment of moderate to severe psoriasis in patients with a medical history of previous or current malignancies.

As a result, cancer patients affected by moderate-to-severe psoriasis, in particular those with multiple comorbidities, are often undertreated. Moreover, safe and effective treatment in these subjects is an unmet need.

Apremilast is a novel oral agent that has recently been made available to dermatologists for the treatment of moderate-to-severe plaque psoriasis and psoriatic arthritis.[4]

Although it is considered as relatively safe molecule with few contraindications, experience with Apremilast in the real-world setting for cancer patients with moderate-to-severe plaque psoriasis is lacking.

Hence, we report the real-life experience in patients with psoriasis and a history of cancer who underwent treatment with Apremilast for 104 weeks.[6,7]

2 | MATERIALS AND METHODS

The retrospective observational study included only patients of our outpatient services suffering from moderate to severe psoriasis (PsO) and/or psoriatic arthritis (PsA). All subjects enrolled have had personal history of cancer. All of them were treated with Apremilast for at least 2 years (104 weeks). The subjects both sexes were aged over 18.

The study was carried out using PASI (Psoriasis Area Severity Index), the score based on the extent of patches, presence of erythema, infiltration and desquamation; BSA (Body Surface Area), calculated as body surface area involved and PGA (Physician Global Assessment) a 5- or 6-point scoring system used to assess psoriasis disease severity. To assess the impairment of quality of life, DLQI (Dermatology Life Quality Index), a questionnaire based on 10 questions concerning the impact of the disease on the patient's quality of life, was used. Finally DAS28 (Disease Activity Score), that assesses the number of painful and swollen joints and disease activity, was used for the evaluation of psoriatic arthritis. DAS-28 is characterized by its rapid and easy implementation in daily practice that allows both the assessment of the disability of the patient to carry out common daily activities at a given time and the assessment of the change in disease activity over time.[8,9]

The different levels of pain were examined through Visual Analogue Scale (VAS) consisting of a straight line with the endpoints defining extreme limits such as 'no pain at all' and 'pain as bad as it could be'.

The five scores described above were investigated at the start (T0), after 24 weeks (T24), 52 weeks (T52), 78 weeks (T78) and after 104 weeks (T104) of Apremilast therapy. The data collected were recorded on a spreadsheet and statistically examined.

3 | RESULTS

The study population comprised 28 adult patients with moderate to severe psoriasis and/or psoriatic arthritis: 16 males (57%) and 12 females (43%); the average age was 64 years. Diagnosis of psoriatic arthritis have had 18 (64%) of them, while 19 (68%) presented cardiometabolic comorbidities.

The psoriatic disease (either cutaneous or arthropathic psoriasis) was present for approximately 14 years, in studied group.

Cutaneous examination revealed: erythema (100%), fissures (93%), bleeding (28%) and xerosis (89%).

Patients also referred itching (86%), burning (57%), and joint pain (43%).

Joint pain complained 43% of subjects. Stinging and itching were present in 86% and 57% respectively.

The skin sites affected by psoriasis were: elbows (78%), knees (71%), upper limbs (53%), lower limbs (50%), trunk (43%), hands (36%), scalp (21%) and genitals (11%).

All patients presented, also, history of oncological pathology, either previous or current, and in particular: colorectal adenocarcinoma (21%), papillary thyroid carcinoma (14%), multiple G3 squamous cellular carcinoma (11%), prostate carcinoma (11%), cervical adenocarcinoma (11%), cutaneous T-cell lymphoma (11%), melanoma (11%), endometrial carcinoma (7%), lung carcinoma (7%), MGUS (3%), breast carcinoma (7%), renal carcinoma (7%), Hodgkin sarcoma (7%) and Kaposi lymphoma (7%).

Most of them were treated previously with anti-cancer therapy, except 7 patients that were undergoing oncological treatment (Tamoxifen, Buserelin and hormone therapy) at the moment of study. Consequently, Apremilast was a therapy of choice for all cases: 30 mg tablets twice daily. Twenty of them (71%) were on Apremilast monotherapy. Instead, 8 patients (28.5%) were taking Methotrexate once a week concurrently with the daily dose of Apremilast, as comedication.

Our study showed that patients started treatment with Apremilast on average 8 years after the diagnosis of the cancer disease.

There were no evidences of serious side effects related to the intake of Apremilast. Adverse events were present in 13 subjects: 11 subjects had diarrhea (36%) and 2 had asthenia (7%) that did not require discontinuation of Apremilast, as they did not compromise the patients' daily activities.

To monitor the therapeutic efficacy and safety and the quality of life the following scores were recorded: PASI, PGA, BSA, DAS 28, VAS and DLQI.

All scores were evaluated at the start (T0) and after to 2 years of Apremilast therapy: particularly at 24 weeks (T24), at 52 weeks (T52), at 78 weeks (T78) and finally at 104 weeks (T104).

The mean values at the beginning of therapy (T0) were: PASI 11, BSA 7, PGA 3, DLQI 16, DAS28 2 and VAS 8. After 24 weeks the indices have achieved these average values: PASI 4.2, BSA 1.3, PGA 0.9, DLQI 4.4, DAS28 1.6 and VAS 5. At T52 of treatment with Apremilast the scores continued to decline: PASI 2.2, BSA 0.9, PGA 0.7, DLQI 1.1, DAS28 1.5 and VAS 4. The average values decreased furthermore at T78: PASI 2, BSA 0.9, PGA 0.6, DLQI 0.9, DAS28 1.4. and VAS 3. At the end of the study (T104), the recorded values reached the following scores: PASI 1.7, BSA 0.6, PGA 0.5, DLQI 0.5, DAS28 1.1 and VAS 2 (Figures 1–2).

In conclusion, after 104 weeks of Apremilast therapy (T104), PASI, BSA, PGA, DLQI, DAS28 and VAS have recorded a reduction of 84,5%, 91%, 83%, 97%, 45% and 75% respectively.

The most common AE was predominantly mild diarrhea, that occurred in half of cases within the first week of treatment and were resolved within the first month, with the intake of probiotics, without resorting to the administration of drug.

Half of patients who reported gastrointestinal symptoms reduced Apremilast dose to 30 mg daily for only 1 month.

4 | DISCUSSION

Managing psoriatic patients with a diagnosis of malignancy may be challenging.[10]

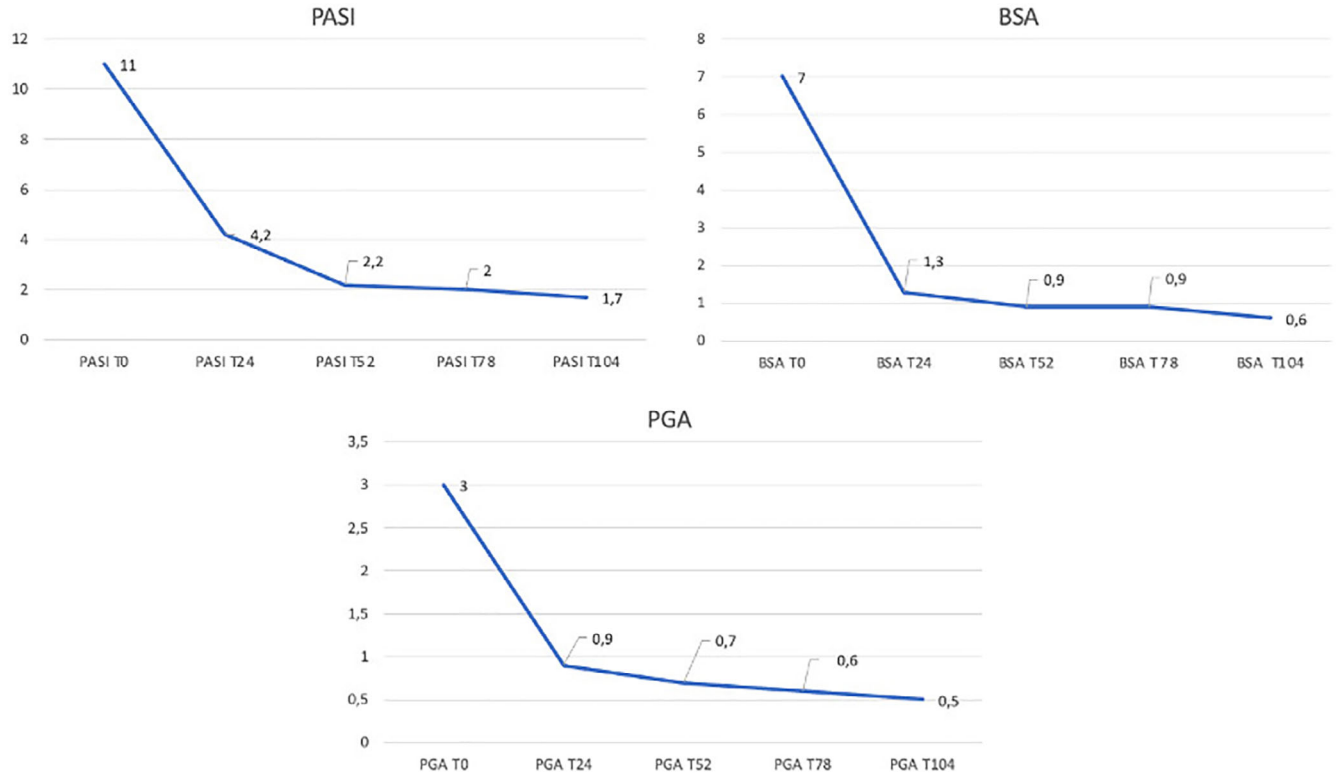

FIGURE 1 The graphs show the trends in PASI, PSA and PGA from the start of therapy (T0) to 2 years of treatment with Apremilast (T104)

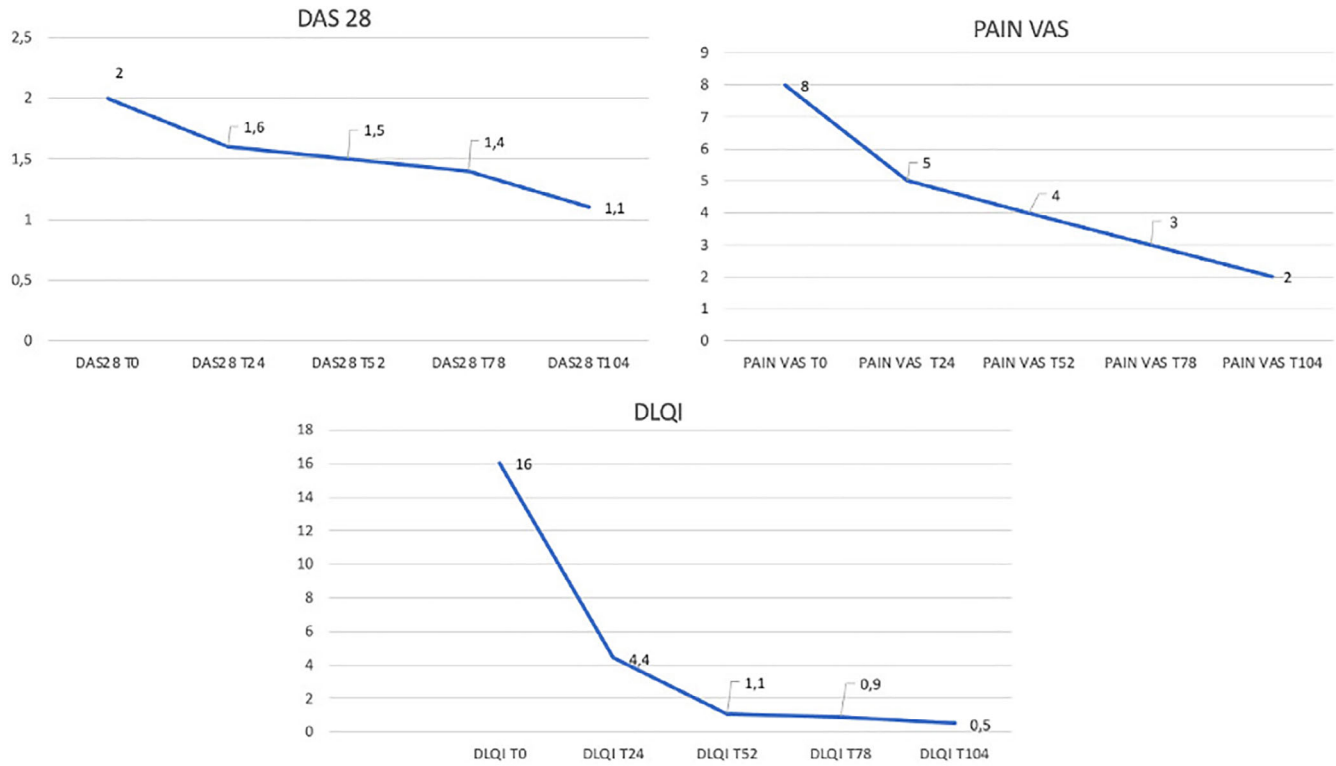

FIGURE 2 The graphs show the trends in DAS 28, PAIN VAS and DLQI from the start of therapy (T0) to 2 years of treatment with Apremilast (T104)

Few evidence-based data are available on the use of traditional systemic or biologic drugs in psoriatic patients with a history of concomitant or previous oncological disease.

Limited data are known about the risk of recurrence or subsequent malignancy in psoriatic patients treated with small molecules, as well.[11,12]

Furthermore, patients with a history of malignancies are frequently ruled out from enrollment in clinical trials and specialist may be inclined not to start immunosuppressive agents in cancer patients.[12]

In approaching the newer biological anti-psoriatic drugs, safety issues are generally heightened by a possible alteration in cancer immune surveillance.

Besides, the risk of progression of a pre-existing malignancy in psoriatic patients treated with biologic agents is still disputed.

Current guidelines indicate consultation with oncologist before starting treatment with biologicals, considering the type and staging of cancer, the risk of recurrence and the burden of psoriasis.[13]

Definitely, most guidelines recommend that history of malignancy within 5 years prior to treatment is a contraindication for treatment with biologic agents.

Apremilast is a systemic therapy indicated for the treatment of moderate to severe psoriasis. It is a phosphodiesterase 4 (PDE4) inhibitor, the so-called small molecule, that interrupts an early point of the inflammatory cascade and plays a central role in the pathogenesis of psoriasis: by blocking degradation of cyclic adenosine monophosphate (cAMP), intracellular levels of cAMP increase and suppressing the excretion of several proinflammatory cytokines, including tumor necrosis factor (TNF)–α and interleukin (IL)–23 and IL-17.[14]

Due to this type of pharmacokinetic mechanism, Apremilast is safe in the management of the vulnerable psoriatic patient.[15]

Additionally, multiple real-world studies have demonstrated the effectiveness and acceptable safety profile of Apremilast in the management of moderate-to-severe plaque psoriasis.[4–7]

Some of above real-life studies, put in evidence the efficacy of oral Apremilast in patients with moderate-to-severe plaque psoriasis and concomitant malignancies.[6]

The studies demonstrated that Apremilast is a valid and effective treatment strategy for moderate to severe psoriasis, as a significant proportion of treated patients achieved a PASI 75 response between week 24 and week 52.

Approximately 98% of patients achieved the European consensus treatment goal of a decrease of ≥5 points in DLQI total score.

Moreover, patients treated with Apremilast showed significantly reduced severity of difficult-to-treat scalp involvement and rapid and significant improvements in pruritus and skin discomfort/pain.

It demonstrated also a rapid onset of action, with clinically meaningful improvements in PASI, pruritus and skin discomfort/pain scores observed as early as week 24.

PASI response was generally maintained over 52 weeks with continued treatment, with.

an acceptable safety profile. Most AEs were mild to moderate and did not lead to discontinuation. Nausea, diarrhea and headache tended to occur more frequently during the first 2 weeks of Apremilast dosing compared with subsequent weeks.

No recurrences or complications related to the preexisting or prior malignancies were detected during the observation period.

All enrolled patients underwent infectious screening (TBC, HIV, HCV, HBV) although not essential for Apremilast treatment.

Malignancy and its treatment may also confer a higher risk of infection, major causes of morbidity and mortality in cancer.[16]

The widespread use of chemotherapeutic and immunosuppressive chemotherapy, highlighting the serious infectious risk represented by granulocytopenia and by high levels of cell-mediated and humoral immunity.[16]

Nevertheless, recurrent infectious events did not occur during observation period, in this study.

5 | CONCLUSIONS

The advent of biological drugs for the treatment of moderate/severe psoriasis has revolutionized the lives of these patients, bringing them into clinical remission and greatly improving their quality of life.

However, some patients with severe infections or malignancies cannot benefit from these therapies, as they are contraindicated.

In addition, a history of previous oncological disease within the last 5 years is also a contraindication for the use of biologics.

On the other hand, Apremilast, which is different from the classic biological drug but has comparable efficacy, appears to be suitable for use in cancer patients and risk-free due to its unique pharmacokinetics. In contrast to the majority of the available systemic antipsoriatic drugs, Apremilast is not contraindicated in case of previous or concomitant malignancy.[15–19]

This real-word study confirmed these concepts: efficacy in patients with moderate to severe cutaneous and/or arthropathic psoriasis, with improvement of subjective symptoms as well as of quality of life.

Furthermore, no side effects on previous or concomitant oncological disease were detected throughout the observation period.

In fact, all patients underwent periodically follow-up by oncologists, according to the protocol. During the 104 week time frame, no one of the examined subjects showed recurrence of their oncological disease.

However, the results of this study confirm the literature data that Apremilast may be useful in this subset of psoriasis patients but regarding its impact on recurrence of malignancy we may have to follow up these patients for a longer period.

In conclusion, Apremilast provides a new therapeutic option for the treatment of cancer patients with moderate-to-severe plaque and/or arthropatic psoriasis and may help address unmet patient needs.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest regarding the publication of this article.

AUTHOR CONTRIBUTIONS

Nicoletta Bernardini, Nevena Skroza, Alessandra Mambrin, Ilaria Proietti, Ersilia Tolino: conceived and designed the study. Anna Marchesiello, Patrizia Maddalena, Federica Marraffa, Giovanni Rossi, Salvatore Volpe: wrote the original draft. Concetta Potenza: supervised the project.

INFORMED CONSENT

The patient has given written informed consent to the publication of his case details.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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