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ORIGINAL RESEARCH

Efficacy and Safety of Apremilast in Oncological Patients with Moderate-to-Severe Plaque Psoriasis: A 5 years Retrospective Observational Study

Caterina Lanna[1], Antonia Rivieccio[1], Martina Vultaggio[1], Ruslana Gaeta Shumak[1], Francesco Maria Bonacci[1], Fabio Artosi[1], Cristiana Borselli[1], Gaetana Costanza[2], Luca Bianchi[1], Elena Campione[1]

[1]Dermatology Unit, Department of Systems Medicine, Università di Roma Tor Vergata, Roma, Italia; [2]Virology Unit, Department of Experimental Medicine, Università di Roma Tor Vergata, Roma, Italia

Correspondence: Caterina Lanna, Dermatologic Unit, Department of Systems Medicine, University of Rome Tor Vergata, Viale Oxford 81, Rome, 00133, Italy, Email caterinalanna.cl@gmail.com

Background: Psoriasis and psoriatic arthritis are chronic autoimmune inflammatory conditions frequently associated with a range of comorbidities, including oncological diseases. Managing these conditions in patients with a history of cancer requires careful consideration of treatment efficacy and safety. Apremilast, an oral phosphodiesterase 4 (PDE4) inhibitor, has shown promise in the treatment of psoriasis and psoriatic arthritis. However, data on its use in oncological patients remain limited.

Methods: This retrospective observational study evaluated the efficacy and safety of Apremilast in 79 patients with a history of cancer who were treated for psoriasis and/or psoriatic arthritis over a period of approximately five years. Clinical outcomes were assessed using the Psoriasis Area Severity Index (PASI), Dermatology Life Quality Index (DLQI), and Visual Analog Scale for pain (PAIN VAS) to monitor disease severity, quality of life, and articular involvement, respectively. Regular oncological assessments were conducted concurrently with Apremilast therapy to ensure patient safety and identify potential interactions.

Results: Over the five-year treatment period, significant improvements were observed in PASI, DLQI, and PAIN VAS scores, indicating effective management of both dermatological and articular symptoms. Patients reported enhanced quality of life and reduced pain levels, reflecting the therapeutic benefits of Apremilast. Oncological evaluations revealed no significant adverse interactions between Apremilast and the patients' cancer history or treatments, underscoring the drug's safety profile in this population.

Conclusion: This study highlights the efficacy and safety of Apremilast as a treatment option for psoriasis and psoriatic arthritis in oncological patients. The findings support its role in improving disease outcomes and quality of life, emphasizing the importance of personalized treatment strategies in managing complex cases involving a history of cancer. Further research is warranted to validate these results in larger patient cohorts.

Keywords: psoriasis, apremilast, cancer, tumors

Introduction

Psoriasis is a chronic, long-lasting, auto-immune T-cell–mediated, inflammatory skin disorder which is estimated to affect about to 2–4% of the population[1] without differences between men and women.[2] It is classically characterized by the presence of reddened plaques coated with silvery-white scaling on extensor surfaces, such as the elbows, knees, trunk, scalp, or lumbosacral area.,[1,3,4] however, it can affect also other sites, called difficult-to-treat area, such as palms and soles, nails and genitalia.[5]

Psoriasis is associated with several comorbidities. Psoriatic arthritis is the most common, affecting close to 30% of psoriatic patients. Other comorbidities include but are not limited to metabolic syndromes, cardiovascular disease,

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psychiatric disorders, inflammatory bowel disease, asthma and non-alcoholic fatty liver disease.[6,7] Other comorbidities, such as infectious and oncological diseases can be frequently present in psoriatic patients and can limit available therapeutic options, including the most recent approved biological therapies (tumor necrosis factor-α inhibitors, interleukin-17 inhibitors, interleukin-12/23 inhibitors, and interleukin-23 inhibitors).[8,9]

Therefore, oncological patients are often under-treated due to the lack of evidence-based data about treatment of moderate-to severe psoriasis in patients with previous or current history of malignancies. The identification of a safe and effective treatment in these subjects is an unmet need.

Apremilast, an oral immunomodulatory phosphodiesterase 4 inhibitor, has shown effectiveness and received approval from the US Food and Drug Administration (FDA) for the treatment of plaque psoriasis and psoriatic arthritis across all levels of disease severity.[10] While considered a relatively safe molecule with few contraindications, thanks to its intracellular mechanism of action, there is a lack of long-term real-life experience on a large scale with Apremilast for oncological patients with moderate-to-severe plaque psoriasis.[11–13]

For this reason, we present our long-term real-life experience of 5 years on 79 psoriatic patients with concomitant history of malignancies treated with apremilast, in order to evaluate its efficacy and safety in this special subpopulation.

Materials and Methods

We conducted a retrospective observational real-life, single-center study on a total of 79 patients referred to our dermatology unit of the University of Tor Vergata from 2017 to 2023. All enrolled patients had a personal history of cancer. All patients underwent treatment with Apremilast for an average period of approximately 5 years.

Inclusion criteria were: 1) adults (>18 years) at the time of informed consent acquisition, 2) presence of cutaneous plaque psoriasis and/or psoriatic arthritis and being treated or eligible to receive Apremilast, naive to biological therapies or bio-experienced. 3) personal history of cancer (current or previous <5 years). The study utilized the following clinical assessment scores: Psoriasis Area Severity Index (PASI), assessing the extent of psoriatic plaques, erythema, infiltration, and desquamation; To evaluate the impact on patients' quality of life, the Dermatology Life Quality Index (DLQI), a 10-question questionnaire with scores ranging from 0 to 30, was used. To evaluate articular involvement, PAIN VAS score was used, assessing trough a visual score (from 0 to 100) the articular pain.

For the evaluation of the concomitant cancer history, we assessed oncological marker, such as CEA, Ca19.9, Ca 15.3, HEF4, Ca125, PSA, LDH, through blood samples.

All the aforementioned scores were evaluated at baseline (T0), and every 6 months until 5 years (T10) of Apremilast therapy.

Moreover, every patient underwent oncological physical and instrumental exam (US, CT) every 6 months.

The collected data were recorded in a spreadsheet and analyzed with descriptive and inferential tests. Differences were analyzed with ANOVA considered statistically significant for $p<0.05$.

Results

We enrolled 79 patients, resulting from the dermatological unit of Tor Vergata hospital for a period of 5 years. 28/79 patients were male and 51/79 were females respectively, with an average age of 59 years (range 30–89) and BMI of 25.5 km/m². All the patients showed up with cutaneous manifestations, but only 21 (26%) displayed concomitant PsA. The mean Pso duration was 25 years (mean value), whereas the average arthritis duration was 20 years. Previous medical history of the analysed population included arterial hypertension (54%), hypercholesterolemia (45.3%), hypertriglyceridemia (13.7%), diabetes mellitus type II (18.9%), and cardiological disease (29.5%). All Patients had a history of oncological pathology previous or current, within 5 years. The types of cancers showed by the patients were: Colorectal adenocarcinoma (10.12%), Papillary thyroid carcinoma (8.9%), breast cancer (25%), Prostate carcinoma (14%), lymphoma (3.8%), Melanoma (12.7%), bladder carcinoma (10%), Kidney carcinoma (1.3%), uterine carcinoma (3.8%), squamous cell carcinoma of head and neck (2.5%), pheochromocytoma (1.3%), lung cancer (6%), ovarian cancer (2.5%), glioblastoma (1.3%). 4 patients showed two types of cancers. (Table 1)

Table 1 Demographical and Clinicopathological Features of Enrolled Patients (Number of Patients=79); Men Age= 59 years Old (Range=30-80 Yrs); Four Patients Showed Two Types of Tumors

		n (%)
Sex	Female	51(65%)
	Male	28(35%)
Type of Tumors	Colorectal adenocarcinoma	8(10.12%)
	Papillary thyroid carcinoma	7(8.9%)
	Breast cancer	20(25%)
	Prostate carcinoma	11 (14%)
	Lymphoma	3 (3.8%)
	Melanoma	10 (12.7%)
	Bladder carcinoma	8 (10%)
	Kidney carcinoma	1 (1.3%)
	Uterine carcinoma	3 (3.8%)
	Squamous cell carcinoma of head and neck	2 (2.5%)
	Pheochromocytoma	1 (1.3%)
	Lung cancer	5 (6%)
	Ovarian cancer	2 (2.5%)
	Glioblastoma	1 (1.3%)

48 patients underwent surgical excision of the cancer, 10 patients underwent just chemotherapy, 2 patients underwent both chemotherapy and radiotherapy, 7 patients underwent hormonal therapy, 20 patients underwent just radiotherapy, 8 patients underwent to immunotherapy. Some patients underwent multiple concomitant oncological treatments. (Table 2)

On average, patients started Apremilast treatment 2 years after cancer diagnosis. All patients received at least one prior topical or systemic anti-psoriatic drug, among which primary anti-TNFalpha inhibitors (20 patients). Methotrexate was previously used by 20 patients, cyclosporine by 16 patients. (Table 3)

Table 2 Cancer Treatment. Some Patients Underwent Multiple Cancer Treatments

Cancer Treatment	**n (%)**
Surgical excision	48 (61%)
Chemotherapy	10 (13%)
Chemotherapy and radiotherapy	2 (0.25%)
Hormonal therapy	7 (0,9%)
Radiotherapy	20 (25%)
Immunotherapy	8 (10%)

Table 3 Previous Anti-Psoriatic Treatments. Some Patients Underwent Multiple Treatments

Previous Anti-Psoriatic Treatment	n (%)
Anti- TNF alpha	20 (25%)
Methotrexate	20 (25%)
Cyclosporine	16 (20%)
Topical steroids	79 (100%)

There were no evidences of serious side effects related to the intake of Apremilast. Adverse events were present in 10 patients: diarrhea (11%) and asthenia (1%) that did not require discontinuation of Apremilast, as they did not compromise the patients' daily activities.

Oncological markers (CEA, Ca19.9, Ca 15.3, HEF4, Ca125, PSA, LDH) did not show any statistical significative variation during the study.

All scores were evaluated at the start (T0) and after 5 years of Apremilast therapy: particularly at after 24 weeks (T1), 52 weeks (T2), 78 weeks (T3), 104 weeks (T4), 128 weeks (T5), and after 156 weeks (T6), 180weeks (T7), 204 weeks (T8), 228weeks (T9), 260 (T10) weeks. At baseline, our cohort displayed an average PASI score of 8.3 and DLQI of 12. Concerning joint involvement, at week 0 mean pain VAS was 46.4. Concerning cutaneous manifestations, mean PASI score and DLQI significantly improved from baseline to week 156 (Figures 1 and 2). The mean PASI and DLQI scores decreased as soon as week T2 (Figures 1 and 2; ANOVA test $p<0.0001$). Also, Pain VAS reduced from baseline to T3 (Figure 3; ANOVA test, $p<0.0001$). All the scores remained almost constant, with slight differences from T3 to the end of the evaluation.

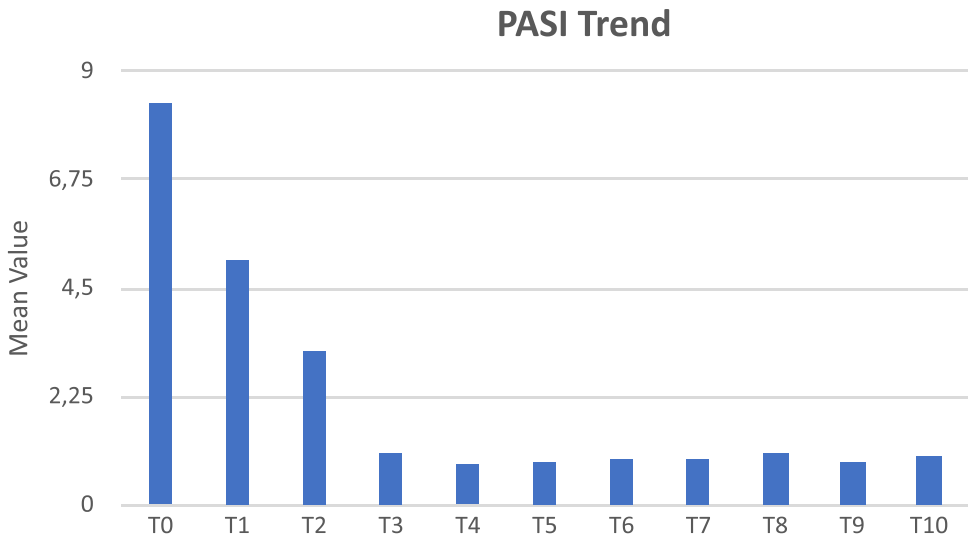

Figure 1 PASI trend in different timepoints. ANOVA test $p<0.0001$.

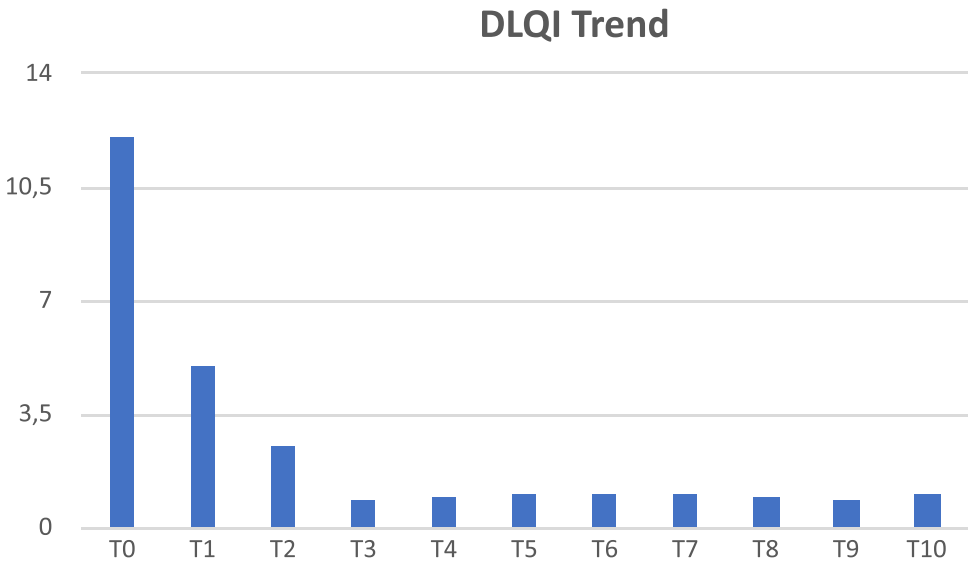

Figure 2 DLQI trend before and after treatment regimen. ANOVA test p<0.0001.

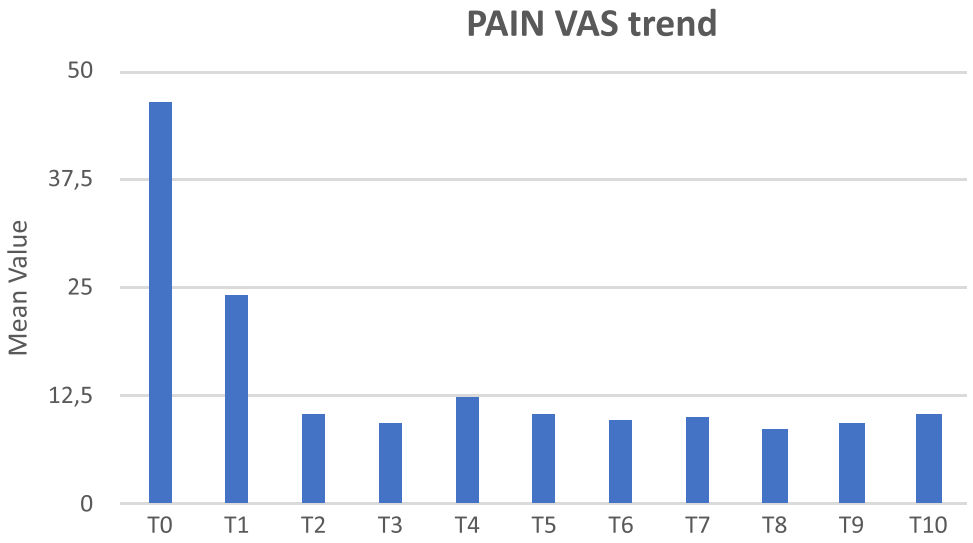

Figure 3 PAIN VAS trend before and after Apremilast treatment. ANOVA test, p<0.002.

Discussion

The management of psoriasis in patients with a history of oncological conditions presents a significant clinical challenge. Our study, conducted on a cohort of 79 patients with moderate-to-severe psoriasis, aimed to assess the safety and efficacy of Apremilast in individuals with concomitant neoplastic diseases, including bladder, lung, breast, and prostate cancer, as well as melanoma. Notably, these patients also exhibited other comorbidities, such as hypertension, cardiovascular disease, diabetes, and dyslipidemia.

Apremilast, a phosphodiesterase 4 (PDE4) inhibitor, acts by modulating a key point in the inflammatory cascade central to the pathogenesis of psoriasis. The drug increases intracellular levels of cyclic adenosine monophosphate (cAMP), which, in turn, regulates the expression of pro-inflammatory cytokines such as tumor necrosis factor (TNF)-α, interleukin (IL)-23, and IL-17.[8] This targeted action effectively reduces inflammation and alleviates psoriasis symptoms, contributing to improved skin health. Its unique mechanism of action ensures safety in patients with multiple underlying conditions, including those with cancer.[14]

The large size and representativeness of our cohort enhance the significance of our findings, allowing a robust evaluation of Apremilast's efficacy and safety in a population with complex clinical profiles. Over the five-year treatment period, no patient experienced recurrence of their oncological disease. Additionally, there were no statistically significant changes in oncological markers or abnormalities detected in biannual physical examinations and imaging studies (eg, ultrasound, CT scans).

These findings underscore the safety profile of Apremilast, demonstrating the absence of adverse oncological outcomes during treatment. While previous studies have investigated the use of Apremilast in patients with psoriasis and cancer, they have been limited in scope.[15,16] Bernardini et al confirmed the drug's safety in patients with a history of cancer but did not specify the time elapsed since cancer diagnosis and treatment.[16] Podevin et al focused on patients with cancer histories within the prior five years but evaluated only 23 cases over an average follow-up of 303.8 ± 252.4 days.[15]

In contrast, our study is the first to assess Apremilast safety over a longer follow-up period (five years) in a larger cohort (79 patients) with a cancer history within five years, a timeframe associated with the highest risk of cancer relapse. Our comprehensive approach included monitoring oncological markers and performing regular imaging, which revealed no changes indicative of cancer progression.

In addition to its safety, Apremilast demonstrated significant efficacy in this population. Patients experienced a marked reduction in PASI scores, alongside significant improvements in pain (PainVAS) and quality of life (DLQI). These results highlight the drug's ability to reduce the severity and extent of psoriasis while enhancing the quality of life in patients with moderate-to-severe disease, particularly within this vulnerable subpopulation.

Adverse events (AEs) associated with Apremilast were generally mild, occurring primarily during the first two weeks of treatment, and did not lead to therapy discontinuation.

Few reports on small cohorts evaluated other anti-psoriatic treatments in patients with a history of malignancies, and it seems that biologic drugs targeting interleukin-17 (IL-17) and interleukin-23 (IL-23) are also safe in this population,[17] suggesting that the selective blockade of specific inflammatory mediators might not interfere with cancer progression. However, notable differences exist between these biologics and Apremilast.

Apremilast acts upstream in the inflammatory cascade by inhibiting phosphodiesterase 4 (PDE4), leading to increased intracellular levels of cyclic adenosine monophosphate (cAMP). This broad regulatory mechanism reduces the production of multiple pro-inflammatory cytokines, including tumor necrosis factor (TNF)-α, IL-23, and IL-17, without fully blocking any single cytokine. This indirect approach may provide a safety advantage in patients with a history of malignancy, as it does not compromise immune surveillance, which is critical for controlling cancer recurrence.

In contrast, anti-IL-17 and anti-IL-23 biologics, while highly effective in rapidly reducing psoriasis severity, have a more targeted mechanism of action. Anti-IL-17 agents (eg, secukinumab, ixekizumab) directly block IL-17, a cytokine with dual roles in cancer biology—pro-tumorigenic in some contexts and anti-tumorigenic in others, depending on the tumor microenvironment. Similarly, anti-IL-23 therapies (eg, guselkumab, risankizumab) inhibit IL-23, an upstream cytokine essential for the differentiation of Th17 cells. While this precise targeting leads to excellent efficacy in psoriasis, it raises theoretical concerns about altering immune responses to malignancies.

Although recent studies suggest that IL-17 and IL-23 inhibitors are safe in patients with a history of cancer, the data are limited, particularly in high-risk populations. Most studies have focused on patients with remote cancer histories, whereas our research evaluates Apremilast in a cohort with a history of malignancy within the critical five-year window of recurrence risk. Furthermore, unlike studies on biologics, our comprehensive monitoring of oncological markers and regular imaging every six months strengthens the evidence of Apremilast's safety.

Future studies on larger scale and longer time of evaluation should be done to draw further conclusions about the oncological safety of apremilast even in comparison with other novel biological drugs, such as anti-IL23 and anti- IL17, identifying the best anti-psoriatic agent in patients with concomitant malignancies.

Ethics Approval

The study was conducted in accordance with the principles of the Declaration of Helsinki. The requirement for patient consent to review medical records was waived by the ethics committee (CET Lazio Area 2) due to the retrospective

observational nature of the study and the use of anonymized data. Patient confidentiality was rigorously maintained throughout the study. Data were de-identified prior to analysis to ensure privacy and prevent the identification of individual patients. All procedures complied with applicable data protection regulations and institutional policies governing the use of medical records for research purposes.

Informed Consent

All subjects provided written informed consent for inclusion before they participated in the study.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare that they have no conflict of interest to disclose.

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