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Original Research Article

EFFICACY AND SAFETY OF APREMILAST IN MODERATE TO SEVERE CASES OF CHRONIC PLAQUE PSORIASIS: A RETROSPECTIVE STUDY

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Abstract: *The objective of this study was to assess the efficacy and safety of Apremilast in patients with moderate-to-severe plaque psoriasis. A retrospective study was conducted in the Dermatology Department of Bakhtawar Amin Trust Hospital Multan from September 2021 to September 2022. A total of 102 patients were included in the study after evaluation. Apremilast was administered in all the patients, and its clinical response was assessed by the extent of Psoriasis Area Severity Index (PASI) reduction 16 weeks after the start of treatment. Our secondary endpoints included examining Dermatology Life Quality Index (DLQI); Physician Global Assessment (PGA); the adverse effects of treatment; survival rate; reasons for discontinuation of treatment, if any, and the rate of patients who managed to reach Psoriasis Area Severity Index reduction up to 50%, 75%, 90% and 100% after 16 weeks. 37 (72.5%) subjects achieved PASI reduction ≥75% or ≥50%, thus achieving the primary endpoint. The majority of the study sample had moderate psoriasis, with a mean baseline DLQI score of 11.2, PASI score of 11.0 and PGA score of 2.6. After 16 weeks, 65% subjects had PGA score ≤1. PASI improved rapidly over 4 (4.8) (P<.001) to 16 weeks (4.3) (P<.001). DLQI at baseline was 11.2; after 16 weeks, it was 3.8 (P<.001). Regarding secondary endpoints, after 16 weeks, 35/37 (94.5%) subjects achieved ΔPASI≥50, 18/37 (48.6%) ΔPASI≥75, 8/37 (21.6%) achieved ΔPASI≥90 and 6/37(16.2%) achieved ΔPASI100. Treatment-related adverse effects occurred in 16/51 (31.3%) patients. In total, treatment was stopped in 6 (11.6%)subjects because of adverse effects; gastrointestinal disorders were the most common. Apremilast is an effective and safe drug for the treatment of patients with moderate-to-severe plaque psoriasis.*

Keywords: Plaque psoriasis, skin disease, apremilast

Introduction

Psoriasis is a common autoinflammatory chronic skin disease (Muddasani et al., 2021). It has various subtypes; the most common is plaque psoriasis(Rendon and Schäkel, 2019). Psoriasis is associated with decreased quality of life and psychological morbidity (Nijakowski et al., 2022). Psoriasis can not be cured completely, but its sign and symptoms can be reduced using therapies such as phototherapy, topical agents, and biological and non-biological agents (Ogdie et al., 2020). However, treatment options are limited by the shortcomings of these therapies. For example, conventional systemic medicines such as cyclosporine, acitretin, and methotrexate have adverse effects like leukocytopenia, nephrotoxicity, and hepatotoxicity (Wollenberg et al., 2022). Biological agents effectively treat psoriasis, but studies show that subjects with moderate to severe plaque psoriasis do not continue treatment with conventional systemic and biological agents because of strict monitoring regimes, intolerable drugs, and limited efficacy (Barbieri et al., 2022). Therefore, more safe and efficacious therapeutic agents must be developed for treating psoriasis.

In 2014, Apremilast, a new oral agent, was developed to treat moderate to severe plaque psoriasis. Apremilast is a phosphodiesterase 4 (PDE4) inhibitor that modifies the inflammatory signaling pathway involved in disease development (Metyas et al., 2019). Two clinical trials show that it is safe and significantly reduces the severity of plaque psoriasis (Crowley et al., 2017; Young and

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Roebuck, 2016). According to these trials, adverse effects of apremilast were headache, nasopharyngitis, nausea, upper respiratory tract infection (URTI), and diarrhea. However, there are limited studies in real-world clinical setups; therefore, data on the real-world results of apremilast treatment are scarce.

Moreover, in clinical trials, the study sample is affected by selection bias. It represents a real-world population with comorbidities like infections, psychiatric diseases, or chronic illnesses. Thus, this study aims to assess the efficacy and safety of Apremilast in patients with moderate-to-severe plaque psoriasis who presented in the Dermatology Department of Nishtar Medical Hospital, Pakistan.

Methodology

A retrospective study was conducted in the Dermatology Department of Bakhtawar Amin Trust Hospital Multan from September 2021 to September 2022. Apremilast was administered to subjects with chronic psoriasis (> six months) and in whom apremilast was not contraindicated. For analyzing efficacy, issues with apremilast treatment for at least a month were involved (n=51). To analyze effectiveness, subjects who had taken at least a single drug dose were included (n=51). Patients who could not complete treatment or did not visit for follow-up were excluded. A total of 102 patients were included in the study. Patients were evaluated at baseline, after 4 and 16 weeks. The study's primary endpoint was to analyze the clinical response to the drug based on the extent of Psoriasis Area Severity Index (PASI) reduction after 16 weeks of treatment. PASI score reduction ≥75% (ΔPASI≥75) was considered a treatment success. ΔPASI≥50% was regarded as the intermediate response. Clinical outcomes were categorized as intermediate response or treatment success. PASI reduction < 50% was considered a treatment failure. Our secondary endpoints included examining the PASI; Dermatology Life Quality Index (DLQI); Physician Global Assessment (PGA); Psoriasis Scalp Severity Index (PSSI); the adverse effects of treatment; survival rate; reasons for discontinuation of treatment, if any, and rate of patients who managed to reach Psoriasis Area Severity Index reduction up to 50%, 75%, 90% and 100% after 4 months. Data were analyzed using SPSS 21.0. Continuous variables were represented as mean. Categorical variables were described as percentages. Kaplan -Meier analysis was done assessing drug survival. P value< 0.05 was considered statistically significant.

Results

For analyzing efficacy, 51 patients were prescribed apremilast. The mean age of the subjects was 50 years, and the mean duration of the disease was 22.1 years. All subjects had received systematic treatment previously; however, data regarding previous treatment was available for 30/51. According to this data, 6/30 subjects received biological therapy, and 24/30 received conventional routine treatment. Thirty-one subjects had comorbidities like hyperlipidemia, obesity, coronary artery disease, and hypertension. 5 patients had a smoking habit**.** All subjects had chronic plaque psoriasis. In 6 patients, palmoplantar psoriasis was present. 80% of subjects had scalp psoriasis. 6 (11.7%) patients had psoriatic arthritis. In 3 patients, another systemic treatment (cyclosporine or methotrexate) was given as bridge treatment along with apremilast.

37 (72.5%) subjects achieved PASI reduction ≥75% or ≥50%, thus achieving the primary endpoint. Most of the study sample had moderate psoriasis, with a mean baseline DLQI score of 11.2, PASI scores of 11.0 and PGA score 2.6. After 16 weeks, 65% subjects had PGA score ≤1. PASI improved rapidly over 4 weeks(4.8) (P<.001) to 16 weeks (4.3) (P<.001). DLQI at baseline was 11.2; after 16 weeks, it was 3.8 (P<.001). Regarding secondary endpoints, after 16 weeks, 35/37 (94.5%) subjects achieved ΔPASI≥50, 18/37 (48.6%) ΔPASI≥75, 8/37 (21.6%) achieved ΔPASI≥90 and 6/37(16.2%) achieved ΔPASI100 (Table I, II). A total of 13/51 (25.4%) subjects discontinued treatment because of inefficacy and 6 because of adverse effects. In detail, after 16 weeks, 8 patients had unsatisfactory treatment outcomes with ΔPASI <75%. For the subjects who discontinued treatment, the mean duration was 99 days; for subjects who continued treatment, the mean duration was 223.6 days. According to Kaplan Meier analysis, drug survival was 67.5% in the 24th week.

Table I Clinical outcomes of the treatment

	Number of patients	**Percentage**
Primary endpoints		
ΔPASI ≥ 75	31	88.7%
ΔPASI 50 and DLQI≤5	6	16.2%
Total	37	72.5%
Secondary endpoints		
ΔPASI 50	35	94.5%
ΔPASI 75	18	48.6
ΔPASI 90	8	21.6%
ΔPASI 100	6	16.2%

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Treatment-related adverse effects occurred in 16/51 (31.3%) patients. In total, treatment was stopped in 6 (11.6%) subjects because of adverse effects; the most common were gastrointestinal disorders. These adverse effects were temporary in most patients, except in 2 subjects where the drug was discontinued. The drug was discontinued in 4 other patients due to mood disturbance and other psychological effects (Table III).

Table II Week wise outcomes of the treatment

Mean score (range)	Week 0	Week 4	Week 16
PGA	2.6 (0 -6)	1.6 (0 -4)	1.2 (0-2)
DLQI	11.2 (0 -25)	6.1 (0 -16)	3.7 (0 -15)
PSSI	7.5 (0 -61)	3.5 (0 -15)	2.7 (0 -11)
PASI	11.0 (0 -51)	4.8 (0 -13.5)	4.3 (0 -16.7)

Table III Treatment associated adverse effects

Adverse effect	Number of patients	Percentage
Total patients with adverse effects	16	31.3%
No. of Adverse effect/patient		
1 adverse effect	13	25.4%
< 1 adverse effect	3	5.8%
Treatment discontinuation due to adverse effects	6	11.7%
Serious adverse effect	0	0
Type of adverse effect		
Gastrointestinal	11	21.5%
Headache	2	3.9%
Weight loss	1	1.9%
Infection	2	3.9%
Fatigue	1	1.9%
Sleep disturbance	1	1.9%
Mood disturbance	1	1.9%

Discussion

Currently, there is limited data on the safety and efficacy of apremilast. In this study, moderate to severe cases of psoriasis were treated with apremilast. The result of this study shows better effectiveness of apremilast than those reported by previous studies(Muddasani et al., 2021) (Rendon and Schäkel, 2019). In our study, the mean PGA score was 2.6, and the mean PASI score was 11.0 compared to the PASI score of 19 and PGA of 3.3 in these clinical trials. Moreover, in this study, results were not based on PASI but also were assessed by a secondary endpoint combining Quality of Life and skin. More than 2/3rd subjects achieved PASI reduction ≥75% or ≥50%, thus achieving the primary endpoint; this shows superior efficacy compared to those reported by clinical trials.

Regarding secondary endpoints, 94.5% of subjects achieved ΔPASI≥50 compared to 58.6% reported by a previous study (Tampouratzi et al., 2022), and 21.6% achieved ΔPASI≥90 compared to 9.8%. In the current study, DLQI at baseline was 11.2; after 16 weeks, it was 3.8. A previous study showed that after 16 weeks of treatment, DLQI was 4.0(Rajagopalan et al., 2021). It was observed that throughout treatment DLQI and PASI improved rapidly. Moreover, in our study, the prevalence of scalp disease in 80% is in line with the findings of previous studies(Papadavid et al., 2016; Reich et al., 2017). Our study's mean baseline DLQI score was 11.2, the PASI score was 11.0, and the PGA score was 2.6. A previous study reported a mean baseline PASI score of 10.45 and a DLQI of 13.8(Mayba and Gooderham, 2017).

The safety profile reported in this study is comparable to that reported by previous clinical trials (Muddasani et al., 2021). In 11.6% of subjects, treatment was discontinued because of adverse effects, and 25.4% of patients left treatment due to inefficacy. In a previous study, the prevalence of treatment-associated side effects was 16 %(Liu et al., 2022). The most common adverse effect was gastrointestinal disorders, the same reported by a previous study(Mayba and Gooderham, 2017). Moreover, in this study, drug ineffectiveness was the most common reason for treatment discontinuation. In this study, 25.5% population discontinued treatment due to inefficacy; this is higher than reported by a previous study(Vujic et al., 2018). It can be because, in our research, apremilast monotherapy was used.

Conclusion

Apremilast is an effective and safe drug for the treatment of patients with moderate-to-severe plaque psoriasis.

Conflict of interest

The authors declare no conflict of interest.

References

Barbieri, J. S., Beidas, R. S., Gondo, G. C., Fishman, J., Williams, N. J., Armstrong, A. W., Ogdie, A. R., Mehta, N., and Gelfand, J. M. (2022). Analysis of specialist and patient perspectives

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on strategies to improve cardiovascular disease prevention among persons with psoriatic disease. *JAMA dermatology* **158**, 252-259.

Crowley, J., Thaçi, D., Joly, P., Peris, K., Papp, K. A., Goncalves, J., Day, R. M., Chen, R., Shah, K., and Ferrándiz, C. (2017). Long-term safety and tolerability of apremilast in patients with psoriasis: Pooled safety analysis for≥ 156 weeks from 2 phase 3, randomized, controlled trials (ESTEEM 1 and 2). *Journal of the American Academy of Dermatology* **77**, 310-317. e1.

Liu, Y., Li, Y., and Du, H. (2022). Efficacy of apremilast for psoriasis: a meta-analysis of randomized controlled studies. *Advances in Dermatology and Allergology/Postępy Dermatologii i Alergologii* **39**.

Mayba, J. N., and Gooderham, M. J. (2017). Real-world experience with apremilast in treating psoriasis. *Journal of cutaneous medicine and surgery* **21**, 145-151.

Metyas, S., Tomassian, C., Messiah, R., Gettas, T., Chen, C., and Quismorio, A. (2019). Combination therapy of apremilast and biologic agent as a safe option of psoriatic arthritis and psoriasis. *Current Rheumatology Reviews* **15**, 234-237.

Muddasani, S., Fleischer, A. B., and Feldman, S. R. (2021). Treatment practices for psoriasis and how they are changing. *Journal of the American Academy of Dermatology* **84**, 579-581.

Nijakowski, K., Gruszczyński, D., Kolasińska, J., Kopała, D., and Surdacka, A. (2022). Periodontal Disease in Patients with Psoriasis: A Systematic Review. *International Journal of Environmental Research and Public Health* **19**, 11302.

Ogdie, A., Coates, L. C., and Gladman, D. D. (2020). Treatment guidelines in psoriatic arthritis. *Rheumatology* **59**, i37-i46.

Papadavid, E., Katsimbri, P., Kapniari, I., Koumaki, D., Karamparpa, A., Dalamaga, M., Tzannis, K., Boumpas, D., and Rigopoulos, D. (2016). Prevalence of psoriatic arthritis and its correlates among patients with psoriasis in Greece: results from a large retrospective study. *Journal of the European Academy of Dermatology and Venereology* **30**, 1749-1752.

Rajagopalan, M., Dogra, S., Saraswat, A., Varma, S., and Banodkar, P. (2021). the use of apremilast in psoriasis: an Indian perspective on real-world scenarios. *Psoriasis: Targets and Therapy* **11**, 109.

Reich, K., Bomas, S., Korge, B., Manasterski, M., Schwitchtenberg, U., Mentz, H., and Groegel, K. (2017). First" Real-World" Insights on Apremilast Treatment for Patients with Plaque Psoriasis from the LAPIS-PSO Study: An Interim Analysis. *SKIN The Journal of Cutaneous Medicine* **1**, s15-s15.

Rendon, A., and Schäkel, K. (2019). Psoriasis pathogenesis and treatment. *International journal of molecular sciences* **20**, 1475.

Tampouratzi, E., Papakonstantis, M., Katsantonis, J., Sidiropoulos, T., Delli, F., Efthymiadis, K., Sfaelos, K., Christodoulou, A., Chasapi, V., and Panagakis, P. (2022). Clinical evidence on the use of brodalumab for the treatment of psoriasis in Greece: Experience from clinical practice of four tertiary hospitals. *Dermatologic Therapy*, e15532.

Vujic, I., Herman, R., Sanlorenzo, M., Posch, C., Monshi, B., Rappersberger, K., and Richter, L. (2018). Apremilast in psoriasis–a prospective real-world study. *Journal of the European Academy of Dermatology and Venereology* **32**, 254-259.

Wollenberg, A., Kinberger, M., Arents, B., Aszodi, N., Avila Valle, G., Barbarot, S., Bieber, T., Brough, H., Calzavara Pinton, P., and Christen-Zäch, S. (2022). European guideline (EuroGuiDerm) on atopic eczema–part II: non-systemic treatments and treatment recommendations for special AE patient populations. *Journal of the European Academy of Dermatology and Venereology* **36**, 1904-1926.

Young, M., and Roebuck, H. L. (2016). Apremilast, an oral phosphodiesterase 4 (PDE4) inhibitor: A novel treatment option for nurse practitioners treating patients with psoriatic disease. *Journal of the American Association of Nurse Practitioners* **28**, 683-695.

[Citation: Khan, S., Farooq, M., Tariq, F., Ahmed, R., Aslam, M.A. (2023). Efficacy and safety of apremilast in moderate to severe cases of chronic plaque psoriasis: a retrospective study. *Biol. Clin. Sci. Res. J.*, **2023***: 180*. doi: https://doi.org/10.54112/bcsrj.v2023i1.180]

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