

TREATMENT RESPONSE TO APREMILAST IN PATIENTS WITH LICHEN PLANUS PRESENTING TO A TERTIARY CARE HEALTH FACILITY

APREMILAST IN PATIENTS WITH LICHEN PLANUS

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DOI: <https://doi.org/10.5281/zenodo.22895287>

Keywords

Apremilast; Lichen Planus; Quality of Life; Pruritus; Physician Global Assessment; Subject Global Assessment.

Article History

Received: 19 April, 2025

Accepted: 23 June, 2025

Published: 19 July, 2025

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ABSTRACT

Background: Lichen planus (LP) is a chronic immune-mediated inflammatory condition that affects the skin and mucous membranes, and can cause considerable morbidity and reduced quality of life. Traditional treatment options are limited by inadequate response and side effects. The phosphodiesterase-4 inhibitor apremilast has shown promise and appears to be safe.

Objective: To assess the treatment response to apremilast in Lichen planus patients and to determine the clinical factors associated with treatment response.

Materials and Methods: A total of 90 patients with biopsy-proven lichen planus who did not respond to topical steroids were enrolled in this single arm prospective Cohort study. All patients received apremilast 30 mg twice daily for 12 weeks as per the routine departmental protocol. Efficacy was measured as improvement in Physician Global Assessment (PGA) of at least 2 grades. The secondary outcomes were Subject Global Assessment (SGA), pruritus Visual Analog Scale (VAS), Dermatology Life Quality Index (DLQI) and Target Area Lesion Symptom Score (TALSS).

Result: Efficacy was achieved in 27.8% of patients, while 44.4% demonstrated $\geq 50\%$ improvement in SGA. Complete clearance occurred in 5.6%. Significant improvements were observed in PGA, pruritus VAS, DLQI, and TALSS ($p < 0.001$). Shorter disease duration and lower body surface area involvement were associated with treatment response, whereas presence of diabetes mellitus was inversely associated with treatment response.

Conclusion: Apremilast was well tolerated and associated with treatment response treatment in patients with lichen planus, especially in the early stages and mild disease. It presents a good alternative to traditional systemic treatments.

Introduction

Lichen planus (LP) is an immune-mediated chronic inflammatory skin condition that affects the skin, mucous membranes, hair follicles and nails. LP is a significant burden to patients due to severe itching, pain and the possibility of

deforming complications.¹ LP occurs worldwide with a prevalence of 0.5% to 2.0% of the population. Solimani et al (2021) noted two-thirds of patients are aged between 30 and 60 years.²

LP is equally common in both genders in its cutaneous form, but has female predominance (60-75%) in the oral form.³ Giuliani and colleagues (2019) reported that hypertrophic and mucosal LP have a 1% risk of transformation into squamous cell carcinoma, requiring ongoing follow-up.⁴ This malignant potential, especially in erosive oral LP, demands regular follow-up and histopathological examination, contributing to the disease burden and costs.

LP is an immunologically mediated disease. Gupta and Jawanda (2015) revealed cytotoxic T-cell infiltrates involving attack on basal keratinocytes that express unknown antigens.⁵ This immune reaction is mediated by activated CD8⁺ T cells specific to unknown antigens expressed by basal keratinocytes.

The immune response may be triggered or sustained by a range of factors, including viral infections (especially hepatitis C), stress, genetic factors (links to HLA-DR1 and HLA-DQ1) and drugs. The relapsing course of LP is a manifestation of the sustained inflammatory activity, which poses a challenge for clinicians to manage the disease in the long term.

Current approaches to therapy are not optimal. Initial treatment is based on potent topical steroid therapy,⁶ but patients with resistant disease need systemic therapies such as oral corticosteroids, retinoids, methotrexate, cyclosporine and phototherapy. Current systemic therapies are sub-optimal in efficacy, have significant side effects (including immunosuppression, hepatotoxicity, nephrotoxicity, and metabolic problems) with long-term use, and require laboratory monitoring, limiting their use. Therefore, there is a need for better and safer systemic therapies with minimal monitoring.

Oral phosphodiesterase-4 inhibitor apremilast offers a new hope. Ravichandran and Kheterpal (2020) have outlined its mechanism of elevating intracellular cAMP, leading to protein kinase A activation and inhibiting the transcription of several proinflammatory cytokines, such as TNF- α , IFN- γ , IL-2 and IL-17, that play a role in the pathogenesis of LP.⁷ Apremilast does not require periodic laboratory monitoring and has an excellent safety profile, making it a promising alternative for long-term use in chronic skin disorders.

Apremilast has been effective in LP in prior trials. Paul and colleagues (2013) demonstrated that 30% of patients who got 12-week Physician Global Assessment (PGA) scores recorded at least a 2-grade improvement.⁸ It was reported that 34.61% ($p < 0.0001$) achieved the same outcome, with an improvement of the target area lesion symptom scores.⁹ The article by Rafique, Malik, Umbreen, Safdar, Babar, and Malik (2025) recently reported a 65.3% response rate in 72 Pakistani patients, indicating that it may be even more effective in South Asian populations.¹⁰ One of the gaps in knowledge, which Radu and colleagues (2023) confirmed, is the odds ratio of 2.99 of developing oral LP.¹¹ in patients with hypothyroidism. Mallah and colleagues (2022) discovered that LP patients are at a higher risk of developing diabetes mellitus (1.87 times higher).¹² These co-morbidities could impact drug performance but no study has reported their effects on apremilast. There is also no large scale study in Pakistan which has studied apremilast keeping in view these clinical factors.

Thus, the present study is justified. Due to scant data from the South Asian region and no studies documenting comorbidities that have an impact on treatment response, there is a need for a prospective assessment of the efficacy of apremilast in patients with lichen planus and to examine the relationship between demographic and clinical variables (age, sex, duration of disease, body surface area, body mass index, and associated comorbidities) and their impact on treatment response and quality of life.

Methodology

This Single Arm Prospective Cohort Study was conducted in Department of Dermatology, Liaquat University of Medical and Health Sciences (LUMHS), Jamshoro, Hyderabad for 7 months. This study included patients of either sex aged 18 years or above with a histopathologically confirmed diagnosis of cutaneous or mucosal lichen planus presenting to the outpatient department. The inclusion criteria were patients who were refractory to topical corticosteroids and who had a baseline Physician Global Assessment (PGA) score of ≥ 3 . Topical steroid resistant patients were defined as those who did not have satisfactory control of the disease after one month of potent topical

steroids (such as clobetasol propionate 0.05%) once or twice daily.

Patients were excluded if they were known to have a drug allergy to apremilast or any component of the product, were prescribed apremilast for more than 4 weeks before enrolment in the study, or their clinical history was suggestive of lichenoid drug eruption (specifically antihypertensives and non-steroidal anti-inflammatory drugs). Women who were pregnant or breastfeeding, women of childbearing potential who did not practice adequate contraception, or patients with significant medical comorbidities, such as cardiovascular, renal, hepatic disease or psychiatric illness, were also excluded. Finally, patients receiving concomitant strong CYP450 inducers (rifampin, phenytoin, carbamazepine) were excluded.

The sample size was determined by the World Health Organization sample size calculator for a single proportion. The sample size was calculated assuming a 95% confidence level, an expected treatment response to apremilast of 30% (based on the published literature by Paul and colleagues (2013)⁸ and Viswanath and colleagues (2022)⁹ and an absolute precision of 10%. The sample size was 81 patients. To compensate for potential missing data or drop out, an additional 10% was added, bringing the total number of patients to 89, which was rounded up to 90 patients.

The study was approved by the Institutional Research Ethics Committee of LUMHS (LUMHS/REC/-517). In a consecutive manner, all eligible patients were invited to participate in the study after a detailed description of the study, procedures, risks, and benefits. All participants provided informed consent in their native languages (Urdu or Sindhi). Patient data were deidentified and no identifying information was published. Study participants were given the option to withdraw from the study at any time without compromising their health care.

All patients had a baseline assessment. Age and sex data were collected. Clinical variables recorded include disease duration, type of lichen planus (cutaneous, mucosal or both), percent of body surface area involvement (a palm is considered as 1% of the body surface area), body mass index (BMI, calculated as weight in

kilograms divided by square of the height in meters), and baseline Physician Global Assessment (PGA) score on a 0-5 scale. Itch and quality of life measures included pruritus visual analog scale (0-10, 0=no itch, 10=worst imaginable itch) and the Dermatology Life Quality Index (DLQI), a validated questionnaire with ten questions scored from 0 to 30, with higher scores reflecting worse quality of life.

The area of lesion assessment (target area) was defined as the most affected body region and this was well documented at baseline for future lesion assessment. The Target Area Lesion Symptom Score was the total of three individual scores for erythema, elevation and pruritus, each scored as 0-3 (0=none, 1=mild, 2=moderate, 3=severe) for a total of 0-9. Comorbid conditions recorded included diabetes mellitus, hypertension and hypothyroidism, defined as ever diagnosed by a physician or currently taking medication for the condition. Health-related lifestyle factors, such as smoking, were documented as never, ex- or current smoker. Prior therapies included topical corticosteroids (defined as potency and duration of use) and systemic therapies (defined as type, duration and response).

All the participants received 12-week oral therapy of apremilast 30 mg twice daily with a five-day titration protocol as per routine departmental protocol. The five-day protocol involved the day 1: 10 mg once a day, day 2: 10 mg twice a day, day 3: 10 mg once in the morning and 20 mg in the evening, day 4: 20 mg twice a day and from day 5 onwards: 30 mg twice a day.

For week 12, reassessment was done by the same investigator in order to maintain consistency. The results that were noted included the PGA score, SGA score (improvement of the patient's lesions measured using a six-point scale, where 0 indicated an absence of residual lesion activity, 1 indicated greater than 75% improvement, 2 indicated 50%-75% improvement, 3 indicated 25%-50% improvement, 4 indicated less than 25% improvement, and 5 indicated worsened lesions), Target Area Lesion Symptom Score with component scores, pruritus visual analog scale (VAS) score, and Dermatology Life Quality Index (DLQI) score. Improvement of at least two grades in PGA score from the baseline after 12 weeks of treatment constituted the main efficacy

endpoint. All the adverse effects were noted as type and frequency and had to be notified immediately. Serious adverse effects were to be reported to the ethics committee within 24 hours.

All data were collected using SPSS 26. For quantitative data including age, duration of disease, body surface area, body mass index, pruritus visual analog scale score, Dermatology Life Quality Index score, Physician Global Assessment scores (baseline and week 12), and Target Area Lesion Symptom Scores (baseline and week 12), mean and standard deviation were used for normally distributed data; whereas median and interquartile range were used for non-normally distributed data. Categorical data including gender, lichen planus subtype, diabetes mellitus, hypertension, hypothyroidism, smoking status, and efficacy were described by frequency percentage.

The first measure of effectiveness is the percent of patients achieving at least 2-point improvement at week 12 on the Physician Global Assessment. This proportion and its 95% Confidence interval are reported. All continuous secondary effectiveness measures, including changes in Physician Global Assessment, Dermatology Life Quality Index, Pruritus Visual Analog Scale, and Target Area Lesion Symptom Score from baseline to week 12, are analyzed using a paired t-test if the data are normally distributed; otherwise, the Wilcoxon signed-rank test is used.

Secondary outcomes are the percentage of patients to whom at least 50% of improvement in the Subject Global Assessment (SGA, score ≤ 2) was observed after 12 weeks of treatment, the mean SGA score change from baseline to 12 weeks and the percentage of patients to whom complete clearance of the Target Area Lesion Symptom Score (TALSS, score 0 or 1) was achieved at week 12.

Due to the ordinal nature of baseline patient characteristics and outcome measures, Spearman rank correlation coefficients was applied to determine the relationship of each of the following variables DLQI scores, PGA scores and SGA scores at week 12: age, disease duration, BSI (body surface area) involvement, and BMI (body mass index). Correlation coefficients were interpreted as follows: 0.00–0.19 as very weak, 0.20–0.39 as weak, 0.40–0.59

as moderate, 0.60–0.79 as strong, and 0.80–1.00 as very strong. Also, baseline Physician Global Assessment (PGA) and Subject Global Assessment (SGA) at 12 weeks were compared to determine agreement between physician and patient assessments.

Associations between baseline categorical characteristics and treatment response were examined using the chi-square test or Fisher's exact test, as appropriate. A p-value of less than 0.05 was considered statistically significant for all analyses.

Results

The total number of patients enrolled in this study was 90 and all of them completed the 12 weeks' treatment protocol and none were lost to follow-up (Figure 1). As far as the age of patients goes, the study population consists mainly of middle-aged patients with the majority belonging to adult age categories, signifying that lichen planus in this study population is a disease that affects the middle aged more so than any other age group. This patient population had a slight male predilection. Most of the study population consisted of non-smokers, while fewer patients were either currently smoking or were ex-smokers.

As far as the co-morbid condition is concerned, DM was the most prevalent condition, followed by hypertension, while hypothyroidism was much less prevalent among this population. Regarding clinical features, cutaneous LP was the most commonly seen type of LP, followed by mixed and mucosal type. Baseline data showed most patients with moderately severe and severely affected patients signifying a significant level of disease severity among patients (Table 1). A considerable number of patients had improvements according to patient-based evaluation criteria at the 12-week follow-up period, whereas a relatively larger number of patients had improvements according to physicians' evaluation criteria. Some patients had achieved complete clearance after the treatment, suggesting that there were more cases of partial improvement in their conditions, but not complete elimination of the condition.

Overall adverse event occurred in 12(13.3%) patients, (Figure 2). Among these adverse events headache was observed in 7 (7.8%), gastrointestinal discomfort noted in 4(4.45%)

and others in 1(1.1%). However, no serious adverse events or treatment discontinuation was noted. There were improvements in patient based outcomes measures from baseline to week 12 across all measures (Table 2). Median PGA fell (IQR -1.0 to -3.0), but did not become more challenging (no deterioration; Wilcoxon $p<0.001$). Mean pruritus VAS decreased from 6.59 ± 1.54 to 4.60 ± 2.48 (mean change -1.98, 95% CI -2.36 to -1.61, paired t-test $p<0.001$), though 9 patients (10.0%) reported worsened pruritus. Median DLQI decreased from 15.0 (IQR 11-18) to 11.0 (IQR 5-17) (median change -4.0, Wilcoxon $p<0.001$), with worsening reported in 15 patients (16.7%). Median TALSS Total went from 6.0 (IQR 5-7) to 4.0 (IQR 2-6) (median change -2.0, Wilcoxon $p<0.001$), with no declines.

Univariate analysis showed that disease duration, extent of body surface area involvement, presence of diabetes mellitus, and baseline disease severity were associated with treatment response. There was no significant association between other demographic factors (age and gender) or other comorbidities and outcomes, however.

In multivariable analysis, both disease duration and extent of involvement of body surface area remained associated with treatment response, indicating that earlier disease and less extensive body surface area involvement was associated with a greater likelihood of treatment response. Despite of the fact that the disease duration fails to reach the significance level after adjustment (p value=0.053). Diabetes mellitus was highly inversely associated with the treatment response as the adjusted OR was 0.08, 95% CI 0.01-0.76, $p=0.028$. This reveals that diabetic patients markedly less likely to respond treatment, this

relationship should be addressed cautiously, because of the small number of patients in the present study. After the adjustment, baseline disease severity did not have an independent association, suggesting that this association might be accounted for by the relationship with disease duration and BSA (Table 3). In view of the number of events versus the number of predictors (25 versus 4), these multivariable estimates (especially for diabetes mellitus and baseline PGA) are meant to be considered exploratory. Smoking status (univariate $p=0.140$) and BMI (univariate $p=0.168$) also had pre-specified p -values less than 0.05 but were not included because of that. The overall pattern of association remained similar when both were included in a sensitivity analysis with the four main predictors (smoking status: adjusted OR 1.94, 95% CI 0.94-4.01, $p=0.073$; BMI: adjusted OR 0.92, 95% CI 0.81-1.04, $p=0.311$), but neither had a strong enough effect on the other predictors to materially alter their direction or significance.

At baseline, the correlations of greater BSA with week-12 outcomes were moderate for DLQI ($\rho=0.482$, $p<0.001$), PGA ($\rho=0.544$, $p<0.001$) and mild for SGA ($\rho=0.372$, $p<0.001$) (moderate for both DLQI and PGA; mild for SGA). There was a weak correlation between age and week-12 DLQI ($\rho=0.264$, $p=0.012$) but not with PGA or SGA. BMI showed a weak correlation with week-12 DLQI ($\rho=0.231$, $p=0.028$) only. There was a weak correlation of disease duration with week-12 PGA ($\rho=0.233$, $p=0.027$) but not with DLQI or SGA (Table 4). There was good agreement between physician- and patient-reported assessments at week 12 (Spearman $\rho=0.705$ for PGA vs SGA, $p<0.001$).

Figure 1 Patient Flow diagram

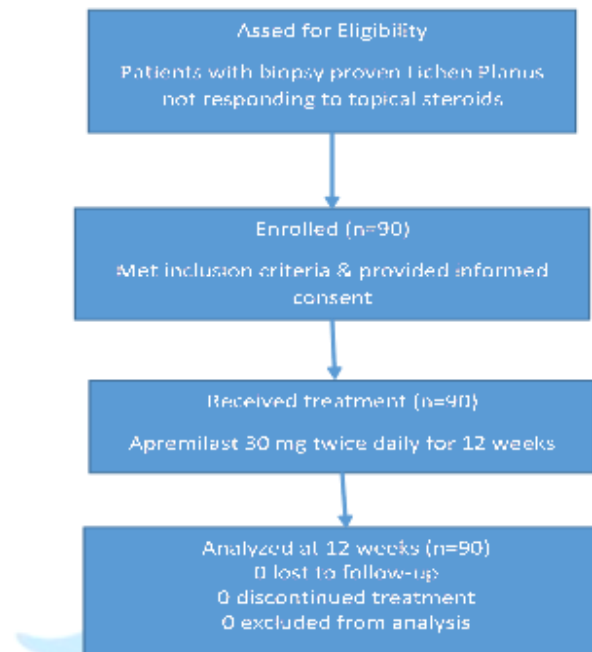


Table 1: Baseline Demographic and Clinical Characteristics (n = 90)

Variable	Value
Age (years)	41.82 ± 11.42
BMI (kg/m ²)	27.26 ± 3.76
Disease duration (months)	9.67 ± 4.05
Body surface area (%)	15.53 ± 6.37
Baseline Pruritus VAS	6.59 ± 1.54
Baseline DLQI	14.71 ± 4.66
Baseline TALSS Total	6 (5-7)
Gender	
• Male	50 (55.6%)
• Female	40 (44.4%)
Smoking status	
• Never	59 (65.6%)
• Former	15 (16.7%)
• Current	16 (17.8%)
Diabetes mellitus	20 (22.2%)
Hypertension	19 (21.1%)
Hypothyroidism	10 (11.1%)
Lichen planus subtype	
• Cutaneous	50 (55.6%)
• Mucosal	19 (21.1%)

• Both	21 (23.3%)
Baseline PGA	
• Moderate	38 (42.2%)
• Severe/Very severe	52 (57.8%)

BMI: Body Mass Index, VAS: Visual Analogue Scale, DLQI: Dermatology Life Quality Index, TALSS: Target Area Lesion Symptom Score, PGA: Physician Global Assessment

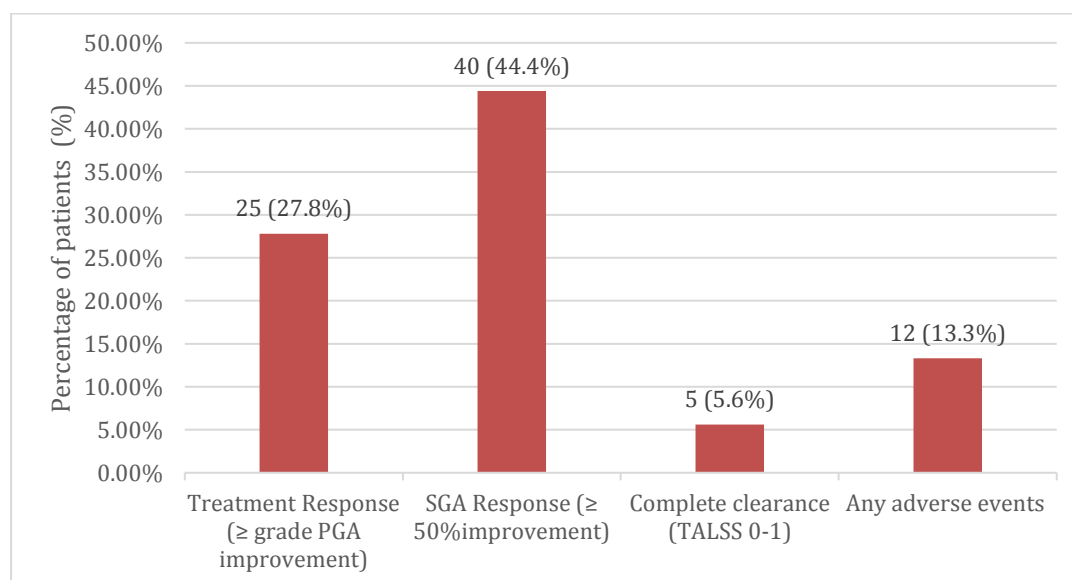


Figure 2: Treatment Outcomes at Week 12 (N=90)

Table 2: Comparison of Baseline and Week 12 Outcomes

Variable	Baseline	Week 12	Change (95% CI)	p-value
PGA, median (IQR)	4.0 (3-4)	3.0 (2-4)	-1.0 (-1.0 to 0.0)*	<0.001
Pruritus VAS, mean±SD	6.59 ± 1.54	4.60 ± 2.48	-1.98 (-2.36 to -1.61)**	<0.001
DLQI, median (IQR)	15.0 (11-18)	11.0 (5-17)	-4.0 (-5.0 to -2.0)*	<0.001
TALSS Total, median (IQR)	6.0 (5-7)	4.0 (2-6)	-2.0 (-2.0 to -1.0)*	<0.001

PGA: Physician Global Assessment, VAS: Visual Analogue Scale, DLQI: Dermatology

Life Quality Index, TALSS: Target Area Lesion Symptom Score. * Wilcoxon signed-rank test applied, ** T test applied

Table 3: Univariate and Multivariable Logistic Regression Analysis of Factors Associated with Treatment Response

Variable	Unadjusted OR (95% CI)	p-value	Adjusted OR (95% CI)	p-value
Age	0.98 (0.94-1.02)	0.402	—	—
Disease duration (months)	0.88 (0.77-0.99)	0.038	0.85 (0.72-1.00)	0.053
BSA (%)	0.88 (0.81-0.96)	0.003	0.86 (0.75-0.98)	0.028
Diabetes mellitus	0.10 (0.01-0.80)	0.030	0.08 (0.01-0.76)	0.028
Baseline PGA	0.20 (0.08-0.49)	<0.001	0.53 (0.17-1.60)	0.259

OR: odds ratio, CI: confidence interval, BSA: body surface area, PGA: physician global assessment variables with $p \leq 0.20$ in univariate

analysis and clinically relevant variables were included in the multivariable model. Bold P-values: significant

Table 4: Correlation of Outcomes at 12 weeks and baseline variable

Variables	DLQI	PGA	SGA
Age	$\rho=0.264$, $p=0.012$	$\rho=0.143$, $p=0.180$	$\rho=0.130$, $p=0.223$
Disease duration	$\rho=0.147$, $p=0.168$	$\rho=0.233$, $p=0.027$	$\rho=0.114$, $p=0.285$
BSA (%)	$\rho=0.482$, $p<0.001$	$\rho=0.544$, $p<0.001$	$\rho=0.372$, $p<0.001$
BMI	$\rho=0.231$, $p=0.028$	$\rho=0.169$, $p=0.111$	$\rho=0.034$, $p=0.750$

DLQI: Dermatology Life Quality Index, PGA: Physician Global Assessment, SGA: Subject Global Assessment, BSA: body surface area, BMI: body mass index.

Discussion

This is a valuable prospective study of the effectiveness of Apremilast and the clinical factors associated with treatment response in Lichen planus (LP) patients in a south Asian tertiary care setting. The results indicate that apremilast is associated with clinically significant improvement in both physician-assessed and patient-reported parameters as well as lesion-specific parameters and remains safe. The findings are consistent with other results that have been reported and offer further evidence of the usefulness of apremilast in treatment of refractory LP in populations in which there is limited data.

Most of these patients in this study had moderate to severe LP, reflecting the population that is most likely to benefit from systemic therapy, making this population relevant to assess newer therapies like apremilast in this population.

The main efficacy endpoint of this study was a ≥ 2 grade improvement in the Physician Global Assessment (PGA), which was met by 27.8% of patients. This is largely in line with previous researches conducted by Paul et al.,⁸ who found improvement in around 30% of patients, and by Viswanath et al.,⁹ who found a comparable improvement rate of 34.61%. The lower response rate in the current study may be due to differences in baseline disease activity, presence of mucosal and mixed variants and the diversity commonly observed in patients in clinical practice. Notably, Rafique et al.,¹⁰ reported a higher response rate (65.3%) in a Pakistani cohort, suggesting that there may be differential treatment response between populations, which

may be due to genetic, environmental, or healthcare-related factors.

While the benefit of apremilast is clinically relevant, only 5.6% of patients were completely clear. Lichen planus is a chronic disease that tends to go in waves and fluctuations in activity, particularly reduction in symptoms and lesion severity, can be meaningful to patients. A strong association of

LP with thyroid disorders was reported by Radu et al.,¹¹ and an increased risk of diabetes mellitus in LP patients was reported by Mallah et al.,¹² indicating that systemic comorbidities may influence disease persistence and treatment responses. Furthermore, Friedl et al.,¹³ noted that hypertrophic LP is chronic and resistant to treatment, which could account for the comparatively low complete clearance rates observed in clinical trials.

Therapy of lichen planus (LP) is becoming more targeted immunomodulation. In inflammatory skin diseases, phosphodiesterase-4 inhibition has been noted as having great potential for use, and in immune-mediated diseases, targeted therapy has been growing in significance, as noted by Liang et al. and Rosset et al., respectively.^{14, 15} This is especially important in LP because T cell-driven inflammation is at the heart of the disease pathogenesis. Apremilast has a more targeted and selective mechanism of action compared to traditional systemic immunosuppressants by targeting intracellular signaling pathways and cytokine production.

The safety outcomes observed in this study are in line with existing evidence. Overall, apremilast was well tolerated, with adverse events reported in 13.3% of patients, and mostly mild. It was clinically proven to be beneficial by

Bettencourt et al.¹⁶ in oral LP and by AbuHilal et al.¹⁷ in challenging cases. This was further supported by Hafner et al.,¹⁸ who noted that it plays a role in mucosal LP which is often more resistant to standard therapies and more morbid. Overall, these results reinforce the safety and appropriateness of apremilast for longer-term use.

Diabetes mellitus was found to be a significant factor in this study, with diabetes being an independent risk factor for poor treatment response (adjusted OR 0.08, 95% CI 0.01–0.76). This is biologically plausible because diabetes has been linked to a chronic low-grade inflammatory condition, immune system changes in T-cells and reduced microvascular function, all of which could dampen the anti-inflammatory effect of PDE4 inhibitors in the treatment of lichen planus. Alternatively, there may be a difference in the pharmacokinetics of the drugs used in diabetic patients or an inflammatory status that is higher than that in a normal patient, and remains unaffected by modulation treatment over 12 weeks. This study should be interpreted as hypothesis generating and the large range of the confidence interval is due to the small number of diabetic patients (n=20, only 1 responder) in the study; larger studies are necessary to confirm whether diabetes status should be a factor in the selection of patients to receive apremilast treatment in lichen planus. Bansal et al.,¹⁹ have identified a correlation of LP and endocrine disorder, which indicate that systemic inflammatory and metabolic pathways are likely to play a role in the behavior of the disease. Chronic and relapsing course of LP was described by Chainani-Wu et al.,²⁰ which suggests duration of the disease and systemic health as possible factors in treatment response.

This study has one great advantage in that patients reported improvement in their outcomes. There was significant improvement in both pruritus severity scores and Dermatology Life Quality Index (DLQI) scores following treatment. As highlighted by Gupta et al.,⁵ pruritus is a key contributor to disease burden in lichen planus, and reducing it can greatly enhance patient well-being. Similarly, improvements in DLQI scores indicate clinically significant improvements in daily functioning

and psychosocial health particularly relevant for chronic skin disease.

Consistent with the demonstrated mechanism of action of apremilast via elevation of cAMP and suppression of pro-inflammatory cytokines, these findings indicated good safety characteristics without the need for intensive laboratory monitoring, which was also observed by Mehta et al.⁶

The factors predicting treatment response are another important contribution of this study. Therapy was more likely to be successful in patients with a shorter disease duration and less extent of involvement of body surface area. This shows the importance of initiating treatment early in lichen planus to prevent it from worsening and to enhance the chances of a good outcome. More widespread disease, as manifested by greater BSA involvement, however, likely represents more advanced inflammatory status and may be associated with more difficult to effectively treat disease.

In recent years, the use of apremilast in dermatology has been the subject of numerous studies. Kim-Lim et al.,²¹ reported favorable clinical results with apremilast in the treatment of oral lichen planus in a case report and Wessel et al.,²² reported favorable outcomes in case series, including cases with treatment-resistant disease. Its varied use and acceptance in the clinic were further illustrated by the reports of Demirbaş et al.,²³ and Bubna et al.,²⁴ that reported its use in a variety of dermatologic conditions in an off-label manner. This was also confirmed by Maloney et al.,²⁵ in a detailed review who pointed out that it is safe and effective in treating a range of inflammatory skin conditions.

Although these are promising findings there are some caveats to be taken into account. Since there was no control group, it is hard to make definitive causal conclusions, and the interval between follow-up periods is relatively short, which may underestimate long-term results or relapse patterns. Moreover, because of the single center study design and moderate sample size, the generalizability of findings may be limited. Nevertheless, there is strength in the prospective design, detailed assessment of outcomes and incorporation of clinically relevant variables in this study.

Conclusion

In all, the study has demonstrated that Apremilast is a promising addition to the treatment options available for lichen planus especially for moderate to severe and refractory patients due to its favourable safety profile, ease of use and clinical benefits. The results highlight

the importance of early treatment and reduced disease severity for improved results. The observed association with metabolic comorbidities is interesting, and should be studied further in larger multicenter Clinical trial.

Abbreviations

BMI:	Body Mass Index
BSA:	Body Surface Area
cAMP:	Cyclic Adenosine Monophosphate
CI:	Confidence Interval
DLQI:	Dermatology Life Quality Index
DM:	Diabetes Mellitus
IFN- γ :	Interferon Gamma
IL:	Interleukin
LP:	Lichen Planus
LUMHS:	Liaquat University of Medical and Health Sciences
OR:	Odds Ratio
PGA:	Physician Global Assessment
SGA:	Subject Global Assessment
SPSS:	Statistical Package for the Social Sciences
TALSS:	Target Area Lesion Symptom Score
TNF- α :	Tumor Necrosis Factor Alpha
VAS:	Visual Analog Scale

Acknowledgment: We acknowledge the participation of all patients enrolled in the study

Competing Interest / Funding: none.

Authors' Contribution

Maria Asad: Substantial contributions to the conception or design of the work

Hafiz Bashir Ahmed: Provided supervision and/or project administration, including oversight of the research activity planning and execution

Saba Dahri & Muhammad Ahsan: Acquisition, analysis, and interpretation of data; methodology.

Bushra & Shahzeen Karamullah: Drafting the manuscript or revising it critically for important intellectual content

Declaration

Consent to Participate: Written informed consent was obtained from all participants prior to inclusion in the study.

Consent for Publication: All authors provided consent for the publication.

Conflict of Interest: none.

Use of AI-Assisted Technologies: No AI tool was used to generate data, perform statistical analysis or create figures. However, it was used for spelling and grammar checking of the final draft only

References

- Tekin B, Xie F, Lehman JS. Lichen Planus: What is New in Diagnosis and Treatment? *Am J Clin Dermatol*. 2024 Sep;25(5):735-764. doi: 10.1007/s40257-024-00878-9
- Solimani F, Forchhammer S, Schloegl A, Ghoreschi K, Meier K. Lichen planus - a clinical guide. *J Dtsch Dermatol Ges*. 2021 Jun;19(6):864-882. doi: 10.1111/ddg.14565.
- Pelet del Toro N, Strunk A, Garg A, Han G. Prevalence and Treatment Patterns of Lichen Planus. *J Am Acad Dermatol*. 2025;92(4):717-723. doi: 10.1016/j.jaad.2024.09.081

- González-Moles MÁ, Ramos-García P. An Evidence-Based Update on the Potential for Malignancy of Oral Lichen Planus and Related Conditions: A Systematic Review and Meta-Analysis. *Cancers*. 2024;16(3):608. doi: 10.3390/cancers16030608
- Gupta S, Jawanda MK. Oral Lichen Planus: An Update on Etiology, Pathogenesis, Clinical Presentation, Diagnosis and Management. *Indian J Dermatol*. 2015 May-Jun;60(3):222-9. doi: 10.4103/0019-5154.156315.
- Mehta H, Sharma A, Dogra S. Evolving utility of apremilast in dermatological disorders for off-label indications. *Clin Exp Dermatol*. 2022 Dec;47(12):2136-2149. doi: 10.1111/ced.15377.
- Ravichandran S, Kheterpal MK. Apremilast for the off-label treatment of lichenoid and interface dermatoses. *J Am Acad Dermatol*. 2020;83(5):1489-91. <https://doi.org/10.1016/j.jaad.2020.05.112>
- Paul J, Foss CE, Hirano SA, Cunningham TD, Pariser DM. An open-label pilot study of apremilast for the treatment of moderate to severe lichen planus: a case series. *J Am Acad Dermatol*. 2013 Feb;68(2):255-61. doi: 10.1016/j.jaad.2012.07.014.
- Viswanath V, Joshi P, Dhakne M, Dhoot D, Mahadkar N, Barkate H. Evaluation of the Efficacy and Safety of Apremilast in the Management of Lichen Planus. *Clin Cosmet Investig Dermatol*. 2022 Dec 2;15:2593-2600. doi: 10.2147/CCID.S390591.
- Rafique A, Malik LM, Umbreen S, Safdar A, Babar H, Malik S. Efficacy of Apremilast in Patients with Moderate to Severe Lichen Planus. *Indus J Bio Res*. 2025;3(5):1117-22. DOI: <https://doi.org/10.70749/ijbr.v3i5.2712>
- Radu AM, Carsote M, Nistor C, Dumitrascu MC, Sandru F. Crossroads between Skin and Endocrine Glands: The Interplay of Lichen Planus with Thyroid Anomalies. *Biomedicines*. 2023 Dec 28;12(1):77. doi: 10.3390/biomedicines12010077.
- Mallah N, Varela-Centelles PI, Seoane-Romero J, Takkouche B. Diabetes mellitus and oral lichen planus: A systematic review and meta-analysis. *Oral Dis*. 2022;28(8):2100-9. doi:10.1111/odi.13909
- Whittington CP, Saleh JS, Bresler SC, Patel RM. Hypertrophic Lichen Planus: An Up-to-Date Review and Differential Diagnosis. *Arch Pathol Lab Med*. 2024 Jun 1;148(6):659-665. doi: 10.5858/arpa.2022-0515-RA.
- Liang X, Zheng J, Huang X, Tan M, Liao J. Apremilast treatment of immune-mediated inflammatory skin diseases: a narrative review. *Frontiers in Pharmacology*. 2025 Aug 21;16:1633426. doi:10.3389/fphar.2025.1633426
- Rosset F, Sciamarrelli N, Mastorino L, Pala V, Boskovic S, Bongiovanni E, et al. Monoclonal Antibodies and Small-Molecule Therapies for Lichen Planus: Targeted Immunomodulation and Emerging Evidence. *Antibodies*. 2025;14(3):71. doi:10.3390/antib14030079
- Bettencourt M. Oral Lichen Planus Treated with Apremilast. *J Drugs Dermatol*. 2016 Aug 1;15(8):1026-8.
- AbuHilal M, Walsh S, Shear N. Treatment of recalcitrant erosive oral lichen planus and desquamative gingivitis with oral apremilast. *J Dermatol Case Rep*. 2016;10(4):56-7. doi:10.3315/jdcr.2016.1232
- Hafner J, Gubler C, Kaufmann K, Nobbe S, Navarini AA, French LE. Apremilast is effective in lichen planus mucosae-associated stenotic esophagitis. *Case Rep Dermatol*. 2016;8(2):224-226. <https://doi.org/10.1159/000447051>
- Bansal PV, Raj K, Gupta N, Dwivedi D, Sethi A, Prabhakar N, et al. Prevalence of oral lichen planus in patients with hypothyroidism versus nonhypothyroidism. *J Pharm Bioall Sci*. 2024;16:S2159-61. DOI: 10.4103/jpbs.jpbs_111_24

- Louisy A, Humbert E, Samimi M. Oral Lichen Planus: An Update on Diagnosis and Management. *Am J Clin Dermatol*. 2024 Jan;25(1):35-53. doi: 10.1007/s40257-023-00814-3
- Kim-Lim P, Thomas C. Crushed apremilast for the treatment of oral lichen planus. *JAAD Case Rep*. 2023 May 19;37:114-115. doi: 10.1016/j.jdcr.2023.05.013.
- Wessel S, Baltazar D, Harview C, Kessler M, Ackerman L. 64728 Oral Lichen Planus and Apremilast: Case Series and Literature Review. *J Am Acad Dermatol*. 2025;93(3):AB261.
- Demirbaş A, Demirbaş GU, Diremsizoglu E. Expanding therapeutic horizons: apremilast for refractory inflammatory dermatological conditions. *Arch Dermatol Res*. 2025;317(1):673. doi:10.1007/s00403-025-04081-6
- Bubna AK, Viplav V. An In-depth Review of the Off-label Use of Apremilast in Dermatology. *J Pharmacol Pharmacother*. 2025;16(2):143-63. <https://doi.org/10.1177/0976500X241303186>
- Maloney NJ, Zhao J, Tegtmeyer K, Lee EY, Cheng K. Off-label studies on apremilast in dermatology: a review. *J Dermatolog Treat*. 2020;31(2):131-40. doi:10.1080/09546634.2019.1589641.