RESEARCH LETTER

Can Week 4 PASI Response Serve as an Early Predictor of Apremilast Efficacy in Psoriasis? A Single-Centre Preliminary Study

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To the Editor,

Apremilast is an oral phosphodiesterase-4 inhibitor used for moderate to severe plaque psoriasis and psoriatic arthritis. Efficacy studies for psoriasis vulgaris show that PASI 75 response rates vary between 30% and 70% over a 12- to 16-week treatment period (1–3). In our own clinical practice, we have observed that the efficacy of apremilast varies among patients, with some responding significantly while others remain unresponsive. This may prolong the transition to effective treatment for some patients, increase the period of time they live with a low quality of life and lead to additional economic burdens. Therefore, there is a need for indicators that can predict treatment response in the early stages. This study aimed to evaluate the predictive value of week 4 PASI response in achieving week 12 PASI 75 response.

Patients starting apremilast treatment at Etlik City Hospital Psoriasis Outpatient Clinic (December 2023–June 2025) were retrospectively reviewed. Patients completing ≥12 weeks' treatment with documented PASI scores at baseline, week 4, and week 12 were included. Statistical analysis was performed using IBM SPSS 26 (IBM Corp, Armonk, NY, USA).

The study included 33 patients: 22 males (66.7%) and 11 females (33.3%), mean age 47.36 ± 14.60 years. Among patients, 23 (69.7%) had prior conventional therapy, 4 (12.1%) had prior conventional and biologic therapy, and 6 (18.2%) were treatment-naive. Median baseline PASI score was 4.00 (0.0–17.9), mean week 4 PASI score was 2.59 ± 1.35, and median week 12 PASI score was 2.0 (0.0–6.0). Median 4-week PASI response was 40.0% (–100.0–100.0), and median 12-week PASI response was 52.0% (–100.0–100.0). At week 4; PASI 50, 75, and 90 responses were achieved by 12 (36.4%), 4 (12.1%), and 2 (6.1%) patients, respectively. By week 12; these numbers increased to 17 (51.5%), 13 (39.4%), and 4 (12.1%). Baseline characteristics and outcomes are presented in **Table I**.

Analysis of early PASI response predictive value revealed that week 4 PASI 50 response strongly predicts week 12 PASI 75 response with 76.9% sensitivity, 90.0% specificity, 83.3% positive predictive value, and odds ratio of 30.0 ($p < 0.001$). In practical terms, 83.3% of week 4 PASI 50 responders achieved week 12 PASI 75 response. Individual patient PASI response trajectories (Fig. S1) demonstrate considerable inter-patient variability in treatment response and illustrate how early response patterns tend to persist over time.

ROC analysis demonstrated excellent discrimination (AUC: 0.938) with optimal cutoff at week 4 PASI 40.58 response (Youden index: 0.773, sensitivity: 92.3%, specificity: 75.0%) for predicting week 12 PASI 75 response (**Fig. 1**).

Statistical significance was assessed using Fisher's exact test ($p < 0.001$) and Cohen's w calculated as 0.680. *Post hoc* power analysis demonstrated 97.42% statistical power with the current sample size of $n = 33$ (GPower 3.1.9.7, $\alpha = 0.05$).

Our findings showing early response patterns are consistent with existing literature on apremilast's early efficacy. The ACTIVE study by Nash et al. (4) showed apremilast's effect in psoriatic arthritis patients began significantly at week 2 (16.4% vs 6.4%, $p = 0.025$) and was sustained through to week 52. The UNVEIL study by Strober et al. (5) demonstrated apremilast's early effect at week 4 with significant reductions in IL-17A, IL-17F, and IL-22 levels compared with placebo. The PROMINENT study by Okubo et al. (6) evaluated Static Physician Global Assessment (sPGA) response, defined as clear or almost clear skin. Among patients achieving sPGA response at week 16, 15.9% reached this at week 2 and 54.0% at week 4.

Early response to treatment has clinical and economic impact. The etanercept study by Nast et al. (7) found median discontinuation duration of 80 days due to inefficacy, with 77.9% of discontinuing patients failing to achieve PASI 25, while only 1 PASI 75 responder discontinued treatment. These findings demonstrate that patients failing adequate early response tend to discontinue therapy, with approximately 80 days representing a critical threshold.

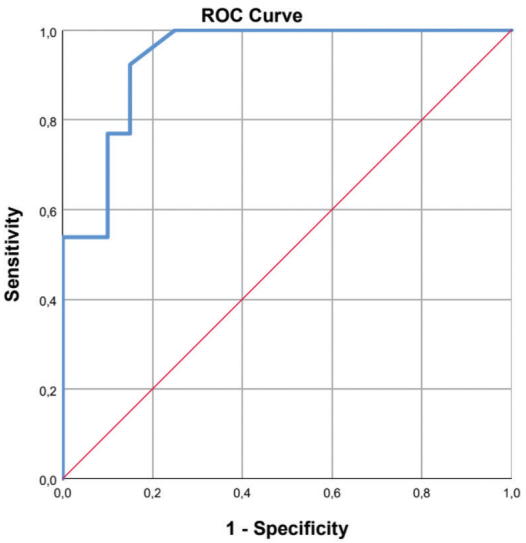
This single-centre preliminary study demonstrated that week 4 PASI response strongly predicts week 12 treatment success in apremilast therapy. ROC analysis revealed excellent discrimination (AUC: 0.938) with an optimal cut-off of PASI 40.58, achieving 92.3% sensitivity and 75.0% specificity. These performance metrics suggest that week 4 PASI > 40 response can be used as a reliable guide for treatment decisions.

Our results suggest that the PASI response at week 4 may provide an objective criterion for decisions to continue or modify treatment, enable stratification of patients before the critical 80-day period, and help reduce both

Table I. Baseline patient characteristics and treatment outcomes by PASI 75 response status at week 12

Characteristic	Total ($n = 33$)	PASI 75 responders ($n = 13$)	Non-responders ($n = 20$)	Sig.
Demographics				
Age, years, mean±SD	47.4±14.6	45.1±14.2	48.6±11.9	0.412[b]
Median (IQR)	47.0 (38.0–56.0)	46.0 (33.0–55.0)	47.5 (40.0–57.0)	
Gender, *n* (%)				0.616[a]
Male	22 (66.7%)	8 (61.5%)	14 (70.0%)	
Female	11 (33.3%)	5 (38.5%)	6 (30.0%)	
Prior treatment history, *n* (%)				
Treatment-naive	6 (18.2%)	4 (30.8%)	2 (10.0%)	**0.037**[a]
Conventional systemic only	23 (69.7%)	9 (69.2%)	14 (70.0%)	0.956[a]
Conventional+biologic	4 (12.1%)	0 (0.0%)	4 (20.0%)	**0.046**[a]
Baseline disease severity				
Baseline PASI, mean±SD	5.0±4.0	5.9±5.4	4.4±2.6	0.328[b]
Baseline PASI, median (IQR)	4.0 (2.0-6.5)	4.0 (1.9-6.6)	3.8 (2.0-6.0)	0.487[c]
Baseline PASI ≥ 10, *n* (%)	3 (9.1%)	2 (15.4%)	1 (5.0%)	0.347[a]
Early treatment response				
Week 4 PASI response, mean±SD	30.1±41.8	64.6±20.1	9.8±40.2	**0.000**[b]
Week 4 PASI response, median (IQR)	40.0 (16.7–55.3)	67.4 (50.0–80.0)	20.0 (0.0–40.0)	**0.000**[c]
Week 4 PASI 50 response, *n* (%)	12 (36.4%)	11 (84.6%)	1 (5.0%)	**0.000**[a]
Week 12 treatment outcomes				
Week 12 PASI response, mean±SD	31.2±69.4	84.5±10.4	−2.7±70.1	**0.000**[b]
Week 12 PASI response, median (IQR)	52.0 (20.0–75.0)	80.0 (75.0–94.3)	20.0 (−11.1–47.4)	**0.000**[c]
Response categories at week 12				
PASI 90 response	4 (12.1%)	4 (30.8%)	0 (0.0%)	**0.008**[a]
PASI 75 response	13 (39.4%)	13 (100.0%)	0 (0.0%)	**0.000**[a]
PASI 50 response	17 (51.5%)	13 (100.0%)	4 (20.0%)	**0.000**[a]
Negative response (< 0%)	7 (21.2%)	0 (0.0%)	7 (35.0%)	**0.009**[a]
PASI 75 response by prior treatment				
Treatment-naive patients	4/6 (66.7%)	4 (30.8%)	2 (10.0%)	**0.037**[a]
Conventional systemic patients	9/23 (39.1%)	9 (69.2%)	14 (70.0%)	0.956[a]
Conventional+biologic patients	0/4 (0.0%)	0 (0.0%)	4 (20.0%)	**0.046**[a]

[a]χ^2 test or Fisher's exact test for categorical variables; [b]Independent samples *t*-test for normally distributed continuous variables; [c]Mann–Whitney *U* test for non-parametric continuous variables.
Prior treatment: 0 = treatment-naive, 1 = conventional systemic only, 2 = conventional+biologic.
Psoriasis Area and Severity Index (PASI) response = [(Baseline PASI - Current PASI)/Baseline PASI] × 100.
SPSS case processing summary: valid cases: 33 (100.0%), missing cases: 0 (0.0%), total: 33 (100.0%).
Age and PASI variables tested for normality using Shapiro–Wilk test.
SD: standard deviation; IQR: interquartile range. Statistically significant values ($p < 0.05$) are shown in bold.



Area Under the ROC Curve

Test Result Variable(s)	Area
week 4 PASI response	,938

Coordinates of the Curve

Test Result Variable(s): week 4 PASI response

Positive if Greater Than or Equal To	Sensitivity	1 - Specificity
8,3333	1,000	,650
16,6667	1,000	,650
18,3333	1,000	,550
20,0000	1,000	,500
20,5263	1,000	,450
25,4386	1,000	,400
34,1430	1,000	,350
38,9277	1,000	,300
39,6970	1,000	,250
40,5882	,923	,150
43,0882	,846	,150
46,8590	,769	,150
49,3590	,769	,100
52,6316	,538	,100
56,5789	,538	,050
62,6430	,538	,000
67,8226	,462	,000
70,7937	,385	,000
76,6667	,308	,000
81,0615	,231	,000
87,3258	,154	,000
96,2644	,077	,000
101,0000	,000	,000

The test result variable(s): week 4 PASI response has at least one tie between the positive actual state group and the negative actual state group.

Fig. 1. ROC curve analysis for predicting PASI 75 response at week 12 using 4-week PASI response percentage. Area under the ROC curve (AUC) = 0.938, indicating excellent predictive accuracy.

the time patients spend with poor quality of life, and healthcare costs.

Although our single-centre design and limited sample size ($n=33$) restrict generalizability, 97.42% statistical power supports result reliability. Future multicentre, larger-sample studies with apremilast and other conventional treatments will strengthen the clinical utility of early response assessment. This study may advance evidence-based, personalized treatment algorithms in psoriasis management.

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In this article, Claude AI (Anthropic, San Francisco, CA, USA) was used to refine the linguistic expression.

Data are available upon reasonable request due to privacy restrictions.

Previous presentations: Parts of our results will be presented at the Turkish National Dermatology Congress, to be held in Antalya, Turkey, on 22–26 October 2025.

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The authors have no conflicts of interest to declare.

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