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Predictive Factors of Early Super-Response to Biologic Agents in Psoriasis: Insights from Real-World Evidence

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Background/Objectives: The concept of early super-response (ESR) in psoriasis, characterized by rapid and sustained complete skin clearance, has recently gained clinical relevance. However, evidence regarding predictors of ESR remains limited. This study aimed to identify clinical and laboratory factors associated with ESR in patients with psoriasis vulgaris treated with biologics.

Methods: In this retrospective study, 299 patients with psoriasis vulgaris receiving biologic therapy were evaluated. ESR was defined as achieving a PASI 100 response at week 4 and maintaining PASI < 1 through week 48. Demographic, clinical, and laboratory parameters were compared between ESR and non-ESR groups. Variables with $p < 0.1$ in univariate analyses were entered into multivariate logistic regression to identify independent predictors.

Results: Bio-naïve status (OR = 2.16, 95% CI 1.17–3.96, p = 0.013) and higher baseline neutrophil count (OR = 1.26, 95% CI 1.04–1.53, p = 0.016) were independent positive predictors of ESR, while palmoplantar involvement (OR = 0.27, 95% CI 0.13–0.58, p = 0.001) was a strong negative predictor. Smoking (OR = 0.57, 95% CI 0.29–1.11, p = 0.099) showed a borderline negative association, and platelet-to-lymphocyte ratio (PLR) (OR = 1.005, 95% CI 0.999–1.01, p = 0.083) demonstrated a borderline positive effect. At the biologic class level, no statistically significant differences in ESR rates were observed. Moreover, biologic class was not independently associated with ESR in multivariable analyses after adjustment for clinically relevant covariates.

Conclusion: Bio-naïve status and elevated baseline neutrophil count predicted rapid and sustained complete clearance with biologic therapy, whereas palmoplantar involvement impaired early response. These findings emphasize the prognostic role of baseline inflammatory and phenotypic features in guiding personalized psoriasis management.

Keywords: psoriasis vulgaris, biologic therapy, early super-response, predictive biomarkers, systemic inflammation

Introduction

Psoriasis is a chronic inflammatory disease that affects approximately 2–3% of the global population, with prevalence varying across different geographic regions and populations.[1] In about 20% of cases, psoriasis is accompanied by psoriatic arthritis. Moreover, individuals with moderate-to-severe psoriasis have a significantly higher likelihood of developing several comorbid conditions compared to the general population, including cardiovascular and cerebrovascular diseases, type 2 diabetes mellitus, nonalcoholic fatty liver disease, and metabolic syndrome.[2–7]

Recent advances in the immunopathogenesis of psoriasis have revealed that it is not merely a classic Th1-mediated inflammatory disease driven by IFN-γ, but is also closely associated with Th17 and Th22 immune responses. Pro-inflammatory cytokines produced by T cells—including IL-17, IL-21, IL-22, and IFN-γ—together with dendritic cell–derived cytokines such as TNF-α, IL-6, IL-20, and IL-23, as well as antimicrobial peptides and chemokines secreted by keratinocytes, all play crucial roles in psoriasis pathogenesis. A pathogenic triad consisting of IL-23-producing dendritic cells, IL-17-secreting Th17 cells, and activated keratinocytes forms the central axis of psoriatic inflammation. Targeting

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these key pathways with biologic agents directed against TNF-α, IL-17, and IL-23, which also suppress systemic inflammation, has revolutionized the treatment of psoriasis.[8–10] Among clinical parameters influencing the achievement of a PASI 90 response at month 6 with biologic therapy, prior biologic exposure, older age, higher body mass index, and current or past smoking have been identified as negative predictors of treatment outcomes.[11] Findings from studies investigating laboratory parameters predictive of treatment response have been inconsistent, and to date, no universally accepted biomarker has been established in this regard.

In recent years, the rapidity and sustainability of clinical response to biologic therapies have gained increasing importance, leading to the emergence of the concept of "super-response". However, a clear consensus on the definition of super-response has yet to be established. While some authors have defined it as achieving a PASI 100 response at weeks 16, 20, 24, or 28, others have proposed alternative definitions, such as reaching a PASI score below 1 or 2 at similar time points.[12–17] In addition, certain definitions also include the maintenance of this response through weeks 48 or 52.[15–17] In addition to these definitions, in recent years, an even more challenging concept—early super-response—has been introduced, referring to achieving a PASI 100 response as early as week 4 and, according to some authors, maintaining this response up to week 48.[17–19]Importantly, predictors of early super-response should be conceptually distinguished from predictors of overall treatment response, as they reflect not only the magnitude but also the rapidity of clinical improvement. Several studies have identified early treatment response as a strong predictor of long-term efficacy, as a potential indicator for identifying patients eligible for dose modification and long-term drug survival.[16,17,20–22] Therefore, the identification of clinical and laboratory markers capable of predicting early super-response would help to determine both patients who are likely to maintain a long-term response and those who may benefit from individualized dose adjustments. Moreover, improving modifiable factors could potentially increase the proportion of patients achieving this response.

This study aimed to identify predictive biomarkers by comparing the clinical and laboratory characteristics of patients with psoriasis vulgaris who achieved an early super-response to biologic therapy with those who did not.

Materials and Methods

Population and Study Design

This real-life, retrospective, single-center study was conducted at the Department of Dermatology and Venereology, Uşak University, and included adult patients (≥18 years) who received standard-dose biologic therapy with an anti-TNF, anti–IL-12/23, anti–IL-17, or anti–IL-23 agent between June 2020 and January 2025. Eligible patients had moderate-to-severe psoriasis, defined as a Psoriasis Area and Severity Index (PASI) >10 and an inadequate response or contraindication to conventional systemic therapies, or a PASI ≤10 with involvement of at least one sensitive area. Patients were required to have continued the initiated biologic therapy for at least 48 weeks to be included in the study. Demographic and clinical data, including age, sex, disease duration, age at disease onset, baseline PASI, family history of psoriasis, presence of comorbidities such as psoriatic arthritis (PsA), type 2 diabetes mellitus, hypertension, dyslipidemia, coronary artery disease, and nonalcoholic fatty liver disease, body mass index (BMI), obesity (defined as BMI ≥ 30 kg/cm2), current or past smoking status, previously used systemic and/or biologic therapies, bio-naïvety, the type and duration of the current biologic agent, and the presence of scalp, genital, inverse, palmoplantar, or nail involvement (defined as special area involvement), were obtained from patients' medical files and electronic health records.

Exclusion criteria included age <18 years, pregnancy, follow-up duration of less than 48 weeks, absence of PASI assessment at week 4, presence of guttate, erythrodermic, or pustular psoriasis, concomitant use of other immunosuppressive therapies, and lack of baseline demographic data, hemogram results, or C-reactive protein (CRP) values prior to treatment initiation. At week 4 of the current biologic therapy (ie, after the first injection), patients who achieved a PASI 100 response and maintained a PASI score of <1 at week 48 were classified as "early super-responders (ESR)". The remaining patients were categorized as "non–early super-responders (nESR)".

Both groups were compared in terms of baseline demographics, clinical, and laboratory characteristics. Laboratory parameters compared between the groups included CRP, neutrophil count, and several hemogram-derived inflammatory indices, namely the neutrophil-to-lymphocyte ratio (NLR), derived NLR (d-NLR), systemic immune–inflammation index

(SII), systemic inflammation response index (SIRI), aggregate index of systemic inflammation (AISI), and platelet-to-lymphocyte ratio (PLR). The hemogram-derived inflammatory indices were calculated using the following formulas: NLR = neutrophil count/lymphocyte count; d-NLR = neutrophil count/(white blood cell count – neutrophil count); PLR = platelet count/lymphocyte count; SII = (neutrophil count × platelet count)/lymphocyte count; SIRI = (neutrophil count × monocyte count)/lymphocyte count; AISI = (neutrophil count × platelet count × monocyte count)/lymphocyte count; and PLR = platelet count/lymphocyte count.

Approval for the study was obtained from the Non-Interventional Clinical Research Ethics Committee of Uşak University Faculty of Medicine (approval date and number: 11.09.2025/830–830-19).

Statistical Analysis

Statistical analyses were performed using IBM SPSS Statistics version 23.0 (IBM Corp., Armonk, NY, USA). The Kolmogorov–Smirnov or Shapiro–Wilk tests were used to assess the normality of data distribution. Continuous variables were expressed as median with interquartile range (IQR), and categorical variables as frequencies and percentages. Between-group comparisons of quantitative variables were conducted using the Mann–Whitney *U*-test or the independent-samples *t* test, as appropriate. Categorical variables were compared using the chi-square test or Fisher's exact test, when applicable. Univariate logistic regression analysis was performed for disease duration, baseline PASI score, presence of PsA, family history of psoriasis, presence of obesity, special site involvement, scalp, genital, inverse, palmoplantar, and nail involvement, smoking status, bio-naïve status, and laboratory parameters including CRP, neutrophil count, NLR, d-NLR, SII, SIRI, AISI and PLR. All variables with $p < 0.1$ in the univariate analysis were considered for inclusion in the multivariate logistic regression model to identify the most suitable predictive model for early super response. Special area involvement and SIRI were not included due to their conceptual and statistical overlap with palmoplantar involvement and neutrophil count, respectively, both of which showed stronger significance levels. A p-value of <0.05 was considered statistically significant.

Results

Baseline Demographic and Clinical Characteristics

Of the 299 patients included in the study, 172 (57.5%) were male. The mean age was 50.54 ± 15.23 years, the median age at disease onset was 30 years (IQR 24), and the median disease duration was 17 years (IQR 16). Before initiation of their current treatment, the mean baseline PASI score was 13.3 ± 7.27. A total of 192 patients (64.2%) had at least one special area involvement, the most frequently affected being the scalp (47%, n = 142). The median BMI, calculated for 135 patients, was 27.8 (IQR 6.3), and 41 of them (30.4%) were obese. PsA was present in 102 patients (34.1%), a family history of psoriasis in 62 (20.7%), and a current or past history of smoking in 64 (21.4%). The most common comorbidities were hypertension (16.1%), type 2 diabetes mellitus (14.7%), and coronary artery disease (8%).

Among conventional systemic therapies, methotrexate was the most frequently used agent (89.6%, n = 268). A total of 208 patients (69.6%) were bio-naïve. Among bio-experienced patients, secukinumab was the most commonly used previous biologic (n = 32, 10.7%). At the time of data collection, 143 patients (47.8%) were receiving anti–IL-17 agents (secukinumab, ixekizumab, or bimekizumab), 139 (46.5%) were on anti–IL-23 therapy (guselkumab or risankizumab), 14 (4.7%) were on anti-TNF therapy (adalimumab or certolizumab), and 3 (1.0%) were on anti–IL-12/23 therapy (ustekinumab). The median duration of current biologic treatment was 104 weeks (IQR 75), and 228 patients (76.3%) were classified as early super responders. The demographic and clinical characteristics of the patients are summarized in Table 1.

Comparison of Early Super-Responders and Non-Early Super-Responders

There were no statistically significant differences between the two groups in terms of demographic and clinical characteristics, including age, sex, disease duration, age at disease onset, baseline PASI score, BMI, obesity, presence of concomitant PsA, family history of psoriasis, comorbidities (hypertension, type 2 diabetes, coronary artery disease, dyslipidemia, and non-alcoholic steatohepatitis), presence of any special area involvement, or the category of current

Table 1 Baseline Demographic and Clinical Characteristics of the Patients

Number of Patients	299
Gender, n (%)	
Female	127 (42.5)
Male	172 (57.5)
Age (year), mean ± SD	50.54 ± 15.232
Disease duration (year), median (IQR)	17 (16)
Age of disease onset (year), median (IQR)	30 (24)
Baseline PASI, mean ± SD	13.3 ± 7.27
Special area involvement n (%)	192 (64.2)
Scalp	142 (47.5)
Nail	91 30.4)
Genital	50 (16.7)
Palmo-plantar	36 (12)
Inverse	9 (3)
Psoriatic arthritis, n (%)	102 (34.1)
Co-morbidities, n (%)	
Hypertension	48 (16.1)
Type 2 diabetes mellitus	44 (14.7)
Coronary artery disease	24 (8)
Dyslipidemia	21 (7)
Non-alcoholic steatohepatitis	9 (3)
Current/past smoking, n (%)	64 (21.4)
Family history of psoriasis, n (%)	62 (20.7)
Bio-naïve status, n (%)	208 (69.6)
Previous treatments, n (%)	
Conventional treatments	
Methotrexate	268 (89.6)
Acitretin	113 (37.8)
Cyclosporine	51 (17.1)
Phototherapy	8 (2.7)
Apremilast	7 (2.3)
Biologic agents	
Adalimumab	19 (6.4)
Etanercept	4 (1.3)
Infliximab	2 (0.7)
Certolizumab pegol	6 (2)
Ustekinumab	20 (6.7)
Secukinumab	32 (10.7)
Ixekizumab	13 (4.3)
Guselkumab	7 (2.3)
Risankizumab	4 (1.3
Current treatment, n (%)	
Anti TNF-α	14 (4.6)
Adalimumab	7 (2.3)

(*Continued*)

Table 1 (Continued).

Certolizumab pegol	7 (2.3)
Anti IL-12/23 (Ustekinumab)	3 (1)
Anti IL-17	143 (48.8)
Secukinumab	92 (30.7)
Ixekizumab	49 (16.3)
Bimekizumab	2 (0.6)
Anti IL-23	139 (45.5)
Guselkumab	57 (19)
Risankizumab	82 (27.4)
Early super-responder status, n (%)	228 (76.3)

Abbreviations: SD, standard Deviation; IQR, Interquartile Range; PASI, Psoriasis Area and Severity Index; TNF, Tumor Necrosis alpha; IL, Interleukin.

treatment. When special area involvement was analyzed by subgroups, palmoplantar involvement was significantly more frequent in the nESR group compared with the ESR group (25.4% vs. 7.9%, $p < 0.001$, Figure 1). In addition, 73.7% of the ESR patients were bio-naïve, which was significantly higher than the proportion observed in the nESR group (56.3%, $p = 0.006$, Figure 2). Current/past smoking history was more frequent in the nESR group, showing a trend toward statistical significance ($p= 0.055$). Although there was no categorical difference between the two groups regarding the class of biologic agents currently used (anti-TNF, anti–IL-12/23, anti–IL-17, or anti–IL-23), ixekizumab use was significantly more frequent among ESR patients compared to nESR patients (19.3% vs. 7.0%, $p = 0.015$). Similarly, the proportion of patients receiving risankizumab was higher in the ESR group compared to the nESR group; however, this difference was not statistically significant (29.8% vs. 19.7%, $p = 0.096$). The rates of secukinumab use were comparable between the two groups (29.8% vs. 33.8%, $p = 0.526$). Conversely, guselkumab use was more common in the nESR group (28.1%) than in the ESR group (16.2%), and this difference was also statistically significant ($p = 0.025$).

There were no statistically significant differences between the two groups in median CRP, NLR, d-NLR, SII, or AISI values. However, the ESR group had significantly higher median neutrophil counts, SIRI, and PLR values compared to the nESR group ($p = 0.046$, 0.05, 0.005, respectively). The demographic and clinical parameters of both groups presented in Table 2.

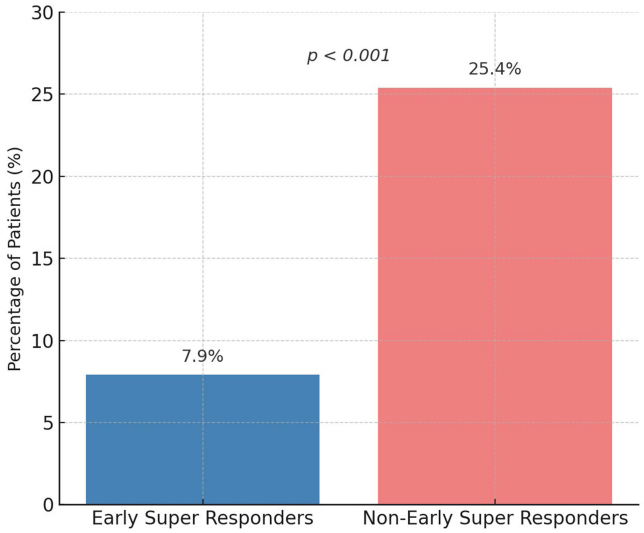

Figure 1 Comparison of palmoplantar involvement between early super-responders and non–early super-responders. Bars represent the proportion of patients (%) in each group. Palmoplantar involvement was significantly less frequent among early super-responders compared with non–early super-responders ($p < 0.001$).

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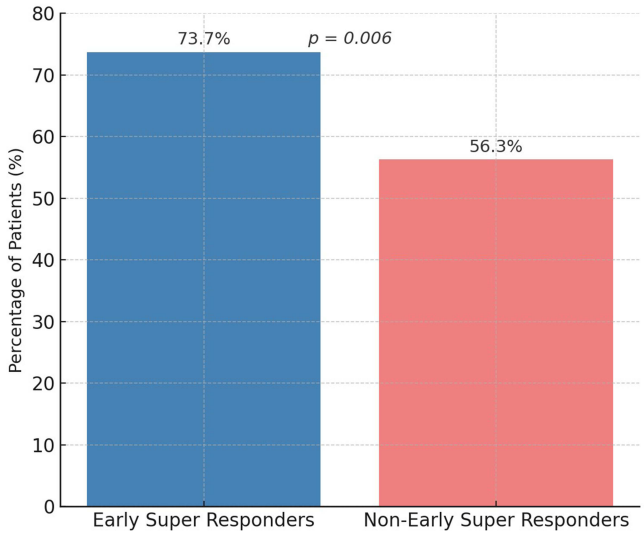

Figure 2 Comparison of biologic-naïve status between early super-responders and non–early super-responders. Bars represent the proportion of patients (%) in each group. Biologic-naïve status was significantly more common among early super-responders (p = 0.006).

Predictors of Early Super-Response

In the univariate logistic regression analysis, bio-naïve status, palmoplantar involvement, neutrophil count, and PLR were significantly associated with early super response to biologic therapy. Bio-naïve patients were more likely to achieve an early super response (OR: 2.171, 95% CI: 1.247–3.780, $p = 0.006$), whereas the presence of palmoplantar involvement

Table 2 Comparison of Baseline Demographic, Clinical, and Laboratory Characteristics Between Early Super-Responders (ESR) and Non–Early Super-Responders (nESR)

Parameter	ESR n=228	nESR n=71	*p* value
Gender (male), n (%)	132 (57.9)	40 (56,3)	0.817
Age (year), mean ± SD	48.28 ± 13.94	49.9 ± 14.54	0.397
Disease duration (year), median (IQR)	19 (17)	11 (18)	0.499
Age of disease onset (year), median (IQR)	28 (24)	33.5 (24.25)	0.342
Baseline PASI, mean ± SD	14.19 ± 6.9	12.99 ± 6.88	0.206
Special area involvement n (%)	140 (61.4)	52 (73.2)	0.206
Scalp	110 (48.2)	32 (45.1)	0.640
Nail	69 (30.3)	22 (31)	0.908
Genital	41 (18)	9 (12.7)	0.295
Palmo-plantar	18 (7.9)	18 (25.4)	**0.000**
Inverse	8 (3.5)	1 (1.4)	0.091
Psoriatic arthritis, n (%)	80 (35.1)	22 (31)	0.524
Co-morbidities, n (%)			
Hypertension	37 (16.2)	11 (15.5)	0.883
Type 2 diabetes mellitus	30 (13.2)	14 (19.7)	0.173
Coronary artery disease	20 (8.8)	4 (5.6)	0.395
Dyslipidemia	16 (7)	5 (7)	0.173
Non-alcoholic steatohepatitis	8 (3.5)	1 (1.4)	0.691

(*Continued*)

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Table 2 (Continued).

Parameter	ESR n=228	nESR n=71	*p* value
BMI (kg/cm^2), median (IQR)	27.9 (6.7)	27.75 (4.9)	0.900
Current/past smoking, n (%)	43 (18.9)	21 (29.6)	**0.055**
Family history of psoriasis, n (%)	49 (21.5)	13 (18.3)	0.564
Bio-naïve status, n (%)	168 (73.7)	40 (56.3)	**0.006**
Current treatment, n (%)			0.316
Anti TNF-α	8 (3.5)	6 (8.5)	0.085
Adalimumab	4 (1.8)	3 (4.2)	0.363
Certolizumab pegol	4 (1.8)	3 (4.2)	0.363
Anti IL-12/23 (Ustekinumab)	2 (0.9)	1 (1.4)	0.558
Anti IL-17	112 (49.1)	31 (42.3)	0.311
Secukinumab	68 (29.8)	24 (33.8)	0.526
Ixekizumab	44 (19.3)	5 (7)	**0.015**
Bimekizumab	0 (0.0)	2 (2.8)	0.056
Anti IL-23	105 (46)	34 (47.9)	0.837
Guselkumab	37 (16.2)	20 (28.1)	**0.025**
Risankizumab	68 (29.8)	14 (19.7)	0.096
CRP (mg/dL), median (IQR)	2.3 (4.4)	2.94 (3.9)	0.845
Neutrophil count (x10^3/μL), median (IQR)	4.17 (2.79)	4.14 (2.3)	**0.046**
NLR, median (IQR)	1.955 (0.996))	1.740 (0.893)	0.226
d-NLR, median (IQR)	1.52 (0.78)	1.38 (0.63)	0.390
SII, median (IQR)	446.42 (301.02)	429.91 (344.24)	0.582
SIRI, median (IQR)	0.86 (0.60)	0.83 (0.59)	**0.05**
AISI, median (IQR)	190.19 (205.73)	183.46 (257.29)	0.233
PLR, median (IQR)	90.83 (101.99)	30.30 (67.29)	**0.005**

Note: Bold values indicate statistically significant *p* values ($p < 0.05$).
Abbreviations: SD, Standard Deviation; IQR, Interquartile Range; PASI, Psoriasis Area and Severity Index; BMI, Body Mass Index; TNF, Tumor Necrosis alpha; IL, Interleukin; CRP, C-Reactive Protein; NLR, Neutrophil-to-Lymphocyte Ratio; d-NLR, derived Neutrophil-to-Lymphocyte Ratio; SII, Systemic Immune–Inflammation Index; SIRI, Systemic Inflammation Response Index; AISI, Aggregate Index Of Systemic Inflammation; PLR, Platelet-to-Lymphocyte Ratio.

was negatively associated with this outcome (OR: 0.252, 95% CI: 0.123–0.518, $p < 0.000$). Higher neutrophil count (OR: 1.199, 95% CI: 1.007–1.428, $p = 0.041$) and elevated PLR (OR: 1.006, 95% CI: 1.001–1.011, $p = 0.030$) were also significant predictors of super response in the univariate model.

In the multivariate analysis, after adjustment for confounders, bio-naïve status remained an independent positive predictor (OR: 2.16, 95% CI: 1.17–3.96, $p = 0.013$), whereas palmoplantar involvement persisted as a strong negative predictor (OR: 0.27, 95% CI: 0.13–0.58, $p = 0.001$). Neutrophil count also retained significance (OR: 1.26, 95% CI: 1.04–1.53, $p = 0.016$), while PLR showed a borderline association (OR: 1.005, 95% CI: 0.999–1.01, $p = 0.083$). Smoking demonstrated a borderline inverse association with super response in the multivariate model (OR: 0.57, 95% CI: 0.29–1.11, $p = 0.099$), suggesting a potential negative but non-significant effect (Table 3 and Figure 3). Although biologic class was entered into the multivariate logistic regression model, no statistically significant independent association with super-response was observed.

Table 3 Univariate and Multivariate Logistic Regression Analyses of Predictors for Early Super-Response to Biologic Therapy in Psoriasis Patients

	Univariate Logistic Regression Analysis		Multivariate Logistic Regression Analysis	
	OR (95% CI)	***p***	**OR (95% CI)**	***p***
Disease duration	1.006 (0.983–1.029)	0.618	–	–
Baseline PASI	1.026 (0.986–1.068)	0.206	–	–
PsA	1204 (0.680–2.133)	0.525	–	–
Bio-naïve status	2.171 (1.247–3.780)	**0.006**	2.16 (1.17–3.96)	**0.013**
Biologic class		0.34*	-Reference	0.630*
Anti-TNF	Reference	-	1.99 (0.15–25.73)	-
Anti IL-12/23	1.56 (0.14–17.73)	0.720	2.21 (0.17–28.37)	0.597
Anti IL-17	1.87 (0.16–21.29)	0.615	1.06 (0.07–16.62)	0.544
Anti IL-23	0.67 (0.05–9.19)	0.762	-	0.968
Family history	1.221 (0.619–2.409)	0.564	-	-
BMI	1.013 (0.941–1.090)	0.734	-	-
Special area involvement	0.581 (0.322–1.048)	**0.071**	0.27 (0.13–0.58)	-
Palmoplantar involvement	0.252 (0.123–0.518)	**0.000**	-	**0.001**
Scalp involvement	1.136 (0.666–1.940)	0.640	-	-
Inverse psoriasis	2.545 (0.313–20.707)	0.382	-	-
Genital psoriasis	1.510 (0.695–3.284)	0.298	-	-
Nail involvement	0.967 (0.543–1.721)	0.908	0.57 (0.29–1.11)	-
Smoking	0.553 (0.301–1.017)	**0.057**	-	0.099
CRP	1.009 (0.982–1.036)	0.529	1.26 (1.04–1.53)	-
Neutrophil count	1.199 (1.007–1.428)	**0.041**	-	**0.016**
NLR	1.258 (0.927–1.707)	0.140	-	-
d-NLR	1.289 (0.866–1.918)	0.211	-	-
SII	1.000 (0.999–1.001)	0.484	-	-
SIRI	1.447 (0.942–2.221)	**0.091**	-	-
AISI	1.000 (0.999–1.001)	0.567	1.005 (0.999–1.01)	-
PLR	1.006 (1.001–1.011)	**0.030**		0.083

Note: Bold values indicate p values ($p < 0.1$). *overall *p*.

Abbreviations: OR, Odds Ratio; CI, Confidence Interval; PsA, Psoriatic Arthritis; TNF, Tumor Necrosis alpha; IL, Interleukin; BMI, body mass index; CRP, C-Reactive Protein; NLR, Neutrophil-to-Lymphocyte Ratio; d-NLR, derived Neutrophil-to-Lymphocyte Ratio; SII, Systemic Immune–Inflammation Index; SIRI, Systemic Inflammation Response Index; AISI, Aggregate Index Of Systemic Inflammation; PLR, Platelet-to-Lymphocyte Ratio.

Discussion

In this study, certain demographic, clinical, and laboratory parameters were found to influence both the achievement of a PASI 100 response at week 4 and the maintenance of a PASI score < 1 up to week 48. Among these, bio-naïve status, absence of palmoplantar involvement, and higher baseline neutrophil count emerged as independent predictors of early super-response (ESR). In contrast, current/past smoking history showed a borderline negative association, whereas a higher platelet-to-lymphocyte ratio (PLR) demonstrated a borderline positive association with achieving this response.

In the literature, particularly in studies evaluating patients treated with guselkumab, the term "super-response" has been introduced to describe patients achieving a PASI 100 response at weeks 20 or 28. In these studies, bio-naïve patients were significantly more likely to achieve this response, whereas bio-experienced status was identified as an independent negative predictor of super-response.[12,13,16,23] In another study assessing plaque psoriasis patients treated with brodalumab, prior exposure to three or more systemic agents, including biologics, was found to negatively influence the likelihood of achieving a super-response defined achieving PASI ≤ 1 at week 12/16.[24] Similar to our study, bimekizumab trials that defined achieving PASI 100 at week 4 as an indicator of early super-response have also identified bio-naïve status as a positive predictor of this outcome.[18,19] Similar findings have also been reported in a cohort of patients treated with ixekizumab, secukinumab, ustekinumab, adalimumab, and guselkumab.[17] In our study as well, bio-naïve status was

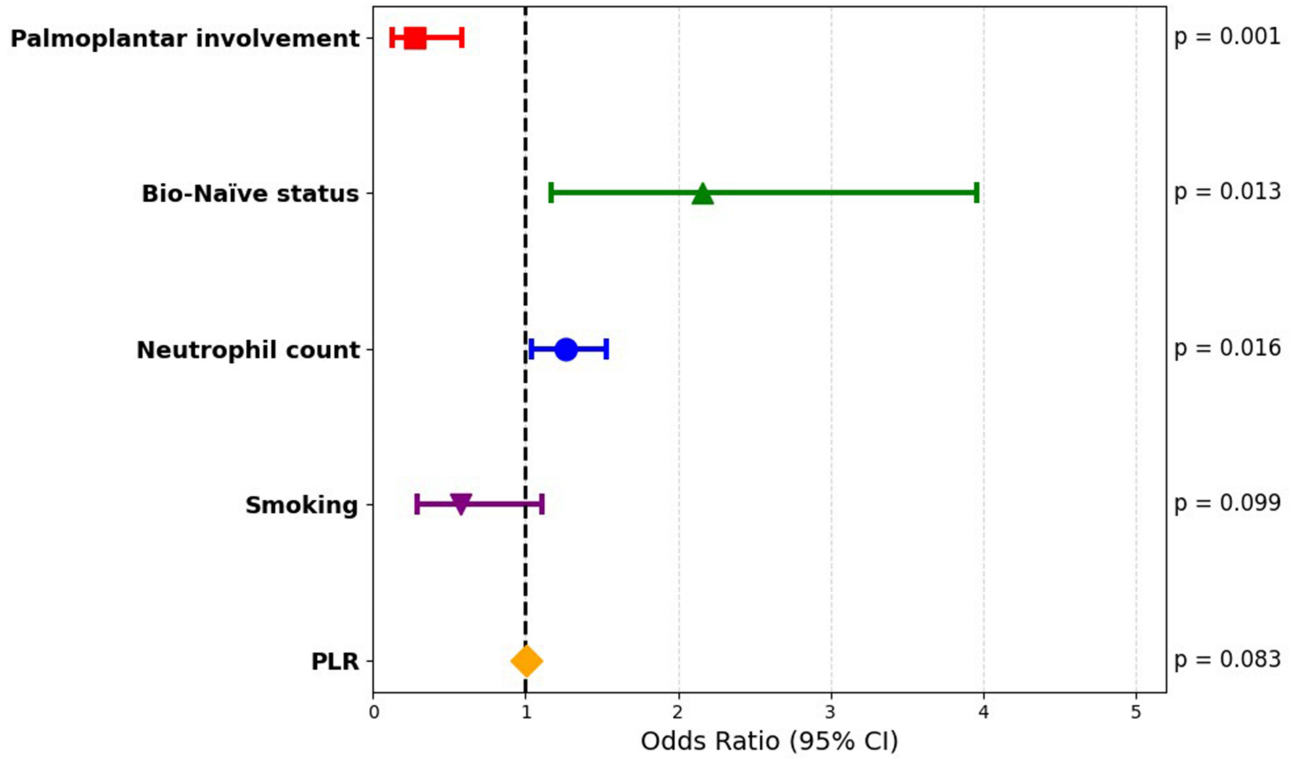

Figure 3 Forest plot showing adjusted odds ratios (ORs) with 95% confidence intervals derived from multivariate logistic regression analysis for predictors of early super-response to biologic therapy in patients with psoriasis. The vertical dashed line indicates the null value (OR = 1). Variables are ordered according to effect size. Predictors with borderline statistical significance are presented for completeness and should be interpreted with caution. Red squares indicate palmoplantar involvement, green triangles indicate bio-naïve status, blue circles indicate neutrophil count, purple inverted triangles indicate smoking status, and Orange diamonds indicate PLR (platelet to lymphocyte ratio).

identified as a strong predictive factor for early super-response, consistent with and supporting the findings of previous studies in the literature.

ESR has been primarily evaluated in the context of anti–IL-17 inhibitors, particularly bimekizumab, and to our knowledge no studies to date have directly compared IL-17 and IL-23 inhibitors with respect to this parameter.[18,19] In a study where patients achieving a PASI $\leq$ 1 response at week 16 and maintaining it through weeks 28 and 52 were classified as super-responders, no significant difference was observed among anti–IL-23 agents including risankizumab, guselkumab, and tildrakizumab.[15] In our study as well, no significant difference was detected among biologic agent classes (anti–IL-17, anti–IL-23, anti–IL-12/23, and anti-TNF) in terms of achieving an ESR. However, when individual biologic agents were analyzed separately, the proportion of patients achieving ESR was significantly higher in the ixekizumab group, whereas the opposite trend was observed in the guselkumab group. Although both guselkumab and risankizumab have demonstrated strong efficacy in moderate-to-severe psoriasis, literature on "early super-response" is limited. In our cohort, guselkumab showed lower rates of early super-response, and for risankizumab no statistically significant difference was noted, which may reflect the scarcity of studies using such an aggressive early endpoint for IL-23 inhibitors. To our knowledge, early super-response has not been directly compared between ixekizumab and secukinumab in head-to-head studies; most pivotal trials reported early clearance separately for each agent, with ixekizumab studies placing greater emphasis on very early responses.[20,25,26]

The involvement of special areas, which are known to be difficult-to-treat regions, is one of the key factors influencing therapeutic decision-making in psoriasis. In most studies investigating super-response, the potential impact of special area involvement has not been specifically evaluated.[12,14,16,22,24] A few available studies have reported no significant association between special area involvement and super-response.[15,23] However, in a study assessing factors influencing the response to biologic agents and small molecules, scalp involvement was found to negatively affect the likelihood of achieving a PASI 100 response at month 6.[27] In another study evaluating super-response to guselkumab

(defined as PASI 100 at weeks 20/28), patients who achieved a super-response had less frequent nail involvement compared to non-responders.[13] In one of the studies evaluating early super-response, the presence of nail involvement was likewise identified as a negative predictor.[18] In our study, although there was no overall difference in special area involvement between the ESR and nESR groups, palmoplantar involvement was found to be significantly higher in the nESR group and emerged as a strong negative predictor of early super-response. Consistent with our findings, a study assessing bimekizumab response reported that palmoplantar involvement not only negatively affected the PASI 100 response at week 4, but was also associated with lower PASI 75 and PASI 90 responses at the same time point.[19]

In our study, a history of current or past smoking was nearly significantly higher in the nESR group and was identified as a borderline negative predictor of achieving an early super-response in the multivariate regression analysis. Although smoking has been recognized as a negative determinant of treatment response to biologic agents at month 6, it has rarely been addressed as a parameter in studies predicting super-response or early super-response.[11,28] In a study that employed a terminology similar to ours for defining ESR, current or past smoking history was likewise found to be significantly more frequent among ESR patients, consistent with our findings.[17]

In recent years, several complete blood count-derived parameters have been identified as biomarkers reflecting systemic inflammation. Although not all studies have demonstrated consistent associations for each parameter, it has been shown that neutrophil count, NLR, PLR and SII levels are significantly higher in patients with psoriasis compared to healthy controls, correlate with disease activity, and decrease significantly following biologic therapy.[29–31] In our study, the ESR group showed higher baseline neutrophil counts, PLR, and SIRI levels compared to the nESR group. In the multivariate regression analysis, elevated baseline neutrophil count retained its positive predictive value, while PLR was identified as a borderline positive predictor of early super-response. Other neutrophil-related markers were not included in the analysis due to their strong correlations with neutrophil count. These findings suggest that a higher baseline inflammatory state may be associated with a more rapid treatment response. In studies evaluating super-response or early super-response to biologic therapies in psoriasis, these parameters have not been widely emphasized. However, a study assessing PASI 100 response at month 6 reported that elevated baseline d-NLR and SIRI levels were independent predictors of super-response, partially supporting our findings. Conversely, another study evaluating early super-response found that NLR was lower in the responder group.[17] Consequently, although a higher inflammatory burden at baseline may indicate a phenotype more responsive to targeted biologic therapy, this should be interpreted in the context of other clinical factors, and this association should therefore be interpreted with caution.

The limitations of our study include its retrospective design, the lack of restriction or standardized recording regarding concurrent topical therapy during biologic treatment, and the absence of an evaluation of the impact of early super-response on drug survival. The requirement for complete 48-week follow-up data may have introduced selection bias, since patients discontinuing biologic therapy due to primary or secondary inefficacy were excluded, potentially leading to an underrepresentation of non–early super-responders.

Conclusion

In this real-world study, bio-naïve status and higher baseline neutrophil count were identified as strong positive predictors of early super-response to biologic therapy, while palmoplantar involvement emerged as a negative predictor. These findings suggest that baseline systemic inflammation and disease phenotype may influence the rapidity of clinical response. Observations related to individual biologic agents should be considered exploratory and hypothesis-generating, as the study was not powered or designed to draw definitive comparative conclusions at the agent level. Further prospective studies are warranted to validate these predictors and to explore their potential role in optimizing personalized treatment strategies for patients with psoriasis.

Artificial Intelligence/Digital Assistance Statement

The authors confirm that ChatGPT (OpenAI) was employed solely for language editing purposes and that all scientific content was developed by the authors.

Data Sharing Statement

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

Ethical Statement

Approval for the study was obtained from the Non-Interventional Clinical Research Ethics Committee of Uşak University (approval date and number: 11.09.2025/830-830-19). Due to the retrospective design of the study, which involved only the review of existing medical records, the requirement for informed patient consent was waived by the ethics committee. All patient data were anonymized and handled in accordance with data confidentiality principles. The study was conducted in compliance with the Declaration of Helsinki.

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

Sema Koç Yıldırım has received speaker honoraria from AbbVie, Novartis, Janssen, and UCB Pharma. Neslihan Demirel Öğüt has received speaker honoraria and has served on advisory boards for AbbVie, UCB Pharma, Janssen, Lilly, Novartis, Sanofi, and Pfizer. Ece Erbağcı has received speaker honoraria from AbbVie and Novartis. Simge Ünal has received speaker honoraria from AbbVie, Janssen, and UCB Pharma. Ece Gökyayla has received speaker honoraria from AbbVie and Janssen. The authors declare no other conflicts of interest related to this work.

References

1. Parisi R, Iskandar IYK, Kontopantelis E, Augustin M, Griffiths CEM, Ashcroft DM. National, regional, and worldwide epidemiology of psoriasis: systematic analysis and modelling study. *BMJ*. 2020;369:m1590. doi:10.1136/BMJ.M1590
2. Alinaghi F, Calov M, Kristensen LE, et al. Prevalence of psoriatic arthritis in patients with psoriasis: a systematic review and meta-analysis of observational and clinical studies. *J Am Acad Dermatol*. 2019;80(1):251–265.e19. doi:10.1016/J.JAAD.2018.06.027
3. Tang X, Chen L. The risk of organ-based comorbidities in psoriasis: a systematic review and meta-analysis. *An Bras Dermatol*. 2022;97(5):612–623. doi:10.1016/J.ABD.2021.10.007
4. Zhang L, Wang Y, Qiu L, Wu J. Psoriasis and cardiovascular disease risk in European and East Asian populations: evidence from meta-analysis and Mendelian randomization analysis. *BMC Med*. 2022;20(1):421. doi:10.1186/S12916-022-02617-5
5. Li Z, Gu Z, Xiang J, Zhang X. The incidence of metabolic syndrome in psoriasis patients and its correlation with disease activity: a systematic review and meta-analysis. *Front Med Lausanne*. 2025;12:1593003. doi:10.3389/FMED.2025.1593003
6. Patrick MT, Stuart PE, Zhang H, et al. Causal relationship and shared genetic loci between psoriasis and type 2 diabetes through trans-disease meta-analysis. *J Invest Dermatol*. 2020;141(6):1493. doi:10.1016/J.JID.2020.11.025
7. Bellinato F, Gisondi P, Mantovani A, Girolomoni G, Targher G. Risk of non-alcoholic fatty liver disease in patients with chronic plaque psoriasis: an updated systematic review and meta-analysis of observational studies. *J Endocrinol Invest*. 2022;45(7):1277. doi:10.1007/S40618-022-01755-0
8. Sieminska I, Pieniawska M, Grzywa TM. The immunology of psoriasis—current concepts in pathogenesis. *Clin Rev Allergy Immunol*. 2024;66(2):164. doi:10.1007/S12016-024-08991-7
9. Sbidian E, Chaimani A, Garcia-Doval I, et al. Systemic pharmacological treatments for chronic plaque psoriasis: a network meta-analysis. *Cochrane Database Syst Rev*. 2022;2022(5):CD011535. doi:10.1002/14651858.CD011535.PUB5
10. Lebwohl MG, Carvalho A, Asahina A, et al. Biologics for the treatment of moderate-to-severe plaque psoriasis: a systematic review and network meta-analysis. *Dermatol Ther*. 2025;15(7):1633. doi:10.1007/S13555-025-01423-0
11. Hjort G, Schwarz CW, Skov L, Loft N. Clinical characteristics associated with response to biologics in the treatment of psoriasis: a meta-analysis. *JAMA Dermatol*. 2024;160(8):830. doi:10.1001/JAMADERMATOL.2024.1677
12. Mortato E, Talamonti M, Marcelli L, et al. Predictive factors for super responder status and long-term effectiveness of guselkumab in psoriasis: a multicenter retrospective study. *Dermatol Ther*. 2025;15(5):1239–1250. doi:10.1007/S13555-025-01394-2
13. Schäkel K, Reich K, Asadullah K, et al. Early disease intervention with guselkumab in psoriasis leads to a higher rate of stable complete skin clearance (‘clinical super response’): week 28 results from the ongoing phase IIIb randomized, double-blind, parallel-group, GUIDE study. *J Eur Acad Dermatol Venereol*. 2023;37(10):2016–2027. doi:10.1111/JDV.19236
14. Menéndez Sánchez M, Muñiz de Lucas A, Pérez Fernández E, Llamas Velasco M, Ruiz Genao DP, López Estébaranz JL. Super-responders in psoriasis under interleukin 23 inhibitor treatments, experience in two centres. *J Eur Acad Dermatol Venereol*. 2023;37(11):e1321–e1322. doi:10.1111/JDV.19310
15. Di Giulio S, Falcidia C, Foggi G, et al. Predictors of super-responder status to Anti-IL-23 therapies in moderate-to-severe plaque psoriasis: a real-world monocenter study. *J Clin Med*. 2025;14(18). doi:10.3390/JCM14186371

16. Herranz-Pinto P, Alonso-Pacheco ML, Feltes-Ochoa R, et al. Real-world Performance of a new strategy for off-label use of guselkumab in moderate to severe psoriasis: super-responder patients as the epitome of efficacy and optimisation. *Clin Drug Investig*. 2023;43(7):517–527. doi:10.1007/S40261-023-01280-9
17. Liu Y, Hu K, Duan Y, Chen X, Zhang M, Kuang Y. Characterization and treatment outcomes of biologic therapy in super-responders and biologic-refractory psoriasis patients: a single-center retrospective study in China. *J Am Acad Dermatol*. 2025;93(1):46–54. doi:10.1016/j.jaad.2025.02.063
18. Fratton Z, Bighetti S, Bettolini L, et al. Real-world experience of bimekizumab in a cohort of 109 patients over 48 weeks and identification of predictive factors for an early super response and risk of adverse events. *Psoriasis*. 2025;15:145–158. doi:10.2147/PTT.S514249
19. Çetinarslan T, Mergen MA, Türel Ermertcan A, et al. Predictive factors for early super response to bimekizumab in 341 patients with psoriasis-a 24-week short-term multicenter real-life experience. *J DermatolTreat*. 2025;36(1):2563657. doi:10.1080/09546634.2025.2563657
20. Augustin M, Gallo G, See K, et al. Early response is associated with stable long-term response in psoriasis patients receiving ixekizumab or ustekinumab. *J Drugs Dermatol*. 2022;21(2):122–126. doi:10.36849/JDD.6063
21. Akdogan N, Mutlu ÖK, Karabulut E, Yalici-Armagan B, Gulseren D, Dogan Gunaydın S. Early response is a strong predictor of the long-term response in psoriasis patients receiving risankizumab or guselkumab in the real-world: a retrospective analysis. *Expert Rev Clin Pharmacol*. 2025;18(6):417–423. doi:10.1080/17512433.2025.2527098
22. Eyerich K, Asadullah K, Pinter A, et al. Noninferiority of 16-week vs 8-week guselkumab dosing in super responders for maintaining control of psoriasis: the GUIDE randomized clinical trial. *JAMA Dermatol*. 2024;160(9):953–963. doi:10.1001/JAMADERMATOL.2024.2463
23. Marcelli L, Belcastro A, Talamonti M, et al. Characterization of super-responder profile in chronic plaque psoriatic patients under guselkumab treatment: a long-term real-life experience. *J Clin Med*. 2024;13(17). doi:10.3390/JCM13175175
24. Rompoti N, Politou M, Stefanaki I, et al. Brodalumab in plaque psoriasis: real-world data on effectiveness, safety and clinical predictive factors of initial response and drug survival over a period of 104 weeks. *J Eur Acad Dermatol Venereol*. 2023;37(4):689–697. doi:10.1111/JDV.18825
25. Leonardi CL, See K, Burge R, et al. Number needed to treat network meta-analysis to compare biologic drugs for moderate-to-severe psoriasis. *Adv Ther*. 2022;39(5):2256–2269. doi:10.1007/S12325-022-02065-W
26. Paller AS, Seyger MMB, Alejandro Magariños G, et al. Efficacy and safety of ixekizumab in a Phase III, randomized, double-blind, placebo-controlled study in paediatric patients with moderate-to-severe plaque psoriasis (IXORA-PEDS). *Br J Dermatol*. 2020;183(2):231–241. doi:10.1111/bjd.19147
27. Morariu SH, Cotoi OS, Tiucă OM, et al. Blood-count-derived inflammatory markers as predictors of response to biologics and small-molecule inhibitors in psoriasis: a multicenter study. *J Clin Med*. 2024;13(14). doi:10.3390/JCM13143992
28. Schwarz CW, Loft N, Rasmussen MK, et al. Predictors of response to biologics in patients with moderate-to-severe psoriasis: a Danish nationwide cohort study. *Acta Derm Venereol*. 2021;101(10). doi:10.2340/ACTADV.V101.351
29. Ye JH, Zhang Y, Naidoo K, Ye S. Neutrophil-to-lymphocyte ratio and platelet-to-lymphocyte ratio in psoriasis: a systematic review and meta-analysis. *Arch Dermatol Res*. 2024;316(3). doi:10.1007/S00403-024-02823-6
30. Zhang Y, Qian H, Kuang YH, Wang Y, Chen WQ, Zhu W. Evaluation of the inflammatory parameters as potential biomarkers of systemic inflammation extent and the disease severity in psoriasis patients. *Arch Dermatolog Res*. 2024;316(6):1–11. doi:10.1007/S00403-024-02972-8
31. Şener G, Inan Yuksel E, Gökdeniz O, Karaman K, Canat HD. The Relationship of Hematological Parameters and C-reactive Protein (CRP) with disease presence, severity, and response to systemic therapy in patients with psoriasis. *Cureus*. 2023;15(8). doi:10.7759/CUREUS.43790