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Systemic Immune-Inflammation Index and Systemic Inflammation Response Index in Psoriasis: Limited Utility for Monitoring Response to IL-23 Inhibitors

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ABSTRACT

Introduction: Psoriasis is a chronic inflammatory skin disease frequently associated with systemic inflammation. Recently, blood cell-derived markers such as the Systemic Immune Inflammation Index (SII) and Systemic Inflammation Response Index (SIRI) have been proposed as potential biomarkers for disease activity and treatment monitoring. However, their clinical relevance in patients undergoing biological therapy, particularly IL-23 inhibitors, has not been fully explored.

Objectives: To evaluate the utility of SII and SIRI in monitoring disease activity in patients with severe psoriasis treated with guselkumab, risankizumab, or tildrakizumab.

Methods: This retrospective observational study included 120 patients with moderate-to-severe psoriasis treated with IL-23 inhibitors over 12 months. SII, SIRI, and Psoriasis Area and Severity Index (PASI) were assessed at baseline, six months, and 12 months. Correlations between inflammatory indices and some comorbidities were analyzed.

Results: Despite significant PASI improvement across all treatment groups, SII and SIRI values showed inconsistent fluctuations and did not parallel clinical response. While SII decreased slightly in

the tildrakizumab group, no consistent trend was observed in guselkumab and risankizumab cohorts. SIRI demonstrated similarly variable behavior. Weak-to-moderate correlations were noted between inflammatory indices and comorbidities such as obesity, diabetes mellitus, and hypertension.

Conclusions: SII and SIRI do not reliably reflect treatment response in psoriasis patients receiving IL-23 inhibitors. Their variability and correlation with comorbidities suggest limited value as psoriasis-specific biomarkers. More targeted indicators are needed for accurate monitoring of systemic inflammation in this setting.

Introduction

Psoriasis is a chronic inflammatory skin disease with systemic involvement that affects approximately 2–3% of the global population. It is characterized by immune dysregulation, leading to hyperproliferation of keratinocytes and increased production of pro-inflammatory cytokines, particularly those involved in the interleukin (IL)-23/IL-17 axis [1]. Given the systemic nature of inflammation in this condition, recent research has explored hematological biomarkers to assess disease severity and response to treatment [2]. Among these, the Systemic Immune Inflammation Index (SII) and Systemic Inflammation Response Index (SIRI) have emerged as potential indicators of systemic inflammation in various diseases, including cancer, cardiovascular, autoimmune, and infectious diseases [3]. Those derived from routine blood tests are particularly interesting because they are inexpensive, widely available, and easy to perform [4]. Recent studies have suggested that SII and SIRI could be valuable tools for evaluating systemic inflammation in psoriasis [3,5,6]. These indices, derived from routine blood count parameters, have been linked to psoriasis severity and systemic inflammatory burden. However, their clinical utility remains controversial, especially in the context of biologic therapy targeting IL-23, IL-17, and TNF-α [3,5-7]. Despite initial reports indicating a correlation between high SII and SIRI values and increased psoriasis severity [8,9], recent findings have raised concerns regarding their reliability in monitoring treatment response [6]. Notably, discrepancies exist in the observed effects of biological therapy on these markers, with some studies reporting significant reductions in SII and SIRI posttreatment, while others fail to establish consistent trends [2,10].

Objectives

Our study aimed to critically evaluate the relevance of SII and SIRI in psoriasis by analyzing their fluctuations in patients undergoing treatment with IL-23 inhibitors.

Material and Methods

This retrospective observational study analyzed data from a cohort of 120 adult patients with severe plaque psoriasis (defined as PASI ≥10) treated with guselkumab, risankizumab, or tildrakizumab. Other clinical psoriasis subtypes, apart from chronic plaque psoriasis, were not included. Data were collected from patient medical records at IRCCS, Policlinico di Sant'Orsola (Bologna, Italy) over a 12-month period (year 2024), with assessments at baseline (T0), six months (T6), and 12 months (T12). The study population included 45 patients treated with guselkumab, 42 with risankizumab, and 33 with tildrakizumab. Demographic, clinical, and laboratory data were extracted from electronic health records. The primary variables analyzed included the SII and the SIRI, recorded at T0, six months, and 12 months. Comorbidities such as obesity (body mass index–BMI ≥30), arterial hypertension (previous clinical diagnosis), diabetes mellitus (DM), and prior anti-TNFα therapy history were also documented. Descriptive statistics were used to summarize baseline characteristics and longitudinal changes in PASI, SII, and SIRI. Continuous variables are expressed as mean ± standard deviation (SD), while categorical variables are reported as frequencies and percentages. The Shapiro-Wilk test was applied to assess data normality. Spearman correlation analysis was performed to evaluate the association between inflammatory indices (SII, SIRI) and comorbidities. A p-value of <0.05 was considered statistically significant. The study was conducted in accordance with the principles of the Declaration of Helsinki. Data confidentiality was maintained throughout the research process.

Results

A total of 120 patients were included in the study across three treatment cohorts. In the guselkumab cohort (45 patients), 57.8% were male (26 patients) and 42.2% were female (19 patients), with a mean age of 49.3 ±12.4 years (range: 30–70). The risankizumab cohort included 42 patients, with 57.1% male (24 patients) and 42.9% female (18 patients), and a mean age of 47.8 ±11.9 years (range: 30–72). In the tildrakizumab cohort (33 patients), 60.6% were male (20 patients) and 39.4% were female (13 patients), with a mean age of 50.1 ±13.2 years (range: 31–71). The mean PASI, SII, and SIRI values at different time points across the three treatment groups were as follows:

- Guselkumab: PASI at baseline was 18.5 ±6.4, at T6: 6.0 ±3.8 (25% reached PASI 0), and at T12: 2.1 ±1.5 (50% reached PASI 0). The mean SII at baseline was 547.65 ±237.31, with a slight decrease at six months (541.53 ±244.73) and an increase at 12 months (564.39 ±381.51). The mean SIRI at baseline was 1.07 ±0.61, increasing at six months (1.21 ±0.98) and 12 months (1.26 ±1.12).
- Risankizumab: PASI at baseline was 19.2 ±5.8, at T6: 4.5 ±3.1 (30% reached PASI 0), and at T12: 1.3 ±1.0 (55% reached PASI 0). The mean SII at baseline was 484.74 ±275.71, decreasing at six months (470.10 ±211.30) and increasing slightly at 12 months (486.68 ±246.20). The mean SIRI at baseline was 0.96 ±0.64, increasing at six months (1.03 ±0.75) and remaining stable at 12 months (0.99 ±0.63).
- Tildrakizumab: PASI at baseline was 17.8 ±6.1, at T6: 7.2 ±4.0 (20% reached PASI 0), and at T12: 2.8 ±1.7 (45% reached PASI 0). The mean SII at baseline was 759.18 ±363.16, decreasing at six months (604.19 ±331.32) and further at 12 months (557.83 ±197.92). The mean SIRI at baseline was 1.58 ±0.74, decreasing at six months (1.15 ±0.57) and remaining stable at 12 months (1.13 ±0.47).

Results are fully summarized in Table 1 and graphically represented in Figure 1.

Regarding comorbidities, obesity was present in 53.3% of the guselkumab cohort, 30% of the risankizumab cohort, and 36.4% of the tildrakizumab cohort. Hypertension was recorded in 60% (guselkumab), 57.1% (risankizumab), and 54.5% (tildrakizumab) of patients. DM was present in 33.3% (guselkumab), 28.6% (risankizumab), and 27.3% (tildrakizumab). A history of prior biological therapy was noted in 80% of guselkumab patients, 78.6% of risankizumab patients, and 81.8% of tildrakizumab patients.

Correlation analysis revealed the following significant associations: obesity showed a negative correlation with SII at 6 months (r=-0.31, *P*=0.038) and 12 months (r= -0.40, *P*=0.006) in the guselkumab group, while in the risankizumab cohort, obesity was negatively correlated with both SII and SIRI (-0.40 to -0.63). In the tildrakizumab group, obesity showed weak positive correlations with both indices (0.10 to 0.30). Hypertension demonstrated weak negative correlations with SII (-0.19 to -0.35) and weak positive correlations with SIRI (0.20 to 0.36) in the risankizumab cohort, while in the tildrakizumab group, it correlated moderately with SIRI at six months (0.54). DM showed weak positive correlations with SII (0.19 to 0.22) and weak negative correlations with SIRI (-0.26 to -0.41) in the risankizumab cohort, while in the tildrakizumab group, DM had weak-to-moderate negative correlations with both indices (-0.26 to -0.42). Prior biological therapy did not exhibit any strong correlation with inflammatory markers in any group.

Discussion

Our findings indicate that SII and SIRI do not exhibit a consistent trend in patients with severe psoriasis treated with IL-23 inhibitors, questioning their reliability as inflammatory biomarkers in this setting (Figure 1). While some studies suggest that these indices correlate with disease severity [3,9], our results demonstrate considerable variability in their levels over time, with fluctuations that do not parallel PASI improvement. This inconsistency aligns with prior research showing that IL-23 inhibitors, unlike IL-17 inhibitors, do not significantly impact systemic inflammatory markers [4,10]. The observed variability in SII and SIRI values may stem from multiple factors. Firstly, previous reports indicate that while SII and SIRI are elevated in untreated psoriasis patients, their response to biological therapy is inconsistent [2]. Our data align with studies suggesting that SII and SIRI decrease significantly with IL-17 inhibitors but not with IL-23 inhibitors [4,10]. This discrepancy likely reflects differential effects of these drug classes on systemic inflammation, as IL-17 inhibitors have been shown to exert broader systemic anti-inflammatory effects than IL-23 inhibitors. IL-17 plays a dominant role in promoting inflammatory activity outside the skin, including signals that amplify neutrophil presence and movement in the bloodstream. For this reason, indices calculated from circulating blood cells may decline more coherently when this cytokine is blocked directly. Conversely, inhibiting IL-23 at an earlier step does not fully prevent IL-17 from being released through parallel routes, meaning that blood-based inflammatory trends may remain partially active and variably oriented, even when the skin disease improves substantially [10].

Moreover, some studies propose that SII and SIRI correlate with comorbidities such as obesity, DM, and cardiovascular disease rather than with psoriasis severity per se [8,9]. This association complicates their use as psoriasis-specific biomarkers, as fluctuations may be influenced by underlying metabolic conditions rather than changes in disease activity [6]. In our cohort, the presence of metabolic comorbidities may have contributed to the inconsistent trends observed in SII and SIRI, further questioning their applicability in psoriasis monitoring.

Given that our study exclusively analyzed patients treated with IL-23 inhibitors, the lack of significant reductions in SII and SIRI may further support the notion that these indices are more reflective of broader systemic inflammation rather than psoriasis-specific changes. Taken together, our results reinforce the notion that SII and SIRI are not reliable biomarkers for psoriasis monitoring, particularly in patients treated with IL-23 inhibitors. Their inconsistent trends and potential confounding by comorbid conditions limit their clinical utility. An additional challenge lies in the nature of SII

Table 1. Patient demographics and results. Summary of patient demographics and clinical outcomes across the three treatment cohorts (guselkumab, risankizumab, and tildrakizumab). The table presents the number of patients, sex distribution, mean age, PASI scores at baseline, six months (T6), and 12 months (T12) as well as SII and SIRI values at the same time points. PASI 0 percentages indicate the proportion of patients achieving complete skin clearance at T6 and T12.

Treatment	Patients (N)	Males (%) (N)	Females (%) (N)	Mean age ± SD (years, range)	PASI Baseline (mean ± SD)	PASI T6 (mean ± SD)	PASI T12 (mean ± SD)	SII Baseline (mean ± SD)	SII T6 (mean ± SD)	SII T12 (mean ± SD)	SIRI Baseline (mean ± SD)	SIRI T6 (mean ± SD)	SIRI T12 (mean ± SD)
Guselkumab	45	57.8% (26)	42.2% (19)	49.3 ± 12.4 (30–70)	18.5 ± 6.4	6.0 ± 3.8	2.1 ± 1.5	547.65 ± 237.31	541.53 ± 244.73	564.39 ± 381.51	1.07 ± 0.61	1.21 ± 0.98	1.26 ± 1.12
Risankizumab	42	57.1% (24)	42.9% (18)	47.8 ± 11.9 (30–72)	19.2 ± 5.8	4.5 ± 3.1	1.3 ± 1.0	484.74 ± 275.71	470.10 ± 211.30	486.68 ± 246.20	0.96 ± 0.64	1.03 ± 0.75	0.99 ± 0.63
Tildrakizumab	33	60.6% (20)	39.4% (13)	50.1 ± 13.2 (31–71)	17.8 ± 6.1	7.2 ± 4.0	2.8 ± 1.7	759.18 ± 363.16	604.19 ± 331.32	557.83 ± 197.92	1.58 ± 0.74	1.15 ± 0.57	1.13 ± 0.47

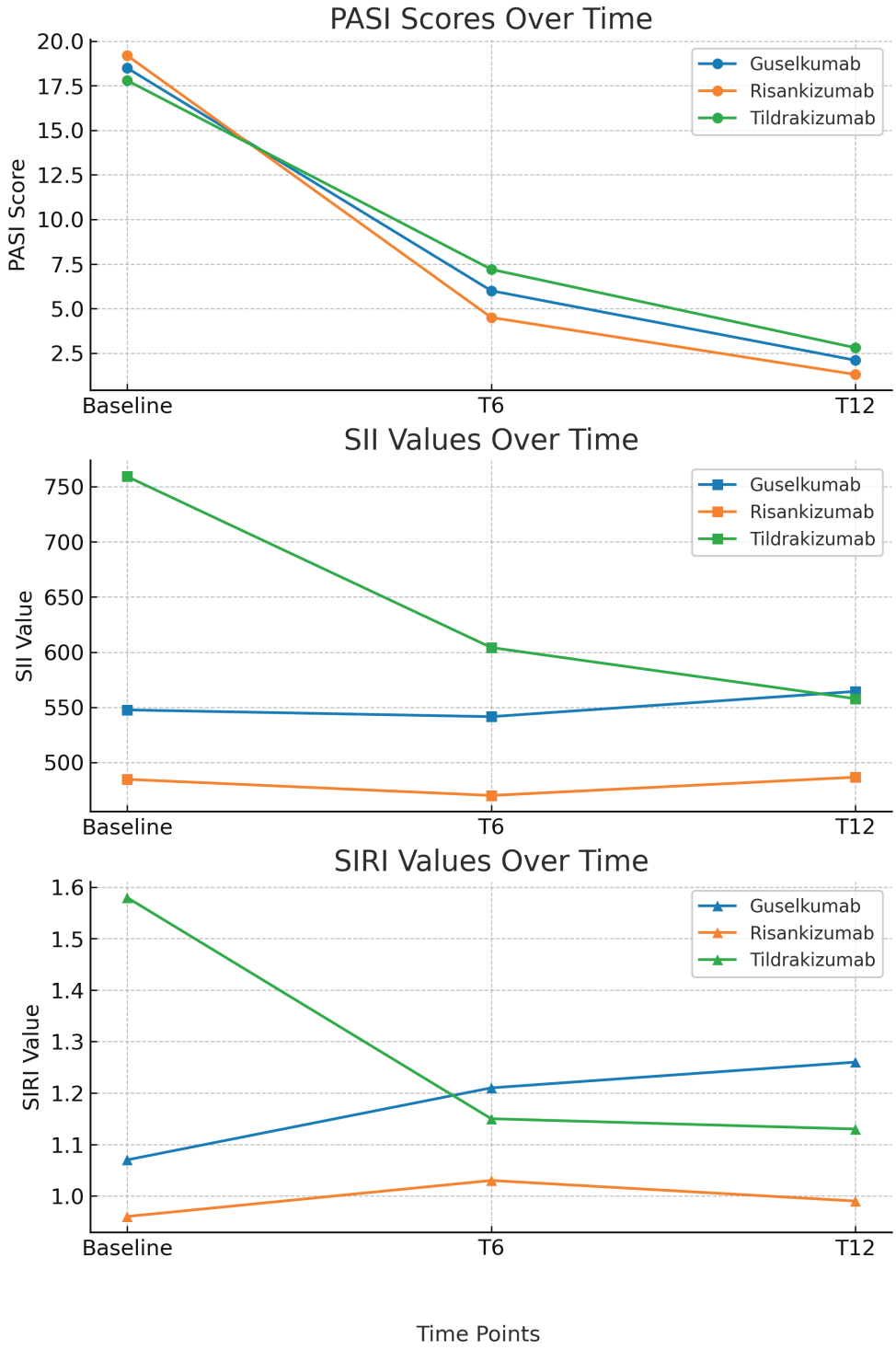

Figure 1. Comparison of PASI, SII, and SIRI values at baseline, six months (T6), and 12 months (T12) for the three treatment cohorts: guselkumab (blue lines), risankizumab (green lines), and tildrakizumab (red lines).

and SIRI themselves, which are derived from complete blood count parameters. These indices can fluctuate due to unrelated factors such as infections, stress, or other inflammatory conditions, raising further concerns about their reliability as psoriasis-specific biomarkers. Future research should focus on identifying more psoriasis-specific biomarkers that can reliably track disease progression and therapeutic response.

This study has some inherent limitations that should be acknowledged. As a retrospective, observational analysis, it does not establish a direct causal relationship between SII, SIRI, and treatment response in psoriasis. The single-center data collection at IRCCS Policlinico di Sant'Orsola in Bologna may limit the generalizability of the findings to broader populations with diverse demographic and clinical

characteristics. Additionally, the lack of a control group, either healthy individuals or psoriasis patients not treated with biologics, prevents a clear distinction between changes in inflammatory markers due to disease progression versus the effect of IL-23 inhibitors. The study's 12-month follow-up period, while sufficient for short-term trends, may not capture the long-term dynamics of SII and SIRI in psoriasis management. Moreover, the inclusion of multiple IL-23 inhibitors (guselkumab, risankizumab, and tildrakizumab) introduces heterogeneity, as these agents may exert varying degrees of systemic inflammation modulation.

Another limitation of this study is that psoriatic arthritis status was not systematically recorded in the cohort, and patients were not grouped based on joint involvement. As a result, we could not clearly distinguish systemic inflammation potentially driven by the joints from changes in the blood-based inflammatory indices. An additional challenge is the inherent clinical complexity of patients with psoriasis, who frequently present multiple comorbid conditions capable of influencing systemic inflammatory levels beyond the skin disease alone. In our study, only a partial comorbidity profile was available, which does not fully reflect the wide spectrum of inflammatory and noninflammatory conditions observed in routine clinical practice. Moreover, transient acute infections, including influenza-like illnesses, were not captured, as systematic correction for short-term infectious episodes would have added substantial complexity to retrospective data abstraction. Collectively, these factors limited our ability to isolate psoriasis-specific systemic inflammation from background inflammatory variability affecting the composite indices.

Conclusion

Our study demonstrates that SII and SIRI are unreliable biomarkers for monitoring treatment response in patients with moderate-to-severe psoriasis treated with IL-23 inhibitors. Although IL-23 blockade led to significant clinical improvements, neither SII nor SIRI consistently mirrored these changes, and their trends were often influenced by comorbidities such as obesity, DM, and hypertension. These findings highlight the limitations of using generalized systemic inflammation indices to assess disease activity in psoriasis and underscore the need for more specific and robust biomarkers tailored to this complex disease. Future prospective studies are warranted to identify and validate more accurate tools for evaluating systemic inflammation and treatment efficacy in psoriatic patients.

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