

## Effect of Treatment With Biologic Agents on the Novel Inflammatory Biomarkers Systemic Immune Inflammation Index and Systemic Inflammation Response Index for Psoriasis

Funda Tamer<sup>1</sup>, Yusuf Can Edek<sup>1</sup>, Ahmet Burhan Aksakal<sup>1</sup>

<sup>1</sup> Department of Dermatology, Gazi University School of Medicine, Ankara, Turkey

**Key words:** biological agents, psoriasis, systemic immune inflammation index, systemic inflammation response index, treatment

**Citation:** Tamer F, Edek YC, Aksakal AB. Effect of Treatment With Biologic Agents on the Novel Inflammatory Biomarkers Systemic Immune Inflammation Index and Systemic Inflammation Response Index for Psoriasis. *Dermatol Pract Concept*. 2024;14(1):e2024065. DOI: <https://doi.org/10.5826/dpc.1401a65>

**Accepted:** April 9, 2023; **Published:** January 2024

**Copyright:** ©2024 Tamer et al. This is an open-access article distributed under the terms of the Creative Commons Attribution-NonCommercial License (BY-NC-4.0), <https://creativecommons.org/licenses/by-nc/4.0/>, which permits unrestricted noncommercial use, distribution, and reproduction in any medium, provided the original authors and source are credited.

**Funding:** None.

**Competing Interests:** None.

**Authorship:** All authors have contributed significantly to this publication.

**Corresponding Author:** Funda Tamer, Gazi Universitesi Hastanesi, Emniyet Mahallesi, 29, 06560, Ankara/ Turkey. Tel: +903122026129. E-mail: fundatmr@yahoo.com.

**ABSTRACT** **Introduction:** Psoriasis is a chronic cutaneous disorder with underlying systemic inflammation. The systemic immune inflammation (SII) and systemic inflammation response indexes (SIRI) are novel biomarkers that indicate systemic inflammation.

**Objectives:** We aimed to evaluate the effect of biological agent treatment on SII and SIRI in psoriasis patients.

**Methods:** Between April 2019 and October 2022, SII and SIRI were retrospectively evaluated in patients with psoriasis before and three months after the initiation of biological agents.

**Results:** This study included 220 patients, 101 females and 119 males. SIRI was significantly higher in male patients compared to females ( $P < 0.001$ ). Although not statistically significant, SII and SIRI were higher in obese patients, patients with severe psoriasis, longer disease duration, nail involvement and patients who received previous biological agent treatment. SII was also higher in patients with hypertension, diabetes, hepatic steatosis, depression and coronary artery disease ( $P = 0.801$ ,  $P = 0.752$ ,  $P = 0.706$ ,  $P = 0.079$ ,  $P = 0.861$ , respectively), whereas SIRI was higher in patients with diabetes and depression ( $P = 0.263$ ,  $P = 0.777$ , respectively). Both SII and SIRI statistically significantly decreased after treatment with adalimumab, infliximab, ixekizumab, secukinumab, ustekinumab and risankizumab.

**Conclusions:** SII and SIRI may indicate the severity of psoriasis as well as SII may be associated with psoriatic arthritis, hypertension, hepatic steatosis and coronary artery disease in patients with psoriasis. There is no consensus on the biomarkers that can be used to create an optimized treatment strategy in psoriasis. Therefore, SII and SIRI may be helpful in making the choice of treatment and in the follow-up of patients with psoriasis treated with biological agents.

## Introduction

Psoriasis is a chronic inflammatory cutaneous disorder which has been related to comorbidities such as psoriatic arthritis, diabetes, obesity, cardiovascular diseases and depression due to underlying systemic inflammation [1]. It has been suggested that proinflammatory cytokines, which have been implicated in the development of cutaneous findings such as tumor necrosis factor (TNF)- $\alpha$ , interleukin (IL)-17, IL-23, were increased in both skin and the circulation [2]. Although the systemic inflammatory response, which is not limited to the skin, may lead to tissue and organ dysfunction, the risk for the development of the disease and pathogenesis of the systemic involvement have not been fully understood [3]. It has been suggested that biological agents used in the treatment of psoriasis might reduce the risk of the development of systemic comorbidities and prevent the progression of existing comorbidities due to their anti-inflammatory effects [4].

It is important to identify biomarkers that can indicate disease activity and remission in psoriasis. Inflammatory biomarkers, especially obtained from blood samples, may be easily performed and used in the follow-up of patients with psoriasis [5]. Various biomarkers such as neutrophil/lymphocytes ratio, platelet/lymphocytes ratio and systemic immune inflammation index have been proposed to be used to detect systemic inflammation in patients with psoriasis [1,5]. However, there is no consensus on the biomarkers that can be used to create an optimized treatment strategy in the management of psoriasis [5].

Systemic immune inflammation index (SII) and systemic inflammation response index (SIRI) are new biomarkers that have been reported to indicate systemic inflammation [6]. SII and SIRI have been associated with various disorders such as hepatic steatosis, cardiovascular diseases, risk of cancer development and depression [6-9]. In a few studies, high SII levels have been reported in patients with psoriasis [10,11]. Recently, Sugimoto et al reported that patients with psoriatic arthritis were likely to have high SIRI levels [1]. However, SII and SIRI have not been adequately studied in patients with psoriasis.

## Objectives

The aim of this study was to evaluate the SII and SIRI in patients with psoriasis treated with biological agents.

## Methods

Gazi University Ethics Committee approved this study (approval number: 2022-1108). Medical records of patients who were admitted for the treatment of psoriasis between April 2019 and October 2022 were retrospectively reviewed. Patients with psoriasis aged 18 years and over and who were treated with biological agents were included in this study. Psoriasis type, psoriasis duration, accompanying psoriatic arthritis and systemic diseases, psoriasis treatment, psoriasis area and severity index (PASI) and body mass index (BMI) were noted.

PASI less than 10 was regarded as mild to moderate psoriasis, whereas PASI greater than 10 was severe disease [12]. Obesity was defined as body mass index (BMI)  $\geq 30$  kg/m<sup>2</sup> [13]. In addition, SII and SIRI were evaluated before and three months after treatment with biological agents. SII and SIRI were calculated using the data obtained from complete blood count; SII= platelet count ( $\times 10^3/\mu\text{L}$ ) X neutrophil count ( $\times 10^3/\mu\text{L}$ ) / lymphocyte count ( $\times 10^3/\mu\text{L}$ ) and SIRI= neutrophil count ( $\times 10^3/\mu\text{L}$ ) X monocyte count ( $\times 10^3/\mu\text{L}$ ) / lymphocyte count ( $\times 10^3/\mu\text{L}$ ) [14,15].

Statistical analysis was performed using SPSS version 25.0. Continuous variables were presented as mean  $\pm$  standard deviation or median (interquartile range), whereas categorical variables were presented as counts and percentages. Kolmogorov-Smirnov test was used to detect the normality of the distribution of the variables. The differences between the groups were evaluated by Mann-Whitney U test and Wilcoxon signed ranks test.  $P < 0.05$  was considered statistically significant.

## Results

This study included 220 patients, 101 (45.9%) females and 119 (54.1%) males with a mean age of  $49.61 \pm 13.29$  years (range: 20-77 years) (Table 1). The median psoriasis duration was 20 (16) years in male patients and 15 (18) years in females ( $p=0.006$ ). The median PASI and BMI was 14 (8.5) and 28.6 (8) kg/m<sup>2</sup>, respectively. Sixty-six (30%) patients were treated with ustekinumab, 56 (25.5%) with ixekizumab, 43 (19.5%) with adalimumab, 24 (10.9%) with secukinumab, 15 (6.8%) with infliximab, 11 (5%) with risankizumab and 5 (2.3%) with guselkumab.

**Table 1. The characteristics of the patients with psoriasis.**

Characteristics	
Gender, N (%)	Female, 101 (45.9%) Male, 119 (54.1%)
Mean age±SD (years)	49.61±13.29
Psoriasis type, N (%)	Psoriasis vulgaris, 195 (88.6%) Palmoplantar psoriasis, 13 (5.9%) Generalized pustular, 12 (5.5%)
Psoriasis duration, median (IQR) (years)	18 (16)
Psoriatic arthritis, N (%)	Present, 66 (30%) None, 154 (70%)
Nail findings, N (%)	Present, 104 (47.3%) None, 116 (52.7%)
Past medical history, N (%)	Unremarkable, 100 (45.5%) Hypertension, 59 (26.8%) Hyperlipidemia, 45 (20.5%) Diabetes mellitus, 32 (14.5%) Hepatic steatosis, 24 (10.9%) Hepatitis B virus carriage, 20 (9.1%) Depression, 19 (8.6%) Coronary artery disease, 16 (7.3%) Thyroid disease, 9 (4.1%) Asthma, 6 (2.7%)
Previous treatment, N (%)	Conventional treatment, 214 (97.3%) Biological agents, 93 (42.3%) Phototherapy, 70 (31.8%)

IQR = interquartile range; SD = Standard deviation.

This study included 220 patients with a mean age of 49.61±13.29 years. Most of the patients (88.6%) had psoriasis vulgaris. The frequency of psoriatic arthritis was 30%.

Although not statistically significant, higher SII levels were detected in male patients, patients with severe psoriasis, psoriasis duration longer than 20 years, patients with psoriatic arthritis, nail involvement, obese patients and patients previously treated with biological agents ( $P = 0.855$ ,  $P = 0.267$ ,  $P = 0.466$ ,  $P = 0.968$ ,  $P = 0.210$ ,  $P = 0.071$ ,  $P = 0.921$ , respectively). SII was also higher in patients with hypertension, diabetes, hepatic steatosis, depression and coronary artery disease ( $P = 0.801$ ,  $P = 0.752$ ,  $P = 0.706$ ,  $P = 0.079$ ,  $P = 0.861$ , respectively) (Table 2).

SIRI was statistically significantly higher in male patients compared to females ( $P < 0.001$ ). Although not statistically significant, higher SIRI levels were detected in patients with severe psoriasis, nail findings, psoriasis duration longer than 20 years, obese patients and patients previously treated with biological agents ( $P = 0.295$ ,  $P = 0.904$ ,  $P = 0.381$ ,  $P = 0.185$ ,  $P = 0.921$ , respectively). SIRI was also higher in patients with diabetes and depression ( $P = 0.263$ ,  $P = 0.777$ , respectively) (Table 3).

SII statistically significantly decreased in all patients with psoriasis three months after biological agent treatment ( $P < 0.001$ ). In addition, SII significantly decreased in treatment groups such as TNF- $\alpha$  inhibitors, IL-17 inhibitors and IL-12/23 inhibitor ( $P < 0.001$ ,  $P < 0.001$ ,  $P < 0.001$ , respectively). SII also statistically significantly decreased in

patients treated with adalimumab, infliximab, ixekizumab, secukinumab, ustekinumab and risankizumab ( $P < 0.001$ ,  $P = 0.002$ ,  $P < 0.001$ ,  $P = 0.004$ ,  $P < 0.001$ ,  $P = 0.013$ , respectively) (Table 4) (Figure 1).

SIRI statistically significantly decreased in all patients with psoriasis three months after biological agent treatment ( $P < 0.001$ ). SIRI also significantly decreased in patients treated with adalimumab, infliximab, ixekizumab, secukinumab, ustekinumab and risankizumab ( $P < 0.001$ ,  $P = 0.001$ ,  $P = 0.002$ ,  $P = 0.018$ ,  $P < 0.001$ ,  $P = 0.041$ , respectively) (Table 5 and Figure 2).

## Conclusions

SII and SIRI have been proposed as novel biomarkers which might indicate systemic inflammation, however, the use of SII and SIRI in patients with psoriasis was evaluated in limited studies [1]. For instance, Yorulmaz et al reported higher SII levels in patients with psoriasis compared to healthy individuals as well as SII was positively correlated with PASI and presence of psoriatic arthritis [10]. Similarly, Melikoglu et al reported an association between disease severity and SII levels in patients with psoriasis. In addition, Melikoglu et al reported no difference in SII levels in patients with different

**Table 2. Systemic immune inflammation index in patients with psoriasis.**

Systemic Immune Inflammation Index median (IQR)		P value
Female 618 (513)	Male 655 (400)	0.855
With arthritis 656 (430)	Without arthritis 642 (419)	0.968
Psoriasis vulgaris 644 (426)	Other types 705 (363)	0.456
Nail involvement 696 (434)	Without nail involvement 600 (401)	0.210
Psoriasis duration (≤20 years) 643 (429)	Psoriasis duration (>20 years) 656 (428)	0.466
Mild/ moderate psoriasis 624 (388)	Severe psoriasis 652 (490)	0.267
Non-obese 642 (428)	Obese 718 (619)	0.071
Previous biological treatment 658 (411)	Biologic-naïve 642 (436)	0.921
Unremarkable medical history 645 (395)	With a chronic disease 648 (461)	0.763
With hypertension 687 (566)	Without hypertension 642 (411)	0.801
With hyperlipidemia 598 (388)	Without hyperlipidemia 658 (436)	0.113
With diabetes mellitus 651 (611)	Without diabetes mellitus 645 (403)	0.752
With hepatic steatosis 735 (461)	Without hepatic steatosis 643 (418)	0.706
With hepatitis B virus carriage 608 (431)	Without hepatitis B virus carriage 650 (421)	0.915
With depression 782 (239)	Without depression 608 (418)	0.079
With coronary artery disease 692 (521)	Without coronary artery disease 643 (416)	0.861

IQR = interquartile range.

Higher SII levels were detected in male patients, patients with severe psoriasis, patients with psoriatic arthritis, nail findings and obese patients. SII may indicate the severity of psoriasis.

types of psoriasis [16]. However, Ibrahim et al reported that patients with pustular psoriasis had higher SII levels compared to those with psoriasis vulgaris and erythrodermic psoriasis [17]. Dincer Rota et al reported higher SII levels in

**Table 3. Systemic inflammation response index in patients with psoriasis.**

Systemic inflammation response index median (IQR)		P value
Female 1.02 (0.83)	Male 1.28 (1.10)	<0.001
With arthritis 1.09 (0.75)	Without arthritis 1.21 (0.99)	0.07
Psoriasis vulgaris 1.18 (0.90)	Other types 1.19 (1.06)	0.956
Nail involvement 1.20 (0.87)	Without nail involvement 1.16 (0.91)	0.904
Psoriasis duration (≤20 years) 1.13 (0.91)	Psoriasis duration (>20 years) 1.25 (0.99)	0.381
Mild/ moderate psoriasis 1.13 (0.75)	Severe psoriasis 1.19 (1.07)	0.295
Non-obese 1.05 (0.74)	Obese 1.30 (1.08)	0.185
Previous biological treatment 1.25 (1.19)	Biologic-naïve 1.16 (0.76)	0.921
Unremarkable medical history 1.16 (1.01)	With a chronic disease 1.19 (0.79)	0.753
With hypertension 1.16 (1.00)	Without hypertension 1.19 (0.87)	0.607
With hyperlipidemia 1.18 (0.67)	Without hyperlipidemia 1.20 (1.01)	0.806
With diabetes mellitus 1.23 (1.11)	Without diabetes mellitus 1.16 (0.89)	0.263
With hepatic steatosis 1.13 (0.98)	Without hepatic steatosis 1.19 (0.90)	0.472
With hepatitis B virus carriage 1.13 (0.98)	Without hepatitis B virus carriage 1.19 (0.90)	0.424
With depression 1.39 (1.22)	Without depression 1.18 (0.89)	0.777
With coronary artery disease 1.01 (0.85)	Without coronary artery disease 1.20 (0.90)	0.185

IQR = interquartile range.

SIRI was statistically significantly higher in male patients compared to females. This result may be related to longer psoriasis duration in male patients than in females.

patients with psoriasis compared to patients with dermatological disorders other than psoriasis. SII was also associated with nail changes due to psoriasis [11]. Kelesoglu Dincer et al reported higher SII levels in patients with psoriatic arthritis

**Table 4.** The effect of biological agent treatment of psoriasis on systemic immune inflammation index.

	Systemic immune inflammation index median (IQR)		P value
	Before treatment	After treatment	
All patients	646 (420)	492 (324)	<0.001
TNF- $\alpha$ inhibitors	607 (384)	408 (341)	<0.001
IL-17 inhibitors	703 (485)	528 (298)	<0.001
IL-12/23 inhibitor	603 (468)	512 (344)	<0.001
IL-23 inhibitor	689 (390)	467 (182)	0.056
Adalimumab	532 (278)	374 (327)	<0.001
Infliximab	867 (356)	487 (469)	0.002
Ixekizumab	682 (432)	539 (314)	<0.001
Secukinumab	744 (624)	454 (276)	0.004
Ustekinumab	603 (468)	512 (344)	<0.001
Risankizumab	559 (392)	443 (145)	0.013
Guselkumab	859 (468)	501 (1147)	0.893

IL = interleukin; IQR = interquartile range; TNF- $\alpha$  = tumor necrosis factor- $\alpha$ .

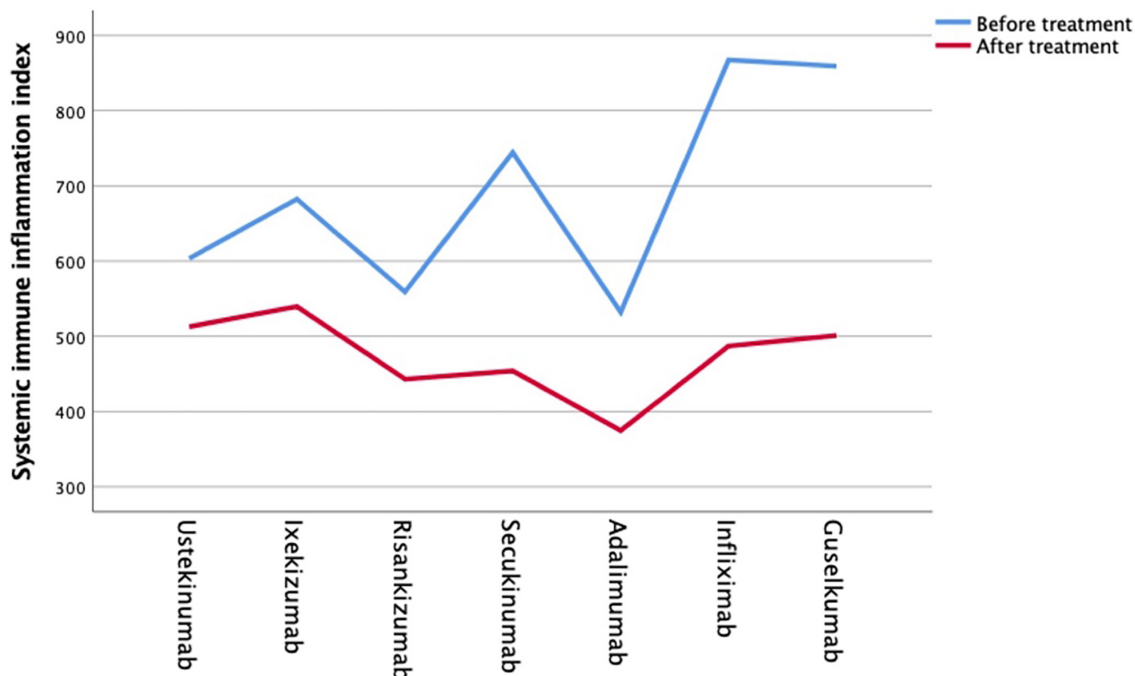
Systemic immune inflammation index decreased in patients treated with adalimumab, infliximab, ixekizumab, secukinumab, ustekinumab and risankizumab. Systemic immune inflammation index may be useful in the follow-up of patients treated with biological agents.

**Table 5.** The effect of biological agent treatment of psoriasis on systemic inflammation response index.

	Systemic inflammation response index median (IQR)		P value
	Before treatment	After treatment	
All patients	1.18 (0.90)	0.95 (0.74)	<0.001
TNF- $\alpha$ inhibitors	1.15 (0.73)	0.8 (0.58)	<0.001
IL-17 inhibitors	1.16 (1.08)	1.00 (0.88)	<0.001
IL-12/23 inhibitor	1.17 (0.79)	0.95 (0.68)	<0.001
IL-23 inhibitor	1.52 (1.42)	0.97 (0.78)	0.056
Adalimumab	1.05 (0.68)	0.78 (0.58)	<0.001
Infliximab	1.73 (1.14)	0.88 (1.04)	0.001
Ixekizumab	1.17 (1.14)	1.00 (0.93)	0.002
Secukinumab	1.07 (1.27)	1.01 (0.94)	0.018
Ustekinumab	1.17 (0.79)	0.95 (0.68)	<0.001
Risankizumab	1.75 (1.69)	0.88 (1.08)	0.041
Guselkumab	1.28 (0.79)	0.98 (3.03)	0.686

IL = interleukin; IQR = interquartile range; TNF- $\alpha$  = tumor necrosis factor- $\alpha$ .

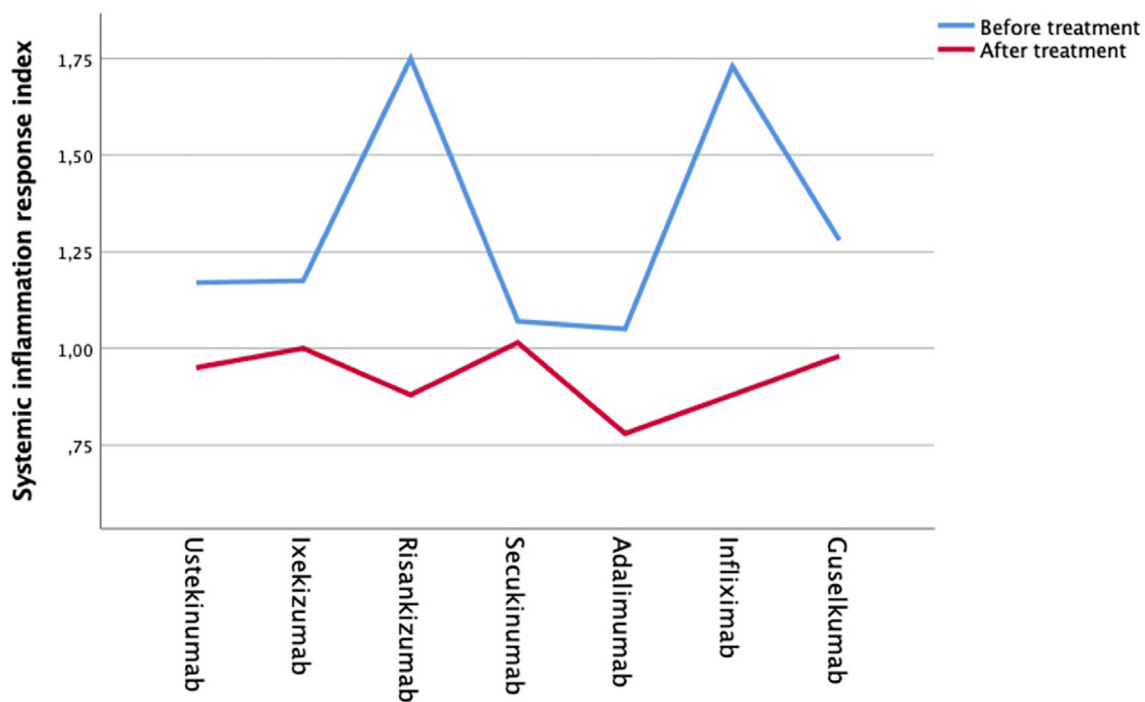
Systemic inflammation response index decreased in treatment groups such as TNF- $\alpha$  inhibitors, IL-17 inhibitors and IL-12/23 inhibitor. Systemic inflammation response index may be useful in the follow-up of patients treated with biological agents.



**Figure 1.** The effect of biological agents on systemic immune inflammation index. Systemic immune inflammation index decreased in all treatment groups.

than in healthy controls as well as positive correlation between SII and severity of psoriatic arthritis [18]. Sugimoto et al reported no significant difference in SII and SIRI levels in patients with psoriasis vulgaris and psoriatic arthritis and

in healthy individuals. On the other hand, a positive relationship was detected between PASI and both SII and SIRI. Sugimoto et al also revealed that SIRI might indicate higher possibility of the diagnosis of psoriatic arthritis. In addition,



**Figure 2.** The effect of biological agents on systemic inflammation response index. Systemic inflammation response index decreased in all treatment groups.

adherence to biological agent treatment of patients with psoriasis vulgaris and psoriatic arthritis was not related to high SII or SIRI levels [1].

Within this study, SII was higher in males, obese patients, patients with severe psoriasis and longer disease duration, patients with psoriatic arthritis, nail findings and patients who received previous biological agent treatment. SII was also higher in patients with comorbidities such as hypertension, diabetes, hepatic steatosis, depression and coronary artery disease. On the other hand, SIRI was statistically significantly higher in male patients compared to females. This result may be related to longer psoriasis duration in male patients than in females. SIRI was also higher in obese patients, patients with severe psoriasis, longer disease duration and nail involvement and patients who received previous biological agent treatment. In addition, SIRI was higher in patients with comorbidities such as diabetes and depression. SII and SIRI were similar in patients with psoriasis vulgaris and in patients with other types of psoriasis. Both SII and SIRI significantly decreased after treatment with TNF- $\alpha$  inhibitors such as adalimumab and infliximab, IL-17 inhibitors such as ixekizumab and secukinumab, IL-23 inhibitor such as risankizumab, as well as ustekinumab.

Our results revealed that both SII and SIRI might indicate severity of psoriasis, however, SII might also be associated with psoriatic arthritis. Furthermore, SII may be associated with hypertension, diabetes, hepatic steatosis, depression and coronary artery disease in patients with psoriasis, whereas SIRI with diabetes and depression. Treatment

with adalimumab, infliximab, ixekizumab, secukinumab, ustekinumab and risankizumab significantly reduced SII and SIRI levels in patients with psoriasis. Herein, we presented a unique and comprehensive study on SII and SIRI in patients with psoriasis treated with biological agents. Although a variety of biological agents have been developed to be used in the treatment of psoriasis, there is lack of biomarkers widely preferred to assess disease severity, psoriatic arthritis and comorbidities and to be used during the course of treatment of psoriasis with biological agents [5,19-21]. Our results will contribute to the literature on the use of SII and SIRI in the management of psoriasis patients with biological agents. Since SII and SIRI can be easily performed, in clinical practice both biomarkers may be helpful in making treatment choice and in the follow-up of patients with psoriasis treated with biological agents.

## References

1. Sugimoto E, Matsuda H, Shibata S, et al. Impact of pretreatment systemic inflammatory markers on treatment persistence with biologics and conventional systemic therapy: a retrospective study of patients with psoriasis vulgaris and psoriatic arthritis. *J Clin Med.* 2023;12(8):3046. DOI: 10.3390/jcm12083046. PMID: 37109382. PMCID: PMC10145777.
2. Korman NJ. Management of psoriasis as a systemic disease: what is the evidence? *Br J Dermatol.* 2020;182(4):840-848. DOI: 10.1111/bjd.18245. PMID: 31225638. PMCID: PMC7187293.
3. Tashiro T, Sawada Y. Psoriasis and systemic inflammatory disorders. *Int J Mol Sci.* 2022;23(8):4457. DOI: 10.3390/ijms23084457. PMID: 35457278. PMCID: PMC9028262.

4. Wu JJ, Kavanaugh A, Lebwohl MG, Gniadecki R, Merola JF. Psoriasis and metabolic syndrome: implications for the management and treatment of psoriasis. *J Eur Acad Dermatol Venereol.* 2022;36(6):797-806. DOI: 10.1111/jdv.18044. PMID: 35238067. PMCID: PMC9313585.
5. Honma M, Nozaki H. Molecular pathogenesis of psoriasis and biomarkers reflecting disease activity. *J Clin Med.* 2021;10(15):3199. DOI: 10.3390/jcm10153199. PMID: 34361983. PMCID: PMC8346978.
6. Xia Y, Xia C, Wu L, Li Z, Li H, Zhang J. Systemic immune inflammation index (SII), system inflammation response index (SIRI) and risk of all-cause mortality and cardiovascular mortality: a 20-year follow-up cohort study of 42,875 US adults. *J Clin Med.* 2023;12(3):1128. DOI: 10.3390/jcm12031128. PMID: 36769776. PMCID: PMC9918056.
7. Fest J, Ruiter R, Mulder M, et al. The systemic immune-inflammation index is associated with an increased risk of incident cancer—a population-based cohort study. *Int J Cancer.* 2020;146(3):692-698. DOI: 10.1002/ijc.32303. PMID: 30924141. PMCID: PMC6916270.
8. Song Y, Guo W, Li Z, Guo D, Li Z, Li Y. Systemic immune-inflammation index is associated with hepatic steatosis: evidence from NHANES 2015-2018. *Front Immunol.* 2022;13:1058779. DOI: 10.3389/fimmu.2022.1058779. PMID: 36466832. PMCID: PMC9718528.
9. Li X, Huan J, Lin L, Hu Y. Association of systemic inflammatory biomarkers with depression risk: results from national health and nutrition examination survey 2005-2018 analyses. *Front Psychiatry.* 2023;14:1097196. DOI: 10.3389/fpsy.2023.1097196. PMID: 36846218. PMCID: PMC9945233.
10. Yorulmaz A, Hayran Y, Akpınar U, Yalcın B. Systemic immune-inflammation index (SII) predicts increased severity in psoriasis and psoriatic arthritis. *Curr Health Sci J.* 2020;46(4):352-357. DOI: 10.12865/CHSJ.46.04.05. PMID: 33717509. PMCID: PMC7948012.
11. Dincer Rota D, Tanacan E. The utility of systemic-immune inflammation index for predicting the disease activation in patients with psoriasis. *Int J Clin Pract.* 2021;75(6):e14101. DOI: 10.1111/ijcp.14101. PMID: 33619821.
12. Conforti C, Currado D, Navarini L, et al. Moderate-to-severe plaque psoriasis, described by PASI  $\geq$ 10%, can be associated with higher cardiovascular risk according to seven risk algorithms: results of a 10-year single-center retrospective study and clinical management of psoriatic patients with cardiovascular risk. *Dermatol Ther.* 2020;33(6):14451. DOI: 10.1111/dth.14451. PMID: 33098612.
13. Liu N, Birstler J, Venkatesh M, Hanrahan L, Chen G, Funk L. Obesity and BMI cut points for associated comorbidities: electronic health record study. *J Med Internet Res.* 2021;23(8):24017. DOI: 10.2196/24017. PMID: 34383661. PMCID: PMC8386370.
14. He L, Xie X, Xue J, Xie H, Zhang Y. Association of the systemic immune-inflammation index with all-cause mortality in patients with arteriosclerotic cardiovascular disease. *Front Cardiovasc Med.* 2022;9:952953. DOI: 10.3389/fcvm.2022.952953. PMID: 36172591. PMCID: PMC9510918.
15. Han K, Shi D, Yang L, et al. Prognostic value of systemic inflammatory response index in patients with acute coronary syndrome undergoing percutaneous coronary intervention. *Ann Med.* 2022;54(1):1667-1677. DOI: 10.1080/07853890.2022.2083671. PMID: 35695557. PMCID: PMC9225721.
16. Melikoglu M, Pala E. Systemic Immune-inflammation index as a biomarker of psoriasis severity. *Arch Basic Clin Res.* 2023;5(2):291-295. DOI: 10.5152/ABCR.2023.22124.
17. Ibrahim SH, Guan M, Li S. Systemic immune inflammatory index is associated with pustular psoriasis: a single center retrospective study. *J Cosmet Dermatol Sci Appl.* 2022;12(4):174-186. DOI: 10.4236/jcdsa.2022.124015.
18. Kelesoglu Dincer AB, Sezer S. Systemic Immune inflammation index as a reliable disease activity marker in psoriatic arthritis. *J Coll Physicians Surg Pak.* 2022;32(6):773-778. DOI: 10.29271/jcpsp.2022.06.773. PMID: 35686411.
19. Ramessur R, Corbett M, Marshall D, et al. Biomarkers of disease progression in people with psoriasis: a scoping review. *Br J Dermatol.* 2022;187(4):481-493. DOI: 10.1111/bjd.21627. PMID: 35482474. PMCID: PMC9796834.
20. Molteni RE. Biomarkers in the pathogenesis, diagnosis, and treatment of psoriasis. *Psoriasis (Auckl).* 2012;2:55-66. DOI: 10.2147/PTT.S24995.
21. Jiménez C, Bordagaray MJ, Villarroel JL, et al. Biomarkers in oral fluids as diagnostic tool for psoriasis. *Life.* 2022;12(4):501. DOI: 10.3390/life12040501. PMID: 35454992. PMCID: PMC9027180.