CODEN [USA]: IAJPBB ISSN : 2349-7750

INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES

SJIF Impact Factor: 7.187
https://doi.org/10.5281/zenodo.8072992

Available online at: http://www.iajps.com *Research Article*

COMPARATIVE ASSESSMENT OF METHOTREXATE AND CYCLOSPORINE AS THERAPEUTIC APPROACHES FOR SEVERE PSORIASIS: ANALYZING CLINICAL EFFICACY AND OUTCOMES

[1]Dr Tasneem Kousar, [2]Dr Muhammad Osama, [3]Dr Tallal Ahmad, [4]Dr Jawadullah Khan, [5]Dr Shehroze Khan Awan, [6]Dr. Abdul Hafeez

[1]Pmdc: 52336p, Institution: Foundation University Medical College,
Emai: drtk1474@gmail.com
[2]38403-6003912-7, [3]38403-6498251-3, [4]Pmdc: 721761-01-M, [5]115614-P, [6]115618-P

Abstract:

Objective: *Skin patches that are thick, red, and scaly with a tendency to reoccur over time are the hallmark of the chronic autoimmune illness psoriasis. Cyclosporine and methotrexate have been two widely used therapies for severe psoriasis for a long time. Our goal in this research is to evaluate the clinical efficacy of methotrexate and cyclosporine as treatments for severe psoriasis. We want to learn about their results and provide some insight into how managing this difficult illness could benefit them.*

Methods: *To learn more about the health of patients who were hospitalized because of severe psoriasis during the previous three years, Mayo Hospital in Lahore thoroughly analyzed their medical data. The goal of this research was to evaluate several outcomes connected to the severity of the illness, including the PASI score for the psoriasis area and severity and the length of hospitalization.*

Results: *There were 26 patients in the research study in all. With a standard deviation of 24.64, the average decrease in the PASI (Psoriasis Area Severity Index) was determined to be 42.8%. In comparison to the methotrexate group, which had a lower drop in PASI (mean of 43.22% with a standard deviation of 24.4%) than the cyclosporine group (mean of 54.88% with a standard deviation of 12.73%), researchers found. In addition, the patients in the cyclosporine group received therapy for an average of 18.83 days on average, with a standard deviation of 9.39, as opposed to 11.65 days on average, with a standard deviation of 5.91, in the methotrexate group.*

Conclusions: *Severe psoriasis has been successfully treated with methotrexate and cyclosporine. Patients receiving cyclosporine therapy, however, can have lengthier hospital stays.*

Keywords: *cyclosporine, methotrexate, psoriasis*

Corresponding author:

Dr.Tasneem Kousar,

Pmdc: 52336p, Institution: Foundation University Medical College,
Emai: drtk1474@gmail.com

QR code

Please cite this article in press Tasneem Kousar et al, ***Comparative Assessment Of Methotrexate And Cyclosporine As Therapeutic Approaches For Severe Psoriasis: Analyzing Clinical Efficacy And Outcomes.,*** *Indo Am. J. P. Sci, 2023; 10 (06).*

INTRODUCTION:

As thick, red, scaly plaques on the skin that come and go, psoriasis is a form of autoimmune disease. This illness is often associated with arthritis in the joints, coronary artery disease, and mental health problems. It is regulated by immunological processes, hereditary vulnerability, and triggering environmental events. (1) From 0.09 to 11.4% of the world's population have psoriasis. Psoriasis is a condition that affects 0.4% of people in Asia. There are several topical medications for psoriasis, including anthralin, tar, corticosteroids, and calcipotriene; light therapy using ultraviolet B (UVB) and psoralen with ultraviolet A (PUVA); and systemic immunosuppressant medications like cyclosporine, methotrexate, and acitretin. (2) By preventing the production of DNA, the folic acid inhibitor propranolol has an antimitotic impact on the skin's outer layer. Having a potent immunosuppressive impact is the cyclic decapeptide cyclosporine. T helper cell activation and the production of cytokines like interleukin-2 (IL-2) are inhibited by its method of action in psoriasis. (3) The treatment of moderate to severe psoriasis has traditionally included the use of cyclosporine and methotrexate. (4) For moderate to serious psoriasis, both medications are still regarded in Pakistan as the first-line systemic therapy. (5) Numerous research investigations have shown the possible side effects of methotrexate and cyclosporine as well as their efficacy as treatments for mild serious psoriasis. For the treatment of nail psoriasis and psoriasis vulgaris, there are additionally some trials that mix the two medications. (6,7)

Figure 1: Severe Psoriasis

In comparison to the more potent and secure biologic treatments, these two drugs perform less well, as demonstrated by a recent meta-analysis. While traditional systemic treatment is being phased out, wealthier countries are increasingly choosing biological medicines. (8,9) Due to their comparatively expensive costs, biologics are not widely used in underdeveloped nations like Pakistan. Therefore, methotrexate and cyclosporine are still preferred medications in clinical settings for traditional systemic therapy. It is necessary to assess the effectiveness of these two drugs in treating Pakistani patients. In this investigation, systemic cyclosporine and methotrexate were used to treat individuals with severe psoriasis to evaluate the clinical results.

METHODS:

Study Design: The researchers received permission from the hospital's ethics committee to perform this retrospective analysis at Mayo Hospital in Lahore. Patients with severe psoriasis who were hospitalized in the Dermatovenereology ward between 2021 and 2023 and were treated with methotrexate or cyclosporine were the main subject of the research.

The demographic data, psoriasis area and severity index (PASI) ratings, duration of hospital stay, and history of therapy were all gathered by the researchers from the patient’s medical records. Severe psoriasis was defined as those with a PASI score higher than 10. The initial PASI scores were determined at the time of admission, and the final PASI values were computed the day following release. The decrease in PASI scores and the duration of hospital stay were the key outcomes tracked in this research. It was thought that the goal of treating psoriasis was to reduce PASI scores by 75% (PASI-75).

The overall goals of this research were to examine the demographics of patients with severe psoriasis, identify the effects of methotrexate and cyclosporine on PASI scores, and examine the influence of these medications on hospital stay. The researchers wanted to provide insightful information on how severe psoriasis patients are managed and treated in a hospital setting.

Statistical Analysis: The PSPP program, a publicly downloadable statistical tool, was used to carry out the statistical study. While Pearson's correlation was utilized to look at correlations between variables, descriptive techniques were used to analyze demographic information and clinical outcomes. The means of the regularly distributed data were compared using paired sample t-tests, whereas the means of the non-normally distributed data were compared using Wilcoxon rank tests.

RESULTS:

26 of the 30 hospitalized individuals with severe psoriasis who were the subject of a study were used in the analysis. Methotrexate and cyclosporine were used throughout the course of the therapy. The average age of the patients was 41.08 years old, with a standard deviation of 16.04 years, and there were around 1.7:1

more men than women among them. All of the patients had initial PASI (Psoriasis Area and Severity Index) scores that were high, with an average of 39.92 and a standard deviation of 15.88. 20 of the patients were treated with methotrexate, while 6 were treated with cyclosporine (Table 1).

Table 1: Demographics of the study population

	n	%	Mean	SD
Age			41.08	16.04
Gender				
Female	9	34.6		
Male	17	65.4		
Systemic treatment				
PASI score			39.92	15.88
Cyclosporine	6	20		
Methotrexate	20	66.7		

With a 12-hour gap between treatments, the methotrexate group was given dosages ranging from 2.5 to 5 mg three times per week, whereas the cyclosporine group got 50 to 100 mg twice daily. In contrast to the cyclosporine group, which had a higher average baseline PASI score of 46.95 (14.50), the methotrexate group had an average baseline PASI score of 37.81 (16.0) before therapy. (Table 2)

Table 2: Average PASI rating for the two treatment groups

		Cyclosporine	Methotrexate
PASI after	**Mean**	21.08	17.03
	SD	8.25	8.29
PASI baseline	**Mean**	46.95	37.81
	SD	4.5	16
p		0.003	<0.001

Significantly lower PASI scores were seen in both therapy groups. For both groups, the average PASI score drop was 45.91%, with a standard deviation of 22.59%. However, the methotrexate group exhibited a lower decrease than the cyclosporine group, with an average reduction of 43.22% (24.4) vs 54.88% (12.73) (Table 2). Only 5% of the methotrexate-treated patients had a PASI-75 response, which indicates a 75% or higher decrease in PASI score. On the other hand, the majority of the cyclosporine-treated patients reduced their PASI scores by between 50 and 75 percent (Figure 2).

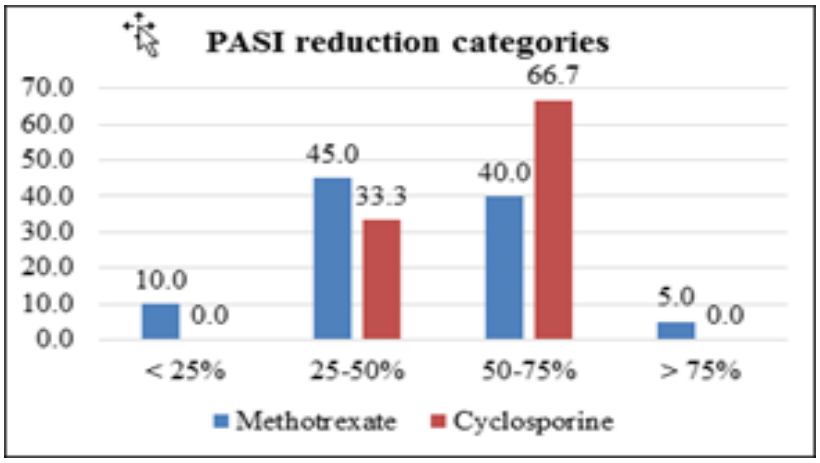

Figure 2: Decrease in (PASI) score divisions between two groups

With an average stay of 13.31 days and a standard variation of 7.33 days, the patient's hospital stays varied from 4 to 34 days. Notably, patients receiving cyclosporine had a lengthier hospital stay, lasting an average of 18.83 days (9.39), while those receiving methotrexate had a shorter stay, lasting an average of 11.65 days (5.91).

The effectiveness of methotrexate and cyclosporine in treating severe psoriasis was assessed in this research. Both medications significantly decreased PASI scores, with the cyclosporine group seeing a greater decline. Only a tiny portion of methotrexate-treated individuals, however, showed a PASI-75 response. Patients receiving cyclosporine treatment spent more time in the hospital than those receiving methotrexate treatment.

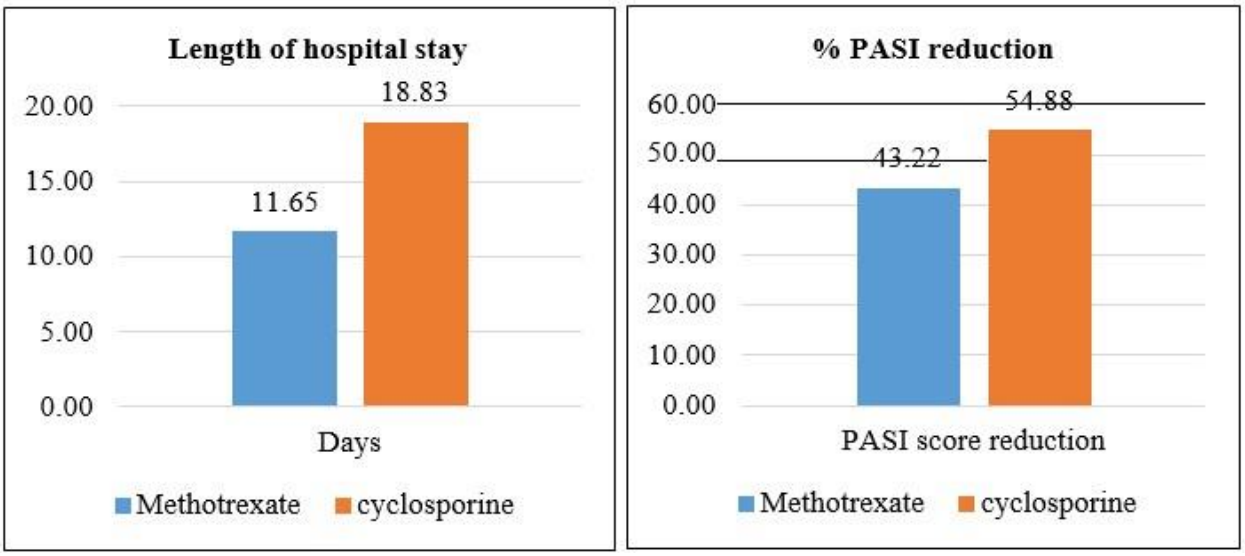

Figure 3: Hospital stay duration and decrease in PASI scores between two groups.

DISCUSSIONS:

Two systemic medications that have traditionally been employed for the treatment of mild-serious psoriasis include cyclosporine and methotrexate. (10) Determining the severity of psoriasis is crucial to selecting the best therapy. The most popular techniques for assessing the degree of severity of psoriasis in medical practice, particularly for patients receiving systemic medication, are PASI and DLQI. In this research, the score obtained from the PASI is employed to evaluate clinical progress. Three severity classifications (mild, moderate, severe) are used in clinics based on the PASI score. PASI 5 indicates mild psoriasis, PASI 5–10 intermediate psoriasis, and PASI >10 severe psoriasis. (11) A tertiary hospital in Indonesia found that cyclosporine and methotrexate were successful in treating severe psoriasis. In this research, patients taking methotrexate or cyclosporine had substantially lower PASI scores. The effectiveness of cyclosporine is greater, although this distinction is not significant. Though there wasn't a statistically significant distinction, cyclosporine was shown to be more efficient than methotrexate in achieving PASI-75. (12) A clinical investigation revealed that cyclosporine 3 mg per day and methotrexate 15 mg per week administered for 16 weeks might lower PASI values in 94 percent of the subjects by a minimum of 25 percent. In the methotrexate group, 60% of participants, and in the cyclosporine group, 71% of subjects, PASI-75 was reached. (13) Another research examined the effects of methotrexate and cyclosporine without using a placebo. With a statistically significant difference, the mean PASI score change for the cyclosporine group was 72% and for the methotrexate group, it was 58%. (14) Both drugs helped treat severe psoriasis, according to a previous study. In this clinical research, methotrexate was more successful than cyclosporine; after 12 weeks of therapy, the PASI score was reduced by 98.5 percent versus 85.6 percent in the cyclosporine group. (15)

The systemic therapy with the greatest evidence to be successful for moderate to severe psoriasis includes biological medicines such as etanercept, ustekinumab, adalimumab, and infliximab, according to a meta-analysis of 48 randomized controlled studies. These biological substances are more efficient than traditional ones such as methotrexate, cyclosporine, fumaric acid, retinoids, alefacept, and alefacept. (16) According to current psoriasis recommendations, those with mild-to-serious psoriasis who cannot take conventional treatment owing to consequences or are

sensitive to it may consider biological therapies. (17,18,19) Conventional systemic therapy is often used as the initial line of treatment since it is less expensive, especially in poor nations like Indonesia. (20) The most important question is when to switch from traditional systemic medication to biological treatment, based on internationally published consensus guidelines. (21) Psoriasis patients' average length of stay (LOS) in Pakistani hospitals seems to be higher than in industrialized nations. In comparison to patients who got cyclosporine, those who took methotrexate had a reduced mean LOS. In the United States, individuals with simple psoriasis spent an average of 4.6 days in the hospital, regardless of the disease's severity. In those with psoriasis who have severe infections, it may increase to 6.6 days. (22) According to further data, psoriasis patients' average LOS was 8.6 days. (23) Hospitalization may be necessary for individuals with moderate to severe psoriasis to complete diagnostic or treatments that cannot be completed at a first or secondary referral hospital. (24) Systemic conditions that need the care of additional experts are commonly present in people with severe psoriasis. Hospitalized psoriasis patients may have a worse quality of life and physical suffering, especially if they are older. (25) A qualitative study found that the reduction in quality of life started to get better right away after the patient was released from the hospital and persisted for three months. (26) It is important to be aware of the adverse effects of both methotrexate and cyclosporine since in certain studies, they affect more than half of the patients. As 14 individuals in the methotrexate group withdrew from the trial due to an unusually elevated liver enzyme, the study showed methotrexate side effects (27). Other side effects mentioned in the reports included nausea, especially on the day the medicine was administered, as well as muscle pain, fatigue, and paraesthesias in the fingers. (28,29) The most frequent cyclosporine adverse effect is elevated creatinine levels, which is subsequently accompanied by high blood pressure, hypertriglyceridemia, anxiety, and headache. (30) The study's shortcomings include the difficulty in establishing methotrexate and cyclosporine's long-term side effects after discharge due to several patients skipping outpatient follow-up appointments.

CONCLUSIONS:

The severity of severe psoriasis has been effectively reduced by cyclosporine and methotrexate. Although cyclosporine has been shown to result in higher decreases in PASI scores, patients using this medicine often remain in the hospital for a longer period. Before contemplating the use of biological medications as an option, it is important to evaluate the clinical response to these therapies.

REFERENCES:

1. Yasmeen, N., Sawyer, L. M., Malottki, K., Levin, L. Å., Didriksen Apol, E., & Jemec, G. B. (2022). Targeted therapies for patients with moderate-to-severe psoriasis: a systematic review and network meta-analysis of PASI response at 1 year. *Journal of Dermatological Treatment*, *33*(1), 204-218.
2. Galluzzo, M., Chiricozzi, A., Cinotti, E., Brunasso, G., Congedo, M., Esposito, M., ... & Parodi, A. (2022). Tildrakizumab for treatment of moderate to severe psoriasis: an expert opinion of efficacy, safety, and use in special populations. *Expert Opinion on Biological Therapy*, *22*(3), 367-376.
3. Megna, M., Fabbrocini, G., Cinelli, E., Camela, E., & Ruggiero, A. (2022). Guselkumab in moderate to severe psoriasis in routine clinical care: an Italian 44-week real-life experience. *Journal of Dermatological Treatment*, *33*(2), 1074-1078.
4. Griffiths, C. E., Papp, K. A., Song, M., Miller, M., You, Y., Shen, Y. K., ... & Blauvelt, A. (2022). Continuous treatment with guselkumab maintains clinical responses through 4 years in patients with moderate-to-severe psoriasis: results from VOYAGE 1. *Journal of Dermatological Treatment*, *33*(2), 848-856.
5. Megna, M., Potestio, L., Fabbrocini, G., & Ruggiero, A. (2022). Long-term efficacy and safety of guselkumab for moderate to severe psoriasis: a 3-year real-life retrospective study. *Psoriasis: Targets and Therapy*, 205-212.
6. Thaçi, D., Strober, B., Gordon, K. B., Foley, P., Gooderham, M., Morita, A., ... & Gottlieb, A. B. (2022). Deucravacitinib in moderate to severe psoriasis: clinical and quality-of-life outcomes in a phase 2 trial. *Dermatology and Therapy*, *12*(2), 495-510.
7. Maurelli, M., Gisondi, P., & Girolomoni, G. (2023). Tailored biological treatment for patients with moderate-to-severe psoriasis. *Expert Review of Clinical Immunology*, *19*(1), 37-43.
8. Chen, Z. T., Chen, R. F., Li, X. L., Wang, Q., Ren, W. W., Shan, D. D., ... & Guo, L. H. (2023). The role of ultrasound in screening subclinical psoriatic arthritis in patients with moderate to severe psoriasis. *European Radiology*, 1-11.
9. Colombo, D., Bianchi, L., Fabbrocini, G., Corrao, S., Offidani, A., Stingeni, L., ... & Zagni, E. (2022). Real-world evidence of biologic treatments in moderate–severe psoriasis in Italy: Results of the CANOVA (EffeCtiveness of biologic treAtmeNts for plaque psOriasis in Italy:

An obserVAtional longitudinal study of real-life clinical practice) study. *Dermatologic Therapy*, *35*(1), e15166.
10. Ruiz-Villaverde, R., Rodriguez-Fernandez-Freire, L., Armario-Hita, J. C., Pérez-Gil, A., & Galán-Gutiérrez, M. (2022). Super responders to guselkumab treatment in moderate-to-severe psoriasis: a real clinical practice pilot series. *International Journal of Dermatology*, *61*(8), 1029-1033.
11. Ghalamkarpour, F., Pourani, M. R., Abdollahimajd, F., & Zargari, O. (2022). A case of severe psoriatic erythroderma with COVID-19. *Journal of Dermatological Treatment*, *33*(2), 1111-1113.
12. Megna, M., Potestio, L., Camela, E., Fabbrocini, G., & Ruggiero, A. (2022). Ixekizumab and brodalumab indirect comparison in the treatment of moderate to severe psoriasis: Results from an Italian single-center retrospective study in a real-life setting. *Dermatologic Therapy*, *35*(9), e15667.
13. Griffiths, C. E., Gooderham, M., Colombel, J. F., Terui, T., Accioly, A. P., Gallo, G., ... & Blauvelt, A. (2022). Safety of ixekizumab in adult patients with moderate-to-severe psoriasis: data from 17 clinical trials with over 18,000 patient-years of exposure. *Dermatology and Therapy*, *12*(6), 1431-1446.
14. Ellis, C. N., Neville, S. J., Sayyouh, M., Elder, J. T., Nair, R. P., Gudjonsson, J. E., ... & Agarwal, P. P. (2022). Epicardial adipose tissue volume is greater in men with severe psoriasis, implying an increased cardiovascular disease risk: A cross-sectional study. *Journal of the American Academy of Dermatology*, *86*(3), 535-543.
15. Crowley, J. J., Langley, R. G., Gordon, K. B., Pinter, A., Ferris, L. K., Rubant, S., ... & Warren, R. B. (2022). Efficacy of risankizumab versus secukinumab in patients with moderate-to-severe psoriasis: subgroup analysis from the immerge study. *Dermatology and Therapy*, *12*(2), 561-575.
16. Lebwohl, M. G., Merola, J. F., Rowland, K., Miller, M., Yang, Y. W., Yu, J., ... & Langley, R. G. (2023). Safety of guselkumab treatment for up to 5 years in patients with moderate-to-severe psoriasis: pooled analyses across seven clinical trials with greater than 8600 patient-years of exposure. *British Journal of Dermatology*, ljad115.
17. Cetkovská, P., Dediol, I., Šola, M., Kojanová, M., Trčko, K., Čarija, A., ... & Mamun, K. (2023). Apremilast use in severe psoriasis: real-world data from Central and Eastern Europe. *Advances in Therapy*, *40*(4), 1787-1802.
18. Tsiori, S., Rompoti, N., Kontoangelos, K., Papageorgiou, C., Papageorgiou, C., Stratigos, A., & Rigopoulos, D. (2022). Psychopathology and alexithymia in patients with moderate-to-severe psoriasis: development of a novel index with prognostic value. *International Journal of Environmental Research and Public Health*, *19*(7), 4029.
19. Lebwohl, M., Rowland, K., & Miller, M. (2022). 33150 Safety of guselkumab in patients with moderate-to-severe psoriasis: Pooled analyses across clinical studies. *Journal of the American Academy of Dermatology*, *87*(3), AB106.
20. Caldarola, G., Zangrilli, A., Bernardini, N., Bavetta, M., De Simone, C., Graceffa, D., ... & Bianchi, L. (2022). Risankizumab for the treatment of moderate-to-severe psoriasis: A multicenter, retrospective, 1 year real-life study. *Dermatologic Therapy*, *35*(6), e15489.
21. Ruiz-Villaverde, R., Rodriguez-Fernandez-Freire, L., Armario-Hita, J. C., Pérez-Gil, A., Chinchay, F. V., & Galán-Gutiérrez, M. (2022). Guselkumab as a switching strategy after anti-TNFα, anti-IL17, or anti-IL12/23 therapies in moderate-to-severe psoriasis. *Dermatologic Therapy*, *35*(10), e15760.
22. Ion, A., Dorobanțu, A. M., Popa, L. G., Mihai, M. M., & Orzan, O. A. (2022). Risks of Biologic Therapy and the Importance of Multidisciplinary Approach for an Accurate Management of Patients with Moderate-Severe Psoriasis and Concomitant Diseases. *Biology*, *11*(6), 808.
23. Thaçi, D., Gerdes, S., Du Jardin, K. G., Perrot, J. L., & Puig, L. (2022). Efficacy of Tildrakizumab Across Different Body Weights in Moderate-to-Severe Psoriasis Over 5 Years: Pooled Analyses from the reSURFACE Pivotal Studies. *Dermatology and Therapy*, *12*(10), 2325-2341.
24. Wang, X., Kaiser, H., Kvist-Hansen, A., McCauley, B. D., Skov, L., Hansen, P. R., & Becker, C. (2022). IL-17 pathway members as potential biomarkers of effective systemic treatment and cardiovascular disease in patients with moderate-to-severe psoriasis. *International Journal of Molecular Sciences*, *23*(1), 555.
25. Dogra, S., Singh, N., Kumar, S., Narang, T., & Handa, S. (2022). Comparison of overall efficacy and safety of oral versus subcutaneous methotrexate in severe psoriasis. *Dermatologic Therapy*, *35*(8), e15656.
26. Michelucci, A., Manzo Margiotta, F., Panduri, S., Tonini, A., Romanelli, M., Morganti, R., ... & Dini, V. (2022). A real-life experience as a proof of Guselkumab effectiveness and safety in

patients with moderate to severe psoriasis. *Dermatologic Therapy*, *35*(4), e15339.
27. Yun, J. S., Scardamaglia, L., Tan, C. G., & McCormack, C. J. (2022). Successful secukinumab treatment of active bullous pemphigoid and chronic severe psoriasis: a case report. *Australasian Journal of Dermatology*, *63*(2), e155-e158.
28. Adamczyk, M., Bartosińska, J., Raczkiewicz, D., Adamska, K., Adamski, Z., Czubek, M., ... & Krasowska, D. (2023). Risankizumab Therapy for Moderate-to-Severe Psoriasis—A Multi-Center, Long-Term, Real-Life Study from Poland. *Journal of Clinical Medicine*, *12*(4), 1675.
29. Lebwohl, M. G., Soliman, A. M., Yang, H., Wang, J., Hagan, K., Padilla, B., & Pinter, A. (2022). Impact of Risankizumab on PASI90 and DLQI0/1 duration in moderate-to-severe psoriasis: a post hoc analysis of four phase 3 clinical trials. *Dermatology and Therapy*, *12*(2), 407-418.
30. Zozaya, N., Abdalla, F., Alfonso Zamora, S., Balea Filgueiras, J., Carrascosa Carrillo, J. M., Delgado Sánchez, O., ... & HIdalgo-Vega, Á. (2022). Assessing the value contribution of bimekizumab for the treatment of moderate-to-severe psoriasis using a multidisciplinary reflective multi-criteria decision analysis. *Expert Review of Pharmacoeconomics & Outcomes Research*, *22*(6), 941-953.