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COVID-19 pandemic and vaccination rate in patients with psoriasis treated with biologics: a single center experience

COVID-19 pandemija i stopa vakcinacije kod obolelih od psorijaze lečenih biološkim lekovima: iskustvo jednog centra

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Abstract

Background/Aim. Psoriasis is a chronic, immune-mediated, genetically determined disease, which is manifested by the appearance of erythematous scaly plaques. Treatment includes conventional therapies and biologics. The coronavirus disease 2019 (COVID-19) raised widespread concern for patients with psoriasis treated with immunosuppressive drugs, especially biologics. Even though there was no data at the beginning of the pandemic on the efficacy and safety of vaccines against COVID-19 in patients with psoriasis treated with biologics, the National Psoriasis Foundation (United States of America) recommended vaccination in these patients. The aim of this study was to evaluate the influence of COVID-19 on clinical characteristics and quality of life of psoriatic patients treated with biologics and evaluate the effectiveness of biologic therapy during the pandemic. **Methods.** A retrospective cross-sectional study was conducted at the Clinic of Dermatology and Venereology of the University Clinical Center of Serbia from March 2020 to January 2022. Data was collected from medical documentation during the consecutive hospitalization of patients with psoriasis who received biologics. **Results.** The study included a total of 181 patients with psoriasis divided into two groups. Patients from each group were treated with different biologics (ustekinumab in 63.0% and secukinumab in 37.0% of patients). They achieved significant improvement regarding their clinical characteristics after a two-year follow-up [Psoriasis Area and Severity Index (PASI) before treatment: 14.1 (0–50.5) and after treatment: 1.2 (0–49.7), $p < 0.001$] and quality of life [Dermatology Life Quality Index (DLQI) before treatment: 15.0 (0–34) and after treatment: 0 (0–28), $p < 0.001$]. Due to unsatisfactory therapeutic response in 4 (2.2%) patients, secukinumab was changed to ustekinumab. The vaccine against COVID-19 was given to 53.0% of patients, but only 20.4% received all three doses. Infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was confirmed in 64 (35.4%) patients, and 68.0% of those infected contracted the disease before the first dose of the vaccine. Therapy with biologics was delayed due to SARS-CoV-2 infection in 52 (28.7%) patients, of which 11 (21.2%) had exacerbation of psoriasis. **Conclusion.** The vaccination rate in patients with psoriasis receiving biologics was hardly 50.0%, and about a third of the vaccinated patients had a milder form of COVID-19. The therapy with biologics was successful regardless of the short-term interruption of drug administration due to the beginning of the COVID-19 pandemic and the worsening of psoriasis in some patients during that time.

Key words:
biological therapy; covid-19; psoriasis; vaccination.

Apstrakt

Uvod/Cilj. Psorijaza je hronična, genetski uslovljena bolest, posredovana imunskim mehanizmima, koja se manifestuje pojavom eritematoznih plakova sa skvamom. Lečenje podrazumeva konvencionalnu i biološku terapiju. Bolest izazvana korona virusom 2019. (*coronavirus disease 2019* – COVID-19) izazvala je zabrinutost za obolele od psorijaze koji se leče imunosupresivnim lekovima, posebno biološkom terapijom. Iako na početku pandemije nije bilo dovoljno podataka o efikasnosti i bezbednosti vakcine protiv COVID-19 kod obolelih od psorijaze na biološkoj terapiji, Nacionalna fondacija za psorijazu (Sjedinjene Američke Države) preporučila je vakcinaciju protiv COVID-19 kod ovih bolesnika. Cilj studije bio je da se ispita uticaj COVID-19 na kliničku sliku i kvalitet života

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obolelih od psorijaze koji su lečeni biološkom terapijom, kao i da se ispita efikasnost biološke terapije tokom pandemije. **Metode.** Retrospektivna studija preseka sprovedena je na Klinici za dermatologiju i venerologiju Univerzitetskog kliničkog centra Srbije, u periodu od marta 2020. do januara 2022. godine. Podaci su prikupljeni iz medicinske dokumentacije tokom konsekutivne hospitalizacije obolelih od psorijaze lečenih biološkom terapijom. **Rezultati.** Istraživanje je obuhvatilo 181 bolesnika obolelih od psorijaze podeljenih u dve grupe. Bolesnici iz obe grupe lečeni su različitim biološkim lekovima (ustekinumab kod 63,0% i sekukinumab kod 37,0% bolesnika). Kod njih je postignuto značajno poboljšanje kliničke slike, koja je praćena tokom dve godine [*Psoriasis Area and Severity Index* (PASI) pre lečenja: 14,1 (0–50,5) i posle lečenja: 1,2 (0–49,7), $p < 0,001$], i kvaliteta života [*Dermatology Life Quality Index* (DLQI) pre lečenja: 15,0 (0–34) i posle lečenja: 0 (0–28), $p < 0,001$]. Zbog nezadovoljavajućeg terapijskog odgovora kod 4 (2,2%) bolesnika, sekukinumab je zamenjen ustekinumabom. Vakcinu protiv COVID-19 primilo je 53,0% bolesnika, ali je sve tri doze primilo samo 20,4% bolesnika. Infekcija virusom *severe acute respiratory syndrome coronavirus 2* (SARS-CoV-2) potvrđena je kod 64 (35,4%) bolesnika a 68,0% od ukupnog broja zaraženih obolelo je pre prve doze vakcine. Terapija biološkim lekovima bila je odložena zbog SARS-CoV-2 infekcije kod 52 (28,7%) bolesnika, od kojih je 11 (21,2%) imalo pogoršanje psorijaze. **Zaključak.** Stopa vakcinacije obolelih od psorijaze koji su primali biološku terapiju bila je jedva 50,0%, a približno trećina vakcinisanih bolesnika imala je blaži oblik COVID-19. Biološka terapija bila je uspešna bez obzira na privremeni prekid kod pojedinih bolesnika usled COVID-19 i pogoršanja psorijaze u tom periodu. Biološka terapija je bila uspešna bez obzira na privremeni prekid lečenja koji je nastao usled početka pandemije COVID-19 i pogoršanja psorijaze kod pojedinih bolesnika u tom periodu.

Ključne reči:
biološka terapija; covid-19; psorijaza; vakcinacija.

Introduction

Psoriasis is a chronic, immune-mediated, genetically determined disease of the skin and nails, with a profound negative impact on the patient's quality of life [1, 2]. It affects 1–3% of the population, which is more than 125 million people worldwide [3]. The most common form of the disease is chronic plaque psoriasis (*Psoriasis vulgaris*), affecting 85–90% of patients [4]. Treatment of psoriasis includes topical and/or systemic therapy, such as retinoids, methotrexate, or cyclosporine, used for moderate-to-severe cases [5]. Since the early 2000s, the treatment of psoriasis was improved by biologics, which include inhibitors of tumor necrosis factor (TNFi) (infliximab, etanercept, adalimumab), interleukin (IL)-17 (secukinumab, ixekizumab, brodalumab), IL-12/23 (ustekinumab), and IL-23p19 (guselkumab, risankizumab) [6]. Currently, only two biologics are available in our country – secukinumab and ustekinumab. In terms of its scope, intensity, and dangers to the population's health, the crisis caused by the Coronavirus disease 2019 (COVID-19) pandemic has been, by far, one of the biggest challenges of the 21st century [7]. As the pandemic continued, COVID-19 vaccines were developed. Four types of vaccines have been approved, and those include whole virus vaccines (Sinopharm), mRNA vaccines (Pfizer BioNTech and Moderna), non-replicating viral vector (Oxford-AstraZeneca, Sputnik V), and protein subunit vaccines (Novavax) [8, 9]. This pandemic has raised widespread concern about the use of immunosuppressive agents in the treatment of several diseases, as well as psoriasis, especially in patients treated with biologics [10]. Owing to the differing methods across different studies, at the beginning of the pandemic, it was unknown whether patients with psoriasis had a higher risk of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection [11]. However, the Italian National Psoriasis Foundation suggested that vaccines play a pivotal role in protecting patients with psoriasis against SARS-CoV-2 infection and that these patients do not have to discontinue their prescribed antipsoriatic therapies [12]. Clinical trials showed high efficacy rates and no major safety concerns regarding the use of vaccines against COVID-19 [13]. Brazzelli et al. [14] conducted an observational monocentric prevalence study where they concluded that patients treated with biologics are not susceptible to COVID-19 compared to other psoriatic patients. The National Psoriasis Foundation (United States of America) recommended the use of vaccines against COVID-19 in patients undergoing biological treatment without the need to discontinue therapy [15]. Wu et al. [16] have reported cases of new-onset psoriasis as well as psoriasis flares as adverse events after COVID-19 vaccination.

The aim of this study was to evaluate the impact of COVID-19 on worsening of clinical manifestations of psoriasis, evaluating Psoriasis Area and Severity Index (PASI) and Body Surface Area (BSA) scores, in patients in whom the polymerase chain reaction (PCR) test has confirmed the infection. Moreover, the aim was to evaluate the vaccination rate in patients with psoriasis treated with biologics. To the best of our knowledge, this is the only study in our region that has evaluated these types of data during the COVID-19 pandemic.

Methods

A cross-sectional retrospective study was conducted at the Clinic of Dermatology and Venereology of the University Clinical Center of Serbia during the COVID-19 pandemic (March 2020 – January 2022). The study included 181 psoriatic patients treated with two biological drugs available in our country – secukinumab and ustekinumab. We collected data on the following: the type of biologics, their therapeutic effects [we evaluated PASI and BSA and Dermatology Life Quality Index (DLQI) scores before and after the treatment, but also after the confirmed infection with SARS-CoV-2], the incidence of COVID-19, vaccination rate and type of COVID-19 vaccine that patients received, possible delay of therapy, as

well as the further course of psoriasis. Data was collected from the computer database during consecutive hospitalizations of patients with psoriasis who received biologics.

The PASI and BSA scores were used to assess the disease severity. Based on PASI, psoriasis can be classified as mild (PASI < 3), moderate (PASI 3–10), and severe (PASI > 10) [17]. BSA measures the affected skin area according to the patient's palm surface. For PASI and BSA scores above 10, systemic therapy is recommended. To evaluate the impact of psoriasis on the patient's quality of life, we used a validated DLQI questionnaire. Scores above 10 require systemic therapy [18, 19].

Statistical analysis

Categorical variables were expressed as counts and percentages, while continuous variables were presented as mean ± standard deviation or range. For comparison between variables, the Chi-square test, Student's *t*-test, and Mann-Whitney rank sum test were applied. All statistical methods were considered statistically significant if the *p*-value was less or equal to 0.05.

Results

Demographic and clinical data are shown in Table 1. Initially, ustekinumab was introduced in 60.8% of patients and secukinumab in 39.2% without a significant difference in the frequency of those medications prescribed between genders. Due to unsatisfactory therapeutic response in 4 (2.2%) patients, secukinumab was changed to ustekinumab. Therefore, 63.0% of patients were treated with ustekinumab and 37.0% with secukinumab. The average PASI score before introducing biologics was 14.1 (0–50.5), and two years later, it was 1.2 (0–49.7), $p < 0.001$. There was a statistically significant improvement in the PASI score for all psoriatic patients. The PASI score for patients before starting secukinumab was 13.25 (0–42.0), and two years later, it was 0.95 (0–16.4), $p < 0.001$. For patients before starting ustekinumab, the PASI score was 14.7 (0–50.5), and two years later, it was 1.3 (0–49.7), $p < 0.001$.

The patients were also evaluated for PASI 50, PASI 75, PASI 90, and PASI 100 scores – PASI reduction of 50%, 75%, 90%, and 100% scores, respectively. In both groups (secukinumab and ustekinumab), PASI 50 was achieved in 89.8%, PASI 75 in 77.3%, PASI 90 in 54.7%, and PASI 100 in 23.2% of all patients. In patients treated with secukinumab, PASI 50 was registered in 95.5%, PASI 75 in 80.9%, PASI 90 in 58.8%, and PASI 100 was achieved in 29.4% of patients. In patients treated with ustekinumab, PASI 50 was observed in 86.4% of patients, PASI 75 in 76.4%, PASI 90 in 52.7%, and PASI 100 was achieved in 19.1% of patients. There were no statistically significant differences between PASI 50, 75, 90, and 100 between patients treated with secukinumab and patients treated with ustekinumab (Table 2).

Table 1

Demographic and clinical data of patients with psoriasis treated with biologics (n = 181)

Parameter	Values
Male/Female	101/80 (56/44)
Age (years)	47.36 ± 15.42 (13–78)
Type of psoriasis	
psoriasis vulgaris	168 (92.8)
psoriatic erythroderma	5 (2.8)
nail psoriasis	5 (2.8)
palmoplantar pustular psoriasis	3 (1.6)
PASI	14.1 (0–50.5)
BSA	20.0 (0–98.0)
DLQI	15.0 (0–34)
Ustekinumab	110 (60.8)
Ustekinumab (male/female)	63/47 (57/43)
Secukinumab	67 (37.0)
Secukinumab (male/female)	36/31 (54/46)
Secukinumab changed to ustekinumab	4 (2.2)

PASI – Psoriasis Area and Severity Index; BSA – Body Surface Area; DLQI – Dermatology Life Quality Index.
Values are expressed as numbers (percentages) or numbers (range), except for age which is shown as mean ± standard deviation (range).

Table 2

PASI 50, 75, 90, and 100 in patients treated with secukinumab and ustekinumab

PASI percentage response rate	Total	Secukinumab	Ustekinumab	*p*-value*
PASI 50	159 (89.8)	64 (95.5)	95 (86.4)	0.051
PASI 75	139 (77.3)	55 (80.9)	84 (76.4)	0.368
PASI 90	98 (54.7)	40 (58.8)	58 (52.7)	0.365
PASI 100	41 (23.2)	20 (29.4)	21 (19.1)	0.100

For abbreviations, see Table 1. Results are shown as numbers (percentages).
***For the level of significance of 0.05 according to the Chi-square test.**

The average BSA score before biologic therapy was 20.0 (0–98.0), and two years later, it was 1.0 (0–85.0), $p < 0.001$. There was a statistically significant improvement in BSA score two years after starting biologic therapy. For patients before starting secukinumab, the BSA score was 20 (0–65), and two years later, it was 1.0 (0–30.0), $p < 0.001$. For patients before starting ustekinumab, the BSA score was 18.0 (0–98.0), and two years later, it was 2.0 (0–85.0), $p < 0.001$. The DLQI score before biologic therapy was 15.0 (0–34), and two years later, it was 0 (0–28.0), $p < 0.001$. For patients before starting secukinumab, it was 15 (0–29), and two years later, it was 0 (0–20), $p < 0.001$. For ustekinumab, before therapy, the DLQI score was 14.5 (0–34), and two years later, it was 0 (0–28), $p < 0.001$.

SARS-CoV-2 infection, proven with standard PCR test, was reported in 64/181 (35.4%) psoriatic patients, with 30/64 (46.9%) females and 34/64 (53.1%) males ($p = 0.0592$). Secukinumab was applied among 22/64 (34.4%) patients and ustekinumab among 42/64 (65.6%) patients, with no statistically significant difference ($p = 0.505$). Of the 46.9% of female COVID-19 patients, 9/30 (30.0%) were on secukinumab and 21/30 (70.0%) were on ustekinumab. Of 53.1% of COVID-19 patients of male gender, 13/34 (38.2%) were on secukinumab, and 21/34 (61.8%) were on ustekinumab, with no statistically significant difference ($p = 0.550$).

Therapy with biologics was delayed due to COVID-19 in 52/181 (28.7%) patients, while in another 14/181 (7.7%) patients, the therapy was postponed due to other medical issues (urinary tract infections, other respiratory diseases). Of the 28.7% of patients who had postponed therapy due to COVID-19, exacerbation of psoriasis occurred in 11/52 (21.2%) patients (seven patients on secukinumab and four on ustekinumab). The mean PASI score before exacerbation was 5.1 (0.8–16.2), and after exacerbation, it was 10.9 (1.7–25.8). There was a significant difference in the PASI score ($p < 0.003$). Patients treated with secukinumab had a significant impairment of the PASI score ($p = 0.018$), while patients treated with ustekinumab did not have a significant increase in the PASI score ($p = 0.068$) (Figure 1). The average therapy delay was two months, but it should be emphasized that some patients had a longer delay not only due to COVID-19 but also due to other medical and non-medical reasons (examinations of other organ systems, lack of health insurance, etc.). The average therapy delay time was significantly longer among psoriatic patients who received ustekinumab than among those treated with secukinumab ($p = 0.002$). There was no association between PASI and delay time.

COVID-19 vaccination was performed in 96/181 (53.0%) of our patients; 9/181 (5.0%) received only one dose, 50/181 (27.6%) received two doses, and 37/181 (20.4%) received all three doses. However, 63/181 (34.8%) patients did not receive the vaccine, while for 22/181 (12.2%) of our patients, we have no record of their vaccination. Among the vaccinated patients, the highest percentage received the Sinopharm vaccine at 25.4%, followed by Pfizer at 17%, and Sputnik at 4.4%. We also had patients who combined vaccines with 3.3% receiving a combination of Sinopharm and Pfizer, 1.8% receiving Pfizer and Sputnik, and 1.1% receiving Pfizer and AstraZeneca (Figure 2). There were 42.0% of vaccinated males and 45.0% of females on secukinumab, while 58.0% of males and 55.0% of females were on ustekinumab ($p = 0.340$). There was no significant difference in gender distribution among vaccinated psoriatic patients according to the use of biologic therapy.

Of the total number of patients, 23.8% got infected with the SARS-Cov-2 virus before getting vaccinated (23.0% of females and 26.3% of males). Of the remaining 11.6% of infected patients (who got COVID-19 after vaccination),

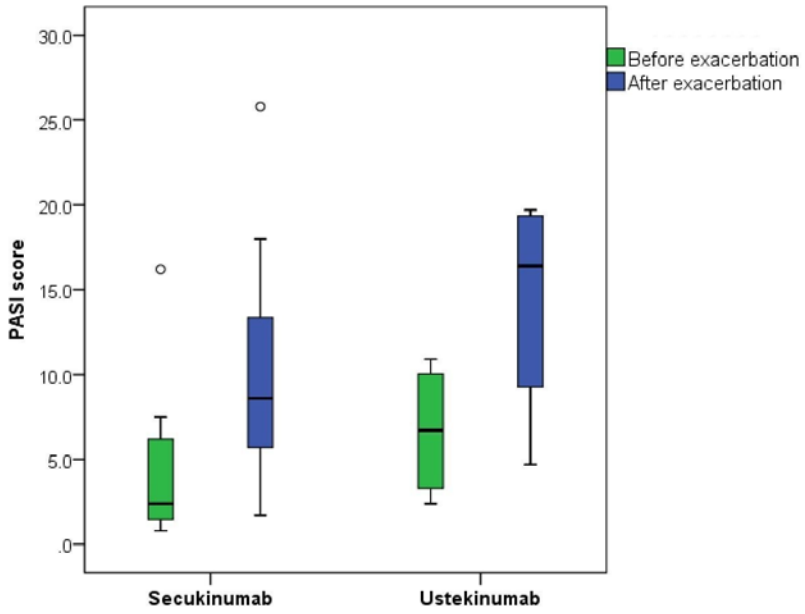

Fig. 1 – Worsening of psoriasis due to coronavirus disease 2019 measured by PASI score.
For abbreviations, see Table 1.

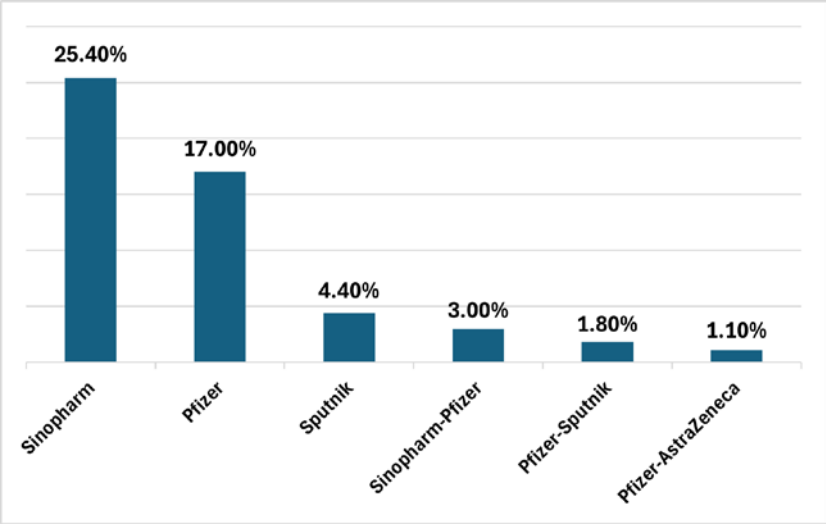

Fig. 2 ─ Vaccination rates in psoriatic patients treated with biologics.

3.1% got COVID-19 a year after two doses of vaccine, 2.0% got COVID-19 right after the second dose, one person (0.55%) got COVID-19 a month after the second dose of the vaccine, and another person (0.55%) got COVID-19 four months after the second dose of the vaccine. Those patients were, in fact, approximately one-fifth of all vaccinated patients, and all of them, except one patient (0.55%), had milder forms of the disease and did not require hospitalization. According to our data, only one male patient treated with ustekinumab died from COVID-19. He was not vaccinated; he had hypertension and a cytokine storm that occurred as part of the COVID-19.

Discussion

This research aimed to investigate the vaccination and SARS-CoV-2 infection rate in patients with psoriasis treated with biologics. We also explored the beneficial effects of treatment with biologics on psoriasis and tried to see if and how the COVID-19 pandemic affected those patients in our country.

In our study, we had a slightly larger number of male patients with psoriasis treated with biologics, which is consistent with other studies [20, 21]. This finding could be related to a slightly higher prevalence of psoriasis and a more severe form of the disease in the male population [22]. For instance, in the Swedish registry for systemic psoriatic treatment (PsoReg), 60.0% of registered patients are men. Other European registries show even bigger numbers in favor of men: Denmark 66.0%, Italy 67.0%, and Spain 63.0% [23]. The introduction of biologics for the treatment of psoriasis has not only drastically changed the course of the disease but also improved the quality of life of these patients. We can conclude this based on the findings of PASI, BSA, and DLQI scores before and after the treatment. PASI 50, PASI 75, PASI 90, and PASI 100 achieved with biologics were also quite satisfactory, as shown in several other studies around the world [24–27]. Complete vaccination was considered the most important means for overcoming the COVID-19 pandemic. Complete vaccination of a significant number of people worldwide helps create collective immunity and drastically decreases the probability of spreading the disease [28]. In a prospective single-center study, Lodde et al. [29] have shown that in people with psoriasis treated with systemic immunosuppressive therapy, as well as in those treated with biologics, an anti-SARS-CoV-2 IgG seroconversion was achieved in 96.1% of patients. Slightly more than half (53.0%) of our patients with psoriasis have been vaccinated against COVID-19, but complete vaccination was conducted in only 20.4%. The most commonly used vaccine was Sinopharm, followed by Pfizer. In a study conducted on Chinese patients with psoriasis, 68.9% received complete vaccination against COVID-19. The most commonly used vaccine among them (89.5%) was the inactivated vaccine (Sinopharm), followed by the protein subunit vaccine (Novavax) in 8.3% of patients, and 2.2% of patients received the adenovirus vector vaccine (AstraZeneca and Johnson & Johnson). The difference in vaccination coverage between Chinese and our patients probably lies in patient awareness, as well as in official recommendations. No severe adverse reactions were reported in vaccinated patients. Moreover, the use of biologics in the treatment of psoriasis was not associated with an increased risk of adverse reactions [30], which is consistent with our experience. The COVID-19 pandemic has influenced and changed the lives of all people around the globe and has certainly affected chronic patients, especially those on immunosuppressive therapy. In our study, we reported that 35.0% of patients had COVID-19 without significant differences in relation to the biological drug they received. Of course, we considered only patients in whom COVID-19 was proven by adequate testing – PCR test for SARS-CoV-2. Due to COVID-19, 29.0% of patients postponed their treatment with biologics, and the average therapy delay was two months. Significant exacerbation of psoriasis presented as an elevated PASI score and was present in one-fifth of the patients. Patients treated with secukinumab had

significant impairment of the PASI score compared with those treated with ustekinumab, which can be explained by the time interval of drug administration (secukinumab is administered every four weeks, while ustekinumab every 12 weeks). Most patients did not have a serious exacerbation of psoriasis. Furthermore, they had mild forms of COVID-19, which did not require hospitalization, and all of them continued therapy with biologics after recovery, and their PASI score improved. Our findings are similar to those from a study by Mroz et al. [20]. They reported that from 57 patients, 19 developed COVID-19, of which three patients on ustekinumab had exacerbation of psoriasis, while only one patient on secukinumab got infected and had no exacerbation of psoriasis. However, all COVID-19 patients had a mild course and did not require hospitalization. One other study conducted in a clinic in central Italy for 136 weeks, including 151 patients with moderate-to-severe plaque psoriasis treated with secukinumab, found that not a single patient reported infection with SARS-CoV-2 [31]. Unfortunately, in our research, one patient treated with ustekinumab died from COVID-19. According to our knowledge, he was not vaccinated, had hypertension, and a cytokine storm occurred as part of the COVID-19 symptoms. He obtained his biologics regularly and was healthy when the treatment was administered. Recent studies showed no adverse impacts from biologics on COVID-19 outcomes in patients with psoriasis [32]. No significant difference was found in the rates of hospitalization when compared to the general population, stratified by age or class of the biologics. Those findings are consistent with other studies that reported that patients with psoriasis on biologics were not at an increased risk of intensive care unit admission or death; they can be, however, at higher risk for testing positive for SARS-CoV-2, to be self-quarantined at home or hospitalized. The authors suggest further application of biologics during the pandemic because there is no evidence that these drugs are responsible for the development of severe complications in COVID-19 [32, 33]. However, some studies suggest that biologics should be discontinued in COVID-19 patients and that the risks and benefits should be carefully weighed in these therapies [34].

Conclusion

The vaccination rate in patients with psoriasis receiving biologics was not satisfactory. Just over half of the patients have been vaccinated against COVID-19, and only one-fifth received all three recommended doses, all without unusual side effects. One-third of all patients had milder forms of COVID-19, but it should be noted that a great majority of them got infected before receiving the vaccine. Almost one-third of the patients discontinued treatment with biologics due to COVID-19, and one-fifth had exacerbation of psoriasis. Fortunately, after re-introducing biologics, the disease subsided, and the biologics were continued according to protocol. We can also confirm that patients treated with both available biologics had very good therapeutic effects and were quite satisfied with the improvement in their quality of life.

Conflict of interest

The authors declare no conflict of interest.

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