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Biological Treatment of Psoriasis: A Different Life

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Abstract: ***Psoriasis has a significant detrimental effect on quality of life and is linked to both anxiety and depression. The introduction of biologics has improved treatment outcomes, but it is not well understood how patients feel about these gains. Aims of the current study was to address the advantages and disadvantages of biologics as a first - line treatment option and revise treatment guidelines in light of new research. The comorbid conditions are included in our discussion. Additionally; to discuss the effect of COVID - 19 on psoriasis patients. Furthermore; to investigate the daily activities of psoriasis patients getting biological therapy in order to better understand their requirements and the care they receive. Methodology: The current study was searched using a variety of key words such as "biologic therapy" "psoriasis", "psoriatic arthritis", "Type of psoriasis", "psoriasis and/or complications", "psoriasis and/or COVID", "psoriasis and/or interstitial pneumonia", "inteleukin - 23" and "interluekin - 17". Those articles were derived from the data related to Psoriasis and reported cases were conducted utilizing seven electronic databases (CINAHL, MEDLINE, ProQuest, PubMed, Scopus, Science Direct, and Cochrane) for studies published in various languages from January 2023 to September 2023. According to the findings, psoriasis is a prevalent inflammatory skin illness with major medical and psychosocial comorbidities that is primarily genetically determined. The number of therapy options available to people with psoriasis is growing as a result of improvements in our understanding of the disease's aetiology. biological treatments that reduce systemic inflammation may improve cardiovascular outcomes in psoriasis patients. Similar to how metabolic syndromecan be well controlled by medicine or lifestyle modifications, psoriasis signs and symptoms may improve as a result.***

Keywords: biologic therapy, psoriasis, biologics; psoriasis; psoriatic arthritis; tumour necrosis factor; inteleukin - 23; interluekin - 17, Psoriasis, biologics, COVID - 19 and psoriasis

1. Introduction

1.1 Background

A prevalent chronic inflammatory skin disorder with many different clinical manifestations is psoriasis. The most prevalent form of psoriasis, psoriasis vulgaris (PV), is primarily caused by dysfunction of the adaptive immune system (***Hu et al., 2021).*** The most uncommon form of psoriasis, pustular psoriasis (PP), is characterized by an overactive innate immune system that results in the distinctive erythematous, scaly skin and pustules that can merge to form pus lakes (***Bachelez, et al., 2020).*** A rare and potentially fatal form of psoriasis known as generalized pustular psoriasis (GPP) is characterized by recurrent fever, systemic flushing, and sterile pustules (***Fujita et al., 2018).*** GPP is a potentially fatal condition that can manifest as a chronic condition with sporadic acute flares involving systemic inflammation (***Haskamp et al., 2020).*** Due to its rarity and lack of established therapeutic standards, therapy of GPP has been restricted even though it may be fatal (***Strober et al., 2022).*** Recent discoveries about the aetiology of GPP have produced cutting - edge therapeutic alternatives, food and drug administration (FDA) approved GPP - specific drug (***Kodali et al.2023 and Morita et al. (2023).*** Therapy with biological agents may be required for severe, refractory cases of pediatric psoriasis or atopic dermatitis; however, this may be challenging due to a lack of therapy alternatives and established treatment guidelines (***Cline, et al., 2020).***

Epidemiologically**;** both men and women can have psoriasis, although women tend to get it earlier and are more likely to have a family history of it. According to ***Parisi and Iskandar (2020),*** its age of onset has a bimodal distribution with maxima for males and women at 30 - 39 and 60 - 69 years old, respectively. Psoriasis affects an estimated 60 million individuals globally, with prevalence rates varying by nation from 0.05% in Taiwan to 1.88% in Australia. High - income locations and those with older populations seem to have it more frequently. According to the ***Global Psoriasis Atlas from 2021***, it affects 1.52% of the general population in the UK.

The underlying pathophysiology connecting psoriasis and metabolic syndrome (MetS) appears to entail shared genetic predispositions and inflammatory pathways, albeit the precise causative relationship between these two conditions is not yet fully defined. Both illnesses are characterized by dysregulation of the IL - 23/Th - 17 immunological signaling system, which may have a significant role in increasing susceptibility to metabolic and cardiovascular disorders in both psoriasis patients and non - psoriasis patients. Therefore, biological therapies for psoriasis that block these signals could diminish the inflammatory burden of psoriasis while simultaneously lowering the risk of atherosclerosis and cardiometabolic disorders. In recent imaging investigations, healing of skin lesions was linked to improvement in vascular inflammation, providing evidence that biological agents' positive effects extend beyond the skin and may assist to fend against cardiovascular disease (CVD) (***Wu, et al., 2022).***

Tumor necrosis factor (TNF), interleukins (IL) 17, 12, and 23, as well as hereditary autoimmune processes are thought to be the cause of the disease. A more thorough understanding of the psoriasis' molecular pathogenesis allowed for the targeted use of biological therapy to treat

moderate to severe instances (***Kisielnicka, et al., 2020).*** Psoriasis has a complex pathophysiology, although genetics plays a major role, particularly in cases of plaque psoriasis with an early beginning (40 years). Heritability was estimated to be between 60 and 90 percent in twin, family - based, and extensive population - level investigations, which proved this. Genome - wide association studies have now found more than 60 susceptibility loci. Many of the probable causative genes are implicated in the IL - 23/Th17 axis (IL23R, IL12B, and TYK2), the skin barrier function (LCE3), NF - kappa B signaling (TNIP1), type 1 interferon pathway (RNF113, and IFIH1), antigen presentation (HLA - C and ERAP1), and type 1 interferon signaling. This shows that T cells interact in a complicated way (***Dand et al., 2020).*** The IL - 23/Th17 axis is the main driver of immune activation, chronic inflammation, and keratinocyte proliferation, and dendritic cells and keratinocytes are believed to be the pathophysiology of psoriasis (***Schön et al., 2018).*** Psoriasis has been linked to environmental triggers such stress, obesity, beta - blockers, smoking, and lithium (***Budu - Aggrey, et al., 2019).*** Pustular psoriasis appears to be genetically unique, and various susceptibility genes, including CARD14, IL36RN, and AP1S3 in people with European heritage, have been implicated (***Raharja et al., 2021).***

Clinically; there are numerous ways that psoriasis can appear, including plaque, flexural, guttate, pustular, or erythrodermic psoriasis. The most prevalent type is plaque psoriasis, which manifests as symmetrical, well - defined salmon pink plaques with silvery - white scale on the scalp, trunk, and extensor surfaces (particularly the elbows and knees). Where scales have been removed, bleeding spots can be seen (Auspitz sign). Flexural psoriasis can affect the axillae, sub - mammary, and vaginal areas and manifests without much scaling. Guttate psoriasis typically, but not always, is preceded by streptococcal infection and manifests as an acute, symmetrical eruption of drop - like papules or plaques that primarily affects the trunk and limbs. Plaque psoriasis can later appear in patients with guttate psoriasis. The broad erythematous rash (erythroderma) caused by severe untreated psoriasis is life - threatening due to potential sequelae include hypothermia, infection risk, acute renal injury, and high - output heart failure. The occurrence of psoriasis in traumatized skin areas is known as the Koebner phenomenon. Up to 50% of patients may experience nail problems, including nail pitting (indentation in the nails), onycholysis (separation of the nail plate from the nail bed), oil spots (nailbed discolouration), dystrophy, and subungual hyperkeratosis (***Raharja, et al., 2021).***

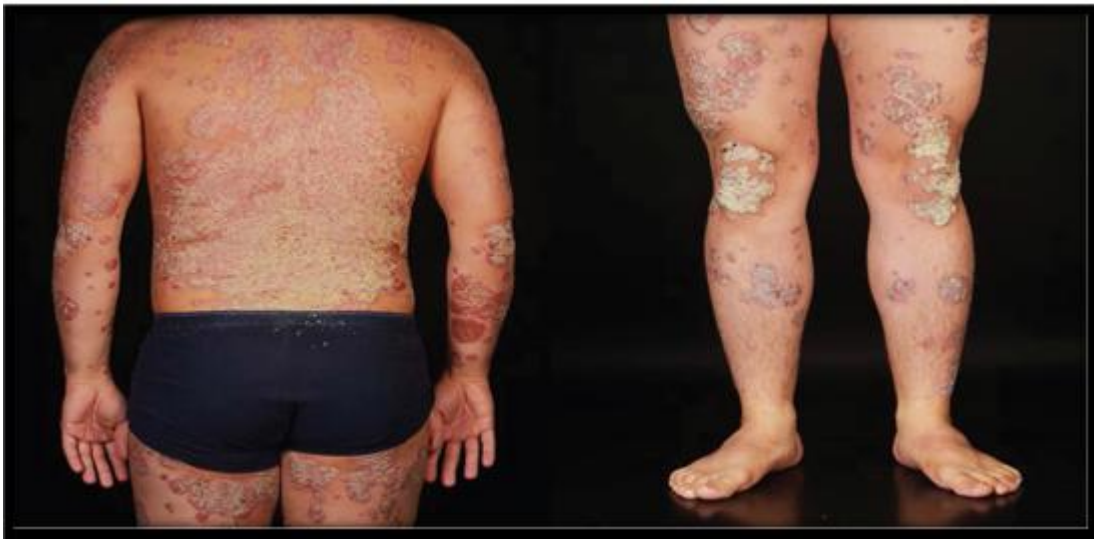

Figure 1: Chronic plaque psoriasis. Widespread, symmetrically distributed and well - demarcated erythematous, scaling plaques. Extensor surfaces such as elbows and knees are typically affected ***(Raharja, et al., 2021).***

Clinical manifestations of psoriasis can take many different shapes, including plaque, flexural, guttate, pustular, or erythrodermic. Psoriasis is thought to impact 60 million individuals worldwide, with 1.52% of the population in the UK being affected. Psoriasis is an immune - mediated inflammatory disease with a significant hereditary component. A holistic and multidisciplinary approach to therapy is necessary because of its link to psoriatic arthritis and elevated incidence of cardiometabolic, hepatic, and psychiatric comorbidities ***(Raharja et al., 2021).*** Body surface area (BSA) and the severity of erythema, induration, and scaling are used to determine the extent of psoriasis as assessment of psoriasis patients. In secondary care, validated scores like the Physician Global Assessment Scale (PGAS) and the Psoriasis Area Severity Index (PASI) are frequently combined with patient - reported outcome measures like the Dermatology Life Quality Index (DLQI). It is crucial to pay attention to its psychological effects as they could cause disengagement and non - adherence to therapy. Multimorbidity screening is an opportunity that arises at every patient interaction ***(Patrick et al., 2021).***

Psoriasis is primarily a skin and joint condition, but it is also a systemic inflammatory disorder that alters innate and adaptive immunity, with effects that go beyond the condition's visible lesions (***Blake et al., 2020).*** Circulating proinflammatory mediators in psoriasis cause a systemic inflammatory response that is typically accompanied by concomitant conditions like CVD and metabolic syndrome. According to ***Gisondi et al. (2018),*** the prevalence of MetS, a complex disorder that is characterized by the coexistence of numerous disorders that raise the risk of CVD, ranges from 20% to 50% in psoriasis patients. It also rises as the severity of the psoriasis gets worse. In comparison to the

general population, family members of psoriasis sufferers are more likely to get the disease, suggesting that psoriasis has at least some hereditary roots. The possibility that a unique genetic background may possibly contribute to the greater propensity for MetS in psoriasis patients is of special interest (***Dand et al., 2020). Figure 2*** provides a summary of the immunological processes that both psoriasis and CVD share. Relationship between cardiovascular health, metabolic syndrome, and the severity of psoriasis (***Wu et al., 2022).***

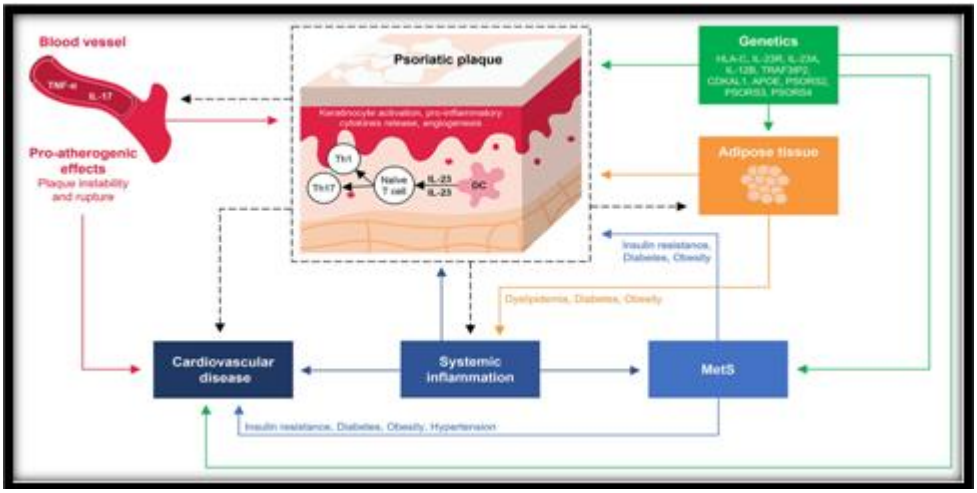

Figure 2: Common underlying immunologic mechanisms of psoriasis and CVD APOE, apolipoprotein E; CDKAL1, CDK5 Regulatory Subunit Associated Protein 1 - Like 1; DC, dendritic cells; HLA, human leukocyte antigen; IL, interleukin; MetS, metabolic syndrome; PSORS, psoriasis susceptibility loci; Th, T helper cells; TNF, tumour necrosis factor; TRAF3IP2, TRAF3 - interacting protein 2 ***(Wu, et al., 2022).***

Psoriasis treatments include topical agents (vitamin D analogues and corticosteroids), phototherapy (narrowband ultraviolet B radiation (NB - UVB) and psoralen and ultraviolet A radiation (PUVA)), standard systemic (methotrexate, ciclosporin and acitretin), biologic (TNF, IL - 17 and IL - 23 inhibitors) or small molecule inhibitor (dimethyl fumarate and apremilast) therapies. The creation of extremely effective and focused treatments has been facilitated by improvements in the understanding of its pathogenesis (***Raharja et al., 2021).*** The choice of psoriasis treatment may be influenced by awareness of multimorbidities in addition to enhancing overall health. For instance, using methotrexate may not be advised if the patient has chronic liver illness. Rheumatologists, hepatologists, and clinical psychologists are frequently involved in a multidisciplinary approach, which is essential (***Patrick et al., 2021).***

One research suggests that using biologic therapy for moderate to severe psoriasis would not increase the likelihood of contracting COVID - 19 infection and associated potentially fatal consequences. In especially during the pandemic phase, when patients are more likely to be influenced by misunderstandings and to acquire psychological problems such as dread and worry, dermatologists play a crucial role in advising and educating the patients. Patients should be reassured that they can maintain their modified lives and biologic therapies with the utmost care to avoid contracting COVID - 19, given that adherence to biologic therapy is strongly connected with decreased incidence of relapses according to ***Polat et al. (2021).***

The treatment of psoriasis and psoriatic arthritis has been significantly improved by the development of biologic medicines over the past 20 years. Given that there are currently 11 FDA - approved biologic treatment options for psoriasis, they have significantly improved. However, there is also misunderstanding among providers as a result of the abundance of possibilities. In addition to the distinctive skin lesions, psoriasis is a persistent systemic inflammatory illness that is accompanied by a number of comorbidities. The most prevalent comorbidity of psoriasis is MetS, which is also a risk factor for CVD, a leading cause of mortality in psoriasis patients. Although the exact causal relationship between these two disorders is not fully established, the underlying pathophysiology linking psoriasis and MetS seems to involve overlapping genetic predispositions and inflammatory pathways (***Brownstone, et al., 2021).***

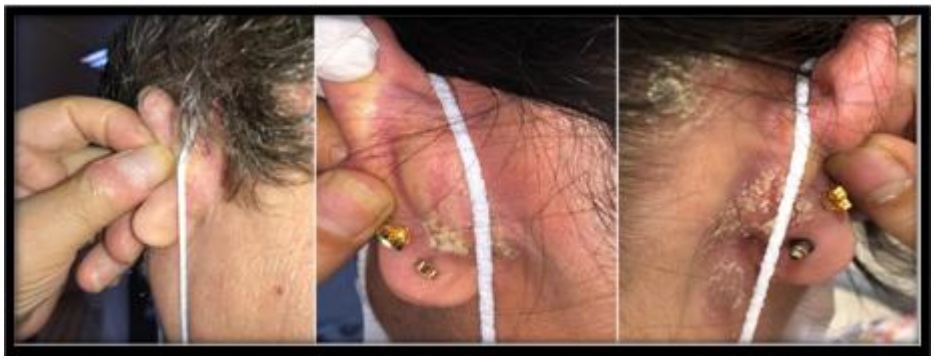

Figure 4: Retroauricular psoriasis lesions due to the use of face mask (***Polat et al.2021).***

Psoriasis patients' treatment plans should be customized to match their unique needs depending on the severity of their condition, how it affects their quality of life, how well they responded to previous medicines, and whether they have any other conditions. Clinical decision - making should take into account the essential data from clinical trials evaluating the safety and effectiveness of biologic medicines and small - molecule medications for psoriasis (***Jiang, et al., 2023).*** For individuals with psoriasis and various concomitant diseases, specific recommendations about first line systemic therapy alternatives are also required.

A chronic inflammatory skin condition called psoriasis is characterized by scaly, indurated erythema. It significantly lowers patients' quality of life. It is now understood to be a systemic illness rather than only a skin condition because it also leads to psoriatic arthritis and mental health issues. Additionally, there is evidence of a link with cardiovascular events. Due to biologics' great efficacy and tolerable safety, psoriasis treatment underwent a significant change with their introduction. Today, psoriasis can be treated with a wide range of biologic medications. But there are differences in traits including onset speed, durability, safety profile, and effects on comorbidities. By making the best decision for each patient based on a better understanding of those characteristics, psoriasis' negative effects on patients' quality of life and persistence are reduced (***Kamata and Tada, 2020).***

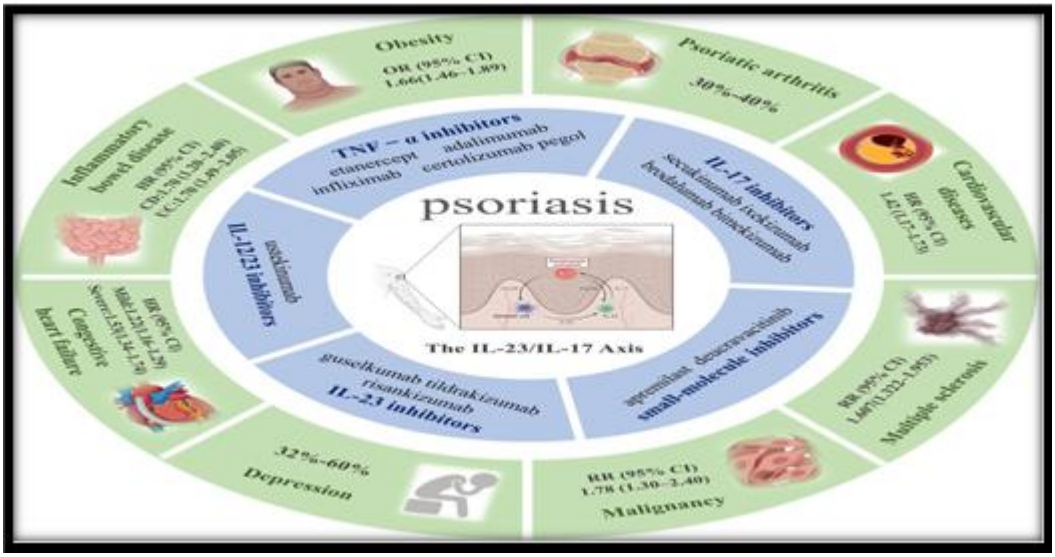

Figure 3: Summary of systemic treatment options and comorbidities in psoriasis. The inner ring depicts current biologic and small - molecule inhibitors for psoriasis, the outer ring depicts the strength of the association between psoriasis and comorbidities.

CI confidence interval, *HR* hazard ratio, *IL* interleukin, *OR* odds ratio, *RR* relative risk, *TNF* tumor necrosis factor, *UC* ulcerative colitis ***(Jiang, et al., 2023).***

1.2 Statement of the problem

According to ***Reich et al. (2015),*** psoriatic patients receiving biological therapy have a higher prevalence of obesity, diabetes, and CVD than those receiving normal systemic medication. Abnormal body mass is linked to a noticeably poor response to all systemic, biological therapies for persistent plaque psoriasis. The issue could become urgent if the population of overweight and obese patients keeps growing. Currently, patients who weigh more than 100 kg make up roughly 25–30% of the subpopulations in clinical trials and exhibit a lower frequency of an optimal response to biological therapy than the control group (***Ehsani, et al., 2016).*** The issue is largely caused by the substance's pharmacokinetic interactions during systemic metabolism. Abundant adipose tissue deregulation of medication clearance expands the drug distribution volume. Set clinical pharmacological doses eventually become insufficient and reduce the likelihood of a successful therapeutic outcome. The issue is particularly severe with biologics that have fixed dosage plans and have brief biological half - lives, such as etanercept and adalimumab, and may need

overweight and obese patients to pay higher therapy expenditures in order to reach therapeutic goals (***Tan, et al., 2013).***

In order to better inform therapy choices and, more specifically, guideline creation, it is urgently necessary to evaluate the relative efficacy and tolerability of psoriasis biologics (***Mahil, et al., 2020).*** In addition to the efficacy of the treatment, it's critical to define and comprehend the long - term dangers of biologic therapy in order to inform therapy choice and, whenever possible, reduce these risks for patients (***Al - Janabi, Yiu, 2022).***

Furthermore, to recognizing psoriasis as a significant non - communicable disease, the World Health Organization also highlighted the suffering caused by incorrect diagnoses, subpar care, and stigmatization of this condition (***World Health Organization, 2016).*** Psoriasis was estimated to have caused 5.6 million all - age disability - adjusted life - years (DALYs) in 2016 by the Global Burden of Disease Study, which is at least three times more than inflammatory bowel disease (IBD) ***(Hay et al., 2017).***

The therapeutic options for the treatment of moderate - to - severe psoriasis have grown as a result of the release of data from biologic clinical trials, the approval of novel biologics, and our improved understanding of the etiology of psoriasis. Tumor necrosis factor inhibitors, interleukin (IL) - 17 inhibitors, ustekinumab (an IL - 12/23 inhibitor), and IL - 23 inhibitors are biologics that are currently licensed for the treatment of psoriasis. For the personalization of patient treatment, data from clinical trials and investigations of the efficacy and safety of biologics are crucial (***Thatiparthi et al., 2021).*** Adalimumab, infliximab, etanercept (TNF - antagonists), and ustekinumab (IL - 12/23 inhibitor) are the four biologics that make up the standard treatment in clinical practice in Europe. Secukinumab and ixekizumab (IL - 17A inhibitors), which were just made available to clinicians, are thought to deliver the best therapy outcomes to date. Except for infliximab, they are delivered at set weight - independent doses that are doubled exclusively for patients receiving ustekinumab who weigh more than 100 kg (***Rnholt and Iversen, 2017).***

In comparison to oral systemic medications, the existing data suggests that biologics, particularly anti - TNFs, may be associated with a better prognosis in the occurrence of COVID - 19. To clearly define the impact of particular medications and other biologics like IL - 17 and IL - 23 inhibitors on the outcome of the COVID - 19, larger datasets are required. Therefore, the current study carried outaimed to address the advantages and disadvantages of biologics as a first - line treatment option and revise treatment guidelines in light of new research. The comorbid conditions are included in current discussion. Additionally; to discuss the effect of COVID - 19 on psoriasis patients. Furthermore; to investigate the daily activities of psoriasis patients getting biological therapy in order to better understand their requirements and the care they receive**.**

1.3 Research Question

- What are the advantages and disadvantages of biologics as a first - line treatment option?
- What are the treatment guidelines in light of new research?
- What are the comorbid conditions of psoriasis patients?
- What is the effect of COVID - 19 on psoriasis patients?
- What are the daily activities of psoriasis patients getting biological therapy in order to better understand their requirements and the care they receive?

1.4 Study Aims

Aim of the current study was to address the advantages and disadvantages of biologics as a first - line treatment option and revise treatment guidelines in light of new research. The comorbid conditions are included in current discussion. Additionally; to discuss the effect of COVID - 19 on psoriasis patients. Furthermore; to investigate the daily activities of psoriasis patients getting biological therapy in order to better understand their requirements and the care they receive**.**

2. Methodology

2.1 Research Design

The current study was designed as integrated literature review to stand on the advantages and disadvantages of biologics as a first - line treatment option and revise treatment guidelines in light of new research. The comorbid conditions are included in current discussion. Additionally; to discuss the effect of COVID - 19 on psoriasis patients. Furthermore; to investigate the daily activities of psoriasis patients getting biological therapy in order to better understand their requirements and the care they receive**.**

2.2 Data collection

The current study was searched using a variety of key words such as “biologic therapy” “psoriasis”, “psoriatic arthritis”, “Type of psoriasis”, “psoriasis and/or complications”, “psoriasis and/or COVID”, “psoriasis and/or interstitial pneumonia”, “inteleukin - 23” and “interluekin - 17”. Those articles were derived from the data related to Psoriasis and reported cases were conducted utilizing seven electronic databases (CINAHL, MEDLINE, ProQuest, PubMed, Scopus, Science Direct, and Cochrane) for studies published in various languages from January 2023 to September 2023. Up until September 2023, we looked for randomized controlled trials (RCTs) in the MEDLINE, PubMed, EMBASE, and Cochrane databases. Data were collected using direct, indirect, and placebo comparisons of different biologics.

2.3 Study inclusion criteria

All studies about the advantages and disadvantages of biologics as a first - line treatment option and revise treatment guidelines in light of new research. The comorbid conditions are included. Additionally; the daily activities of

psoriasis patients getting biological therapy in order to better understand their requirements and the care they receive**.**

3. Discussions

On the word of ***Parisi et al. (2020),*** psoriasis is a chronic, inflammatory skin condition that affects up to 2% of people worldwide. According to ***Szepietowski et al. (2016) and Miller et al. (2013),*** it manifests as well - defined, red, scaly plaques that can be itchy or painful and is linked to concomitant conditions such psoriatic arthritis, hypertension, obesity, and diabetes. Tumor necrosis factor (TNF), interleukin (IL) - 17, and IL - 23 are cytokines that are largely T - helper (Th) 17 and Th1 - driven and mediate psoriatic inflammation (***Duan et al., 2020; Armstrong et al., 2013).*** Broadly acting oral immunomodulators like methotrexate and ciclosporin, as well as biologics, which are monoclonal immunoglobulin - G (IgG) molecules (with the exception of etanercept) that target particular cytokines or receptors involved in the pathogenesis of psoriasis, are systemic treatment options for severe psoriasis. The key outcome measures in psoriasis are typically efficacy endpoints by 12 or 16 weeks, even though Phase III trials are essential for demonstrating the effectiveness and safety of treatments. Comparator arms are typically not included in trial extensions, and patients with substantial comorbidities who may be more susceptible to adverse events are frequently left out of trials (***Mason et al., 2018).*** Additionally, there could be a long delay between drug exposure and the emergence of side effects such cancer (***Al - Janabi, Yiu, 2022).***

Unfortunately, 2 - 4% of people worldwide are affected by psoriasis, a chronic inflammatory skin condition that is linked to higher mortality and multimorbidity. Powerful targeted biologic medicines have been developed as a result of a better understanding of the molecular pathophysiology of psoriasis, and this has drastically changed patient outcomes. There are currently eleven biologics approved for usage in Europe and the USA that target TNF, IL - 12/IL - 23p40, IL - 17A, IL - 17 receptor, and IL - 23p19 (guselkumab, risankizumab, and tildrakizumab). There is an urgent need for comparative efficacy studies to guide clinical decision - making as a result of the quick growth of therapy alternatives. Clinical decision - making must also take into account patient - reported outcomes, such as the change in the dermatological life quality index (DLQI) and measures of therapy tolerance. In a hierarchical cluster analysis, which simultaneously analyzes outcomes related to efficacy and tolerability, these data can be combined (***Mahil et al., 2020).*** Numerous analyses of biologics demonstrated that they were more effective than conventional systemic treatments and did not cause organ damage or serious adverse responses (***Kisielnicka et al., 2020).***

Being treated biologically was viewed as a turning point with profound effects on one's physical, psychological, and emotional well - being. However, psychological side effects including social withdrawal and isolation seemed to be ingrained in the patient's identity; the patient's unfavorable impressions of psoriasis left scars that damaged their sense of self. Patients felt insecure as a result of their perceived dread of stopping their biological treatment, which made them hesitant to bring up their worries with medical personnel. Being accepted for biological treatment could be difficult, but it appeared to mark a turning point in individuals' lives. The use of biologics seemed to shed light on the importance of the biological therapy and the impact that psoriasis had on one's prior daily life (***Trettin, et al., 2020).***

Psoriasis significantly lowers quality of life and is linked to sadness and anxiety (***Geale, et al., 2017).*** Patients with psoriatic arthritis have an even worse quality of life, more comorbid conditions, more healthcare costs, lower income, and higher unemployment rates (***Dalgard, et al., 2015 and Kristensen, et al., 2017).*** Despite advancements in medicine, the majority of psoriasis patients—even those whose condition is under control—remain dissatisfied with their care (***Khoury, et al., 2017).*** This may be the result of patients' discontent with the management of their psoriasis, particularly the lack of sympathy and support shown by health care professionals (HCP) who fail to acknowledge that having psoriasis is a complex, long - term disorder that affects more than just the skin. Psoriasis can have a negative impact on one's self - image and is linked to stigmatization and social exclusion (***Ghorbanibirgani, et al., 2016).*** Psoriasis patients battle with altered body images, pain, redness, and flare - ups. Major life - altering decisions may be impacted by psoriasis, and patients' lives may be shaped in ways that may have been different in the absence of the condition. These views of sickness can be connected to the Common - sense Model of Self - Regulation (CSM), which contends that patients' perspectives of their health are influenced by specific patterns in the way they organize their views of illness (***Martin et al., 2015).***

Psoriasis patients' impressions of their illnesses are cognitive representations made up of individual experiences depending on their social and cultural surroundings. It has been demonstrated that psoriasis patients struggle to restrain their negative feelings, and that the severity of the condition is correlated with how patients perceive their illness. Therefore, investigating patient experiences may help us all understand how people perceive their illnesses. Biologics have enhanced health - related quality of life and treatment outcomes, and they also provide long - term advantages (***Griffiths et al., 2018).*** Biologic use improves physical health and boosts self - assurance, although certain psychosocial effects may linger (***Wasilewska et al., 2016; Chaptini et al., 2016).*** Biologics may alter how patients live their life and how they view their condition, but it is unclear how patients will experience these changes (***Narayanan et al., 2015).***

Prior to the development of biologic medicines, the only systemic treatments for moderate - to - severe psoriasis were oral medications like methotrexate. The safety profile of methotrexate is far from optimal, despite the fact that it was a moderately successful treatment for psoriasis. For instance, methotrexate contains more than ten black box warnings, several of which include the possibility of death. There are also substantial black box warnings for other conventional oral treatments including oral retinoids and cyclosporine. Biologic agents provide alternatives that are significantly more potent than drugs like methotrexate but come with no

black box warnings at all. Another benefit is that some of the more modern biologic medications can be maintained with only four injections per year. It is evident that significant advancements have been made in the safety and effectiveness of biologic therapy for psoriasis. The ongoing advances in our understanding of the pathophysiology of psoriasis have allowed for the development of this novel therapy paradigm. Psoriasis was still predominantly viewed as an issue with epidermal hyperproliferation thirty years ago (***Brownstone et al., 2021).***

The role of the immune system in psoriasis has been highlighted by recent study into the disease's pathophysiology. The molecular basis of which cytokines are involved in the pathophysiology of psoriatic illness is now clearly understood. A number of different cell types, including keratinocytes, natural killer T cells, plasmacytoid dendritic cells, and macrophages, are implicated in the first cascade of psoriasis pathogenesis. These cells release cytokines that cause myeloid dendritic cells to become activated. Myeloid dendritic cells that have been stimulated then release IL - 12 and IL - 23. These two cytokines play key roles in the pathogenesis of psoriasis at the cellular level. Native T cells are transformed into Th1 cells (which secrete IFN - and TNF -) by IL - 12, while Th17 and Th22 cell proliferation is mostly dependent on IL - 23. TNF - , IL - 17, and IL - 22 are all produced by Th17 cells (***Armstrong and Read, 2020).*** In light of all of these various molecular signaling pathways, it is suggested that IL - 23 - mediated activation of the Th17 pathway is the primary cause of the inflammation present in psoriasis.

The greater efficacy of IL - 17 and IL - 23 biologic drugs may indicate that these pathways are more crucial to the pathophysiology of psoriasis and that, generally, psoriasis patients show higher pathology in this particular route. When compared to the era of a more widespread immunosuppression reflected by the old oral drugs, the ability to treat psoriasis has been changed by the fact that biologic agents interact with a particular cytokine (such as TNF - , IL - 17, or IL - 23) in a tailored manner. Targeted immunomodulation has greatly enhanced the safety and efficacy of biologic medicines, resulting in an improved therapy regimen (***Alwan and Nestle, 2015).***

According to ***Warren et al. (2015),*** one of the main reasons for biologic cessation is infection. Adalimumab trial data revealed an infectious adverse event rate of 1.2 occurrences per patient - year versus 0.8 for those who received a placebo (***Menter et al., 2008).*** According to combined trial data for risankizumab, 19–24% of patients experienced infection, compared to 9–16% for placebo (***Gordon et al., 2018).*** However, different studies use different safety outcome measures, do not always collect long - term data, and lack the necessary statistical power to investigate certain undesirable outcomes of interest, such as major infections. A serious infection is one that necessitates intravenous antibiotics, requires hospitalization, or results in death. A systematic review and meta - analysis (pre - print) of 29, 724 participants in psoriasis clinical trials discovered a low rate of serious infection (n=97) at 10 - 16 weeks with no statistically significant difference when compared to placebo or each other (***Manounah et al., 2021 and Penso et al., 2021).***

The immune response to fungus infections depends on IL - 17. According to a systematic evaluation of anti - IL17 trials, people receiving secukinumab, brodalumab, or ixekizumab experienced candida infection at rates of 1.7%, 4%, and 3.3%, respectively, as opposed to 0.3% in the placebo group. One severe case out of the 395 total cases was identified (0.3%). Although the longest follow - up was 56 weeks, phase III study data indicate that between 6% and 19.3% of patients in the bimekizumab groups developed candidiasis (***Warren, et al., 2021).*** In the be radiant phase III trial comparing bimekizumab and secukinumab, 12.9 - 19.3% of people receiving bimekizumab experienced candidal infection, as opposed to 3% of those receiving secukinumab (***Reich et al., 2021).*** These findings suggest that compared to other anti - IL17s, bimekizumab may be more prone to result in candidal infections. Other biologic classes may be better suitable for patients for whom fungal infection is a concern. Real - world data over longer follow - up periods are needed to determine the risk of candida infection in the long term.

Clinical practice guidelines usually advise screening with an interferon gamma release assay prior to the start of a biologic due to the potential risk of tuberculosis (TB) acquisition or reactivation (***Smith, et al., 2020).*** Ankylosing spondylitis, psoriatic arthritis, and rheumatoid arthritis were treated with anti - TNFs in a meta - analysis of RCTs, and it was found that participants on anti - TNFs had an increased risk of acquiring TB compared to controls. According to subgroup analysis, people with rheumatoid arthritis had the highest risk. We are not aware of any trials that are comparable or observational studies of TB risk in psoriasis patients. ***Nogueira et al. (2020)*** summarized information on latent tuberculosis infection rates among treated subjects from psoriasis IL - 17 and IL - 23 inhibitor trial extensions and safety studies. Prior to beginning biologic therapy, patients are typically checked for tuberculosis using an interferon gamma release assay, and any latent tuberculosis is typically treated. The strongest evidence supports the safe use of risankizumab in patients with latent TB who need immediate treatment for psoriasis and cannot wait for anti - TB therapy, but anti - TNFs should be avoided (***Smith et al., 2020).***

Several studies have been carried out in participants with IBD, despite the fact that there is little information available on the post - operative infection risk of anti - TNF medication in psoriasis patients. Anti - TNF medicines have been linked to a higher incidence of post - operative infections in patients with IBD, according to certain meta - analyses (***Ali et al., 2014; Yang et al., 2014),*** whereas other studies have found no such link (***Xu et al., 2019).*** Small sample sizes and the heterogeneity of the studies included in these meta - analyses may be the cause of conflicting data. There was no discernible change in the rate of post - operative wound infection in a small cohort study with 60 individuals who were taking either anti - TNF drugs or ustekinumab (***Shim, et al., 2018).*** There was no non - biologic control group in this study. After conducting a retrospective cohort research on patients receiving infliximab for inflammatory arthritis, psoriasis, or IBD,

George et al showed no change in infection risk after discontinuing treatment for less than 4 weeks compared with 8–12 weeks (OR 0.90, 95% CI 0.6–1.34). The National Psoriasis Foundation (NPF) and the American Academy of Dermatology (AAD) jointly developed guidelines that advise biologic therapy continuation during low - risk surgical procedures, but case - by - case consideration for moderate - or high - risk procedures (***Moosvi, et al., 2020).***

It is likely that biologics could reduce the immune response to severe acute respiratory syndrome coronavirus - 2 (SARS - CoV - 2) and hence raise the likelihood of severe COVID - 19 given the increase in risk of infection with some biologics as discussed above. Gisondi et al. carried out retrospective observational research of 5206 psoriasis patients receiving biologic therapy early in the pandemic and documented clinical information from patient records or contact. In contrast to the incidence rate of 1.6 in the general population, there were no COVID - 19 - related deaths and fewer patients were hospitalized (***Geisen et al., 2021).*** Izadi et al. 's more recent cohort analysis, which included 6077 people using immunomodulators for immune - mediated inflammatory disorders (IMIDs) including psoriasis, included data from several registries spanning several nations and disease domains. According to this study, methotrexate monotherapy and other oral medication regimens were associated with greater chances of hospitalization or death related to COVID - 19 when compared to anti - TNF monotherapy. Anti - TNF monotherapy and anti - TNF coupled with methotrexate did not significantly vary from one another (***Izadi, et al., 2021).*** Unfortunately, as related to ***Al - Janabi, et al., (2021)*** The study's ability to measure anti - nucleocapsid antibodies that are present after infection but not vaccination allowed it to identify individuals with past infection (even asymptomatic illness).

It's crucial to know whether biologics raise the risk of cancer because some tumors are immune - evading. The population's risk of developing skin cancer has been studied recently. ***Mason et al. (2021)*** used BADBIR in two cohort studies to compare the risks of basal cell carcinoma (BCC) and squamous cell carcinoma (SCC) in persons who had no prior history of keratinocyte malignancies to those who had such a history.14 800 participants made up the initial trial, with 9398 belonging to the biologic cohort and 5402 to the non - biologic systemic cohort. In the biologic cohort, there was no higher incidence of BCC or SCC compared to non - biologic systemic therapy. The second trial, which involved 267 people who had already experienced BCC or SCC, revealed no link between biologic therapy and the emergence of BCC or SCC. The key flaw in both studies was the modest number of BCC/SCC cases in both cohorts, which could have concealed the smaller impact of biologic therapy on the risk of keratinocyte cancer (***Mason et al., 2021).***

Therefore, in the authors' opinion, the possibility of cancer risk should not affect the choice of biologic agent. Clinical guidelines advise patients to take part in national cancer screening programs and to weigh the risks and benefits of stopping treatment individually with the help of a multidisciplinary team and oncology input in order to reduce potential risk (***Smith et al., 2020; Menter et al., 2019).*** In contrast to HF, the risk of major cardiovascular events (MACE), such as acute coronary syndromes and strokes, has been investigated in psoriasis patients receiving biologic therapy. According to ***Rungapiromnan et al. (2020),*** there were no changes in the risk of MACE between ustekinumab and anti - TNF, etanercept and adalimumab, or methotrexate and adalimumab. imply that a bigger sample size could be required to assess risk with more accuracy. Additionally, similar to malignancies, there may be a longer delay between exposure and the onset of an adverse effect, necessitating longer follow - up times to catch it. In order to determine if the start of ustekinumab was linked to an increased incidence of MACE in psoriasis patients with either high or low cardiovascular risk, ***Poizeau et al (2020).*** used the French National Health Insurance database.

For those in the low cardiovascular risk category, there was no increase in risk during the risk period. It is challenging to account for variables that are also time - dependent, such the severity of psoriasis, in this type of study design. For instance, patients who begin treatment early may have diseases that are worse managed, increasing the risk of the aforementioned adverse occurrence. The arbitrary choice of 6 months as the risk - period cut - off and the tendency of therapy adverse events to cluster early in susceptible individuals are other potential limitations listed by de ***Brito et al., (2021)*** leaving a relatively healthy cohort for analysis in the later time category. Data for control participants were not available, but combined trial and post - marketing surveillance data reassuringly showed a minimal risk of MACE in psoriasis patients receiving secukinumab (0.3 exposure adjusted incidence rates per 100 patient - years) (***Deodhar, et al., 2019).***

To our knowledge, neither the anti - IL23s nor any other anti - IL17s have had data published looking at the risk of MACE. In conclusion, there is limited evidence to support biologics leading to MACE, such as myocardial infarction or stroke, despite inconsistent evidence associating anti - TNF medicines to the onset or aggravation of heart failure. Anti - TNF medications are thus generally contraindicated in people with heart failure, and other classes may be more appropriate. If heart failure develops or worsens, anti - TNF therapy should be discontinued and a specialist's opinion should be obtained. According to ***Smith et al. (2020),*** there isn't enough solid evidence to support preferential selection of one biologic class over another in patients with a higher risk of MACE.

Biologic therapy during pregnancy has the potential to be teratogenic, raise the chance of spontaneous abortion, and modulate the immune system of the developing fetus. Anti - TNF medications have the most data regarding their use during pregnancy because they have been used to treat psoriasis for the longest. There is no proof of teratogenicity or a higher risk of spontaneous abortion in animal models, despite the fact that anti - TNF medications do pass the placenta (with the exception of certolizumab pegol) (***Yiu, et al., 2014).*** A systematic review of the IBD literature that included 58 trials with 1533 or more pregnant women who had been exposed to anti - TNF found no negative effects on the mother or the newborn (***Nielsen et al., 2013).*** In a recent

systematic evaluation of four cohort studies involving psoriasis patients, it was discovered that anti - TNF treated patients had an elevated risk of teratogenicity or preterm delivery in some trials, but not in all of them (***Pottinger, et al., 2017).*** Due to different sources of bias, inconsistency, and studies being conducted in indirect groups of women without known psoriasis, the GRADE toolkit was modified to classify all four research included in this review as having "very low" levels of evidence quality.

For the fetus' immunological protection, placental transfer of maternal IgG is crucial. This transfer is mediated by the FcRn receptor on syncytiotrophoblast (placental epithelial) cells, which binds to the Fc fragment of IgG (***Palmeira, et al., 2012).*** According to ***Mariette et al. (2018),*** certolizumab pegol is an anti - TNF IgG1 pegylated antibody that does not include the Fc antibody fragment and does not enter the placenta via FcRn - mediated transfer. Certolizumab pegol exposure during pregnancy did not increase the risk of teratogenicity or fetal death when compared to the general population, according to an analysis of prospectively collected data from 528 reported pregnancies with known outcomes (***Clowse, et al., 2018).*** Breastfed newborns of biologic - treated moms don't seem to experience any more difficulties than non - breastfed children or infants not exposed to these treatments, as biologics are protein molecules and are unlikely to be absorbed systemically (***Matro, et al., 2018).*** Certolizumab pegol should be taken into consideration by women who are considering getting pregnant, according to the current review, but decisions about continuing other therapies during pregnancy should be made on a case - by - case basis. Women who wish to breastfeed while receiving biologic therapy should be advised that, while theoretically safe, there is currently no data to support this.

Data on other biologic classes are extremely few. When compared to patients exposed to anti - TNF, one retrospective cohort analysis of ustekinumab - treated IBD patients reported no increase in preterm, fetal death, or teratogenicity (Wils et al., 2021). The sample size, albeit (29 cases and 76 controls), was modest. Although this trial lacked a reference group, it revealed rates of fetal death and teratogenicity to be in line with the general population in 292 patients with maternal exposure to secukinumab used for psoriasis, psoriatic arthritis, ankylosing spondylitis, and other reasons (Warren, et al., 2018). There are no conclusive studies that particularly address biologic exposure in psoriasis during pregnancy, thus it is impossible to draw any strong conclusions about its safety. Treatment choices must be chosen on a case - by - case basis, as is the case with other unknown risks, and clinical practice recommendations may vary. Anti - TNF therapy is safe during pregnancy and breastfeeding, according to the joint ADD - NPF guidelines (American Academy of Dermatology and the National Psoriasis Foundation), although the risk for other classes is uncertain. According to the British Association of Dermatologists (BAD) recommendations, women who are or may become pregnant should utilize reliable contraception while receiving biologic therapy, and certolizumab pegol may be the first choice when beginning biologic therapy in such patients. Furthermore, live immunizations should be avoided in these newborns for the first six months due to the possibility of biologic drug presence in neonates delivered to mothers using biologics beyond 16 weeks of pregnancy.

Psoriasis and depression are known to be related, and biologic use is linked to a decrease in depressive symptoms (***Strober et al., 2018).*** Despite the lack of a clear biological mechanism by which the opposite, i. e., biologics causing or intensifying mental symptoms, could occur, there have been reports of psychiatric adverse events throughout brodalumab's Phase 3 studies.18 The potential for brodalumab to cause psychiatric adverse events was investigated using an examination of brodalumab Phase 2 and 3 clinical trial data (***Lebwohl, et al., 2018).*** Participants in the analysis who had been exposed to brodalumab included 4464 people, of whom 564 had also been treated to ustekinumab. Compared to placebo, a greater percentage of the brodalumab sample experienced improvements in their anxiety and depression levels. The number of individuals who had previous psychiatric problems was comparable across treatment arms at the outset. In the brodalumab group, 3 suicides were reportedly committed. The incidence rates of suicidal ideation and behavior were equivalent between the brodalumab and ustekinumab groups, and rates of mental adverse events were similar across treatment groups. Additionally, a time - to - event analysis showed no temporal connection between these incidents and the commencement of brodalumab. This study has limitations because studies by their very nature cannot be powered to study infrequent adverse events and frequently do not include comparator arms after week 52. According to the most recent research, biologic start is linked to an improvement in psychiatric symptoms rather than a worsening. As a result, psychiatric comorbidity shouldn't prevent someone from receiving biologic therapy or affect their choice of biologic.

Biologics have been linked to a variety of paradoxical inflammatory reactions, including cutaneous adverse events, IBD, and interstitial lung disease. According to ***Garcovich et al. (2019),*** paradoxical psoriasis, eczema, pustular diseases, and lichenoid eruptions are among the cutaneous reactions to biologics that have been reported in patients with rheumatological disorders, IBD, and psoriasis. A systematic review of published cases, observational studies, and trial data on the development of eczema in psoriasis patients receiving biologic treatment revealed that 46% of patients stopped receiving the biologic medication, and there was a significant amount of heterogeneity in the approaches taken to treat the condition. The potential impact of cutaneous adverse events on affected patients is highlighted by this number, notwithstanding the possibility of publication bias inflating it. Uncertain factors may predispose individuals to eczematous reactions, however preceding atopy has been reported in 46% of published instances (***Al - Janabi, et al., 2020).*** Although an integrated safety analysis of ixekizumab trial data discovered an association between prior history of eczema and development of eczema on ixekizumab, ustekinumab, or etanercept, observational studies in psoriasis patients have not been conducted to confirm an association with clinical or demographic factors (***Brunner, et al., 2021).***

In a recent cohort study, the incidence of new - onset IBD was compared in 16, 793 anti - IL17 users with 20, 556 apremilast users and 10, 245 etanercept users using the database of the French national healthcare system (***Penso, et al., 2021).*** After controlling for illness severity, there was a higher incidence of IBD among those taking anti - IL17 than among those taking etanercept, but not as high as among those taking apremilast. Since this is the first study of its kind to date, further comparable research must be done. The use of anti - IL17s in individuals with IBD should be avoided, according to the available research. Investigations should be conducted on patients who begin exhibiting IBD symptoms while taking anti - IL17s, and therapy discontinuation should be considered.

A potential side effect of all biologic classes used to treat psoriasis, interstitial lung disease, has also recently been described (***Kuwana et al., 2021).*** A retrospective assessment of 603 psoriasis patients taking anti - IL17/23 biologics found six cases of interstitial lung disease, with five of those cases improving after stopping the medication (***Penso et al., 2021).*** Eight cases using anti - TNF drugs and one case each for secukinumab, ixekizumab, and ustekinumab were found in a different series (***Matsumoto et al., 2020).*** In contrast to those getting abatacept, rituximab, or tocilizumab for their rheumatoid arthritis, patients treated with anti - TNFs did not have a higher chance of developing interstitial lung disease, according to a retrospective cohort research published in 2015 (***Curtis, et al.).*** Given the lack of information, it is impossible to determine if biologics taken by psoriasis patients actually enhance the risk of interstitial lung disease. An ongoing skin inflammatory condition, psoriasis. However, recent publications in the literature call attention to the treatment - induced weight increase in psoriatic patients, which has become more prominent with the advent of biological therapy. Due to its numerous correlations with the condition and potential significance in the management of clinical practice, it is worthwhile to take into account the impact of body mass index on the biological treatment of chronic plaque psoriasis (***Kisielnicka et al., 2020).***

The recommendations cover topics including assessing the severity of psoriasis and its implications for daily life, prescribing these medications (both as first - line and follow - up treatments), setting treatment objectives, and treatment response. These suggestions serve as a helpful resource for hospital pharmacists, patient associations, hospital management, and health authorities. They also reflect the dermatologists' perspective on the treatment of psoriasis in Spain as described by general practitioners. This revision includes certain changes to earlier declarations, as well as fresh insights into developments in biologic medicines and brand - new global norms based on collected knowledge. Numerous brand - new synthetic compounds and biologics, including biosimilars, are being developed (***Carrascosa et al., 2022).*** Results of the Psoriasis Disease Severity Evaluation Psoriasis patients' disease severity is evaluated in clinical practice using a variety of approved metrics. The body surface area affected (BSA), the psoriasis area and severity index (PASI), and a comprehensive evaluation by either a doctor (PGA) or a patient (PtGA) are the most often utilized metrics. Prior to this consensus statement, general practitioners (GPs) agreed that the absolute PASI score was the best metric for determining if a patient's response to therapy fell within the acceptable range at any point in the disease's progression (***Carrascosa, et al., 2022).***

There is limited research on how the COVID - 19 pandemic affects psoriasis patients who are on biologic therapy.133 individuals with moderate - to - severe psoriasis were receiving maintenance biological treatment at one center in Turkey during the pandemic (mean age: 44.6 13.5 years). To ascertain patients' perspectives, attitudes, and adherence to medication as well as the prevalence of COVID - 19 infection, psoriasis status, and new comorbidities throughout the pandemic, a standardized questionnaire was administered via phone interviews. The biological agents ustekinumab, etanercept, adalimumab, secukinumab, infliximab, ixekizumab, or certolizumab pegol had been administered to every patient. Psoriatic arthritis (35.3%), hypertension (19.5%), diabetes mellitus (16.5%), obesity, coronary artery disease, and dyslipidemia were among the concomitant conditions that were present in 68.4% of the patients. For short (n = 33) or extended (n = 19) periods without seeking medical guidance during the first three months of the pandemic, 39% of patients halted their biological therapy out of fear, worry, and anxiety. Therapeutic counseling led to the restart of drugs in all patients but one. Only one patient with COVID - 19 that was PCR verified out of five who presented suspicious symptoms. Our results imply that, even in the presence of a high frequency of cardiometabolic comorbidities, biologic treatment for moderate - to - severe psoriasis would not pose an additional risk for COVID - 19 infection and its life - threatening complications, provided that all patients are informed and necessary pandemic - directed precautions are well adopted by the patients. COVID - 19, psoriasis, pandemic, biologic treatment, coronavirus, and Sars - Cov - 2 are the key words (***Polat et al., 2021).***

The 2019 coronavirus illness (COVID - 19) has affected both young and old persons without regard to race, age, or gender. Acute respiratory distress syndrome (ARDS), which is the most common cause of mortality from COVID - 19, affects a sizable number of patients. Patients who are receiving immunosuppressive treatments and those who have CVD or metabolic comorbidities are more likely to develop ARDS caused by COVID - 19 (***Huang, et al., 2020; Guan, et al., 2020).*** It was unknown whether biologic treatment, which is frequently used by psoriasis patients who frequently have serious comorbidities like hypertension, diabetes mellitus, CVD, and obesity, increased the risk of contracting COVID - 19 and its potentially fatal complications in the context of dermatology. Data are lacking regarding how these patients are treated, how their biologic therapies are monitored and tailored, and what new comorbidities emerged during the pandemic (***Brownstone, et al., 2020, Conti, et al., 2020 Ebrahimi, et al., and Brownstone, et al., 2020).*** There have been few reports on the incidence and prognosis of COVID - 19 in patients taking biologic agents for psoriasis.

Biologic drugs frequently used to treat psoriasis are divided into three groups: tumor necrosis factor (TNF) - inhibitors, interleukin (IL) - 23 inhibitors, and IL - 17 inhibitors. Although licensed biologic agents vary by country, they may

all be divided into these three categories. TNF - inhibitors include infliximab, adalimumab, etanercept, certolizumab - pegol, and golimumab. Only PsA is treated with golimumab. An anti - IL - 12/23p40 antibody is stekinumab. Anti - IL - 23p19 antibodies include glutelkumab, risankizumab, tildrakizumab, and mirikizumab. These anti - IL - 17A antibodies are secukinumab and ixekizumab. An anti - IL - 17RA antibody is brodalumab. An anti - IL - 17A/F antibody called mekizumab inhibits both IL - 17A and IL - 17F. There have been numerous randomized controlled studies (RCTs), and they have shown that the medications are effective for moderate - to - severe plaque psoriasis. Network meta - analyses have recently made it possible to compare those agents indirectly (***Kamata and Tada, 2020).***

In the clinical trials, biologic medicines showed tolerable safety profiles. However, mounting data showed issues particular to drugs. TNF - inhibitors have reportedly been linked to serious infections (with a slightly higher risk), TB, paradoxical reactions, lupus, and infusion reactions (only with infliximab). Neutropenia, IBD, and candidiasis are linked to IL - 17 inhibitors. There has never been any IL - 23 inhibitor - specific side effects identified as of yet. Interstitial pneumonia and recurrence of the hepatitis B virus are two significant safety worries with biologics. These issues came up when using TNF - inhibitors. The evidence for more recent medications, like IL - 17 and IL - 23 inhibitors, is poor. A body of evidence must be gathered. In terms of immunogenicity, humanized monoclonal antibodies exhibit stronger immunogenicity predispositions than do human monoclonal antibodies. In novel biologic medicines, immunogenicity appears to have a minimal impact on efficacy and safety. However, given that psoriasis is a chronic condition and some patients require long - term treatment with biologics, it may have an impact on the effectiveness and safety of the treatment over time. Further observation is required to make sense of this. Malignancy rates are greater in psoriasis patients than in the adult population overall, although these treatments do not seem to raise the risk of malignancy. In their ***2019*** article, ***Kaushik and Lebwohl*** discuss the proper systematic care for patients with chronic diseases such hepatitis, HIV, and latent tuberculosis as well as pregnant and pediatric patients with moderate - to - severe psoriasis.

The severe acute respiratory syndrome coronavirus 2 (SARS - CoV - 2) pandemic has had a significant impact on Italy, notably in the northern areas (***Rothan and Byrareddy, 2020).*** The increased risk of coronavirus 2019 (COVID 19) in patients receiving biologic therapy has drawn significant attention from medical professionals (***Lebwohl, et al., 2020).*** However, it is yet unknown if biologics increase this risk and/or whether immunosuppressive/immunomodulating treatment worsens the disease's progression. It is debatable whether using biologics for psoriasis should be discontinued in order to avoid serious SARS - CoV - 2 infection - related consequences such interstitial pneumonia. A cytokine storm that includes TNF - a, IL - 6, and IL - 17 appears to be what makes SARS - CoV - 2 infection most lethal (***Liu et al., 2020; Russell et al., 2020).*** In order to treat COVID - 19, biologics are being researched (***Feldmann et al., 2020).***

Patients with psoriasis had considerably greater rates of male sex and comorbidities (obesity, arterial hypertension, and diabetes) than the overall population. In 6501 patients with plaque psoriasis receiving biologic therapies, or 15, 378.5 patient - months of follow - up, we estimated the incidence rate of hospitalization and death for COVID - 19 and compared the results to those from the general adult population of Northern Italy, or 19, 978, 806 subjects and 47, 260, 897.6 patient - months of follow - up. In patients with psoriasis, the incidence rate of COVID - 19 hospitalization was 11.7 per 10, 000 person - months, compared to 14.4 in the general population; the incidence rate of COVID - 19 mortality was 1.3 and 4.7 in these two groups, respectively. There was no statistically significant difference in the rates of hospitalization with the general population when stratifying by age (65 vs. >65 years) or by class of biologic, with the standardized incidence ratio (SIR) of hospitalization and death in patients with psoriasis compared with the general population being 0.94 and 0.42, respectively. Throughout the time of the study, there were no more fatalities from other causes. Of the 6501 individuals we had, 1865 (287%) had psoriatic arthritis. Psoriatic arthritis was present in four of the 18 hospitalized psoriasis patients, but not in any of the deceased. After a period of time ranging from 6 to 15 weeks from being discharged from the hospital, all of the hospitalized patients fully recovered from the viral infection and then resumed biologic medication due to a psoriasis relapse. The study's key finding is that, despite having higher rates of metabolic and cardiovascular comorbidities than the general population, patients with psoriatic disease treated with biologics did not have an elevated risk of hospitalization or death from COVID - 19 (***Gisondi, et al., 2021).***

Accordingly, preliminary research on TNF - a inhibitors and IL - 12/IL - 23 inhibitors in IBD patients revealed that these treatments did not aggravate the clinical course of COVID - 19 when compared to sulfasalazine/mesalamine or no treatment (***Brenner, et al., 2020).*** Contrarily, despite the lack of sufficient data to draw firm conclusions, biologics seemed to be related with a better prognosis (***Bezzio et al., 2020).*** Some SARS - CoV - 2 infection - related systemic problems seem to be correlated with inflammatory and cytokine responses that are over the top. Therefore, medications with direct antiviral activity combined with those that lower the host inflammatory response, such as those that block TNF - a, IL - 6, or IL - 17 pathways, have been proposed and are now being studied for the treatment of COVID - 19 (***Jamilloux, et al., 2020 and Wang, et al., 2020).***

Regrettably children who have dermatological diseases such atopic dermatitis (AD) and psoriasis (PS) are more likely to have low self - esteem, sadness, anxiety, social isolation, and suicide thinking. These illnesses affect a patient's quality of life and should be identified and treated as soon as possible to reduce the likelihood of physical and mental morbidity. The risk profile of topical medicines may be preferred by caretakers over that of systemic drugs, however topical medications frequently fall short of adequately treating moderate - to - severe AD or Ps. Applying topical medications to vast areas of skin on a regular basis is challenging, expensive, and raises the chance of side effects

(AEs). According to ***Cline et al. (2020),*** moderate - to - severe AD or Ps may require systemic treatment with conventional systemic drugs, small molecule inhibitors, or biological agents.

Significant comorbidities like hypertension, diabetes, hyperlipidemia, obesity, and metabolic syndrome are linked to the disease itself and may have serious negative health effects. Body weight exceeding BMI 30 kg/m is specifically taken into account as both a cause of and risk factor for the disease. The biological therapy intervention does not appear to be affected by a number of factors, including patient age, gender, ethnicity, smoking, alcohol use, age at diagnosis, duration and severity of psoriasis, and baseline C - reactive protein levels (***Edson et al., 2014).*** Therefore, BMI appears to be a significant factor modifying the therapy process.

It appears that clinicians are still looking for the optimal treatment in the biological treatment era. Ixekizumab and secukinumab, the most recent biologics to be approved for use in clinical settings, may enable additional research and provide psoriatic patients new hope for more effective treatment outcomes. (***Kiselnicka et al., 2020).*** Regarding the safety and effectiveness of biologics to meet treatment objectives, psoriasis and concomitant diseases necessitate unique treatment strategies. Patients with psoriasis and comorbid conditions now have unique treatment options thanks to newly approved biologics that were developed through clinical trials for the treatment of moderate - to - severe psoriasis. The initial biologic treatment option is dependent on the severity of the disease, the clinical presentation, and the preferences of the patient (***Thatiparthi and colleagues, 2021).***

Finally, but not the end, helping patients through the transition to obtaining biological treatment may be crucial. The worry of patients having their biological treatment stopped is an ongoing problem that medical professionals could address. Our findings underscore the complexity of receiving transformative care and point out psychological problems that cannot be resolved by taking biologics alone. Furthermore, it might be beneficial for HCPs to be aware that patients should be provided the space and chances to talk about their worries about treatment even when they have been adequately taken care of. Key messages; unless a patient has SARS - CoV - 2 infection, biologic cessation in psoriasis patients receiving treatment is not advised to prevent hospitalization and death from COVID - 19.

4. Conclusions

This review summarizes the evidence for the most important dangers of interest, even if it is impossible to cover all potential treatment risks and management techniques. The hazard of several of the concerns listed above is unknown, which emphasizes the value of well - planned, carefully monitored observational studies and registries that gather data prospectively over extended periods of time. Risk management begins with the patient's initial consultation, for instance, by identifying any comorbidities that would prevent the use of specific biologic treatments. Consideration of biologic therapy must take into account the risks vs benefits inherent in clinical practice, especially when the body of available evidence is weak. In conclusion, psoriasis is a prevalent inflammatory skin illness with major medical and psychosocial comorbidities that is primarily genetically determined. The number of therapy options available to people with psoriasis is growing as a result of improvements in our understanding of the disease's aetiology.

There is not much information available about new treatments' long - term efficacy, safety, and effects on comorbidities. To elucidate them, more accumulation is required. There are numerous biologic treatments for psoriasis now on the market. Rapidity of onset, long - term efficacy, safety profile, and effects on comorbidities are among the qualities that differ. When such features are better understood, the best option can be selected for specific patients, increasing persistence, extending medication survival, improving patient satisfaction, and reducing the effect of psoriasis as a disease.

There may be a relationship between the pathophysiology of MetS and psoriasis due to converging inflammatory pathways and hereditary risk. Given this overlap, it is plausible to assume that the conditions are connected, that activity in one condition may be accompanied by activity in the other, and that successful treatment of one condition may lead to improvement of the other. Current research suggests that, within the constraints of small sample sizes and heterogeneity of baseline metabolic parameters, comorbidities, and severity of psoriasis among recruited patients, biological treatments that reduce systemic inflammation may improve cardiovascular outcomes in psoriasis patients. Similar to how MetS can be well controlled by medicine or lifestyle modifications, psoriasis signs and symptoms may improve as a result.

Thus, beyond the requirement to identify people at risk for adverse cardiovascular outcomes, systematic MetS screening in psoriasis patients, as advised by treatment guidelines112, is crucial. Evaluation of the patient's lifestyle and risk factors for co - occurring comorbidities should also be a part of treatment regimens; monitoring body weight, blood pressure, cholesterol, and triglyceride levels, as well as screening for diabetes mellitus, should not be disregarded. Early consideration of systemic psoriasis treatment and the identification of patients in need of cardiovascular preventive measures may arise from a timely diagnosis of concomitant MetS, leading to more effective therapeutic management for both illnesses. Additional study is strongly advised to clarify the drug - specific effects of biological psoriasis treatment on MetS components and CVD risk, as well as the impact of treating MetS components on psoriasis disease activity.

The choice of therapies for patients with moderate - to - severe psoriasis who also have concomitant illnesses is challenging and necessitates careful evaluation of a number of variables, including prices, patient preferences, and the severity of the disease. When selecting a biologic for patients with concomitant PsA, MS, CHF, IBD, hepatitis B, LTBI, lymphoma, NMSC, or COVID - 19 as well as pregnant or pediatric patients, our algorithms may be used as a guidance. The introduction of numerous potent biologic

treatments as well as small - molecule inhibitors has expanded the range of psoriasis therapy options and improved patient results. When creating a customized treatment plan for psoriasis patients, it is crucial to take into account the benefits and drawbacks of each biologic agent because concomitant disease problems frequently make the clinical therapy selection more difficult. We anticipate that by providing dermatologists with evidence - based recommendations, they would be better able to choose the right biologic therapy for patients who have comorbid PsA, obesity, depression, IBD, CHF, MS, and cancer. Accordingly, as new, compelling information accumulates, the recommended treatments should be adjusted.

5. Recommendations

Consequently, the authors advise against judging any currently available biologic therapies negatively based solely on skimming reviews or a quick glance. The authors believe that by thoroughly describing each biologic agent used by dermatologists to treat psoriasis, it will be easier to comprehend the subtle variations among them, which could be crucial for enhancing patient treatment and satisfaction. Hence the currnt study recommended that:

1) The objectives of treatment should be: "Individualized" "Adapted to the characteristics of the patient's disease in each case" "Established independently of the class of drug"
2) The clinician should distinguish between: Optimal goals and clinically acceptable goals while establishing therapeutic objectives.
3) Obtaining a PASI 100 response, an absolute PASI score of 0, or total clearance are the best therapeutic objectives. Absence of any effects on the patient's psychological, emotional, social, or occupational wellbeing. Absence of any clinical signs or symptoms of psoriasis.
4) *Clinically acceptable goals should include:* ◦Achieving a PASI 90 response ◦Achieving an absolute PASI score of ≤3 ◦BSA < 3% and PGA 0 - - - 1 ◦In special areas: PGA ≤ 1 ◦Minimize the impact of disease on quality of life ◦Reduce disease activity to a minimum ◦A DLQI of 0/1 assessed independently of clinical response is not an appropriate treatment goal.
5) Other treatment objectives (a PASI 75 response, an absolute PASI score of 5) can be judged clinically appropriate in certain patients or circumstances (previous treatment failure, concomitant comorbid diseases).

Abbreviations: BSA, body surface area; DLQI, Dermatology Life Quality Index; PASI, Psoriasis Area and Severity Index; PGA, Physician Global Assessment.

References

[1] Ali UA, Martin ST, Rao AD, Kiran RP. Impact of preoperative immunosuppressive agents on postoperative outcomes in Crohn's disease. *Dis Colon Rectum*.2014; 57 (5): 663–674. doi: 10.1097/ DCR.0000000000000099.

[2] Al - Janabi A, Foulkes AC, Mason K, Smith CH, Griffiths CEM, Warren RB. Phenotypic switch to eczema in patients receiving biologics for plaque psoriasis: a systematic review. *J Eur Acad Dermatol Venereol*.2020; 34 (7): 1440–1448. doi: 10.1111/ jdv.16246.

[3] Al - Janabi A, Littlewood Z, Griffiths CEM, et al. Antibody responses to single - dose SARS - CoV - 2 vaccination in patients receiving immunomodulators for immune - mediated inflammatory disease. *Br J Dermatol*.2021; 185 (3): 646–648. doi: 10.1111/ bjd.20479.

[4] Al - Janabi A, Yiu ZZ. Biologics in psoriasis: updated perspectives on long - term safety and risk management. Psoriasis: Targets and Therapy.2022 Jan 6: 1 - 4.

[5] Alwan W, Nestle FO. Pathogenesis and treatment of psoriasis: exploiting pathophysiological pathways for precision medicine. *Clin Exp Rheumatol*.2015; 33 (5 Suppl 93): S2–S6.

[6] Armstrong AW, Harskamp CT, Armstrong EJ. Psoriasis and the risk of diabetes mellitus: a systematic review and meta - analysis. *JAMA Dermatol*.2013; 149 (1): 84–91. doi: 10.1001/2013. jamadermatol.406

[7] Armstrong AW, Read C. Pathophysiology, clinical presentation, and treatment of psoriasis: a review. *JAMA*.2020; 323 (19): 1945–1960. doi: 10.1001/jama.2020.4006

[8] Bachelez H. Pustular psoriasis: the Dawn of a new era. *Acta Derm Venereol*.2020; 100 (3): adv00034. doi: 10.2340/00015555 - 3388.

[9] Bezzio C, Saibeni S, Variola A, Allocca M, Massari A, Gerardi V, et al. Outcomes of COVID - 19 in 79 patients with IBD in Italy: an IG - IBD study. Gut 2020; 69: 1213 - 7.

[10] Blake T, Gullick NJ, Hutchinson CE, Barber TM. Psoriatic disease and body composition: a systematic review and narrative synthesis. PLoS One 2020; 15: e0237598.

[11] Brenner EJ, Ungaro RC, Colombel JF, Kappelman MD. SECURE - IBD Database Public Data Update. Available from: covidibd. org. Accessed May 1, 2020.

[12] Brownstone ND, Hong J, Mosca M, Hadeler E, Liao W, Bhutani T, Koo J. Biologic treatments of psoriasis: an update for the clinician. Biologics: Targets and Therapy.2021 Feb 16: 39 - 51.

[13] Brownstone ND, Thibodeaux QG, Reddy VD, et al. Novel coronavirus disease (COVID - 19) and biologic therapy in psoriasis: infection risk and patient counseling in uncertain times. Dermatol Ther (Heidelb).2020; 10 (3): 1 - 11. https: //doi. org/10.1007/s13555 - 020 - 00377 - 9.

[14] Brownstone ND, Thibodeaux QG, Reddy VD, et al. Novel coronavirus disease (COVID - 19) and biologic therapy for psoriasis: successful recovery in two patients after infection with severe acute respiratory syndrome coronavirus 2 (SARS - CoV - 2). Dermatol Ther (Heidelb).2020; 10 (4): 881 - 885. https: //doi. org/10.1007/s13555 - 020 - 00394 - 8.

[15] Brunner PM, Conrad C, Vender R, et al. Integrated safety analysis of treatment - emergent eczematous reactions in patients with moderate - to - severe psoriasis treated with ixekizumab, etanercept and ustekinumab. *Br J Dermatol*.2021; 185 (4): 865–867. doi: 10.1111/ bjd.20527.

[16] Budu - Aggrey A, Brumpton B, Tyrrell J *et al*. Evidence of a causal relationship between body mass index and psoriasis: A mendelian randomization study. *PLoS Med* 2019; 16: e1002739.
[17] Carrascosa JM, Puig L, Romero IB, Salgado - Boquete L, Del Alcázar E, Lencina JA, Moreno D, de la Cueva P. [Translated article] Practical Update of the Recommendations Published by the Psoriasis Group of the Spanish Academy of Dermatology and Venereology (GPs) on the Treatment of Psoriasis with Biologic Therapy. Part 1. Concepts and General Management of Psoriasis With Biologic Therapy. Actas dermo - sifiliograficas.2022 Mar 1; 113 (3): T261 - 77.
[18] Chaptini C, Quinn S, Marshman G. Durable dermatology life quality index improvements in patients on biologics associated with psoriasis areas and severity index: a longitudinal study. *Australas J Dermatol*.2016; 57: e72 - 5.
[19] Cline A, Berg A, Bartos GJ, Strowd LC, Feldman SR. Biologic treatment options for pediatric psoriasis and atopic dermatitis—a review. The Journal of Clinical and Aesthetic Dermatology.2020 Jun; 13 (6 Suppl): S33.
[20] Clowse MEB, Scheuerle AE, Chambers C, et al. Pregnancy outcomes after exposure to certolizumab pegol. *Arthritis Rheumatol*.2018; 70 (9): 1399–1407. doi: 10.1002/art.40508.
[21] Conti A, Lasagni C, Bigi L, Pellacani G. Evolution of COVID - 19 infection in four psoriatic patients treated with biological drugs. J Eur Acad Dermatol Venereol.2020; 34 (8): e360 - e361. https: //doi. org/10.1111/ jdv.16587.
[22] Curtis JR, Sarsour K, Napalkov P, Costa LA, Schulman KL. Incidence and complications of interstitial lung disease in users of tocilizumab, rituximab, Abatacept and anti - tumor necrosis factor α agents, a retrospective cohort study. *Arthritis Red Ther*.2015; 17 (1): 319. doi: 10.1186/s13075 - 015 - 0835 - 7.
[23] Dalgard FJ, Gieler U, Tomas - Aragones L, Lien L, Poot F, Jemec GB, et al. The psychological burden of skin diseases: a cross - sectional multicenter study among dermatological out - patients in 13 European countries. *J Invest Dermatol*.2015; 135: 984 - 91.
[24] Dand N, Mahil SK, Capon F, Smith CH, Simpson MA, Barker JN. Psoriasis and genetics. *Acta Derm Venereol* 2020; 100: adv00030.
[25] de Brito M, Yiu ZZN. Cardiovascular safety of biologics targeting interleukin (IL) - 12 and/or IL - 23: what does the evidence say? *Am J Clin Dermatol*.2021; 22 (5): 587–601. doi: 10.1007/s40257 - 021 - 00612 - 9.
[26] Deodhar A, Mease PJ, McInnes IB, et al. Long - term safety of secukinumab in patients with moderate - to - severe plaque psoriasis, psoriatic arthritis, and ankylosing spondylitis: integrated pooled clinical trial and post - marketing surveillance data. *Arthritis Res Ther*.2019; 21 (1): 111. doi: 10.1186/s13075 - 019 - 1882 - 2.
[27] Duan X, Liu J, Mu Y, et al. A systematic review and meta - analysis of the association between psoriasis and hypertension with adjustment for covariates. *Medicine (Baltimore)*.2020; 99 (9): e19303. doi: 10.1097/ MD.0000000000019303.
[28] Ebrahimi A, Sayad B, Rahimi Z. COVID - 19 and psoriasis: biologic treatment and challenges. J Dermatolog Treat.2020; 6: 1 - 5.
[29] Edson - Heredia E, Sterling K, Alatorre C, et al. Heterogeneity of response to biologic treatment: perspective for psoriasis. J Investig Dermatol 2014; 134: 18 - 23.
[30] Ehsani A, Mortazavi H, Balighi K, et al. Changes in body mass index and lipid profile in psoriatic patients after treatment with standard protocol of infliximab. Acta Med Iran 2016; 54: 570 - 5.
[31] Feldmann M, Maini RN, Woody JN, Holgate ST, Winter G, Rowland M, et al. Trials of anti - tumour necrosis factor therapy for COVID - 19 are urgently needed. Lancet 2020; 395: 1407 - 9.
[32] Fujita H, Terui T, Hayama K, et al. Japanese guidelines for the management and treatment of generalized pustular psoriasis: the new pathogenesis and treatment of GPP. *J Dermatol*.2018; 45 (11): 1235 - 1270. doi: 10.1111/1346 - 8138.14523.
[33] Garcovich S, De Simone C, Genovese G, Berti E, Cugno M, Marzano AV. Paradoxical skin reactions to biologics in patients with rheumatologic disorders. *Front Pharmacol*.2019; 10: 282. doi: 10.3389/fphar.2019.00282.
[34] Geale K, Henriksson M, Schmitt - Egenolf M. How is disease severity associated with quality of life in psoriasis patients? Evidence from a longitudinal population - based study in Sweden. *Health and quality of life outcomes*.2017; 15: 151.
[35] Geisen UM, Berner DK, Tran F, et al. Immunogenicity and safety of anti - SARS - CoV - 2 mRNA vaccines in patients with chronic inflammatory conditions and immunosuppressive therapy in a monocentric cohort. *Ann Rheum Dis*.2021; 80: 1306–1311. doi: 10.1136/annrheumdis - 2021 - 220272.
[36] George MD, Baker JF, Hsu JY, et al. Perioperative timing of infliximab and the risk of serious infection after elective hip and knee arthroplasty. *Arthritis Care Res*.2017; 69 (12): 1845–1854. doi: 10.1002/acr.23209.
[37] Ghorbanibirgani A, Fallahi - Khoshknab M, Zarea K, Abedi H. The Lived Experience of Psoriasis Patients from Social Stigma and Rejection: A Qualitative Study. *Iranian Red Crescent medical journal*.2016; 18: e27893.
[38] Gisondi P, Fostini AC, Fossa I, Girolomoni G, Targher G. Psoriasis and the metabolic syndrome. Clin Dermatol 2018; 36: 21–28.
[39] Gisondi P, Piaserico S, Naldi L, Dapavo P, Conti A, Malagoli P, Marzano AV, Bardazzi F, Gasperini M, Cazzaniga S, Costanzo A. Incidence rates of hospitalization and death from COVID - 19 in patients with psoriasis receiving biological treatment: A Northern Italy experience. Journal of allergy and clinical immunology.2021 Feb 1; 147 (2): 558 - 60.
[40] Global Psoriasis Atlas. *Statistics*. GPA. http: //global - psoriasis - atlas. apos2. swiss4ward. com/statistics/statistics#KeyMessages [Accessed 15 March 2021].

[41] Gordon KB, Strober B, Lebwohl M, et al. Efficacy and safety of risankizumab in moderate - to - severe plaque psoriasis (UltIMMa - 1 and UltIMMa - 2): results from two double - blind, randomised, placebo - controlled and ustekinumab - controlled phase 3 trials. *Lancet*.2018; 392 (10148): 650–661. doi: 10.1016/S0140 - 6736 (18) 31713 - 6.

[42] Griffiths C, Augustin M, Naldi L, Romiti R, Guevara - Sangines E, Howe T, et al. Patient–dermatologist agreement in psoriasis severity, symptoms and satisfaction: results from a real - world multinational survey. *Journal of the European Academy of Dermatology and Venereology*.2018; 32: 1523 - 9.

[43] Guan WJ, Ni ZY, Hu Y, et al. Clinical characteristics of coronavirus disease 2019 in China. N Engl J Med.2020; 382 (18): 1708 - 1720. https: // doi. org/10.1056/NEJMoa2002032.

[44] Haskamp S, Bruns H, Hahn M, et al. Myeloperoxidase modulates inflammation in generalized pustular psoriasis and additional rare pustular skin diseases. *Am J Hum Genet*.2020; 107 (3): 527 - 538. doi: 10.1016/j. ajhg.2020.07.001.

[45] Hay SI, Abajobir AA, Abate KH *et al*. Global, regional, and national disability - adjusted life - years (DALYs) for 333 diseases and injuries and healthy life expectancy (HALE) for 195 countries and territories, 1990 - 2016: A systematic analysis for the Global Burden of Disease Study 2016. *Lancet* 2017; 390: 1260–344.

[46] Hu P, Wang M, Gao H, et al. The role of helper T cells in psoriasis. *Front Immunol*.2021; 12: 788940. Published 2021 Dec 15. doi: 10.3389/fimmu.2021.788940.

[47] Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet.2020; 395 (10223): 497 - 506. https: //doi. org/10.1016/S0140 - 6736 (20) 30183 - 5.

[48] Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet.2020; 395 (10223): 497 - 506. https: //doi. org/10.1016/S0140 - 6736 (20) 30183 - 5.

[49] Izadi Z, Brenner EJ, Mahil SK, et al. Association between tumor necrosis factor inhibitors and the risk of hospitalization or death among patients with immune - mediated inflammatory disease and COVID - 19. *JAMA Netw Open*.2021; 4 (10): e2129639. doi: 10.1001/jamanetworkopen.2021.29639.

[50] Jamilloux Y, Henry T, Belot A, Viel S, Fauter M, El Jammal T, et al. Should we stimulate or suppress immune responses in COVID - 19? Cytokine and anti - cytokine interventions. Autoimmun Rev 2020; 19: 102567.

[51] Jiang Y, Chen Y, Yu Q, Shi Y. Biologic and Small - Molecule Therapies for Moderate - to - Severe Psoriasis: Focus on Psoriasis Comorbidities. BioDrugs.2023 Jan; 37 (1): 35 - 55.

[52] Kamata M, Tada Y. Efficacy and safety of biologics for psoriasis and psoriatic arthritis and their impact on comorbidities: a literature review. International journal of molecular sciences.2020 Mar 1; 21 (5): 1690.

[53] Kamata, M.; Tada, Y. Safety of biologics in psoriasis. J. Dermatol.2018, 45, 279–286. [CrossRef] [PubMed].

[54] Kaushik, S. B.; Lebwohl, M. G. Psoriasis: Which therapy for which patient: Focus on special populations and chronic infections. J. Am. Acad. Dermatol.2019, 80, 43–53. [CrossRef].

[55] Khoury LR, Skov L, Moller T. Facing the dilemma of patient - centred psoriasis care: a qualitative study identifying patient needs in dermatological outpatient clinics. *Br J Dermatol*.2017; 177: 436 - 44.

[56] Kisielnicka A, Szczerkowska - Dobosz A, Nowicki R. The influence of body weight of patients with chronic plaque psoriasis on biological treatment response. Advances in Dermatology and Allergology/Postępy Dermatologii i Alergologii.2020 Apr 2; 37 (2): 168 - 73.

[57] Kodali N, Blanchard I, Kunamneni S, Lebwohl MG. Current management of generalized pustular psoriasis. Exp Dermatol.2023; 32: 1204 - 1218. doi: 10.1111/exd.14765.

[58] Kristensen LE, Jorgensen TS, Christensen R, Gudbergsen H, Dreyer L, Ballegaard C, et al. Societal costs and patients' experience of health inequities before and after diagnosis of psoriatic arthritis: a Danish cohort study. *Ann Rheum Dis*.2017; 76: 1495 - 501.

[59] Kuwana M, Miyagawa H, Hara H, et al. Characteristics of anti - IL - 17/23 biologics - induced interstitial pneumonia in patients with psoriasis. *PLoS One*.2021; 16 (1): e0245284. doi: 10.1371/ journal. pone.0245284.

[60] Lebwohl M, Rivera - Oyola R, Murrell DF. Should biologics for psoriasis be interrupted in the era of COVID - 19? [published online ahead of print March 18, 2020]. J Am Acad Dermatol. https: //doi. org/10.1016/j. jaad.2020.03.031.

[61] Lebwohl MG, Papp KA, Marangell LB, et al. Psychiatric adverse events during treatment with brodalumab: analysis of psoriasis clinical trials. *J Am Acad Dermatol*.2018; 78 (1): 81–89. e85. doi: 10.1016/j. jaad.2017.08.024.

[62] Liu Y, Zhang C, Huang F, Yang Y, Wang F, Yuan J, et al. Elevated plasma level of selective cytokines in COVID - 19 patients reflect viral load and lung injury. Natl Sci Rev 2020; 7: 1003 - 11.

[63] Mahil SK, Ezejimofor MC, Exton LS, Manounah L, Burden AD, Coates LC, De Brito M, McGuire A, Murphy R, Owen CM, Parslew R. Comparing the efficacy and tolerability of biologic therapies in psoriasis: an updated network meta-analysis. British Journal of Dermatology.2020 Oct 1; 183 (4): 638 - 49.

[64] Manounah L, Yiu ZZN, Mahil SK, et al. Risk of serious infections in patients with psoriasis on biologic therapies: an updated systematic review and meta - analysis. *medRxiv*.2021. doi: 10.1101/2021.08.27.21262722.

[65] Mariette X, Förger F, Abraham B, et al. Lack of placental transfer of certolizumab pegol during pregnancy: results from CRIB, a prospective, postmarketing, pharmacokinetic study. *Ann Rheum*

Dis.2018; 77 (2): 228–233. doi: 10.1136/annrheumdis - 2017 - 212196.

[66] Martin ML, Gordon K, Pinto L, Bushnell DM, Chau D, Viswanathan HN. The experience of pain and redness in patients with moderate to severe plaque psoriasis. *The Journal of dermatological treatment*.2015; 26: 401 - 5.

[67] Mason KJ, Barker JN, Smith CH, et al. Comparison of drug discontinuation, effectiveness, and safety between clinical trial eligible and ineligible patients in BADBIR. *JAMA Dermatol*.2018; 154 (5): 581. doi: 10.1001/jamadermatol.2018.0183.

[68] Mason KJ, Burden AD, Barker JN, et al. Characteristics and skin cancer risk of psoriasis patients with a history of skin cancer in BADBIR. *J Eur Acad Dermatol Venereol*.2021; 35 (8): e498–e501. doi: 10.1111/jdv.17230.

[69] Mason KJ, Burden AD, Barker JN, et al. Risks of basal cell and squamous cell carcinoma in psoriasis patients after treatment with biologic vs non - biologic systemic therapies. *J Eur Acad Dermatol Venereol*.2021; 35 (8): e496–e498. doi: 10.1111/jdv.17282.

[70] Matro R, Martin CF, Wolf D, Shah SA, Mahadevan U. Exposure concentrations of infants breastfed by women receiving biologic therapies for inflammatory bowel diseases and effects of breastfeeding on infections and development. *Gastroenterology*.2018; 155 (3): 696–704. doi: 10.1053/j. gastro.2018.05.04087.

[71] Matsumoto Y, Abe N, Tobita R, et al. The risk of interstitial lung disease during biological treatment in Japanese patients with psoriasis. *Clin Exp Dermatol*.2020; 45 (7): 853–858. doi: 10.1111/ ced.14259.

[72] Menter A, Strober BE, Kaplan DH, et al. Joint AAD - NPF guidelines of care for the management and treatment of psoriasis with biologics. *J Am Acad Dermatol*.2019; 80 (4): 1029–1072. doi: 10.1016/j. jaad.2018.11.057.

[73] Menter A, Tyring SK, Gordon K, et al. Adalimumab therapy for moderate to severe psoriasis: a randomized, controlled phase III trial. *J Am Acad Dermatol*.2008; 58 (1): 106–115. doi: 10.1016/j. jaad.2007.09.010.

[74] Miller IM, Ellervik C, Yazdanyar S, Jemec GB. Meta - analysis of psoriasis, cardiovascular disease, and associated risk factors. *J Am Acad Dermatol*.2013; 69 (6): 1014–1024. doi: 10.1016/j. jaad.2013.06.053

[75] Moosvi Z, Abadir A, Duong J, Nguyen D. Is it safe to continue biologic agents during surgery in patients with inflammatory bowel disease? *Cleve Clin J Med*.2020; 87 (6): 343–346. doi: 10.3949/ccjm.87a.1907152.

[76] Morita A, Choon SE, Bachelez H, et al. Design of Effisayil™ 2: a randomized, double - blind, placebo - controlled study of spesolimab in preventing flares in patients with generalized pustular psoriasis. *Dermatol Ther (Heidelb)*.2023; 13 (1): 347 - 359. doi: 10.1007/s13555 - 022 - 00835 - 6.

[77] Narayanan S, Guyatt V, Franceschetti A, Hautamaki EL. Disease burden and patient reported outcomes among patients with moderate to severe psoriasis: an ethnography study. *Psoriasis (Auckland, NZ)*.2015; 5: 1 - 7.

[78] Nielsen OH, Loftus Jr EV, Jess T. Safety of TNF - α inhibitors during IBD pregnancy: a systematic review. *BMC Med*.2013; 11 (1). doi: 10.1186/1741 - 7015 - 11 - 174

[79] Nogueira M, Warren RB, Torres T. Risk of tuberculosis reactivation with interleukin (IL) - 17 and IL - 23 inhibitors in psoriasis – time for a paradigm change. *J Eur Acad Dermatol Venereol*.2020; 35 (4): 824–834. doi: 10.1111/jdv.16866.

[80] Palmeira P, Quinello C, Silveira - Lessa AL, Zago CA, Carneiro - Sampaio M. IgG placental transfer in healthy and pathological pregnancies. *Clin Dev Immunol*.2012; 2012: 1–13. doi: 10.1155/ 2012/985646

[81] Parisi R, Iskandar IYK, Kontopantelis E *et al*. National, regional, and worldwide epidemiology of psoriasis: Systematic analysis and modelling study. *BMJ* 2020; 369: m1590.

[82] Parisi R, Iskandar IYK, Kontopantelis E, Augustin M, Griffiths CEM, Ashcroft DM. National, regional, and worldwide epidemiology of psoriasis: systematic analysis and modelling study. *BMJ*.2020; 369: m1590. doi: 10.1136/bmj. m1590.

[83] Patrick MT, Stuart PE, Zhang H et al. Causal relationship and shared genetic loci between psoriasis and type 2 diabetes through trans - disease meta - analysis. J Invest Dermatol 2021; 141: 1493–1502.

[84] Penso L, Bergqvist C, Meyer A, et al. Risk of inflammatory bowel disease in patients with psoriasis, psoriatic arthritis and ankylosing spondylitis initiating interleukin 17 inhibitors: a nationwide population - based study using the French national health data system. *Arthritis Rheumatol*.2021. doi: 10.1002/ art.41923.

[85] Penso L, Dray - Spira R, Weill A, Pina Vegas L, Zureik M, Sbidian E. Association between biologics use and risk of serious infection in patients with psoriasis. *JAMA Dermatol*.2021; 157 (9): 1056. doi: 10.1001/jamadermatol.2021.2599.

[86] Poizeau F, Nowak E, Kerbrat S, et al. Association between early severe cardiovascular events and the initiation of treatment with the anti–interleukin 12/23p40 antibody ustekinumab. *JAMA Dermatol*.2020; 156 (11): 1208. doi: 10.1001/jamadermatol.20 20.2977.

[87] Polat Ekinci A, Pehlivan G, Gökalp MO. Surveillance of psoriatic patients on biologic treatment during the COVID-19 pandemic: a single-center experience. Dermatologic Therapy.2021 Jan; 34 (1): e14700.

[88] Pottinger E, Woolf RT, Exton LS, Burden AD, Nelson - Piercy C, Smith CH. Exposure to biological therapies during conception and pregnancy: a systematic review. *Br J Dermatol*.2017; 178 (1): 95–102. doi: 10.1111/bjd.15802

[89] Raharja A, Mahil SK, Barker JN. Psoriasis: a brief overview. Clinical Medicine.2021 May; 21 (3): 170.

[90] Reich K, Mrowietz U, Radtke M, et al. Drug safety of systemic treatments for psoriasis: results from the German Psoriasis Registry PsoBest. Arch Dermatol Res 2015; 307: 875 - 83.

[91] Reich K, Papp KA, Blauvelt A, et al. Bimekizumab versus ustekinumab for the treatment of moderate to severe plaque psoriasis (BE VIVID): efficacy and safety from a 52 - week, multicentre, double - blind, active comparator and placebo - controlled phase 3 trial. *Lancet*.2021; 397 (10273): 487–498. doi: 10.1016/ S0140 - 6736 (21) 00125 - 2.
[92] Reich K, Warren RB, Lebwohl M, et al. Bimekizumab versus secukinumab in plaque psoriasis. *N Engl J Med*.2021; 385 (2): 142–152. doi: 10.1056/NEJMoa2102383.
[93] Rønholt K, Iversen L. Old and new biological therapies for psoriasis. Int J Mol Sci 2017; 18: 2297.
[94] Rothan HA, Byrareddy SN. The epidemiology and pathogenesis of coronavirus disease (COVID - 19) outbreak. J Autoimmun 2020; 109: 102433.
[95] Rungapiromnan W, Mason KJ, Lunt M, et al. Risk of major cardiovascular events in patients with psoriasis receiving biologic therapies: a prospective cohort study. *J Eur Acad Dermatol Venereol*.2020; 34 (4): 769–778. doi: 10.1111/jdv.16018.
[96] Russell B, Moss C, George G, Santaolalla A, Cope A, Papa S, et al. Associations between immune - suppressive and stimulating drugs and novel COVID - 19—a systematic review of current evidence. Ecancermedicalscience 2020; 14: 1022.
[97] Saunte DM, Mrowietz U, Puig L, Zachariae C. Candida infections in patients with psoriasis and psoriatic arthritis treated with interleukin - 17 inhibitors and their practical management. *Br J Dermatol*.2017; 177 (1): 47–62. doi: 10.1111/bjd.15015.
[98] Schön MP, Erpenbeck L. The interleukin - 23/interleukin - 17 axis links adaptive and innate immunity in psoriasis. *Front Immunol* 2018; 9: 1323.
[99] Shim HH, Ma C, Kotze PG, et al. Preoperative ustekinumab treatment is not associated with increased postoperative complications in Crohn's disease: a Canadian multi - centre observational cohort study. *J Can Assoc Gastroenterol*.2018; 1 (3): 115–123. doi: 10.1093/jcag/gwy013.
[100] Smith CH, Yiu ZZN, Bale T, et al. British Association of Dermatologists guidelines for biologic therapy for psoriasis 2020: a rapid update. *Br J Dermatol*.2020; 183 (4): 628–637. doi: 10.1111/bjd.19039.
[101] Strober B, Gooderham M, de Jong EM, et al. Depressive symptoms, depression, and the effect of biologic therapy among patients in Psoriasis Longitudinal Assessment and Registry (PSOLAR). *J Am Acad Dermatol*.2018; 78 (1): 70–80. doi: 10.1016/j. jaad.2017.08.051.
[102] Strober B, Leman J, Mockenhaupt M, et al. Unmet educational needs and clinical practice gaps in the management of generalized pustular psoriasis: global perspectives from the front line. *Dermatol Ther (Heidelb)*.2022; 12 (2): 381 - 393. doi: 10.1007/s13555 - 021 - 00661 - 2.
[103] Szepietowski JC, Reich A. Pruritus in psoriasis: an update. *Eur J Pain*.2016; 20 (1): 41–46. doi: 10.1002/ejp.768
[104] Tan E, Baker C, Foley P. Weight gain and tumour necrosis factor - alpha inhibitors in patients with psoriasis. Austral J Dermatol 2013; 54: 259 - 63.
[105] Thatiparthi A, Martin A, Liu J, Egeberg A, Wu JJ. Biologic treatment algorithms for moderate - to - severe psoriasis with comorbid conditions and special populations: a review. American Journal of Clinical Dermatology.2021 Jul; 22: 425 - 42.
[106] Trettin B, Feldman SR, Andersen F, Danbjørg DB, Agerskov H. A changed life: the life experiences of patients with psoriasis receiving biological treatment. British Journal of Dermatology.2020 Sep 1; 183 (3): 516 - 23.
[107] Wang J, Jiang M, Chen X, Montaner LJ. Cytokine storm and leukocyte changes in mild versus severe SARS - CoV - 2 infection: Review of 3939 COVID - 19 patients in China and emerging pathogenesis and therapy concepts. Journal of Leucocyte Biology.2020 Jul; 108 (1): 17 - 41.
[108] Warren RB, Blauvelt A, Bagel J, et al. Bimekizumab versus adalimumab in plaque psoriasis. *N Engl J Med*.2021; 385 (2): 130–141. doi: 10.1056/NEJMoa2102388.
[109] Warren RB, Reich K, Langley RG, et al. Secukinumab in pregnancy: outcomes in psoriasis, psoriatic arthritis and ankylosing spondylitis from the global safety database. *Br J Dermatol*.2018; 179 (5): 1205–1207. doi: 10.1111/bjd.16901.
[110] Warren RB, Smith CH, Yiu ZZN, et al. Differential drug survival of biologic therapies for the treatment of psoriasis: a prospective observational cohort study from the British Association of Dermatologists Biologic Interventions Register (BADBIR). *J Invest Dermatol*.2015; 135 (11): 2632–2640. doi: 10.1038/ jid.2015.208.
[111] Wasilewska A, Winiarska M, Olszewska M, Rudnicka L. Interleukin - 17 inhibitors. A new era in treatment of psoriasis and other skin diseases. *Advances in Dermatology and Allergology/Postępy Dermatologii i Alergologii*.2016; 33: 247.
[112] Wils P, Seksik P, Stefanescu C, et al. Safety of ustekinumab or vedolizumab in pregnant inflammatory bowel disease patients: a multicentre cohort study. *Aliment Pharmacol Ther*.2021; 53 (4): 460–470. doi: 10.1111/apt.16192.
[113] World Health Organization. *Global report on psoriasis*. World Health Organization, 2016.
[114] Wu JJ, Kavanaugh A, Lebwohl MG, Gniadecki R, Merola JF. Psoriasis and metabolic syndrome: implications for the management and treatment of psoriasis. Journal of the European Academy of Dermatology and Venereology.2022 Jun; 36 (6): 797 - 806.
[115] Xu Y, Yang L, An P, Zhou B, Liu G. Meta - analysis: the influence of preoperative infliximab use on postoperative complications of Crohn's disease. *Inflamm Bowel Dis*.2019; 25 (2): 261–269. doi: 10.1093/ibd/izy246.
[116] Yang Z - P, Hong L, Wu Q, Wu K - C, Fan D - M. Preoperative infliximab use and postoperative complications in Crohn's disease: a systematic review and meta - analysis. *Int J Surg*.2014; 12 (3): 224–230. doi: 10.1016/j. ijsu.2013.12.015.

[117] Yiu ZZN, Griffiths CEM, Warren RB. Safety of biological therapies for psoriasis: effects on reproductive potential and outcomes in male and female patients. *Br J Dermatol*.2014; 171 (3): 485–491. doi: 10.1111/bjd.13060