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Effectiveness of biologic therapies on psoriasis vulgaris

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ABSTRACT

Psoriasis is a chronic proliferative inflammatory condition mediated by the immune system that is characterized by erythematous plaques covered by silvery scales. Psoriasis vulgaris is mediated by T lymphocytes, wherein the activation of innate immune cells and pathogenic T cells leads to inflammation of the skin and excessive growth of keratinocytes. The pathogenesis of psoriasis vulgaris has significantly enhanced comprehension of cutaneous immunology, facilitating an introduction to highly effective therapies. Biologic therapy binds to a specific cytokine such as TNF-α, IL-12, IL-17, or IL-23, unlike non-biologic therapy primarily focuses on resolving clinical manifestation without targeting the underlying causes. A literature review was performed to present the effectiveness of biologic therapies as a part of psoriasis vulgaris management.

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INTRODUCTION

Psoriasis is a chronic proliferative and inflammatory condition of the skin that is mediated by the immune system.(Yang et al., 2018) Clinical presentation of classic psoriasis is characterized by erythematous plaques covered by silvery scales, commonly involves the extensor, scalp, and lumbosacral.(Armstrong et al., 2020) Psoriasis is clinically classified into pustular psoriasis and non-pustular psoriasis. Pustular psoriasis is divided into generalized von Zumbusch pustular psoriasis and localized pustular psoriasis. Non-pustular psoriasis is divided into seven clinical variants, which are psoriasis vulgaris, psoriasis guttate, psoriasis pustulosa, inverse psoriasis, psoriasis erythroderma, psoriasis palmoplantar and psoriasis arthritis.(Koca, 2016) Psoriasis affects 3% of the adult population, around 50% patients have mild disease that involved less than 3% body surface area (BSA) and 78% of patients have moderate disease with less than 10% BSA involved.(Armstrong et al., 2021; Papp et al., 2021) Psoriasis Vulgaris (PV) is the most common clinical variant, where the prevalence is 85% to 90% of the total cases of psoriasis.(Yan et al., 2021)

Management options for psoriasis primarily concentrate on implementing long-term medicines that attempt to regulate its physical symptoms and decrease the extent of the body surface area (BSA) affected. (Ighani et al., 2018) Before the availability of biologic agents, the only systemic treatment options for moderate-to-severe cases of psoriasis were limited to non-biologic therapy with a low safety profile.(Brownstone et al., 2021) Advancements in comprehending the

immunopathogenesis of psoriasis have revealed that interleukin is responsible for the distinctive molecular, cellular, and structural alterations in psoriatic skin. Consequently, this discovery has paved the way for innovative biological agents that specifically target the immune system directly. (Frampton, 2019)The utilization of biological interventions to treat moderate to severe plaque psoriasis is increasing due to their effectiveness in treating the condition and acceptable safety records. (Armstrong et al., 2020)

Several studies compare the effectiveness of biologic versus non-biologic treatments. In a cross-sectional study conducted in Malaysia, biologic therapy demonstrated a more significant reduction in psoriasis patients' Dermatology Life Quality Index (DLQI) scores than non-biologic therapy. Patients with a ≥ 4-point improvement in DLQI scores were approximately two times greater in the biologic-treated group than the non-biologic-treated group.(Robinson et al., 2023) Patients undergoing biologic therapy exhibit higher satisfaction levels with their skin condition and experience an improved quality of life (QoL) compared to those receiving non-biologic therapies. (Wu et al., 2024) Additionally, Canadian survey from July to September 2016 involving 343 participants demonstrated moderate-to-severe psoriasis for satisfaction of biologic therapy users compared with nonbiologic therapy. This study found that ustekinumab and adalimumab were associated with the highest proportions of patient satisfaction among biologic therapy. (Ighani et al., 2018) However, biologic therapy targets inflammatory mediators with great specificity and may allow immune responses to bypass the blockade. This can result in the deterioration of the disease, along with changes in its clinical and immunological features. (Griffiths et al., 2021) Therefore, this review aims to present the effectiveness of biologic therapies as a part of psoriasis vulgaris management.

RESEARCH METHOD

The purpose of this literature review is to determine the role of biologic therapies of in the treatment of psoriasis vulgaris. A total of 46 articles on 4 types of biologic therapies against psoriasis vulgaris were used in this literature review and were taken from databases such as PUBMED, Science Direct, and Google Scholar. The unpatterned search terms used included keywords such as “Biologic Agents”, “Biologic Therapy”, and “Psoriasis Vulgaris”. This search was restricted to studies published during a specified timeframe, specifically from 2016 to 2024, to acquire the most up-to-date knowledge.

RESULT AND DISCUSSION

Pathogenesis of Psosiaris Vulgaris

Pathogenesis of PV consists of two phases: the initiation and maintenance of the pathological state phases. Innate immunity liable for psoriatic inflammation includes dendritic cells (DCs), macrophages, and neutrophils, while adaptive immunity includes B and T cells.(Franziska Grän, 2020) DCs and macrophages are antigen-presenting cells (APCs) that play a significant role in the initial phase. APCs are activated by the damage of the keratinocyte in response to microbial or mechanical injury.(Franziska Grän, 2020) Deoxyribonucleic acid (DNA) of the damaged cell will bind to the LL-37 peptides overexpressed in psoriatic skin, which will induce the plasmacytoid dendritic cells to secrete IFN-α. Myeloid dendritic cells that are activated by IFNα interacting with the naive T cells and produce TNF-α, IL- 23, IL-12, and IL-6.(Armstrong et al., 2020; Rendon & Schakel, 2019) IL-23 and IL-12 induce differentiation of naive T cells to Th17 and Th1 cell subsets, respectively to produce IL-17 and IL-22 through the JAK-STAT pathway.(Tokuyama & Mabuchi, 2020) IL-17 indirectly modulates epidermal hyperplasia by activating signal transducer and activator of transcription-3 (STAT3) and promotes keratinocytes to induce IL-19 and IL-36. (Tokuyama & Mabuchi, 2020) These cytokines alter epidermal

differentiation by stimulating epidermal hyperproliferation and decreasing apoptosis.(Franziska Grän, 2020)

Comparison of Biologic Therapy with Non-Biologic Therapy

There are various treatment options for PV, including topical therapy, phototherapy, and systemic therapy which divided into non-biologic and biologic therapy. (Armstrong et al., 2020; Franziska Grän, 2020) Treatment options for psoriatic patients depend on the disease severity, comorbidities, and healthcare access.(Rendon & Schakel, 2019) Severity of PV determined by the percentage of total body surface area (BSA) affected. BSAs of < 3%, 3% to 10%, and >10% are considered mild, moderate, and severe diseases, respectively. The Psoriasis Area and Severity Index (PASI) is a more precise method for measuring the extent and severity of psoriasis. PASI consists of BSA and the intensity of redness, scaling, and plaque thickness. Final score for PASI ranges from 0 for no disease to 72 for maximum disease severity.(Menter et al., 2020) Systemic therapies are the first choice for patients with moderate to severe psoriasis.(Rendon & Schakel, 2019) Non-biologic therapy such as methotrexate, ciclosporin, acitretin, fumarates, and apremilast primarily focuses on resolving clinical manifestation without targeting the underlying causes.(Griffiths et al., 2021) Usage of non-biologic therapy requires close and frequent blood monitoring, especially methotrexate and cyclosporine because it can result in drug to drug interactions, hepatotoxicity, and nephrotoxicity.(Ighani et al., 2018) This differs from biologic therapy that binds to a specific cytokine such as TNF-α, IL-12, IL-17, or IL-23 has significantly increased in safety and efficacy.(Brownstone et al., 2021; Ighani et al., 2018) Biologic therapy demonstrated a more significant reduction in psoriasis patients' DLQI scores than non-biologic therapy. (Robinson et al., 2023)

Biologic Therapy for Psoriasis Vulgaris

TNF- α inhibitors, IL-12/23 inhibitors, IL-17 inhibitors, and IL-23 inhibitors are the four classes of biologics used to treat PV.

a. TNF- α Inhibitors

Etanercept

Etanercept is a fusion of recombinant human TNF-α receptor protein and the crystallizable fragment portion of IgG1 that binds to soluble and membrane-bound TNF-α and TNF-β. (Brownstone et al., 2021; Rendon & Schakel, 2019) Etanercept is a cytokine that functions by binding to TNF receptor 1 (TNFR1) or TNF receptor 2 (TNFR2), thereby activating key inflammatory pathways such as Nuclear Factor Kappa B (NFkB) and Mitogen-activated protein kinase (MAPK).(Pan & Gerriets, 2023) Recommended dosage is 50 mg subcutaneously (SC) twice weekly for the first 12 weeks, followed by 50 mg once weekly.(Brownstone et al., 2021) In the end of the twelfth weeks, 49% patients who received etanercept administration twice a week achieved PASI 75. (Armstrong et al., 2020; Brownstone et al., 2021) Injection site reactions are the frequent side effects.(Xie et al., 2017) Risk of infection will be increased if etanercept is combined with immunosuppressive medications. Absolute contraindications for all TNF-α inhibitors treatment are patients with active tuberculosis infection or severe infection and congestive heart failure with New York Heart Association (NYHA) class III/ IV.(Nast et al., 2020)

Adalimumab

Adalimumab is a monoclonal IgG1 antibody of human origin that effectively blocks the interaction between cytokine with p55 and p57 cell-surface TNF receptors with a high level of affinity and specificity.(Brownstone et al., 2021; Ellis & Azmat., 2023) Recommended dose for adults consists of initial administration of 80 mg SC at week 0, followed by a dose of 40 mg at week 1. Subsequently, a maintenance dose of 40 mg is administered SC every 2 weeks.(Brownstone et al., 2021) Efficacy of adalimumab in patients at week 16, who achieved PASI 75 was 71% compared to 7% of patients that received a placebo. (Menter et al., 2019) Prospective observational study of 24 weeks in patients with difficult-to-treat PV found that PASI 75 response rates for adalimumab at

week 16 were 88%.(Lanna et al., 2020) Most common reported adverse events (AEs) were nasopharyngitis and headache, affecting over 20% of patients, while injection site reactions were observed in 14%.(Nast et al., 2020; Zangrilli et al., 2020) Combination of adalimumab and immunosuppressive drugs can increase the risk of infection, while combining adalimumab and methotrexate may decrease the likelihood of anti-drug antibody formation. (Nast et al., 2020)

Infliximab

Infliximab is a human chimeric monoclonal IgG1 antibody comprising a mouse variable region and human IgG1-alpha constant region. Infliximab neutralizes the effects of TNF- α by binding to soluble and transmembrane TNF-α molecules.(Brownstone et al., 2021; Menter et al., 2019) Administration of infliximab for PV is 5 mg/kg intravenously (IV) at weeks 0, 2, and 6 followed by subsequent doses every 8 weeks.(Armstrong et al., 2020) The rates of achieving PASI 75 with infliximab for moderate-to-severe PV at week 10 were 75.5% and 70.3% for the 5 mg/kg and 3 mg/kg doses, respectively.(Menter et al., 2019) Efficacy of infliximab decreased over time, with rates of 83.8% at one year, 66.4% at two years, 55.4% at three years, and 38.2% at five years. (Marinas et al., 2018) The most common adverse are mild or moderate, including flushing, pruritus, fever or chills, headache, and urticaria. Approximately 1% of patients experienced severe infusion reactions such as anaphylactic reactions, convulsions, erythematous rash, and delayed-type hypersensitivity reactions resembling serum-sickness manifesting as myalgia, arthralgia, and exanthema occur between one and 14 days after infusion.(Nast et al., 2020; Subedi et al., 2019; Wang et al., 2016)

Certolizumab

Certolizumab pegol (CZP) is a unique humanized antigen-binding fragment of a monoclonal antibody conjugated to a polyethylene glycol (PEG) that inhibits TNF-α in a dose-dependent manner with the absence of Fc fragment.(Brownstone et al., 2021) Certolizumab is minimal transfer across the placenta and has a low relative infant dose during breastfeeding. Therefore, the usage of certolizumab has been approved for pregnancy and breastfeeding.(Lee & Scott, 2020; Rendon & Schakel, 2019) Recommended dosage for patients with > 90 kg is 400 mg SC administered every two weeks, while patient with < 90 kg is 400 mg SC at weeks 0, 2 and 4, then followed by a dose of 200 mg every two weeks.(Brownstone et al., 2021) Efficacy of CZP evaluated in patient who achieved PASI 75 at week 12 was 61.3% and 66.7% for patients receiving CZP 200 mg and CZP 400 mg every two weeks, respectively, compared to 5% for patients receiving placebo.(Esposito et al., 2020) PASI 75 was achieved by 81.6% of patients at week 16, therefore CZP is more effective than other TNF-α inhibitors.(Brownstone et al., 2021) Most common adverse drug reactions were mild to moderate, consisting of nasopharyngitis, upper respiratory tract infections, and headache. Furthermore, there is no opportunistic infections reported. (Esposito et al., 2020; Nast et al., 2020)

b. IL-12/23 Inhibitors

Ustekinumab

Ustekinumab is a human monoclonal antibody that binds to the p40 subunit of IL-12 and IL-23 with high specificity and affinity and, as a result, thereby suppresses IL-12 and IL-23. Ustekinumab has been approved by Food and Drug Administration (FDA) for moderate-to-severe PV in adults and adolescents 12 to 17 years.(Brownstone et al., 2021; Menter et al., 2019) The ustekinumab dosage depends on the patient's age and weight. Adults with a body weight < 100 kg, the recommended loading dose is 45 mg SC initially and 4 weeks after that, followed by a maintenance dose of 45 mg every 12 weeks. While for an adult patient that has a weight exceeding 100 kg, it is recommended to administer a loading dose of 90 mg SC during weeks 0 and 4, followed by a maintenance dose of 90 mg SC every 12 weeks. For adolescents aged 12 to 17 weighing < 60 kg, the dose is 0.75 mg/kg, while for weight 60 to 100 kg, the dose is 45 mg, and for those weighing > 100 kg, the dose is 90 mg. The weight-based dosing regimen is used only for

patients weighing less than 60 kg, while the dosing frequency is unchanged between adults and adolescents. (Armstrong et al., 2020; Menter et al., 2019) Effectiveness of ustekinumab in 320 moderate-to-severe PV patients treated with 45 mg and 90 mg, who achieved PASI 75 rate at week 12 was 66 and 67%, respectively, compared with only 3% in the placebo.(Cingoz, 2009) Ustekinumab exhibits a strong safety profile, and there is also no evidence for an increased risk of tuberculosis.(Brownstone et al., 2021; Ghosh et al., 2019)

c. IL-17 Inhibitors

Secukinumab

Secukinumab is a human IgG1 monoclonal antibody which selectively binds and inhibits IL-17A, has been approved by FDA for treating adult PV. The dosage is 300 mg SC at weeks 0, 1, 2, 3, and 4 for the initial dose, followed by 300 mg SC every 4 weeks for the maintenance dose. (Brownstone et al., 2021; Menter et al., 2019) Greater significant efficacy of secukinumab was found with a dose of 300 mg. Patients who met the criterion for PASI 75 at week 12 was 81.6%, 71.6%, and 4.5% in the 300 mg, 150 mg, and placebo groups, respectively. (Langley et al., 2014) Among all the IL-17 inhibitors, secukinumab has the most extensive safety record in real-world applications. More specifically, secukinumab carries no increased risks for end-organ toxicities, serious infection, multiple sclerosis, reactivation of latent tuberculosis or hepatitis B, leukemia/lymphoma, and nonmelanoma skin cancer.(Blauvelt, 2016) Patients using secukinumab were found to have nasopharyngitis, headache, diarrhea, and upper respiratory tract infection over the first 12 weeks.(Gottlieb et al., 2022) Serious AEs are infrequent, despite a slight rise in superficial fungal and yeast infections.(Blauvelt, 2016) Therefore, early treatment of candida infections, either with topical or systemic treatment is recommended. Relative contraindications are patients with a history of inflammatory bowel disease.(Nast et al., 2020)

Brodalumab

Brodalumab is a human monoclonal antibody that binds to IL-17 receptor and blocks the biologic activities of IL-17A, IL-17F, IL-17A/F, and IL-17E. Brodalumab has a very high efficacy and rapid onset of action, indicated for adults who have failed or lost response to biologic therapies.(Brownstone et al., 2021; Menter et al., 2019) Loading dose of brodalumab is 210 mg SC at weeks 0, 1 and 2, then followed by a maintenance dose of 210 mg SC every 2 weeks. Six hundred and sixty-one patients with severe-to-moderate PV plaque treated with brodalumab 210 mg, brodalumab 140 mg, or placebo every 2 weeks showed a significant improvement, where the endpoint PASI 75 was achieved by 83%, 60%, and 3% respectively by the end of 12th weeks. Administration of brodalumab 210 mg has very high efficacy and rapid onset of action in treating PV, which observed in 43% patient who achieved PASI 100 within a 12-week. Improvement of skin clearance demonstrates a continuous enhancement that extends beyond 12 weeks and remains sustained throughout one year of therapeutic intervention.(Papp et al., 2016) Most common AEs include nasopharyngitis, upper respiratory tract infection, headache, and arthralgia.(Papp et al., 2016) Incidence rates for the risk of fungal or yeast infections and inflammatory bowel disease with an incidence rate of 4 % and less than 1:1000, respectively. Early treatment of candida infections, either with topical or systemic treatment is recommended. Patients with a history of inflammatory bowel disease are included as relative contraindications. (Iznardo & Puig, 2020; Nast et al., 2020)

Ixekizumab

Ixekizumab is a humanized IgG4 monoclonal antibody that selectively binds to IL-17A with a high affinity, and thus it neutralizes IL-17A by inhibiting the binding of IL-17A receptors to its ligand. (Craig & Warren, 2020) Ixekizumab is the only IL-17 therapy that FDA has approved for the treatment of plaque PV in children under 6 years old. The recommended dosage of Ixekizumab as a loading dose is 160 mg SC at week 0 and subsequent doses of 80 mg at weeks 2, 4, 6, 8, 10, and 12 followed by a maintenance dose of 80 mg administered every 4 weeks. Some patients may require 80 mg dose every 2 weeks to maintain response to treatment.(Brownstone et al., 2021)

Ixekizumab 80 mg every 2 weeks was found to superior to placebo. This was revealed in two active-treatment groups received a starting dose of 160 mg of ixekizumab followed by 80 mg of ixekizumab every 2 weeks or 80 mg of ixekizumab every 4 weeks compared to placebo showed higher efficacy in the 2-weeks dosing group than in the 4-weeks dosing group at the end of week 12. It was observed that 89.1% of the patients in the group receiving a 2-week dosing group achieved a PASI 75 response, 70.9% achieved a PASI 90 response, and 35.3% achieved a PASI 100 response.(Gordon et al., 2016) Ixekizumab has a high degree of tolerability and is associated with a low incidence of AEs. The most common AEs reported include nasopharyngitis, upper respiratory tract infection, injection-site reaction, erythema, and headache. The incidence of candidiasis was significantly higher in the 2-week dosing group compared to the placebo group and in the 4-week dosing group. Thus, early treatment of candida infections, topical or systemic, is recommended. Prescribing ixekizumab to patients with inflammatory bowel disease must be cautious because an onset or exacerbation of inflammatory bowel disease has been reported.(Gordon et al., 2016; Nast et al., 2020)

Bimekizumab

Bimekizumab is a novel IgG monoclonal antibody that selectively inhibits downstream signaling of IL-17A and IL-17F. (Armstrong et al., 2022) Bimekizumab demonstrated superior levels of effectiveness compared to placebo, adalimumab, and secukinumab in managing moderate to severe PV. Bimekizumab and its dosage haven't been approved by FDA, nevertheless in Japan, it had been approved and has been granted recently for the therapeutic management of PV, generalized pustular psoriasis, and psoriatic erythroderma in patients who exhibit inadequate response to currently available treatment options. (Brownstone et al., 2021) Bimekizumab at 320 mg SC every 4 weeks for 52 weeks showed an efficacy in achieving PASI 90 for 86% using bimekizumab and 6% placebo-treated patients by week 16.(Asahina et al., 2023) Bimekizumab 320 mg SC had the highest probability of achieving PASI 75, PASI 90 and PASI 100, with response probabilities of 92.3%, 84.0% and 57.8%, respectively within 10-16 weeks of the first injection.(Armstrong et al., 2022) Regarding safety, bimekizumab was well tolerated throughout the evaluated doses, with the highest dose being ≤ 640 mg. Treatment-emergent adverse events (TEAEs) were reported in 88% of patients who received bimekizumab and were mainly mild in severity. The two most common were upper respiratory tract infections and nasopharyngitis.(Oliver et al., 2022)

d. IL-23 Inhibitors

Guselkumab

Guselkumab is a fully human IgG1λ monoclonal antibody that inhibits IL-23 by targeting the p19 subunit of interleukin 23.(Ruggiero et al., 2022) FDA has approved the use of guselkumab in the treatment of moderate-to-severe PV and psoriatic arthritis. The recommended initial administration dose is 100 mg SC at week 0 and week 4, followed by a subsequent maintenance dose of 100 mg SC every 8 weeks.(Brownstone et al., 2021) Safety and effectiveness have shown a superiority in guselkumab compared to placebo, which in week 16, the proportions of patients achieving PASI 75 was 91.2% for guselkumab compared to placebo 5.7%. Guselkumab has an excellent long-term efficacy that was evaluated in week 252, PASI 90 was maintained on 84.1% of patients in VOYAGE 1 and 82% of those in VOYAGE 2. (Reich et al., 2021) Guselkumab is a viable alternative treatment in patients who are unresponsive to other biologic drugs, such as anti-TNF-alpha and anti-IL-17, with a good safety profile. The most common treatment-related AEs were viral upper respiratory tract infection in 2.6% of cases, diarrhea with 1.3% cases, and pruritus in 1.3% cases.(Ruggiero et al., 2022) The absolute contraindication is patients with a history of tuberculosis because of insufficient scientific evidence related to an elevated risk of tuberculosis.(Nast et al., 2020)

Tildrakizumab

Tildrakizumab is a fully humanized IgG1-κ antibody specifically targeting and binding to the p19 subunit of IL-23 with high affinity.(Ruggiero et al., 2022) Tildrakizumab was approved by the FDA for treating PV patients in March 2018.(Bai et al., 2019) Tildrakizumab is the only biologic agent requiring an injection from a healthcare provider. The recommended dose is 100 mg SC at weeks 0 and 4 for the loading dose, followed by 100 mg every 12 weeks as the maintenance. Tildrakizumab has superiority than placebo and etanercept. Different studies show a significant improvement results at weeks 24-28 in terms of PASI 90, which was achieved by 50-91%, and PASI 100, which achieved by 33.3-87%.(Ruggiero et al., 2022) Tildrakizumab has a very safe biologic profile, and the most frequently reported AEs was mild.(Frampton, 2019)

Risankizumab

Risankizumab is a humanized IgG1 monoclonal antibody recently approved for treating adults with moderate-to-severe PV. Risankizumab targets and inhibits IL-23 by binding to the p19 subunit selectively.(Ruggiero et al., 2022) Risankizumab is administered at 150 mg SC using two 75 mg syringes at week 0 and week 4, followed by a maintenance dose of 150 mg every 12 weeks.(Brownstone et al., 2021) Risankizumab has a very high efficacy compared to adalimumab, ustekinumab, and secukinumab. Significant efficacy of risankizumab showed in patients who achieved PASI 90 at weeks 16 and 52, which is 70.3–82.2% and 77.6–85.5%, respectively.(Strober et al., 2020) The most common adverse reactions were upper respiratory infection, headache, fatigue, injection site reactions, and tinea infections. There is no serious AEs were reported from long-term studies at 52 weeks.(Nast et al., 2020; Ruggiero et al., 2022)

Mirikizumab

Mirikizumab is a humanized IgG4 monoclonal antibody which binds to the p19-subunit of IL-23.(Petit et al., 2021) Mirikizumab has not yet been approved by the FDA for treating PV. Five hundred and thirty adult patients with moderate-to-severe PV go through a 52 weeks treatment with mirikizumab, consisting of a 16-week induction period and a 36-week maintenance period. Patients receive mirikizumab 250 mg SC every 4 weeks from weeks 0 to 16, followed by mirikizumab 250 mg every 8 week or mirikizumab 125 mg every 8 weeks. In the 16th week of the study, a significant result was shown by 64.3 % patients achieved PASI 90 compared to a rate of 6.5% who received a placebo. A significant improvement in response to mirikizumab was observed earlier in the 8th week. Significantly by 52nd week, patients treated with mirikizumab by a dose of 250 mg/250 mg and 250 mg/125 mg showed a maintaining treatment to PASI 90 compared to placebo with a rate of 85%, 86%, and 19%, respectively. Serious AEs were observed in 1.2% of cases, while the maintenance period was 1- 3%. Most common AEs were nasopharyngitis, upper respiratory tract, headache, and injection-site pain. (Blauvelt et al., 2022; Brownstone et al., 2021)

Table 1. Biologic treatment of PV

Biologic Agents	Dose Recommended for PV	Effectiveness	Notes
TNF- Alpha Inhibitors			
Etanercept	Loading dose: 50 mg SC twice weekly for the first 12 weeks. Maintenance dose: 50 mg once weekly.	PASI 75 at week 12 was achieved by 49%	-
Adalimumab	Loading dose: 80 mg SC at week 0, 40 mg at week 1. Maintenance dose: 40 mg every 2 weeks.	PASI 75 at week 16 was achieved by 88%	-
Infliximab	Loading dose: 5 mg/kg IV at weeks 0, 2, and 6. Maintenance dose: 5 mg/kg every 8 weeks.	PASI 75 at week 10 patients treated with 5 mg/kg and 3 mg/kg doses were achieved by 75.5% and 70.3%	Efficacy decreased over time.

Biologic Agents	Dose Recommended for PV	Effectiveness	Notes
Certolizumab (CZP)	Loading dose: 400 mg SC at weeks 0, 2 and 4. Maintenance dose: > 90 kg is 400 mg every two weeks. < 90 kg is 200 mg every two weeks.	PASI 75 at week 16 was achieved by 81.6%	Approve for pregnancy and breastfeeding.
IL-12/23 Inhibitors			
Ustekinumab	Loading dose: < 60 kg is 0.75 mg/kg. < 100 kg is 45 mg SC initially. > 100 kg is 90 mg SC at weeks 0 and 4. Maintenance dose: < 100 kg is 45 mg every 12 weeks. > 100 kg is 90 mg every 12 weeks.	PASI 75 at week 12 in patients treated with 45 mg and 90 mg was achieved by 66 % and 67%	Approved for adolescents 12 - 17 years old
IL-17 Inhibitors			
Secukinumab	Loading dose: 300 mg SC at weeks 0, 1, 2, 3, and 4. Maintenance dose: 300 mg SC every 4 weeks.	PASI 75 at week 12 patients treated with 300 mg and 150 mg were achieved by 81.6% and 71.6%.	Most extensive safety record in reactivation of latent tuberculosis.
Brodalumab	Loading dose: 210 mg SC at weeks 0, 1 and 2. Maintenance dose: 210 mg every 2 weeks.	PASI 75 at week 12 was achieved by 83% and 60% for dosages of 210 mg and 140 mg.	High efficacy with rapid onset.
Ixekizumab	Loading dose: 160 mg SC at week 0 and 80 mg at weeks 2, 4, 6, 8, 10, and 12. Maintenance dose: 80 mg every 2 or 4 weeks.	PASI 75 at week 12 was achieved by 89.1% in the group of patients who received a maintenance dose every 2 weeks.	Approved for children below 6 years old.
Bimekizumab	Dosage used in trials. Loading dose: 320 mg SC every 4 weeks. Maintenance dose: 320 mg SC every 4 weeks.	PASI 75, PASI 90, and PASI 100 within 10-16 weeks achieved by 92.3%, 84.0%, and 57.8%.	It hasn't been approved by FDA but had been approved in Japan.
IL-23 Inhibitors			
Guselkumab	Loading dose: 100 mg SC at week 0 and week 4. Maintenance dose: 100 mg every 8 weeks.	PASI 75 at week 16 achieved by 91.2%.	Good for long-term efficacy.
Risankizumab	Loading dose: 100 mg SC at weeks 0 and 4 Maintenance dose: 100 mg every 12 weeks	PASI 90 at weeks 24-28 achieved by 50-91% and PASI 100 achieved by 33.3-87%.	Injection performs by the healthcare.
Tildrakizumab	Loading dose: 150 mg SC using two 75 mg syringes at week 0 and week 4. Maintenance dose: 150 mg every 12 weeks.	PASI 90 at weeks 16 and 52 is achieved by 70.3–82.2% and 77.6–85.5%.	-
Mirikizumab	Dosage used in trials. Loading dose: 250 mg SC every 4 weeks until week 16. Maintenance dose: 250 mg or 125 mg every 8 week.	PASI 90 at week 52 in the group of 250 mg/250 mg and 250 mg/125 mg is 85% and 86%.	It hasn't been approved by FDA.

CONCLUSION

After reviewing all the available options, it has become clear that each biologic agent has their advantages and disadvantages. The only biological agent that is safe for pregnant women and breastfeeding is certolizumab. Treatment options for adolescents 12 to 17 years is ustekinumab,

while for children under 6 years old is ixekizumab. The usage of TNF-α, such as etanercept, infliximab, adalimumab, and certolizumab is contraindicated for patients with active tuberculosis infection or severe infection and congestive heart failure with NYHA class III/ IV. IL-17 inhibitors such as secukinumab, ixekizumab, and brodalumab have a high risk of developing fungal or yeast infections. Secukinumab has the most extensive safety record in the reactivation of latent tuberculosis. Until now, mirikizumab and bimekizumab are being scrutinized for further research. Overall the most effective biologic agent for PV is ixekizumab, where a total of 89.1% of patients in the group receiving 2-weeks dosing group achieved a PASI 75 response at the end of week 12. The authors hope this review can provide scientific knowledge and help enhance psoriasis patient treatment and satisfaction. Clinical trial studies for several biologic agents in patients with psoriasis are ongoing. Authors believed that more and more new biological agents would be discovered. Therefore, the author's advice is not to dismiss any biologic therapies that are now accessible. Suggestions for future studies could carry out meta-analyses that integrate the findings of the newest update and safety profile of biologic agents, including biological agents that the FDA has not approved.

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