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Review Article

Biologic Medications for the Treatment of Psoriasis - Main Groups and Dosing System

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Abstract

This review explores the evolving landscape of psoriasis treatment with a focus on the transformative impact of biologic drugs. Psoriasis, a prevalent and persistent skin condition characterized by red and scaly patches, historically relied on topical, phototherapeutic, and systemic treatments, each with limitations. The advent of biologics represents a significant advancement, offering targeted interventions by addressing specific immunologic mechanisms underlying the disease. Biologics are now considered the preferred systemic therapy for chronic moderate-to-severe plaque psoriasis, particularly when conventional treatments prove ineffective or present disadvantages.

The review delineates the mechanisms of action for biologics targeting tumour necrosis factor-alpha (TNF-α), interleukin-17 (IL-17) and interleukin-23 (IL-23). Specific drugs under each category, including etanercept, infliximab, adalimumab, secukinumab, ustekinumab, and others, are detailed with recommended dosages. Biologics have demonstrated substantial effectiveness, with clinical trials and real-world studies showcasing significant improvements in disease severity and patient's quality of life. Notably, these drugs exhibit rapid action, often yielding noticeable changes within weeks.

While biologics have revolutionized psoriasis treatment, the review emphasizes the importance of judicious use due to potential side effects such as injection-site reactions and respiratory infections. Serious adverse events, including infections and autoimmune reactions, necessitate careful patient selection and monitoring for safety. In conclusion, biologics offer a precise and effective approach to psoriasis treatment, promising marked symptom improvement and enhanced quality of life. The review underscores the need for responsible utilization, considering patient-specific factors, and anticipates ongoing advancements in biologics for improved control over this chronic dermatitis.

More Information

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Introduction

Epidemiology

Psoriasis is a relatively common disorder that occurs in children and adults worldwide, though the prevalence varies among populations. A systematic, worldwide review found the prevalence of psoriasis ranged from 0.5% to 11.4% in adults and 0 to 1.4% in children [1].

There is no clear sex predilection for psoriasis [2]. In addition, psoriasis can begin at any age, though it is less common in children than adults. Peak ages for the onset of psoriasis are between 30 and 39 years and between 50 and 69 years [2].

The incidence of psoriasis may be increasing. A population-based study in the United States found an increase in the incidence of psoriasis between the years 1970 to 1974 (50.8 cases per 100,000) and 1995 to 1999 (100.5 cases per 100,000) [3]. A rise in incidence was also detected among children, increasing from 29.6 cases per 100,000 to 62.7 cases per 100,000 during the same time period [4]. However, changes in diagnostic patterns over time may also contribute to increasing rates of diagnosis [3].

Pathogenesis

Keratinocytes, the primary cellular components of the skin epidermis, serve not only as a physical barrier but also play crucial roles in initiating, sustaining, and regulating the skin's immune response. While participating in the innate immune response by promptly and non-specifically reacting to antigenic stimuli, keratinocytes, despite not being traditional antigen-presenting cells, can process antigens and present

them to T cells. The functionality of keratinocytes is largely influenced by their activation and differentiation status. Under normal conditions, cell differentiation occurs regularly, and the layers undergo constant renewal. In this process, basal layer keratinocytes transform into spiny and granular layers, eventually losing their nucleus and forming the stratum corneum. In psoriatic lesions, however, the terminal differentiation of keratinocytes is incomplete, and there is abnormal cell proliferation. The accelerated cell proliferation leads to inadequate keratinization, resulting in the retention of nuclei within epidermal keratinocytes, a pathological condition known as parakeratosis [5].

The pathogenesis of psoriasis involves the identification of key cytokines IL-17A and IL-23, leading to the development and clinical application of targeted antibodies against these cytokines. Th17 cells are recognized as playing a vital role in psoriasis pathogenesis; however, the complete development of psoriasis cannot be solely attributed to the response of Th17 lymphocytes. Despite targeting cytokines IL-17A or IL-23, a complete cure for psoriasis is not achieved. Recent studies increasingly demonstrate that the intricate interplay among various cytokines and different cell types, including dendritic cells, neutrophils, macrophages, keratinocytes, and Th17 cells, constitutes a complex cascade of events that ultimately contributes to the pathogenesis and progression of psoriasis [5].

Purpose of review

This comprehensive review aims to elucidate the pivotal role of biological drugs in the management of psoriasis, presenting a paradigm shift from traditional treatments such as topical applications, phototherapy, and systemic agents like methotrexate and cyclosporine. The primary objective is to highlight the transformative impact of biologics, which address the specific immunologic mechanisms driving psoriasis, thereby overcoming limitations associated with conventional therapies, including systemic toxicity and long-term reactions.

The review provides a detailed examination of the mechanisms of action of biologics, focusing on their targeting of key components of the immune system, namely tumor necrosis factor-alpha (TNF-α), interleukin-17 (IL-17), and interleukin-23 (IL-23). By exploring the specific agents under each category and their recommended dosages, the review aims to equip healthcare professionals with practical insights into initiating biologic therapy based on factors such as disease severity, treatment side effects, patient preferences, and outcomes.

Additionally, the review underscores the effectiveness of biologic medications through evidence from clinical trials and real-world studies, emphasizing their significant contributions to improvements in disease severity, quality of life, and long-term outcomes for psoriasis patients. The safety profile of biologics is addressed, acknowledging possible side effects while emphasizing the mild and highly tolerable nature of these reactions. The review emphasizes the importance of cautious patient selection, monitoring for safety, and thorough assessments for infections and concomitant conditions before initiating biologic treatment.

In short, the review anticipates the continued evolution of biologics, with growing knowledge about the pathophysiology of psoriasis paving the way for innovative treatments that promise enhanced control over this chronic dermatitis, thereby enhancing the overall well-being of individuals affected by psoriasis.

Challenges faced by psoriasis patients

Visible Symptoms and Social Stigma: Psoriasis appears in the form of red plaques that are thick and are easily visible. Social problems experienced by patients with visible skin conditions, such as misconceptions and stigma, affect the self-perception and mental health of individuals.

Chronic nature and flare-ups: Psoriasis is a chronic disease, and it has cycles with recurrences and remissions. The disease is unpredictable which makes daily life a disruption and causes both physical and psychological problems.

Itchiness and discomfort: Psoriasis is characterized by intense itching, burning, and discomfort. These might include difficulty in controlling blood glucose, which can interfere with sleep and have a negative impact on an individual's well-being.

Association with comorbidities: Psoriasis is associated with psoriatic arthritis, cardiovascular disorders, diabetes mellitus, and poor mental health among others. These are interrelated health issues that most patients have a hard time managing.

Impact on daily activities: Psoriasis lesions may be so severe that regular exercise, wearing a particular piece of clothing, or interacting with others becomes difficult.

Challenges with the evolution of psoriasis treatments

While treatments for psoriasis were emerging, patients would suffer from side effects and challenges with using these medications.

Old remedies: Records of history have shown many natural remedies which include oils, herbs, and even minerals in the relief of the psoriasis symptom. Many ancient societies treated symptoms by using topical applications and baths.

Coal Tar and Sulphur: Sulphurous preparations of coal tar were also used in skin disease treatment during the 19th century and the beginning of the 20th century. Many thought these substances had anti-inflammatory effects.

Introduction of corticosteroids: Corticosteroid use

in psoriasis was introduced in the mid-20th century. The preferred approach was topical steroids which gave anti-inflammatory properties and symptomatic relief.

UV light therapy: It is noteworthy that phototherapy, which involves the application of UV light, became one of the most popular modalities in the second half of the 19th century. These include natural sunshine, and artificial UVB and PUVA treatment regimes.

Systemic medications: Systemic drugs like methotrexate and cyclosporin came into use as psoriasis treatment in the later part of the twentieth century. The purpose of these drugs was symptom management through targeting the immune system.

Biologic revolution: The past few years have witnessed a new revolution in the treatment of psoriasis with biological drugs aimed at parts of the immune system pathway. The newer drugs such as those that inhibit TNF-α, IL-17, and IL-23 provide more targeted and better alternatives.

Treatment side effects: While some traditional treatment options for psoriasis like systemic drugs produce mild effects on a patient's health, others are more severe.

Psoriasis is a very common long-lasting skin condition, showing symptoms of red scaly patches and in some cases white ones on the skin too. Most of the cases do not have any impact on physical well-being and are managed in the outpatient setup. The landscape of treatment of people living with chronic moderate-to-severe plaque psoriasis suitable for systemic therapy or phototherapy is changing quickly. On one hand, the arrival of biological remedies stands among the most impressive advancements in handling psoriasis patients. This review paper discusses the use of biologic drugs in psoriasis therapy, including their mechanisms of action, therapeutic efficacy, and side effects profile.

Biologic's role in the management of psoriasis

Historically, the management of psoriasis has included topical treatments, phototherapy, and systemic treatments, including methotrexate, and cyclosporine, among other agents. Despite their successes, these therapies are accompanied by limitations like systemic toxicity and long-term reactions. However, biologic treatments for psoriasis proved to be game changers in how we approach the management of this condition because they offer targeted interventions addressing the actual immunologic mechanisms at play in the disease.

Topical therapies

Emollients serve as valuable and cost-effective supplements to psoriasis therapy. Maintaining the softness and moisture of psoriatic skin is instrumental in reducing symptoms like itching and tenderness. Proper skin hydration also aids in preventing irritation and the potential development of new psoriatic lesions at sites of trauma, a phenomenon known as Koebnerization.

Ointments: Such as petroleum jelly or thick creams, are particularly effective, especially when applied immediately after a hydrating bath or shower. However, in practical terms, the choice of moisturizer depends on the patient's preference.

Topical corticosteroids: Despite the emergence of newer agents, topical corticosteroids remain the primary treatment for psoriasis. The exact mechanism by which corticosteroids act in psoriasis is not fully elucidated. Nevertheless, they exhibit anti-inflammatory, antiproliferative, and immunosuppressive effects by influencing gene transcription.

Topical vitamin D analogues: Topical vitamin D analogues for the treatment of psoriasis include calcipotriene (calcipotriol), calcitriol, and tacalcitol. Although topical vitamin D analogues are effective as monotherapy for some patients, a systematic review found that combination therapy with a topical corticosteroid is more effective than either treatment alone [6].

Tazarotene: Tazarotene is a topical retinoid that was safe and effective in two randomized, vehicle-controlled trials that included 1303 patients with psoriasis [7].

Calcineurin inhibitors: Topical tacrolimus 0.1% and pimecrolimus 1% are effective in the treatment of psoriasis in sensitive areas. Facial and intertriginous areas may be well suited to these treatments, which can allow patients to avoid or minimize chronic topical corticosteroid use.

Ultraviolet light ultraviolet (UV)

The beneficial impact of ultraviolet (UV) irradiation on the management of psoriatic skin lesions has been acknowledged for an extended period. UV radiation is believed to exert antiproliferative effects by slowing down keratinization and anti-inflammatory effects by inducing apoptosis of pathogenic T cells present in psoriatic plaques. When opting for UV therapy, it is essential to consider the potential of UV radiation to hasten photodamage and elevate the risk of cutaneous malignancy.

Supervised by a dermatologist trained in these treatment modalities, office-based phototherapy and photochemotherapy are necessary. Despite their high efficacy and safety, the utilization of office-based phototherapy has diminished in the United States due to administrative issues and the emergence of new systemic medications [8].

Systemic therapies

Methotrexate: Methotrexate, a folic acid antagonist, has proven successful in treating psoriasis. It also demonstrates effectiveness in addressing psoriatic arthritis and psoriatic nail disease. Initially, the perceived mechanism of action revolved

around methotrexate's antiproliferative impact on DNA synthesis in epidermal cells. However, subsequent evidence indicates that the immunosuppressive effects of methotrexate on activated T cells play a crucial role in managing psoriasis.

Methotrexate has many contraindications. Absolute contraindications include pregnancy, nursing, alcoholism, alcoholic liver disease or other chronic liver disease, immunodeficiency syndromes, bone marrow hypoplasia, leukopenia, thrombocytopenia, significant anaemia, or hypersensitivity to methotrexate. In addition to the risk of hepatotoxicity associated with it.

Acitretin: Systemic retinoids (derivatives of vitamin A) are used for patients with severe psoriasis, including pustular and erythrodermic forms, and in patients with HIV-associated psoriasis. The retinoid of choice in psoriasis is acitretin. Acitretin requires monitoring for hypertriglyceridemia and hepatotoxicity. Common side effects include cheilitis and alopecia. Acitretin is teratogenic; it is only indicated in men and in women of nonreproductive potential. Pregnancy is contraindicated for three years after discontinuing the drug [9].

Cyclosporine: A T-cell suppressor, proves effective for individuals with severe psoriasis. Typically administered orally at doses ranging from 3 to 5 mg/kg per day, noticeable improvement is often evident within four weeks. For cases where a more consistently absorbed modified microemulsion form of cyclosporine is prescribed, lower doses (1 to 3 mg/kg per day) are deemed more suitable. Cyclosporine therapy is contraindicated for individuals with a history of prior PUVA treatment, abnormal renal function, uncontrolled hypertension, malignancy, or hypersensitivity to cyclosporine. Caution should be exercised in cases of major infections or poorly controlled diabetes. Additionally, cyclosporine is associated with multiple drug interactions.

Apremilast: Classified as a phosphodiesterase 4 inhibitor, is an additional oral medication used to address plaque psoriasis. By inhibiting phosphodiesterase 4, it diminishes the production of various cytokines implicated in the development of psoriasis. Apremilast is relatively expensive, aligning its cost more closely with biologics than with methotrexate. Additionally, it has shown efficacy in the treatment of psoriatic arthritis. Apremilast is associated with short-term risk of diarrhoea. Other documented adverse effects of apremilast encompass nausea, upper respiratory infections, headaches, potential drug interactions, and weight loss. Regular weight checks are advised for monitoring purposes. Additionally, patients, their caregivers, and families should remain vigilant for signs of exacerbated depression, suicidal thoughts, or alterations in mood during treatment, given a slight elevation in the risk of depression.

Biologic agents

According to US FDA Biologics are: Biological products include a wide range of products such as vaccines, blood and blood components, allergenics, somatic cells, gene therapy, tissues, and recombinant therapeutic proteins. Biologics can be composed of sugars, proteins, nucleic acids, or complex combinations of these substances, or may be living entities such as cells and tissues. Biologics are isolated from a variety of natural sources - human, animal, or microorganism - and may be produced by biotechnology methods and other cutting-edge technologies.

Currently, biologics are considered the initial and preferred systemic therapy for patients with chronic mild to moderate to severe plaque psoriasis who have been considered suitable candidates for systemic therapy or phototherapy. These drugs are usually used in situations where topical treatment and light therapy do not work well enough or cannot be used due to certain disadvantages. Factors such as disease severity, treatment side effects, patient choice, and treatment outcomes influence the decision to initiate biologic therapy.

Mechanisms of action

Biologic medications used in the treatment of psoriasis target specific components of the immune system that play a crucial role in the development of the disease. The most common targets include tumour necrosis factor-alpha (TNF-α), interleukin-17 (IL-17), and interleukin-23 (IL-23). These cytokines are known to be overactive in individuals with psoriasis, leading to excessive inflammation and abnormal skin cell growth.

1. TNF-α Inhibitors

Medications work by inhibiting TNF-α, a pro-inflammatory cytokine. By blocking TNF-α, these biologics reduce inflammation and slow down the progression of psoriatic skin lesions. The mechanism of action is still a matter of debate. Initially, it was suggested that anti-TNF agents inactivate the proinflammatory cytokine TNF by direct neutralization, thus resulting in the suppression of inflammation.

The main agents under this group include etanercept, infliximab, and adalimumab (Table 1) [10].

A-Etanercept

Adults' dose of subcutaneous 50 mg twice weekly for the initial three months of therapy, followed by a 50 mg SC once weekly for maintenance therapy [11]. Etanercept is approved for patients aged four years or older [12].

Effectiveness: In a randomized trial involving 652 adult patients with active yet stable plaque psoriasis covering a minimum of 10% of the body surface area, three subcutaneous etanercept doses (25 mg weekly, 25 mg twice weekly, 50 mg twice weekly) demonstrated significant superiority over placebo [13]. The study observed that after 12 weeks, there

Table 1: Clinical guidelines for TNF inhibitor use [10].

	Infliximab	Adalimumab	Etanercept
Administration	Intravenous infusion	Subcutaneous injection	Subcutaneous injection
Dosing schedule			
Induction	Weeks 0, 2, 6 = 5 mg/kg	Week 0 = 80 mg Week 1 = 40 mg	Months 0-2 = 50 mg twice weekly
Maintenance	Every 8 weeks = 5 mg/kg	Every 2 weeks = 40 mg	Every week = 50 mg
Efficacy			
Short-term	10 weeks: 80% of patients = PASI-75	12 weeks: 80% of patients = PASI-75	12 weeks: 49% of patients = PASI-75
Long-term	50 weeks: 61% of patients = PASI-75	60 weeks: 68% of patients = PASI-75	59% of patients = PASI-75
Baseline monitoring			
Required	PPD	PPD	PPD
Recommended	LFT, CBC, hepatitis panel	LFT, CBC, hepatitis panel	LFT, CBC, hepatitis panel
Ongoing monitoring			
Recommended	Yearly PPD	Yearly PPD	Yearly PPD
	Periodic history and physical	Periodic history and physical	Periodic history and physical
	Periodic LFT, CBC	Periodic LFT, CBC	Periodic LFT, CBC
Pregnancy class	B	B	B
Toxicities			
Common	Serum sickness	Injection site reaction/pain	Injection site reaction/pruritis
	Infusion reaction	Flu-like symptoms	Flu-like symptoms
Rare	Serious infection (TB)	Serious infection (TB)	Serious infection (TB)
	Lymphoma	Lymphoma	Lymphoma
	New onset CHF, lupus, MS, cytopenia	New onset CHF, lupus, MS, cytopenia	New onset CHF, lupus, MS, cytopenia
	Cancer	Cancer	Cancer

was a minimum of a 75% improvement in the PASI score in 14%, 34%, 49% and 4% of patients, respectively. Following 24 weeks, such improvement was noted in 25%, 44% and 59%, respectively (with no patients receiving a placebo beyond 12 weeks). Etanercept exhibited good tolerance, with adverse events and infections occurring at comparable rates across all four groups.

B-Infliximab

Adults dose IV infusion of 5 mg/kg at weeks 0, 2, and 6, followed by every eight weeks thereafter. The onset of action of infliximab is faster than several other commercially available biological agents according to a systematic review [14].

Effectiveness: In a multicentre randomized trial involving 249 patients with severe plaque psoriasis, infliximab demonstrated efficacy. In comparison to a placebo, a higher percentage of patients treated with intravenous infliximab at doses of 3 mg/kg or 5 mg/kg (administered at weeks 0, 2, and 6) achieved PASI 75 at week 10 (6% *vs.* 72% and 88%, respectively) [15]. The trial suggested that the duration of response was potentially longer with the higher dosage. However, more patients treated with infliximab experienced serious adverse events (12 *vs.* 0), including four cases that the authors deemed reasonably associated with treatment: squamous cell carcinoma, cholecystitis, diverticulitis, and pyelonephritis with sepsis.

C-Adalimumab

Adult dose: initial SC 80 mg of adalimumab followed by 40 mg given every other week, beginning one week after the initial dose.

Effectiveness: A randomized trial in 147 patients with moderate to severe plaque psoriasis compared adalimumab by subcutaneous injection of 40 mg every other week, 40 mg weekly, and placebo [16]. After 12 weeks, more patients treated with adalimumab every other week or weekly achieved PASI 75 (53% and 80%, respectively) *vs.* 4% with placebo. In an open-label extension of the study, improvements were sustained for 60 weeks.

2. IL-17 Inhibitors

IL-17 Inhibitors: Drugs target IL-17, another key player in psoriasis-related inflammation. These biologics help normalize immune responses and alleviate psoriatic symptoms.

Mechanism of action: Keratinocytes are the major target for IL-17 in psoriasis, with IL-17 stimulation causing increased keratinocyte expression of inflammatory cytokines and other effects that contribute to epidermal hyperproliferation and barrier dysfunction. Clinical trials have demonstrated that IL-17 inhibitors are very efficacious for plaque psoriasis [17].

The main agents under this group include Secukinumab, Ixekizumab, Brodalumab, and Bimekizumab.

A-Secukinumab

Adult dose: 300 mg SC once weekly at weeks 0, 1, 2, 3, and 4 followed by 300 mg every four weeks, and doses of 150 mg are sufficient for some patients.

Effectiveness: The effectiveness of secukinumab for moderate to severe plaque psoriasis is supported by two 52-week phase 3 placebo-controlled trials, namely the ERASURE trial and the FIXTURE trial. In both trials, secukinumab was administered at doses of 300 mg or 150 mg once weekly for the first five weeks, followed by once every four weeks. In the ERASURE trial involving 738 participants, 82% of patients in the 300 mg secukinumab group and 72% in the 150 mg secukinumab group achieved PASI 75 at week 12, compared to only 5% in the placebo group. The FIXTURE trial (n = 1306), which included similar secukinumab doses, demonstrated the superiority of secukinumab over both etanercept (50 mg twice weekly for 12 weeks, then once weekly) and placebo. After 12 weeks, PASI 75 was attained by 77% in the 300 mg secukinumab group, 67% in the 150 mg secukinumab group, 44% in the etanercept group, and 5% in the placebo group [18].

B-Ixekizumab

Adult dose: 160 mg at week 0, followed by 80 mg at weeks 2, 4, 6, 8, 10, and 12. The maintenance dose of 80 mg is given every four weeks.

Effectiveness: In the UNCOVER-2 trial (n = 1224) and UNCOVER-3 trial (n = 1346), individuals with moderate to severe plaque psoriasis were randomly assigned to receive either 80 mg of ixekizumab every two weeks following a 160 mg initial dose, 80 mg of ixekizumab every four weeks after a 160 mg initial dose, etanercept (50 mg twice weekly), or placebo, with a distribution ratio of 2:2:2:1. By week 12, a higher percentage of patients treated with either ixekizumab every two weeks or ixekizumab every four weeks achieved PASI 75 compared to those receiving etanercept or placebo. In UNCOVER-2, PASI 75 rates were 90%, 78%, 42%, and 2%, respectively. For UNCOVER-3, PASI 75 rates were 87%, 84%, 53%, and 7%, respectively [19].

C-Brodalumab

Adult dose: 210 mg given at weeks 0, 1, and 2 and then every two weeks.

In the US, the use of the drug will require participation in a REMS program due to concerns regarding the risk of suicidal ideation. However, the causal relationship between Brodalumab treatment and suicidal ideation and behaviour has not been confirmed.

Effectiveness: Evidence from phase 3 randomized trials demonstrates the effectiveness of brodalumab in treating moderate to severe plaque psoriasis [20,21]. In two trials with identical designs, namely AMAGINE-2 (n = 1831) and AMAGINE-3 (n = 1881), patients were randomly allocated in a 2:2:1:1 ratio to receive brodalumab at doses of 210 mg every two weeks, brodalumab at doses of 140 mg every two weeks, standard ustekinumab dosing on day 1, week 4, and then every 12 weeks (45 mg dose for individuals with a bodyweight ≤ 100 kg, and 90 mg dose for those with a bodyweight > 100 kg), or a placebo. By week 12, a higher proportion of patients receiving 210 mg or 140 mg of brodalumab achieved PASI 75 compared to those in the placebo group (86%, 67%, and 8%, respectively, in AMAGINE-2, and 85%, 69%, and 6%, respectively, in AMAGINE-3). Furthermore, the rate of complete skin disease clearance (PASI 100) at week 12 was greater in patients given 210 mg of brodalumab compared to those receiving ustekinumab (44% *vs.* 22%, respectively, in AMAGINE-2, and 37% *vs.* 19%, respectively, in AMAGINE-3). Although a statistically significant advantage of the 140 mg dose of brodalumab over ustekinumab for achieving PASI 100 was observed in AMAGINE-3 at week 12, this was not evident in AMAGINE-2. The occurrence of mild to moderate Candida infections was more frequent in the brodalumab groups than in the ustekinumab and placebo groups, and neutropenia was more frequent in the brodalumab and ustekinumab groups than in the placebo group. Additionally, two suicides were reported in patients receiving brodalumab during crossover and open-label phases of AMAGINE-2.

D-Bimekizumab: An adult dose is 320 mg given every four weeks for the first 16 weeks, followed by 320 mg given every eight weeks.

Patients weighing ≥ 120 kg who have an inadequate response after 16 weeks may benefit from maintaining the four-week treatment interval.

Effectiveness: Clinical trials comparing bimekizumab with adalimumab or secukinumab also provide evidence supporting the superior efficacy of bimekizumab. In a 56-week phase 3 trial known as the BE SURE trial, adults with moderate to severe plaque psoriasis were randomly assigned to receive bimekizumab (320 mg every four weeks for 56 weeks), bimekizumab (320 mg every four weeks for 16 weeks and then every eight weeks until week 56), or adalimumab (80 mg followed by 40 mg one week later and then 40 mg every two weeks until week 24). Patients initially assigned to the adalimumab group subsequently received bimekizumab (320 mg every four weeks from weeks 24 to 56). By week 16, 86% (275 of 319 patients) receiving bimekizumab achieved PASI 90, in contrast to 47% (75 of 159 patients) receiving adalimumab (adjusted risk difference 28.2% points, 95% CI 19.7-36.7). Notably, these positive responses were sustained through week 56 with both dosing regimens for bimekizumab [22].

3. IL-23 Inhibitors

IL-23 inhibitors target IL-23, which is involved in the

differentiation and activation of T cells. By blocking IL-23, these medications interrupt the autoimmune response that drives psoriasis.

Mechanism of action: Monoclonal antibody directed against the common p40 subunit of IL-12 and IL-23. IL-12 promotes Th1 activity and related TNF-α and IFN-γ production, while IL-23 activates Th17 cells that produce IL-17A, which regulates tissue inflammation and autoimmune responses.

The main agents under this group include Ustekinumab, Guselkumab, Tildrakizumab, and Risankizumab

A-Ustekinumab

The dosing of Ustekinumab is weight-based.

For adults ≤ 100 kg is 45 mg given at weeks 0, 4, and every 12 weeks thereafter.

Adults > 100 kg is 90mg given at weeks 0, 4, and every 12 weeks thereafter.

Ustekinumab is a human monoclonal antibody that targets IL-12 and IL-23.

Ustekinumab is approved for the treatment of adults and children 12 years and older with moderate to severe psoriasis.

Effectiveness: In a randomized trial involving 766 patients with moderate to severe plaque psoriasis, a higher proportion of individuals treated with ustekinumab at doses of 45 or 90 mg achieved at least PASI 75 at week 12 compared to those treated with a placebo (67% and 66% *vs.* 3%, respectively). Ustekinumab was administered through monthly subcutaneous injections for the initial two doses, followed by injections every 12 weeks. Responders who continued the therapy generally maintained improvements in psoriasis for at least 76 weeks. Rates of serious adverse events were comparable between the ustekinumab and placebo groups [23].

B-Guselkumab

Guselkumab is a human IgG1 lambda monoclonal antibody that binds to the p19 subunit of IL-23. IL-39 also contains this p19 subunit. The mechanism of action in psoriasis is thought to involve the inhibition of IL-23 signalling.

The adults' dose of 100 mg at weeks 0, 4, and then every 8 weeks.

Effectiveness: In the initial 24 weeks of the 48-week phase 3 VOYAGE 2 trial involving 992 adults with moderate to severe plaque psoriasis, participants were randomly assigned in a 2:1:1 ratio to guselkumab, placebo followed by guselkumab, or adalimumab groups, following dosing regimens similar to those in VOYAGE 1. Like the findings in VOYAGE 1, guselkumab demonstrated superior efficacy compared to adalimumab and placebo at week 16. By week 28, patients had the option to either continue (or start) guselkumab or transition to placebo followed by guselkumab upon the loss of response. Rerandomization occurred for guselkumab-treated patients who had achieved at least PASI 90, and among these rerandomized patients, continued therapy was associated with higher maintenance of response compared to withdrawal. Specifically, 89% maintained PASI 90 through week 48 in the continued therapy group, whereas only 37% in the withdrawal group did so [24].

C-Tildrakizumab

Tildrakizumab is a human IgG1 kappa monoclonal antibody that binds to the p19 subunit of IL-23.

Adult dose: 100 mg given subcutaneously at weeks 0 and 4 and then every 12 weeks.

Effectiveness: Results from Phase 3 trials (reSURFACE 1, reSURFACE 2) indicate the superiority of tildrakizumab over placebo and etanercept. In reSURFACE 1, 772 adults with moderate to severe plaque psoriasis were randomly assigned to receive tildrakizumab 200 mg, tildrakizumab 100 mg, or placebo at weeks 0 and 4, followed by dosing every 12 weeks. After 12 weeks, PASI 75 was achieved by 62%, 64%, and 6% of patients in the 200 mg, 100 mg, and placebo groups, respectively. The reSURFACE 2 trials included 1090 patients randomly assigned to similar groups, with an additional etanercept group. At the 12-week mark, PASI 75 was attained by 66%, 61%, 6%, and 48% of patients in the tildrakizumab 200 mg, tildrakizumab 100 mg, placebo, and etanercept groups, respectively. Rates of serious adverse effects were comparable among the groups in both reSURFACE 1 and reSURFACE 2. Notably, one patient in the tildrakizumab 100 mg group died of an unclear cause during reSURFACE 2 [25].

D-Risankizumab

Risankizumab is a humanized monoclonal antibody directed against the p19 subunit of IL-23 and IL-39.

Adult dose: 150 mg at week 0 and week 4, then every 12 weeks.

Effectiveness: Risankizumab demonstrated superior efficacy compared to ustekinumab and placebo in phase 3 trials. In the 16-week blinded phase of the 52-week UltIMMA-1 (n = 506) and UltIMMa-2 (n = 491) trials, individuals with moderate to severe plaque psoriasis were randomly assigned to receive risankizumab (150 mg), ustekinumab (45 or 90 mg based on weight), or placebo in a 3:1:1 ratio. Doses in this phase were administered at zero and four weeks. In UltIMMa-1, PASI 90 was achieved by 75%, 42%, and 5% of patients, respectively, at 16 weeks. In UltIMMa-2, 75%, 48%, and 2% achieved this endpoint, respectively. Overall,

Table 2: Safety Profile. Summary of Unique Biologic Therapies Licensed for Plaque Psoriasis [27].

Biologic	Structure	Target	Standard Dosing	Average Half-Life
Adalimumab	Human IgG1κ	TNF-α	Loading dose 80 mg; 40 mg every 2 weeks	14 days
Etanercept	TNFR and IgG Fc fusion protein	TNF-α	50 mg weekly	3 days
Infliximab	Human-murine chimeric IgG1	TNF-α	5 mg/kg at weeks 0, 2, and 6, then every 8 weeks	8–9.5 days
Secukinumab	Human IgG1κ	IL-17A	300 mg weeks 1–5, then 300mg monthly.	27 days
Ixekizumab	Humanized IgG4	IL-7A	160 mg at week 0, 80mg at weeks 2, 4, 6, 8, 10, and 12, then 80mg every 4 weeks	13 days
Brodalumab	Human IgG2	IL-17RA	210 mg weeks 0, 1, and 2, then every 2 weeks	11 days
Bimekizumab	Humanized IgG1	IL-17A, IL-17F, IL-17AF	320 mg weeks 0, 4, 8, 12, 16 then every 8 weeks	23 days
Ustekinumab	Human IgG1κ	p40 subunit of IL-12 and IL-23	45 mg weeks 0 and 4, then every 12 weeks	21 days
Guselkumab	Human IgG1λ	p19 subunit of IL-23	100 mg weeks 0 and 4, then every 8 weeks	15–18 days
Risankizumab	Humanized IgG1	p19 subunit of IL-23	150 mg weeks 0 and 4, then every 12 weeks	28–29 days
Tildrakizumab	Humanized IgG1κ	p19 subunit of IL-23	100 mg weeks 0 and 4, then every 12 weeks	23.4 days

Table 3: Adverse Events of Interest Caused by Biologics Used for Psoriasis and Risk Management Strategies [27].

Adverse Event Type	Summary	Risk Management Strategies
Infections		
Serious infections	Increased risk with infliximab and lower risk with ustekinumab in observational studies.	Consider avoiding infliximab in patients at high risk of infection
Fungal infections	Trial data suggests candida infection in all anti-IL17 agents, particularly bimekizumab	Consider alternative biologic classes in patients where avoiding candida infection is a priority
Tuberculosis	Increased odds of developing TB on anti-TNFs in a meta-analysis of rheumatoid arthritis trials. No reactivation in 31 risankizumab-treated patients with latent TB	Screen for TB with interferon-gamma release assay prior to initiation of biologic therapy. Treat latent TB prior to biologic initiation. Consider risankizumab if psoriasis treatment is required before anti-TB therapy.
Post-operative infections	Lack of data on post-operative risk in psoriasis patients.	Case-by-case consideration on whether to pause biologic therapy, or whether to time surgery prior to the next dose of biologic if the risk of psoriasis flare is high.
COVID-19 infection	Anti-TNFs may be associated with a better prognosis in the event of COVID-19 compared with conventional systemic agents. Data lacking for other biologic classes.	Insufficient data to inform risk management,

the incidence of adverse effects was comparable among the three groups; however, infections were more frequent in the risankizumab and ustekinumab groups than in the placebo group [26].

Effectiveness and management strategies

The effectiveness of biologic medications in the treatment of psoriasis has been well-documented. Clinical trials as mentioned have shown that biologics often lead to significant improvements in disease severity, quality of life, and long-term outcomes for patients. Biologics help many people regain control over their psoriasis, as they achieve clearer or virtually clear skin (Table 2).

They are especially helpful for those people having moderate to severe plaque psoriasis as they can attain a very high rate of skin clearance compared with traditional medication. Additionally, biologics generally act faster — patients may notice changes in their asthma control within weeks of starting the medication.

As biologics transformed treatment for psoriasis, there are still some possible side effects and risks involved with their use. Side effects may include injection-site reactions, upper respiratory tract infections, and headaches. These side effect profiles, however, tend to be mild and highly tolerable.

Severe adverse events, including invasive infections, reactive latent TB, and rare autoimmune reactions, have been reported in association with biologic medications. Thus, patient selection and close observation must be done while on these drugs. Before initiating biological treatment, patients should be checked for infections and concomitant conditions and undergo regular monitoring for safety (Table 3).

Conclusion

With biologicals changing the treatment game for psoriasis. They provide a precise approach that attacks the immune mechanisms fuelling the illness, often resulting in marked improvement in disease symptoms and the patient's overall quality of life. These drugs work very well but must be utilized judiciously, through cautious patient selection and monitoring for safety. With growing knowledge about the pathophysiology of psoriasis, we can expect innovative biologics will emerge, which can provide better control over this chronic dermatitis for sufferers.

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