Narrative Review

Ixekizumab, An Effective Biologic Agent Therapy in Various Cases of Psoriasis: A Narrative Review

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Abstract

Psoriasis is a chronic inflammatory skin condition with immune involvement, characterized by skin inflammation and epidermal hyperplasia, increased risk of arthritis, cardiovascular disorders, and psychosocial burden. In the current management of psoriasis, the use of biologic therapy is increasingly being studied. This paper is aimed to increase understanding of ixekizumab in psoriasis management, so that its utilization can be optimized. Currently, the main biological agents have action on two crucial pathways in the psoriasis development and its chronicity, namely the IL-23/Th17 pathway and the TNF-α signaling pathway. Biological agents targeting the IL-17 receptor have shown higher efficacy and safety compared to those targeting TNF-α and IL-23 receptors in treating moderate to severe plaque-type psoriasis. Ixekizumab, one of the selective IL-17A pathway inhibitor, plays a crucial role in managing the occurrence of psoriasis. FDA has approved the use of ixekizumab for moderate to severe psoriasis (PsO) and psoriatic arthritis (PsA) . Numerous clinical trials have demonstrated the safety and efficacy of ixekizumab in treating both plaque psoriasis and PsA. The side effects are generally mild, in the form of nasopharyngitis, pain at the injection site, and upper respiratory tract infections.

Keywords: Psoriasis, IL-17 Inhibitor, Ixekizumab, Biologic agent.

Received: 16-06-2024 **Revision:** 20-11-2024 **Accepted:** 18-04-2025

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Introduction

Psoriasis is a persistent skin condition characterized by inflammation and an abnormal immune response, often influenced by genetics. The usual development of psoriasis involves ongoing inflammation, which causes an overgrowth of skin cells in the form of keratinocyte hyperproliferation.[1] The prevalence of psoriasis varies from 0.09% to 11% of the population worldwide and the incidence has been increasing in the last three decades.[2] This prevalence varies by age, sex, ethnicity, and geographic region. Psoriasis prevalence is found to be lower in African and Asian compared to Scandinavian and Caucasian populations.[3]

In the current psoriasis management, the biologic therapy is being increasingly used. Currently, biologic agents being used mainly act on two crucial pathways in the development and chronicity of psoriasis, namely the IL-23/Th17 pathway and the TNF-α signaling pathway.[1] Interleukin inhibitors represent a group of biological agents that work more specifically than others in the treatment of psoriasis. Because these drugs preferentially target the most specific and significant inflammatory pathways in the psoriasis pathophysiology, they are safer and more effective than conventional therapy and TNF-α inhibitors.[4]

Ixekizumab, a human monoclonal antibody, inhibits the IL-17A pathway. As compared to a placebo, ixekizumab exhibited a noticeably quicker action during the first week of treatment, and the response to therapy, in the form of

improvement in the PASI score, was found to be satisfactory. Psoriasis of the scalp and nails, two clinical variants that do not respond well to topical therapy, have been demonstrated to respond well to ixekizumab.[1]

A better understanding of ixekizu-mab, from the mechanism of action of ixekizumab in inhibiting the pathogenesis of psoriasis, indications and contra-indications for its use as well as the dosage and method of use, is needed so that the utilization of this preparation can be optimized. Evaluation of the success of therapy and the side effects caused by this treatment need to be understood further.

Psoriasis

Psoriasis is a chronic inflammatory skin disease mediated by the immune system. Common clinical symptoms are well-defined erythematous plaques with silvery white scales.[5] Psoriasis prevalence worldwide varies, ranging from 0.09% to 11%. Its incidence has been increasing for the last three decades with a low incidence in Asia, where it is 0.4% of the total population.[5]

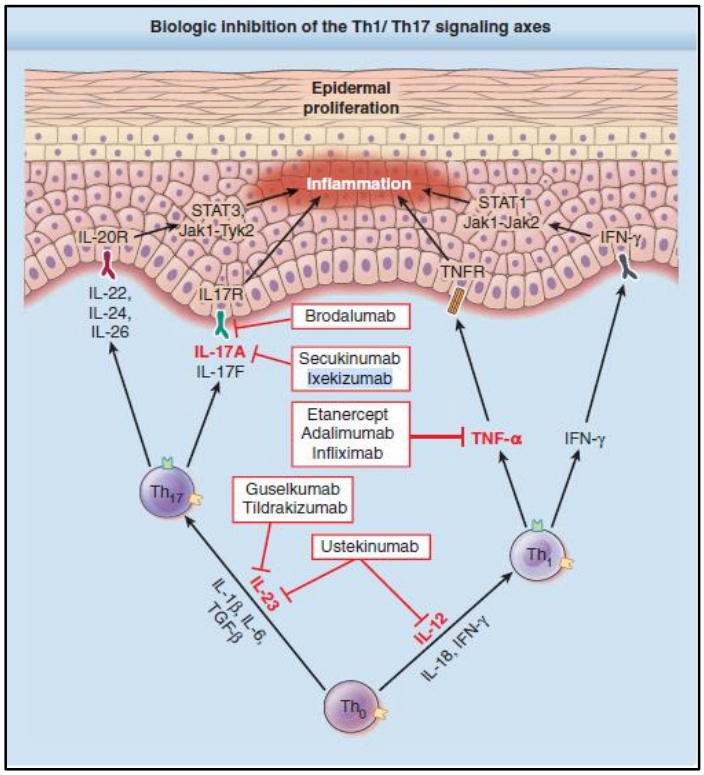

Figure 1: The point of action of biological agents on the Th1/Th17 signaling pathway. IFN, interferons; IL, interleukins; STAT, signal transducer and activator of transcription; TGF, transforming growth factor; Th, T-helper; TNFR, tumor necrosis factor receptor.[5]

Table 1: *Recommendations of Use for IL-17 Antagonist Ixekizumab.15*

No	Recommendation	Recommendation Level
6.1	Ixekizumab is recommended as a monotherapy option for use in adult patients with moderate to severe plaque psoriasis	A
6.2	The recommended initial ixekizumab dose is 160 mg via subcutaneous injection, followed by 80 mg at week 2, week 4, week 6, 8, 10, and week 12	A
6.3	The recommended continued dose of ixekizumab after the first 12 weeks is 80 mg every 4 weeks	A
6.4	Ixekizumab is recommended as a monotherapy option for use in adult patients with moderate to severe plaque psoriasis involving the scalp.	B
6.5	Ixekizumab is recommended as a monotherapy option for use in adult patients with erythrodermic psoriasis	B
6.6	Ixekizumab is recommended as a monotherapy option for use in adult patients with moderate to severe plaque psoriasis involving the nails	B
6.7	Ixekizumab is recommended as a monotherapy option for use in adult patients with generalized pustular psoriasis	B
6.8	Ixekizumab is recommended as a monotherapy option for use in adult patients with plaque psoriasis associated with psoriatic arthritis	A

Current psoriasis treatment is focused to the needs of each patient, given according to the degree of disease severity and disease activity, involvement of joints and other organs, associated comorbidities, medication adherence, and previous therapy failures.[6,7] IL-17 inhibitors are a new class

of biologics that has high specificity and efficacy and have been approved by FDA for use in psoriasis treatment. this group is considered capable of providing optimal efficacy and safety than conventional therapy or TNF-α inhibitors. This is because IL-17 inhibitors work at a specific point in the pathogenesis of psoriasis, in contrast to conventional therapy and TNF-α inhibitors which work by suppressing the overall immune response.[4,8,9]

Ixekizumab as A Biological Agent

Ixekizumab, Brodalumab, and Secukinumab are three biologic agents that have been used in clinical settings as IL-17 inhibitors. Each of these drugs targets a different site in psoriasis pathway, with ixekizumab and secukinumab targeting IL-17A and brodalumab targeting IL-17RA.10,11 The use of ixekizumab has demonstrated high efficacy in the UNCOVER clinical trial program, achieving a PASI75 response in 77.5-84.2% of patients and a PASI 90 response in 59.7-65.3% of patients and a PASI 100 in 30.8- 35% of patients after 12 weeks of therapy.[12] Improvement in PASI scores was maintained up to week 52 of therapy. Ixekizumab is also well tolerated, with less serious adverse drug reactions and low off-drug relapse rates.[13]

High-affinity recombinant humanized monocle-nal antibody, Ixekizumab, specifically targets the pro-inflammatory cytokine IL-17A pathway which is the primary effector of Th17 cells [Fig. 1].[12] IL-17A activity is inhibited and this directly reduces the ongoing inflammatory process and suppresses keratinocyte proliferation.[10] Having a specific point of action on the IL-17A pathway, ixekizumab is able to work very quickly and effectively in reducing the inflammatory process that occurs in psoriasis which is characterized by significantly reduced signs and symptoms in patients, providing a significant improvement in their quality of life.[10,13]

Of all the IL-17 inhibitor class agents, administrations of 80 mg ixekizumab biweekly has better efficacy in obtaining PASI 75. This may be due to the isotype and antibody class (IgG4) or the ability to bind high affinity to IL-17 molecules. Additionally, achievement ofPASI90, which is a benchmark for successful psoriasis therapy, was also found in those receiving treatment with IL-12/23, IL-17 and IL-23 inhibitors. Ixekizumab 80 mg administered biweekly had the highest benefit: risk ratio for reaching PASI-90.[4]

Currently, the FDA has approved the use of ixekizumab for psoriatic arthritis (PsA) and moderate-to-severe plaque psoriasis (PsO). It has been demonstrated that ixekizumab works effectively in treating nail and scalp psoriasis, two psoriasis variants frequently resistant to conventional topical therapy.[14] Furthermore, it has been demonstrated that ixekizumab is beneficial for treating individuals with generalized pustular psoriasis (GPP) and erythrodermic psoriasis, with clinical improvement observed after 12 weeks of treatment (Table 1).[14]

IxekIZumab Therapy and Dosage in Psoriasis Patients

Prior to initiating ixekizumab therapy, physicians are recommended to register their patients on an available form, perform a specific objective assessment (PASI/BSA/PGA), assess the patient's health-related quality of life (HRQoL), review their medical history, perform a physical examination, and look for prior exposure to cancer, tuberculosis, Crohn's disease, and medications (e.g., warfarin).[16] Blood work (CBC, lipid profile, LFT, RFT, serum electrolytes and ASTO titer), urinalysis, and histopathology examination are among the tests performed prior to medication. In addition, patients are urged to have a pregnancy test when applicable, screening for tuberculosis, hypersensitivity, skin cancer, and other infections like HIV and Hepatitis B and C. Special condition such as breastfeeding and contraception use must also be recognized since they might influence drug bioavailability.[15]

Ixekizumab 80 mg is now globally available as an autoinjector pen and 1 mL prefilled syringes. They should be stored at 2°C to 8°C and allowed to cool to room temperature prior to administration for 15 to 30 minutes with the

Table 2: *Level of evidence for the use of the IL-17 antagonist Ixekizumab.10*

Recommendation	Recomm. No	Level of Evidence
Monotherapy in adults		
Therapeutic dose	6.1-6.3	I-II
• 160 mg at week 0, then 80 mg every 2 weeks until week 12		
• Maintenance dose 80 mg every 4 weeks		
Psoriasis Type:		
• Scalp	6.4	I-II
• Erythrodermic	6.5	I-II
• Nails	6.6	I-II
• GPP	6.7	I-II
Monotherapy for psoriasis in psoriatic arthritis (PsA)	6.8	I

needle cap removed. Avoid preparations from exposure to direct sunlight. The contents of the autoinjector pen or prefilled syringe should be administered within 1 hour of being removed from the refrigerator. any product remaining in the pen must be discarded.[16,17]

The recommended initial dose for ixekizumab is 160 mg. This can be administered subcutaneously at week 0, followed by ixekizumab 80 mg biweekly for the first 12 weeks. In the maintenance phase, ixekizumab 80 mg should be administered once a month (Table 2).[5,15]

Ixekizumab in Clinical Practice

Currently, ixekizumab is being used in clinical practice for the treatment of psoriasis. Magdaleno-Tapial conducted a study to assess ixekizumab's safety profile and effectiveness in treating psoriasis patients in a clinical setting. This retrospective study was conducted on 75 patients at two dermatology departments in Valensia, Spain for 1 year, and the results showed the effective use of ixekizumab with a PASI-75 response of 74.6% and a PASI-90 response of 62.7% after 52 completed weeks of treatment. No serious side effects were found in patients.[18,19] A similar study was also conducted by Rivera by observing 301 patients of psoriasis. The final results showed a response to PASI-90 in 80.1% of subjects after 52 weeks of therapy. It was also found that the effectiveness of therapy was more in patients who had never been given biologic therapy before.[20]

A case study conducted on patients with generalized pustular psoriasis, which is a life-threatening subtype of psoriasis, found that after administration of an initial dose of 160 mg of ixekizumab, the patient showed improvement in symptoms in the form of desquamation of pustules and reduced edema and erythema. The patient was sent home on the third day after administration of ixekizumab and the outpatient evaluation showed good results without side effects.[21]

Another study on 10 cases of generalized pustular psoriasis (GPP) who had previously received ineffective systemic therapy for psoriasis showed the effectiveness of therapy after administration of ixekizumab as monotherapy. Because ixekizumab has been shown to be successful for the treatment of GPP regardless of mutations in IL36RN and CARD14, this agent should be considered as an option for patients with GPP.[22,23]

IxEkizumab Contraindications and Side Effects

Contraindications to the administration of IL-17 inhibitors, especially ixekizumab, can be either relative or absolute. A relative contraindication is a history of active IBD, while an absolute contraindication is a history of allergic reactions to therapeutic agents or their carriers.[9] for short-term use (12-16 weeks), selective inhibitors of IL-12/23 and IL-17 are considered safe and well tolerated. Side effects include an increased risk of serious infection, tuberculosis, nasopharyngitis, diarrhea, upper respiratory tract infections, hypersensitivity reactions, and IBD exacerbations, with nasopharyngitis as the most common side effect.[12]

Conclusion

Ixekizumab, a high-affinity recombinant humanized monoclonal antibody, specifically targets the proinflammatory cytokine IL-17A pathway. It works very quickly and effectively in reducing the inflammatory process that occurs in psoriasis which is characterized by a significant reduction in signs and symptoms in patients, resulting in a satisfactory improvement in the health-related quality of life (HRQoL) in individuals with psoriasis. FDA has currently approved the use of ixekizumab for the treatment of psoriatic arthritis (PsA) and moderate-to-severe psoriasis (PsO). Numerous clinical trials have demonstrated its safety and efficacy in treating patients with PsA as well as plaque psoriasis. The side effects are generally mild, in the form of nasopharyngitis, pain at the injection site, and upper respiratory tract infections.

Conflict of Interest

There was no conflict of interest to be declared by any author.

Funding Source: None.

Author's Contribution

NDP: Study conception, design, analysis, and interpretation of results.

SA: Data collection, drafting, and manuscript preparation.

All authors approved the final version of the manuscript to be published.

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