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Secukinumab

Sekukinumab

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Abstract

Secukinumab is a human immunoglobulin G1/κ monoclonal antibody targeting interleukin-17A. In clinical trials, 77-81% of the secukinumab patients achieved a PASI75 response in 12 weeks. As well as in chronic plaque psoriasis, secukinumab has also been found effective and safe as monotherapy in nail and hairy skin psoriasis and psoriatic arthritis. Secukinumab should be used with caution in patients or their first-degree relatives who have inflammatory bowel disease. It has a safe side effect profile in terms of latent tuberculosis activation.
Keywords: Anti-IL-17, secukinumab, psoriasis

Öz

Sekukinumab interlökin-17A'ya yönelik, insan kaynaklı immünoglobulin G1/κ tipinde bir monoklonal antikordur. Klinik araştırmalarda PAŞİ75 yanıtı elde edilen hasta oranı 12. haftada %77 ile 81 arasında değişmektedir. Kronik plak tip psoriasis yanı sıra tırnak ve saçlı deri psoriasisi ile psoriatik artritte de tek başına etkili ve güvenli bulunmuştur. Kendisinde ya da birinci derece yakınlarında inflamatuar barsak hastalığı bulunanlarda dikkatli kullanım gerektiren sekukinumab, latent tüberküloz aktivasyonu açısından güvenli bir yan etki profiline sahiptir.
Anahtar Kelimeler: Anti-IL-17, sekukinumab, psoriasis

Introduction

Secukinumab is an entirely human monoclonal antibody developed to act against IL-17A. It received a FDA approval in 2015 for the treatment of moderate to severe chronic plaque psoriasis in adults who do not respond to conventional systemic treatments or for whom such treatments are contraindicated.

Mechanism of action

IL-17A is the most known and effective member of the IL-17 cytokine family that plays an important role in the pathogenesis of psoriasis. Secukinumab is an immunoglobulin G1/κ isotype recombinant high-affinity human monoclonal antibody that selectively binds to IL-17A to neutralize it. It shows its action by targeting IL-17A to inhibit its interaction with the IL-17 receptor, which is expressed in various cell types including keratinocytes. As a result of this, secukinumab inhibits secretion of proinflammatory cytokines, chemokines and mediators of tissue injury[1].

Dosage/treatment scheme

The recommended dose is 300 mg via subcutaneous injection, initial doses to be administered at weeks 0, 1, 2, 3 and 4 followed by a monthly maintenance dose to be administered every 4 weeks.

Each 300 mg dose is administered as two 150 mg subcutaneous injections[2]. Secukinumab should be used for

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the diagnosis and treatment of conditions it is indicated for under the guidance and supervision of an experienced physician[3].

Efficacy

The efficacy of secukinumab has been evaluated by four 52-week randomized, double-blind, placebo controlled Phase 3 studies. In the ERASURE study, the PASI75, 90 and 100 responses for secukinumab 300 mg and placebo at week 12 were found to be 81.6%, 59.2%, 28.6% and 4.5%, 1.2%, 0.8% respectively. In the FIXTURE study where it was compared to etanercept, the PASI75, 90 and 100 responses for secukinumab 300 mg and etanercept 2x50 mg/week turned out to be 77.1%, 54.2%, 24.1% and 44.0%, 20.7%, 4.3% respectively[4]. In the CLEAR study, a total of 676 patients were assessed and those who were randomized to secukinumab therapy received a 300 mg dose at weeks 0, 1, 2 and 3, then the same dose was administered once a month starting from week 4. The patients who were randomized to ustekinumab were administered the regimen specified on the product label (45 mg to patients weighing ≤100 kg at baseline and 90 mg to those weighing >100 kg at baseline).

The 16th week results of the study showed that the secukinumab therapy was superior to the ustekinumab therapy with respect to the PASI90 response (79.0% and 59.6% respectively). The percentage of the patients whose Dermatology Life Quality Index score was 0/1 (at week 16) was found significantly higher in the secukinumab group (71.9%) than in the ustekinumab group (57.4%). The safety profile of secukinumab was found similar to that of ustekinumab and consistent with the basic Phase 3 secukinumab studies[5].

As in chronic plaque psoriasis, secukinumab was also found fast-acting and effective as a monotherapy in the treatment of psoriasis involving special regions such as palmoplantar, nail and hairy skin[6-8]. In the TRANSFIGURE study, when NAPSI responses at week 16 were compared to the baseline in patients with moderate to severe plaque psoriasis with nail involvement, secukinumab 300 mg was found to be superior to placebo 46.1% for 300 mg, 11.7% for placebo[6]. In the GESTURE study, secukinumab 300 mg was found to be superior to placebo at week 16 based on the pIGA 0-1 (clean-almost clean) recovery rating for patients with moderate to severe palmoplantar plaque psoriasis (33.3% for 300 mg, 1.5% for placebo)[7]. Another study assessing 102 patients with moderate to severe hairy skin psoriasis with 30% involvement of hairy skin surface compared the efficacy of secukinumab 300 mg with that of placebo at week 12 and found secukinumab significantly superior to placebo based on the PASI90 responses (52.9% and 2.0%) and pIGA 0-1 for only hairy skin (56.9% and 5.9%)[8]. Secukinumab has also been found effective in the treatment of psoriatic arthritis and is recommended as a monotherapy in this type of treatment[9]. There are studies demonstrating that it is fast-acting and effective also in the treatment of palmoplantarpustular and erythrodermic psoriasis and its use is recommended[10,11]. It was assessed in terms of immunogenicity and neutralizing anti-secukinumab antibody generation in 2,842 patients who used secukinumab for 52 months in clinical trials was found to be 0.4%, but these antibodies were shown to cause no loss of effect or to have any clinical significance[12].

Follow-up

Achieving PASI75-90 response by week 12-16 of a secukinumab therapy is the main indicator of efficacy. The treatment will be continued with monthly doses as long as the efficacy prevails and no side effects develop. During patient follow-up, routine tests should be carried out, a rheumatic survey administered, and IBD symptoms questioned at every visit.

Adverse effects/safety

The safety of secukinumab has been compared to that of placebo in 4 different placebo controlled Phase 3 clinical studies conducted with 2076 patients[4,13]. Common adverse reactions included nasopharyngitis, herpes labialis, running nose, diarrhoea, and in some patients, increased mucosal and cutaneous candida infections. Other less common adverse effects were tinea pedis, external otitis, neutropenia, conjunctivitis, and urticaria. Most of these reactions did not necessitate discontinuation of the treatment and could be resolved easily. Incidence of serious infections was 0.14% in secukinumab taking patients and 0.3% in placebo taking patients. Neutropenia was more common in the secukinumab group (0.5%) but they were mostly mild and reversible[3,13]. According to clinical studies and real world experiences, it has a quite safe profile in terms of latent TBC activation[14]. A review of 27 clinical studies showed that no active tuberculosis had been reported in the 5-year follow-up of 12,319 patients using secukinumab[15]. Since there is an alert that anti-IL-17s may trigger, or worsen the course of, inflammatory bowel disease in those who themselves or first degree relatives have this disease, it is recommended to use them with caution or to monitor such patients together with gastroenterology[16,17].

Contraindications

Secukinumab is contraindicated in patients who are oversensitive to its active substance or any of its excipients and who have a clinically serious active infection.

It has a relative contraindication in patients with IBD[3].

Drug interactions

Its mean elimination half-life was 27 days, ranging between 18 and 46 days, in the psoriasis studies where the drug was administered intravenously. Secukinumab should not be used concurrently with live vaccines[3].

Pregnancy and lactation

Data on the use of secukinumab in pregnant women is not sufficient. Although no negative effects have been shown in animal trials with respect to pregnancy, birth or intrauterine and postpartum development, it is preferable to avoid using it during pregnancy. Whether or not secukinumab passes into human milk is not known.

There are no studies conducted with pregnant women. In animal trials, no negative effect on the development of foetus has been shown even at high doses, but there was an increase in neonatal deaths. No study was conducted to see whether or not it passes into the milk during lactation[3,16].

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EVIDENCE-BASED TREATMENT SUGGESTIONS

- It is an entirely human IgG1 monoclonal antibody developed to act against IL-17A. It is indicated for the treatment of moderate to severe chronic plaque psoriasis in adults who do not respond to conventional systemic treatments or for whom such treatments are contraindicated.
- The recommended dose is 300 mg via subcutaneous injection, initial doses to be administered at weeks 0, 1, 2, 3 and 4 followed by a monthly maintenance dose to be administered every 4 weeks.
- Alongside chronic plaque psoriasis, it is also fast-acting and highly effective in psoriatic arthritis and palmoplantar, nail and hairy skin psoriasis and its use as a monotherapy is recommended.
- Its common adverse effects have been reported to be nasopharyngitis, herpes labialis, running nose, diarrhoea, and in some patients, increased mucosal and cutaneous candida infections, but all of these could easily be managed requiring no interruption in the treatment.
- It is highly safe in terms of latent TB activation and active TB. It is recommended to use it with caution in those who themselves or first degree relatives have inflammatory bowel disease or to monitor these patients together with gastroenterology.

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