DOI: 10.4274/turkderm.galenos.2022.06337
Turkderm-Turk Arch Dermatol Venereol 2022;56(Suppl 1):61-6



# Interleukin-23 inhibitors

## *İnterlökin-23 inhibitörleri*

Esra Adışen

Gazi University Faculty of Medicine, Department of Dermatology and Venereology, Ankara, Turkey

### Abstract

For adult patients with moderate to severe plaque psoriasis scheduled for systemic therapy, FDA-approved agents that act via interleukin-23 (IL-23) inhibition are guselkumab, tildrakizumab, and risankizumab. Response to treatment should be evaluated after a 12-week treatment period in psoriasis patients being treated with IL-23 inhibitors. In patients with partial response, dose increase may be planned, or topical corticosteroids, vitamin D analogs, methotrexate, or phototherapy (UVB) may be added to the treatment.
**Keywords:** IL-23 inhibitor, guselkumab, tildrakizumab, risankizumab

### Öz

Sistemik tedavi planlanan orta ve şiddetli plak tip psoriasisli erişkin hastalarda interlökin-23 (IL-23) inhibisyonu yoluyla etki eden ajanlardan FDA onayı alanlar guselkumab, tildrakizumab ve risankizumabtır. IL-23 inhibitörleri ile tedavi edilen psoriasisli olgularda tedaviye yanıt 12 haftalık tedavi sonrası değerlendirilmelidir. Kısmi yanıt veren hastalarda doz artışı planlanabilir ya da tedaviye topikal kortikosteroidler, D vitamini analogları, metotreksat, fototerapi (UVB) eklenilebilir.
**Anahtar Kelimeler:** IL-23 inhibitörü, guselkumab, tildrakizumab, risankizumab

## Introduction

Interleukin-23 (IL-23) is a member of the IL-6/IL-12 cytokine family. IL-23 is a heterodimer consisting of two subunits, p19 and p40. The p40 subunit is common for both IL-23 and IL-12. IL-12 has also a p35 subunit, and IL-23 a p19 subunit. IL-23 shows its action by binding to CD4, CD8 and γδ T-cell subgroups as well as to the IL-23 receptor complex found in NK cells, neutrophils, mast cells, lymphoid cells, and macrophages. IL-23 is believed to have a role in the development of cutaneous inflammation in psoriasis. In rat models, when IL-23 is intradermally given to the skin, it causes inflammation and epidermal thickening resembling psoriasis. While IL-23p19 and IL-12/23p40 mRNA levels are high in psoriatic skin lesions, IL-12p35 levels are normal. Similarly, IL-23 serum levels have been found significantly higher in patients with psoriasis than in healthy controls. In the light of these data, use of IL-23 inhibitors in the treatment of psoriasis has been suggested[1-3].

The agents showing their actions by way of IL-23 inhibition in adult patients with moderate to severe plaque psoriasis who are eligible for systemic treatment are guselkumab (2017), tildrakizumab (2018) and risankizumab (2019) in the order of their receiving FDA approval[1-3]. As of January 2021, these 3 agents were not available in our country.

## Guselkumab

### Mechanism of action

It is an entirely human immunoglobulin G1λ (IgG1λ) monoclonal antibody administered subcutaneously, which

**Address for Correspondence/Yazışma Adresi:** Esra Adışen MD, Gazi University Faculty of Medicine, Department of Dermatology and Venereology, Ankara, Turkey
**E-mail:** adisenesra@gmail.com **Received/Geliş Tarihi:** 07.02.2022 **Accepted/Kabul Tarihi:** 11.02.2022
**ORCID:** orcid.org/0000-0002-8768-231X

**Cite this article as:** Adışen E. Interleukin-23 inhibitors. Turkderm-Turk Arch Dermatol Venereol 2022;56(Suppl 1):61-6

binds to p19 subunit of IL-23 to prevent IL-23 from binding to IL-23 receptors on the surfaces of various immune cells[4].

## Instructions for use and dosage

Geselkumab is administered subcutaneously in a 100 mg dose at weeks 0 and 4 and then 100 mg every 8 weeks (Table 1). The drug's half-life is 15-18 days[2,5].

## Efficacy

By binding with high affinity and specificity to IL-23 cytokine, guselkumab prevents interaction of IL-23 with its receptors on cell surfaces and hence secretion of proinflammatory cytokines. Guselkumab also plays an important role in decreasing mRNA expression of IL-17F and IL-22, and increasing the level of IFN-γ produced by Th1 cells. Owing to this, it shows its action by allowing protection of IL-12/Th1 and inhibiting IL-23/Th17 pathway.

The efficacy of subcutaneous guselkumab in moderate to severe psoriasis was investigated in 4 multicenter Phase 3 studies. These studies included patients aged over 18 years with moderate to severe psoriasis who had a PASI score of 12 or above for over 6 months, whose BSA was above 10, and who had a Investigator Global Assessment (IGA) score of 3 and above[4-6].

VOYAGE-1 (n=837) was a Phase 3 study comparing the efficacy of the drug with both placebo and adalimumab. In the study where guselkumab 100 mg was administered at week 0 and 4, and then every 12 weeks, and adalimumab in its authorized dose, the PASI90 values achieved with guselkumab, adalimumab and placebo at week 16 were 73.3%, 49.7% and 2.9%, respectively. The percentage of patients who achieved IGA0/1 values in the guselkumab, adalimumab and placebo groups at week 16 turned out to be 85.1%, 65.9% and 6.9%, respectively. These data demonstrate the superiority of guselkumab to both placebo and adalimumab in terms of all parameters taken into consideration at week 16. Assessments at week 48 also showed that guselkumab had a more effective profile compared to placebo and adalimumab in the treatment of moderate to severe psoriasis. Guselkumab had a higher patient percentage than adalimumab at each checkpoint and the ratio of patients who achieved a PASI100 response was higher in the guselkumab group at week 16 (37.4% vs 17.1%), at week 24 (44.4% vs 24.9%) and at week 48 (47.4% vs 23.4%). Guselkumab was shown in the VOYAGE-1 study to be more effective than adalimumab in nail, hairy skin and hand-foot involvements of psoriasis. The Health-Related Quality of Life and Dermatology Life Quality Index (DLQI) scores of patients showed a higher rate of recovery in the guselkumab group than in the adalimumab group at both week 2 and week 48 assessments[5-11].

Similar to the VOYAGE-1 study, the VOYAGE-2 study (n=992) also investigated the efficacy and safety of guselkumab compared to those of adalimumab and placebo. The patients were first randomized to receive guselkumab, placebo or adalimumab. Those who achieved a PASI90 response at week 28 were randomized again into placebo and guselkumab groups. Alongside an efficacy and safety comparison with placebo and adalimumab, the study also aimed at assessing the effectiveness of guselkumab in patients who did not respond to adalimumab and the effects of withdrawal from guselkumab. Guselkumab was superior to both adalimumab and placebo at week 16 as shown by the rates of achieving PASI90 (70.0%, 46.8% and 2.4%) and IGA 0/1 (84.1%, 67.7% and 8.5%). The rate of PASI100 response was 34.1% in the guselkumab group and 20.6% in the adalimumab group. In week 24 analyses, guselkumab again achieved higher rates than adalimumab in IGA0/1 (83.5% vs 64.9%), PASI75 (89.1% vs

**Table 1. Treatment of psoriasis with IL-23 inhibitors[1-3]**

| | |
|---|---|
| Posology | Guselkumab subcutaneous 100 mg at weeks 0 and 4, and every 8 weeks thereafter,<br>Tildrakizumab subcutaneous 100 mg at weeks 0 and 4, and every 12 weeks thereafter,<br>Risankizumab subcutaneous 150 mg at weeks 0 and 4, and every 12 weeks thereafter, |
| Baseline tests | CBC<br>Complete metabolic profile<br>Chest X-ray<br>PPD or Quantiferon Gold for latent TB<br>Markers of hepatitis B and C infections<br>HIV |
| Follow-up tests | Every 3 months to twice a year depending on response and duration of treatment<br>Periodical anamnesis and physical examination including nonmelanoma skin cancer screening<br>Follow-up for infections (Latent TB, hepatitis B and C, HIV) |
| Side effects | Guselkumab, tildrakizumab and risankizumab have been tolerated well, but there is an increased risk of infections.<br>The most common side effects are infections, often in the form of nasopharyngitis and other upper respiratory tract infections.<br>Accompanying methotrexate use increases the risk of infections and side effects.<br>Elevated liver transaminase level has rarely been reported. |
| Contraindications | They should not be used in those with a history of allergic reaction to therapeutic agents or their carriers.<br>They should not be started or used in the periods of an inflammatory disease that requires an antibiotic therapy. |
| Need for induction in intermittent treatment | Similar to other biologics, induction treatment is recommended only if a period of time 3-4 times the half-life has passed after the previous dose. |
| Vaccination | Live vaccines are not recommended during the treatment. |
| Pregnancy and lactation | There is no data on their safety during pregnancy.<br>Whether IL-23 inhibitors pass into the mother's milk is also unknown. |

71.0%), PASI90 (75.22% vs 54.8%) and PASI100 (44.2% vs 26.6%). An analysis of the week 48 treatment responses of the patients who did not respond to adalimumab and continued with guselkumab showed that 66.1% of them achieved a PASI90 response and 28.6% a PASI100 response. In this study, guselkumab was found more effective than placebo and adalimumab, a result which supported the VOYAGE-1 data. Additionally, the time it took for PASI90 response to disappear was found to be 15.2 weeks[6-11].

NAVIGATE (n=268) was another Phase 3 study which investigated the efficacy and safety of guselkumab in patients who did not respond to ustekinumab. In this study, patients who used ustekinumab according to its authorized posology were assessed at week 16 and 268 patients whose IGA was 2 or more severe were randomized again, 135 of them to receive guselkumab and 133 to continue with ustekinumab.

It was seen in the study that more patients taking guselkumab achieved IGA0/1 at weeks 28 and 52 as compared to the ustekinumab group (31.1% vs 14.3% at week 28 and 36.3% vs 17.3% at week 52). In the same study, guselkumab achieved higher response rates than ustekinumab at week 52 in PASI90 (51.1% vs 24.1%), PASI100 (20.0% vs 7.5%) and DLQI0/1 (38.8% vs 19.0%). The study also showed that guselkumab was effective in patients who did not benefit from ustekinumab[3,4,9-12].

ECLIPSE (n=1048) was a double-blind, randomized, controlled, multicenter study comparing one-to-one the efficacy and safety of secukinumab with those of guselkumab in the treatment of moderate to severe psoriasis. The primary endpoint in this study was the percentages of patients who achieved PASI90 response in the guselkumab and secukinumab groups at week 48. In the study, 84.5% of the guselkumab group and 70.0% of the secukinumab group achieved a PASI90 response at week 48. Other data showed that the rate of achieving a PASI75 response was 89.3% with the guselkumab therapy and 91.6% with secukinumab and a PASI90 response was 69.1% vs 76.1% at week 12, but the assessments at week 48 revealed that the PASI 90 responses were 84.5% vs 70.0%, IGA 0/1 responses 85.0% vs 74.9%, PASI100 responses 58.2% vs 48.4% in favour of guselkumab[3,4,9-12].

## Safety data

Guselkumab was tolerated well in adults with moderate to severe plaque psoriasis in 4 Phase 3 trials. In the first 16-week period, nasopharyngitis, headache and upper respiratory tract infection were the most common side effects. Other infections included gastroenteritis, herpes simplex infections and dermatophytic infections. Gastroenteritis cases were seen at a rate of 4.6% at week 156 of the treatment; they were mild and did not require discontinuation of the treatment. Other infections and infections requiring an antibiotic therapy occurred at comparable rates in all treatment groups until week 48. Neutropenia and candidiasis were at low rates in all treatment groups and there was no difference between the groups with respect to the prevalence of other laboratory abnormalities. Crohn's disease was not reported. No new side effects that would jeopardize safety were observed in the extension phases of the Phase 3 studies up to week 156[1,3,4,9-11].

In studies comparing guselkumab with adalimumab, ustekinumab and secukinumab, data consistent with the safety profiles of these drugs in their phase studies were observed. The NAVIGATE study has not provided any new safety data in relation to patients switching from ustekinumab to guselkumab without a washout period. One or more side effects were seen in 64% of the patients randomized to guselkumab and in 56% of those randomized to ustekinumab. Serious side effects occurred in 7% of the guselkumab group and in 5% of the ustekinumab group and 2% of each group withdrew from the treatment due to an adverse event. The ECLIPSE study reported at least one adverse event in 77.9% of the subjects taking guselkumab and 81.6% of those taking secukinumab. A serious adverse event was reported in 6.2% of the patients taking guselkumab and 7.2% of those taking secukinumab.

An injection site reaction was observed in 2.6% of the patients treated with guselkumab and 6.9% of those treated with adalimumab. The rate of injection site reactions was found to be 0.7% in week 156 assessments.

In guselkumab Phase 3 studies, drug antibodies were detected at a rate of 5.3% at week 44, 6.6% at week 48, 9% at week 60 and 9% at week 156. Association of antibodies with clinical efficacy or injection site reactions has not been shown[13].

The efficacy and safety of guselkumab in generalized pustular psoriasis and erythrodermic psoriasis have been demonstrated in a small patient group consisting of 21 patients. Its efficacy in psoriatic arthritis is still being investigated. In a randomized, double-blind, placebo-controlled Phase 2 study, guselkumab exhibited marked improvements in joint symptoms, physical functioning, enthesitis, dactylitis, and quality of life. Its efficacy in Crohn's disease is being investigated[3,4,9-11].

## TILDRAKIZUMAB

### Mechanism of action

Tildrakizumab is a high-affinity humanized monoclonal Ig-G1κ antibody that selectively inhibits IL-23p19[14].

## Instructions for use and dosage

The recommended way of using tildrakizumab is subcutaneous administration of 100 mg at weeks 0 and 4, and then every 12 weeks (Table 1). Its half-life is 23 days[2].

## Efficacy

The efficacy of tildrakizumab in moderate to severe plaque psoriasis has been investigated in comparison to placebo and etanercept in multicenter, randomized, double-blind, placebo-controlled Phase 3 clinical studies. These studies included patients aged 18 and older with moderate to severe chronic plaque psoriasis whose BSA was ≥10%, Physician Global Assessment (PGA) score ≥3 and PASI ≥12[14].

The efficacy and safety of tildrakizumab was investigated in these Phase 3 studies that included 1549 patients with moderate to severe psoriasis. These studies presented the efficacy and safety analyses and data of both 100 mg and 200 mg subcutaneous administrations up to week 64. Tildrakizumab was compared to placebo in reSURFACE1 (n=772) and to both placebo and etanercept in reSURFACE2 (n=777). The patients in both studies received 100 or 200 mg tildrakizumab at weeks 0 and 4, and continued with the treatment receiving their initial

doses every 12 weeks. Efficacy analyses were carried out at weeks 12 and 28 using the ratios of patients who satisfied PASI75, PGA0/1 and DLQI0/1. In reSURFACE1, the PASI75 response at week 12 was 64% with 100 mg tildrakizumab and 62% with 200 mg tildrakizumab compared to 6% in the placebo group. The rates in the same groups were 35%, 35% and 3% for PASI90 and 14%, 14% and 1% for PASI100, respectively. The response rates at week 12 for PASI75 (61%, 66% and 6%), PASI90 (39%, 37% and 1%) and PASI100 (12%, 12% and 0%) in reSURFACE2 were reported to have a similar distribution to that in reSURFACE1. Etanercept was included in the reSURFACE2 group as an active control group and the treatment responses were found to be PASI75: 48%, PASI90: 21%, PASI100: 5%[15-17].

When the patients who achieved PASI75 response with 100 mg or 200 mg of tildrakizumab at week 28 continued their current therapy for 3 years, this efficacy achieved by 91% of the 100 mg group and %92 of the 200 mg group was maintained for 3 years. Patients who gained partial or no benefit from etanercept at week 28 continued their treatment with tildrakizumab 200 mg after having a 4-week break and the efficacy was found to increase. When the dose was changed to 200 mg in a group of patients who were receiving tildrakizumab 100 mg at week 28, the ratio of patients who achieved a PASI75 response increased from 39% at week 32 to 65% at week 52. When a transition to tildrakizumab 100 mg was made in a group of patients who used tildrakizumab 200 mg until week 28, the ratio of PASI75 patients at weeks 32 and 52 remained to be similar (98.2% and 94.2%)[16-18].

The long-term data on tildrakizumab generally indicate that most of the patients who respond to tildrakizumab at the beginning (patients achieving PASI75 at week 28) retain the clinical efficacy if they continue the treatment with tildrakizumab. Eight out of ten subjects continuing with tildrakizumab 100 mg or 200 mg without a break maintained their PASI75 response throughout a 148-week therapy. The PASI90 and PASI100 responses also remained stable in these studies and a PASI90 response was seen in 60% of the patients at week 148[17-20].

In the group where the tildrakizumab therapy was discontinued, the median relapse time turned out to be 226 days in the 100 mg group and 258 days in the 200 mg group[17-20].

## Safety data

In Phase 2 and Phase 3 studies of tildrakizumab, approximately a half of the patients had a treatment-related adverse event. Most frequently reported side effects were headache (24-27%) and nasopharyngitis (8-39%). Other common side effects included coughing, upper respiratory tract infections, bronchitis and gastroenteritis. The number of these side effects was higher in the tildrakizumab 200 mg group than in the group taking 100 mg, which is the authorized dose.

Among the subgroups formed by randomizing the patients again at week 28, most frequent side effects occurred in the subjects using tildrakizumab 100 mg or 200 mg on a continuous basis[1,17,19].

Drug antibodies were seen in 7.3% of the subjects, but did not change the efficacy of the drug. Injection site complications such as haematoma, pain and erythema were seen in 1-15% of the subjects.

In relation to safety, no new or unpredicted adverse events have been defined in time with respect to these drugs. During a period of 148 weeks, tildrakizumab 100 mg or 200 mg therapy proved to be low-risk for infections, severe infections, malignancies, nonmelanoma skin cancers and major adverse cardiovascular events and made a change comparable to placebo. The frequency of candida infections was very low. No new or unpredicted side effects were reported during 148 weeks other than those identified previously. Adverse events did not necessitate discontinuation of the therapy and no dose-related increase was seen[1,15,17,19,20].

# RISANKIZUMAB

### Mechanism of action

Risankizumab is a humanized IgG1 monoclonal antibody developed to bind to the p19 subunit of IL-23 to prevent IL-23 from interacting with the IL-23 receptor[3].

## Instructions for use and dosage

The recommended way of using risankizumab is subcutaneous administration of 150 mg at weeks 0 and 4, and then every 12 weeks (Table 1). The drug's half-life is 28 days[2].

## Efficacy

The efficacy of risankizumab has been investigated in comparison to placebo, adalimumab, ustekinumab and secukinumab in multicenter, randomized, double-blind, placebo-controlled Phase 3 clinical studies. These studies included patients aged 18 and older with moderate to severe chronic plaque psoriasis whose BSA was ≥10%, Physician Global Assessment (PGA) score ≥3 and PASI ≥12[1,3].

In the IMMhance Phase 3 study (n=507), patients were randomized to risankizumab 150 mg, risankizumab 100 mg or placebo arms. In week 16 assessments, risankizumab was more effective than placebo in achieving PASI75 (89% vs 7%), PASI90 (73.2% vs 2%), PASI100 (47% vs 1%), sPGA0/1 (84% vs 7%), and sPGA0 (46% vs 1%) responses. Patients who achieved sPGA0/1 at week 28 in this study were further randomized to risankizumab (maintenance treatment) or placebo (withdrawal from treatment) groups. The assessment at week 52 showed that 87% of the patients in the maintenance group and 61% of those in the placebo group were able to maintain sPGA0/1. In the assessment at week 104, 81% of the patients in the maintenance group and 7% of those in the placebo group could remain in a sPGA0/1 satisfying status. These data have shown that risankizumab could maintain the efficacy it achieved at week 16 until week 104. In this study, 80.9% of the patients who were made to withdraw from risankizumab were found to have relapses and the median time passed until a relapse was 295 days.

In the UltIMMa-1 (n=506) and UltIMMa-2 (n=491) studies, patients were randomized to risankizumab 150 mg, ustekinumab 45 mg/90 mg or placebo arms. Risankizumab was administered subcutaneously at weeks 0, 4, 16, 28, 40 and 52. After week 16, a transition to risankizumab 150 mg was made in the placebo group. In the UltIMMa-1 and UltIMMa-2 studies, the ratio of patients who previously used biological agents were 34% in UltIMMa-1 and 41% in UltIMMa-2[3,21-23].

In the UltIMMa-1 study, 75.3% of the subjects in the risankizumab group, 42% in the ustekinumab group and 4.9% in the placebo group achieved a PASI90 response at week 16. The rates of achieving

sPGA0/1 in the risankizumab, ustekinumab and placebo groups were 87.8%, 63.0% and 7.8%, PASI100 response 35.9%, 12.0% and 0%, and DLQI0/1 65.8%, 43.0% and 7.8%, respectively[24-27].

In the UltIMMa-2 study, 74.8% of the subjects in the risankizumab group, 47.5% in the ustekinumab group and 2% in the placebo group achieved a PASI90 response at week 16. The rates of achieving sPGA0/1 in the risankizumab, ustekinumab and placebo groups were 83.7%, 61.6% and 5.1%, PASI100 response 50.7%, 24.2% and 2%, and DLQI0/1 66.7%, 46.5% and 4.1%, respectively.

In these studies, risankizumab achieved more effective treatment responses than ustekinumab and placebo in both week 16 and week 52 assessments. The PASI100 results at week 52 showed that PASI100 response was maintained in more than half of those continuing the treatment with risankizumab[24-27].

In the IMMvent study (n=605), the efficacy and safety of risankizumab was compared to adalimumab. Risankizumab was administered at weeks 0 and 4 and then every 12 weeks, and adalimumab in a 80 mg dose at week 0 and then every other week. At week 16, 72% of the subjects in the risankizumab group and 47% of those in the adalimumab group achieved a PASI90 response. The rates of achieving sPGA0/1 in the risankizumab and adalimumab groups were 84% and 60%, PASI100 response 40% and 23%, and DLQI0/1 66% and 49%, respectively. In this study, those patients in the adalimumab group who could not achieve a PASI50 response at week 16 continued their treatment with risankizumab without a washout period. Those who achieved a response between PASI50 and PASI90 were randomized again to continue with adalimumab or to make a transition to risankizumab and those who achieved a PASI90 response continued to take adalimumab. In week 28 assessments, 66.0% of the subjects who switched to risankizumab could achieve PASI90 and 39.6% PASI100, whereas the same values in those who continued with adalimumab were 21.4% and 7.1%, respectively[3,21,22,28-30].

In the IMMerge (n=327) Phase 3 study, risankizumab 150 mg and secukinumab 300 mg were compared at weeks 16 and 52 with respect to the number of patients who achieved PASI90. The patients who were treated with risankizumab (n=164) had a higher rate of achieving PASI90 than those treated with secukinumab (n=163) both at week 16 (73.8% vs 65.6%) and at week 52 (86.6% vs 57.1%). Risankizumab was also found superior to secukinumab with respect to all secondary endpoints, which were PASI100, PGA0/1 and PASI75[31].

## Side effects

The safety profiles of risankizumab, ustekinumab and placebo were similar in these Phase 3 studies. The UltIMMa-1 and UltIMMa-2 studies have reported more infections in patients taking risankizumab and ustekinumab than in those taking placebo. The most common side effect was viral infections of the upper respiratory tract. However, there were no significant differences between the risankizumab, ustekinumab and placebo treatment groups until week 16 in terms of serious adverse events and other side effects that required discontinuation of the study drug.

In the UltIMMa studies, the side effect rates and general safety profiles were similar in the risankizumab and ustekinumab treatment groups during a period of 52 weeks. Latent tuberculosis were reported in 2 patients while on risankizumab therapy although they were Quantiferon negative at the beginning. In the IMMvent study, the safety data of the patients who switched from adalimumab to risankizumab without a washout period did not show any difference. In risankizumab studies, major adverse cardiovascular events occurred in 3 patients who had additional risk factors for intestinal adenocarcinoma, hepatic cancer and cardiovascular disease, but these side effects were not found associated with the drug[3,21-23].

## Use of IL-23 inhibitors during COVID-19 pandemic

Treatment of patients with psoriasis in the period of COVID-19 pandemic should be patient specific considering severity of the disease and comorbidities. The American National Psoriasis Foundation recommends continuation of psoriasis treatments of patients during the COVID-19 pandemic[32]. No side effects restricting the use of IL-23 inhibitors during the pandemic have been reported[32-35]. IL-23 inhibitors are not available in our country.

**SUGGESTIONS**

- Response to treatment should be evaluated after a 12-week treatment period in psoriasis patients being treated with IL-23 inhibitors. In patients giving partial response, dose increase may be planned or topical corticosteroids, vitamin D analogues, methotrexate or phototherapy (UVB) may be added to the treatment.

## References

1. Menter A, Strober BE, Kaplan DH, et al.: Joint AAD-NPF guidelines of care for the management and treatment of psoriasis with biologics. J Am Acad Dermatol 2019;80:1029-72.
2. Yeung J, Gooderham MJ, Grewal P, et al.: Management of Plaque psoriasis with biologic therapies in women of child-bearing potential consensus paper. J Cutan Med Surg 2020;24(Suppl1):3S-14.
3. Chiricozzi A, Antonioli L, Panduri S, Fornai M, Romanelli M, Blandizzi C: Risankizumab for the treatment of moderate to severe psoriasis. Expert Opin Biol Ther 2019;19:1-8.
4. Amin M, Darji K, No DJ, Wu JJ: Review of phase III trial data on IL-23 inhibitors tildrakizumab and guselkumab for psoriasis. J Eur Acad Dermatol Venereol 2017;31:1627-32.
5. Blauvelt A, Papp KA, Griffiths CE, et al.: Efficacy and safety of guselkumab, an anti-interleukin-23 monoclonal antibody, compared with adalimumab for the continuous treatment of patients with moderate to severe psoriasis: Results from the phase III, double-blinded, placebo- and active comparator-controlled VOYAGE 1 trial. J Am Acad Dermatol 2017;76:405-17.
6. Gordon KB, Blauvelt A, Foley P, et al.: Efficacy of guselkumab in subpopulations of patients with moderate-to-severe plaque psoriasis: a pooled analysis of the phase III VOYAGE 1 and VOYAGE 2 studies. Br J Dermatol 2018;178:132-9.
7. Griffiths CEM, Papp KA, Kimball AB, et al.: Long- term efficacy of guselkumab for the treatment of moderate-to-severe psoriasis: results from the phase 3 VOYAGE 1 trial through two years. J Drugs Dermatol 2018;17:826-32.
8. Reich K, Griffiths CEM, Gordon KB, et al.: Maintenance of clinical response and consistent safety profile with up to 3 years of continuous treatment with guselkumab: Results from the VOYAGE 1 and VOYAGE 2 trials. J Am Acad Dermatol 2020;82:936-45.
9. Yiu ZZ, Warren RB: Guselkumab for psoriasis: a critical appraisal of Phase III studies. Immunotherapy 2018;10:67-75.
10. Nakamura M, Lee K, Jeon C, et al.: Guselkumab for the treatment of psoriasis: a review of phase III trials. Dermatol Ther (Heidelb) 2017;7:281-92.

11. Reich K, Armstrong AW, Foley P, et al.: Efficacy and safety of guselkumab, an anti-interleukin-23 monoclonal antibody, compared with adalimumab for the treatment of patients with moderate to severe psoriasis with randomized withdrawal and retreatment: Results from the phase III, double-blind, placebo- and active comparator-controlled VOYAGE 2 trial. J Am Acad Dermatol 2017;76:418-31.
12. Langley RG, Tsai TF, Flavin S, et al.: Efficacy and safety of guselkumab in patients with psoriasis who have an inadequate response to ustekinumab: results of the randomized, double-blind, phase III NAVIGATE trial. Br J Dermatol 2018;178:114-123.
13. Zhu Y, Marini JC, Song M, et al.: Immunoenicity of guselkumab is not clinically relevant in patients with moderate-to-severe plaque psoriasis. J Invest Dermatol 2019;139:1830-4.e6.
14. Gordon KB, Reich K, Crowley JJ, et al.: Disease activity and treatment efficacy using patient-level Psoriasis Area and Severity Index scores from tildrakizumab phase 3 clinical trials. J Dermatolog Treat 2020:1-10.
15. Frampton JE. Tildrakizumab: A review in moderate-to-severe plaque psoriasis. Am J Clin Dermatol 2019;20:295-306.
16. Papp KA, Reich K, Blauvelt A, et al.: Efficacy of tildrakizumab for moderate-to-severe plaque psoriasis: pooled analysis of three randomized controlled trials at weeks 12 and 28. J Eur Acad Dermatol Venereol 2019;33:1098-106.
17. Pithadia DJ, Reynolds KA, Lee EB, Liao W, Wu JJ: Tildrakizumab in the treatment of psoriasis: latest evidence and place in therapy. Ther Adv Chronic Dis 2019;10:2040622319865658.
18. Blauvelt A, Sofen H, Papp K, et al.: Tildrakizumab efficacy and impact on quality of life up to 52 weeks in patients with moderate-to-severe psoriasis: a pooled analysis of two randomized controlled trials. J Eur Acad Dermatol Venereol 2019;33:2305-12.
19. Kimball AB, Papp KA, Reich K, et al.: Efficacy and safety of tildrakizumab for plaque psoriasis with continuous dosing, treatment interruption, dose adjustments and switching from etanercept: results from phase III studies. Br J Dermatol 2020;182:1359-68.
20. Reich K, Warren RB, Iversen L, et al.: Long- term efficacy and safety of tildrakizumab for moderate-to-severe psoriasis: pooled analyses of two randomized phase III clinical trials (reSURFACE 1 and reSURFACE 2) through 148 weeks. Br J Dermatol 2020;182:605-17.
21. Haugh IM, Preston AK, Kivelevitch DN, Menter AM: Risankizumab: an anti-IL-23 antibody for the treatment of psoriasis. Drug Des Devel Ther 2018;12:3879-83.
22. Blair HA. Risankizumab: A review in moderate to severe plaque psoriasis. Drugs 2020:80:1235-45. Erratum in: Drugs. 2020;80:150.
23. Cline A, Feldman SR: Risankizumab for psoriasis. Lancet 2018;392:616-7.
24. Strober B, Menter A, Leonardi C, et al.: Efficacy of risankizumab in patients with moderate-to-severe plaque psoriasis by baseline demographics, disease characteristics and prior biologic therapy: an integrated analysis of the phase III UltIMMa-1 and UltIMMa-2 studies. J Eur Acad Dermatol Venereol 2020;34:2830-8.
25. Blauvelt A, Leonardi CL, Gooderham M, et al.: Efficacy and safety of continuous risankizumab therapy vs treatment withdrawal in patients with moderate to severe plaque psoriasis: a phase 3 randomized clinical trial. JAMA Dermatol 2020;156:1-11.
26. Papp KA, Blauvelt A, Bukhalo M, et al.: Risankizumab versus Ustekinumab for Moderate- to-Severe Plaque Psoriasis. N Engl J Med 2017;376:1551-60.
27. Gordon KB, Strober B, Lebwohl M, et al.: Efficacy and safety of risankizumab in moderate-to-severe plaque psoriasis (UltIMMa-1 and UltIMMa-2): Results from two double-blind, randomised, placebo-controlled and ustekinumab-controlled phase 3 trials. Lancet 2018;392:650-61.
28. Reich K, Gooderham M, Thaçi D, et al.: Risankizumab compared with adalimumab in patients with moderate-to-severe plaque psoriasis (IMMvent): a randomised, double-blind, active-comparator- controlled phase 3 trial. Lancet 2019;394:576-86.
29. Al-Janabi A, Warren RB: Risankizumab vs. adalimumab for moderate-to-severe plaque psoriasis: a critical appraisal. Br J Dermatol 2020;183:220-1.
30. Witjes H, Khatri A, Diderichsen PM, Mandema J, Othman AA: Meta-analyses of clinical efficacy of risankizumab and adalimumab in chronic plaque psoriasis: supporting evidence of risankizumab superiority. Clin Pharmacol Ther 2020;107:435-42.
31. Warren RB, Blauvelt A, Poulin Y, et al.: Efficacy and safety of risankizumab vs. secukinumab in patients with moderate-to-severe plaque psoriasis (IMMerge): Results from a phase 3, randomised, open-label, efficacy assessor- blinded clinical trial. Br J Dermatol 2021;184:50-9.
32. Gelfand JM, Armstrong AW, Bell S, et al.: National psoriasis foundation COVID-19 task force guidance for management of psoriatic disease during the pandemic: Version 1. J Am Acad Dermatol 2020;83:1704-16.
33. Elston DM: COVID, Biologics, and psoriasis therapy. J Am Acad Dermatol 2020;83:1577-8.
34. Sadeghinia A, Daneshpazhooh M: Immunosuppressive drugs for patients with psoriasis during the COVID-19 pandemic era. A review. Dermatol Ther 2021;34:e14498.
35. Ricardo JW, Lipner SR: Considerations for safety in the use of systemic medications for psoriasis and atopic dermatitis during the COVID-19 pandemic. Dermatol Ther 2020;33:e13687.