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MEDICINE

A Nonsystematic Review on Risankizumab: a Novel Drug Recently Approved for Moderate to Severe Psoriasis

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Abstract

In April 2019, the USFDA has approved the humanized monoclonal antibody IgG, Risankizumab, that targets the protein p19 subunit of interleukin (IL-23), for the treatment of moderate to severe plaque psoriasis. The drug was developed by the AbbVie in collaboration with known Boehringer Ingelheim for the management similar immune-mediated inflammatory disorders like inflammatory bowel disease, rheumatic arthritis, etc. The recommended treatment in the case of plague psoriasis with Risankizumab was to begin with 2 initial doses amounts to 150 mg given at baseline (week 0) and again at week 4 that will be followed by 150 mg thereafter by 2 injections every 12 weeks. This article provides a hand on review regarding the drug with all the recent trials and indications.

Keywords Psoriasis · Monoclonal antibody · Risankizumab · IL-23

Introduction

Psoriasis is one of the common skin disorders that are associated with a burden that affects psychological and physical health. Psoriasis is a genetic disease that is immunologically mediated that manifests in the skin, joints, or both with systemic symptoms. The data from North America and Europe shows that its prevalence distributed equally in both sexes, and it is approximately about 2% [1]. Earlier studies have shown that the severity of the disease is higher in men than women [1, 2]. Psoriasis classified based on its clinical presentation into 5 types among that the most common type is plaque psoriasis/psoriasis vulgaris with other types are guttate, inverse psoriasis, pustular psoriasis, or with generalized psoriasis with pustules and the erythrodermic type of psoriasis. The last two subtypes of psoriasis are tagged as the rare but with serious in their clinical course [1]. Monoclonal antibodies (mAB) are directed towards specific pathway that enabled in the management of incurable and resistant diseases, therefore mAB becoming a mainstay therapy in the crucial management of the troublesome moderate to debilitating severe psoriatic types [3]. According to the joint guidelines of the "American Academy of Dermatology (AAD)" and the "National Psoriasis Foundation (NPF)," mild to moderate psoriasis is managed with topical medication or phototherapy, moderate to severe disease managed either with biologic or combined with topical or phototherapy [4]. Risankizumab is a mAB, recently received the global approval for the crucial management of moderate to troublesome severe psoriasis as an important monotherapy.

The pathogenesis involved in the development of immune mediated psoriasis explained in Fig. 1 [5, 6, 20, 22].

Pharmacodynamic Properties Interleukin-23 (IL-23) plays an important central role in the pathogenesis of lesions in psoriasis as explained in the above diagram. IL-23 is having two subunits p19 and p40. Risankizumab specifically has an affinity and binds to the protein p19 subunit of interleukin IL-23

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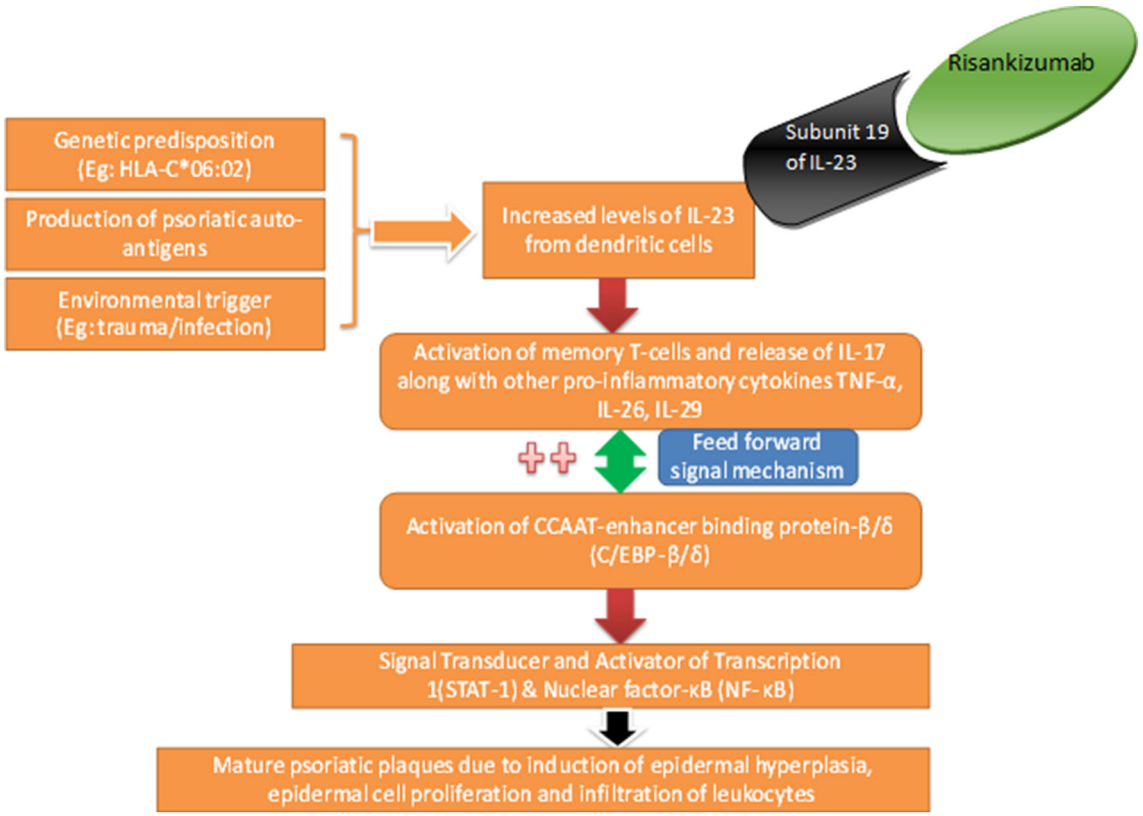

Fig. 1 Pathogenesis of psoriatic plaques and mechanism of the drug

and prevents sequence of the various events in the progression of disease [6]. IL-23 is greatly associated with the orchestra of the T helper cell 17 (Th-17) lineage and its differentiation. It is seen that the initial differentiation of native T cell lymphocytes to the lineage of Th17 needs proteins and cytokines like growth factor-β (GF-β), IL-6, and IL-1β. So IL-23 in the presence of the above said factor is needed for the activation and maintenance of Th17 that then causes the secretion of pro-inflammatory cytokine interleukins (IL-17, IL-22, IL-21, tumor necrosis factor alpha) that helps in the formation of the plaques in psoriasis. The advantages of selective inhibition of IL-23 are that as it is essential for the major differentiation and the important activity of immune cells that contributes such as immune Th-17 and T-helper cell 22 (Th-22). IL-23 also helps the induction of a self-initiation and the applicator loop on the expression of additional interleukin (IL-23) receptors that will be inhibited by monoclonal antibodies as explained in the above flow chart [7].

Skin biopsy specimens of patients with symptoms of moderate–severe type of plaque psoriasis in the first phase of the clinical trial by Krueger and others demonstrated that after 8 weeks of treatment with a single dose of Risankizumab (0.25 mg/kg) was reduced significantly ($p < 0.05$) lesions in the epidermis and dermis such as epidermal acanthosis, hyperkeratosis with more parakeratosis, and generalized inflammation of the body. Immunohistochemistry findings, which are markers of keratin 16 (K16) keratinocyte layer thickening, Ki67 hyperproliferation, cluster differentiation 3 (CD3) for the dermal infiltration by T cells, neutrophil gelatinase lipocalin (NGL) for neutrophils, and CD11c and dendritic cell lysosomal-associated membrane glycoprotein (DC-LAMP) for the dendritic cells and b-defensin 2, and S100 calcium-binding protein A7 (S100A7) for the various tissue inflammation significantly reduced compared with baseline. RNA sequence analysis showed that the various genes associated with the interleukin interaction (IL-23/IL-17) axis are significantly reduced [8]. These findings are consistent with clinical findings assessed with the Psoriasis Area and Severity Index (PASI) scores at the end of eighth week [8]. In ULTIMMA-1 and ULTIMMA-2, a phase 3 trial showed sustained response (i.e., PASI 90) than active comparator Ustekinumab and placebo [9].

Pharmacokinetic Properties of the Drug

The first in clinical trials in human as the "proof-of-concept" study was conducted by Krueger et al. [8] to study pharmacokinetics of the drug along with safety and efficacy in patients with moderate to severe plaque psoriasis type. The route of administration is either intravenous (IV) or subcutaneous (sc). After administration, first dose blood samples were collected

at baseline, 0.5-h, 1-h, 2-h, 4-h, 8-h, and 16-h interval on days 1, 2, 3, 7, 14, and 28 followed by every 4 weeks until 24th week. In this study, bioavailability of the drug assessed using area under curve ($AUC_{0\text{-}inf}$), distribution by volume of distribution (Vd), and maximum concentration in the serum (Cmax), metabolism of the drug assessed by using specific CYP-enzyme probe to identify which microsomal enzymes involved in metabolism and elimination of the drug by half-life ($t1/2$) and mean clearance (Cl).

Absorption and Distribution the Drug Absorption of the drug showed linear pharmacokinetics as there is a direct correlation with dose of the drug and the bioavailability. As the dose of the drug increased, the bioavailability also increased. Bioavailability of the drug after subcutaneous administration was 59%, and Cmax of the drug reached between days 4 and 10 [8]. These findings are described in Table 1. Steady-state plasma (SSP) concentration reached after the 12th day of dosing schedule and plasma concentration at SSP was 2 μg/mL. These findings are similar in other studies [18, 19].

Metabolism of the Drug To test the metabolism of the drug by cytochrome, P-450 enzyme done by using a single oral dose of sensitive probe substrates of CYP enzymes. For this, tests were conducted on day 1 and after 12-week drug administration. In vivo activity of CYP-450 enzymes (CYP 1A2, CYP2C9, CYP2C19, CYP2D6, or CYP3A) showed that there was no effect on the activity of these enzymes. This implies that drug less likely to have potential drug-drug interaction [10].

Excretion of the Drug Elimination of half-life of the drug ranged from 20 to 28 days. Therefore, dose scheduling done on every 4 weeks.

Effect of Drug on Lactation and Pregnancy Till now, no well-controlled studies conducted to prove the teratogenic effect of the drug if it is administered during pregnancy and lactation. There is a need to conduct such studies because Risankizumab is a human IgG antibody molecule, and as a normal IgG molecule, it can cross the blood-placental barrier and can be secreted in the milk. But such concern with regard to use of the drug during lactation can be alleviated as its levels in milk will be very low and its absorption from infant gastro intestinal tract (GIT) is unlikely, because it is a very large molecule and it gets destroyed by gastric enzymes in infants GIT [11]. Its use during the pregnancy needs to be evaluated.

Table 1 Various pharmacokinetic parameters of Risankizumab

Pharmacokinetic parameters	Intravenous (IV) route
Area under curve (AUC)	2.93 to 1650 day mg/mL
Maximum serum concentration (Cmax)	0.311 to 110 mg/mL
Clearance (Cl)	0.33 L/day
Volume of distribution (Vd)	10.8 L
Half-life ($t1/2$)	20 to 28 days

Treatment-Emergent Anti-Drug Antibodies Risankizumab is an antibody that needs to be evaluated for the presence of anti-drug antibodies in patients because it has a direct correlation with its efficacy. Ohtsuki et al., in SustaIMM phase 2/3 trial, observed that antibodies namely antidrug antibodies (ADAs) were noticed in about 39 of the total 171 (23%) patients after 52 weeks of study period, but there was no notable change in the efficacy [12]. PK/PD modeling to demonstrate the correlation between plasma concentration and its efficacy in reducing free IL-23 and improving PASI 100 has demonstrated that Risankizumab was more potent than other currently available antibiotic antibodies in the management of moderate to severe psoriasis. The order of sensitivity was Ustekinumab < Tildrakizumab < Guselkumab < Risankizumab. This was tested by using accelerator mass spectrometry (AMS) to measure the concentration and pharmacokinetics of human recombinant [C]-IL-23 following an intravenous trace dose in cynomolgus monkeys [13].

Therapeutic Efficacy

To assess the therapeutic efficacy of the Risankizumab, these are the common endpoints used: PASI. This index is an objective criterion for calculation of severity of disease based on body surface area with disease, erythema, and indurations and scaling. This index expressed in PASI 75, PASI 90, PASI 100, etc. expression, this index, for example, PASI 75, represents the percentage or the number of patients who have achieved at least 75% or more reduction in their PASI score from the baseline values [14]. Static Physician Global Assessment (sPGA) scores use extent of disease and localized plaques for its calculation. This index uses static variation more commonly than the dynamic variables. It is expressed in percentage of improvement from the baseline. Dermatology Life Quality Index (DLQI) is an objective-based questionnaires aimed to assess the improvement of patient prospective using 10 questions. This index directly relates to improvement in the quality of life of patient [14].

The PASI score along with treating Physician Global Assessment and with respect to quality of life measures provides a complement of measures for studies of severity range of moderate to troublesome severe psoriasis that offer objectivity and are nicely understandable to clinicians that yield a comprehensive view of the impact of disease in patients.

In this review, we summarize the PASI 90 index as all the studies used it as primary endpoint and DLQI given special emphasis because this index gives a real improvement of patient prospective.

In the phase 2 study by Papp et al., 166 patients were randomly administered the drug by subcutaneous (SC) injections of one of the three planned dosage regimens of 18-mg single dose at baseline week (0), 90 or 180 mg at baseline week (0), 4th week and 16th week, and Ustekinumab (45 mg or 90 mg as per weight, at week 0, week 4, and week 16). In this study, score PASI 90 responses at 12th week were 32.6% (14/43), 73.2% (30/41), and 81.0% (34/42) in Risankizumab patients who were administered 18 mg, 90 mg, and 180 mg, respectively, and 40.0% (16/40) in Ustekinumab patients. The improvement was significantly higher in 90 mg and 180 mg of the Risankizumab group than the Ustekinumab [15]. But this study was sponsored by Boehringer Ingelheim for the development of this drug. This implies that there is a chance of potential conflict of interest. An independent study can be conducted to prove Risankizumab superiority over Ustekinumab.

Phase 3 clinical trials were conducted on subjects with severity of moderate to severe plaque type of psoriasis in "ULTIMMA-1, ULTIMMA-2, SustaIMM, IMMHANCE, and IMMVENT" trials. Enrolled subjects were more than 18 years of age with a severity scale of moderate to severe type plaque psoriasis.

ULTIMMA-1 and ULTIMMA-2 [9] enrolled 997 subjects and randomized into Risankizumab, Ustekinumab and placebo group. Subjects received treatment at week 0 baseline, at week 4, and at every 12 weeks thereafter. The primary endpoints in trials ULTIMMA-1 and ULTIMMA-2 are PASI 90 and sPGA at 0 or 1 at 16 weeks versus placebo. Dosing schedule in ULTIMMA-1 was at day 0, then at weeks 4, 16, 28, and 40. At the end of 16 weeks, PASI 90 index in Risankizumab, Ustekinuzumab and placebo group, respectively, are 75.3%, 42%, and 4.9% ($p < 0.001$) in ULTIMMA-1. In ULTIMMA-2 trial, also results are similar to the earlier one in its efficacy.

SustaIMM phase 2/3 trial [12] dosing schedule was similar to the above two trials that is week 0, 4, then every 12 weeks. The results showed that PASI 90 index is significantly higher in 75 mg and 150 mg received group compared with the placebo group with $p < 0.001$. Similarly, in sPGA, PASI 100 and patient-reported outcome were computed using DQLI index.

IMMVENT study [23] designed to compare between Risankizumab with Adalimumab. In this study 605, subjects are enrolled (301 randomized to Risankizumab and 304 to Adalimumab). Risankizumab group received doses of 150 mg of treatment at week 0, week 4, and at every 12 weeks thereafter, and the Adalimumab groups received at a dose of 80 mg at week 0, dose of 40 mg at week 1, and again 40 mg every other week till 15th weeks. Starting at week 16, subjects who were receiving Adalimumab continued or switched treatment based on response: PASI 90 continued to receive Adalimumab; less than PASI 50 were switched to Risankizumab, and those who are falling between PASI 50 to PASI 90 were randomized to either Adalimumab or Risankizumab group. In this study, analysis done at the 16th week proved that there was a significant clinical improvement in the group with Risankizumab than the Adalimumab (sPGA 83.7% vs. 60.2% ($p < 0.001$) and PASI 90–72.4% vs. 47.4% ($p < 0.001$), and at the 28th weeks, patients are analyzed only who are shifted from Adalimumab to Risankizumab therapy (PASI 90 seen in 66.0% vs. 21.4% ($p < 0.001$) (Table 2).

IMMHANCE trial [16] enrolled 507 subjects (407 randomized to Risankizumab 150 mg and 100 to placebo). Subjects received treatment at week 0, 4, and at every 12 weeks thereafter from week 4. Analysis was done at 16 weeks using sPGA and PASI 90 at 0 or 1 at 16th weeks. The results proved that Risankizumab was superior to placebo to meet primary endpoints sPGA 0/1 (83.5% Risankizumab vs. 7.0% placebo) and PASI 90 (73.2% Risankizumab vs. 2.0% placebo) (R29). In the second part of the study, the patients are re-allocated/randomized to the group Risankizumab and placebo for the group earlier receiving Risankizumab and analyzed at 52nd week and patients in placebo group put on Risankizumab therapy. In this study, 31 subjects are diagnosed with latent tuberculosis in which 11 patients who did not receive prophylaxis did not develop any active tuberculosis during the mean period of follow-up till 55 weeks on Risankizumab.

Long-Term Treatment Analysis of the patients in trials ULTIMMA-1, ULTIMMA-2, and SustaIMM phase 2/3 was done at the end of 52 weeks shown in Table 3 to assess the long-term response. In ULTIMMA-1 and ULTIMMA-2 trial's subjects in the group, placebo is shifted to Risankizumab 150-mg group whereas the other group continued same till week 52 after randomization. The difference in the number of patients improved between Ustekinumab, and patients shifted from placebo to Risankizumab were significant with $p < 0.001$ higher in both of the studies. Details are described in Table 2.

In SustaIMM phase 2/3 trial after 16 weeks, patients are re-randomized to Risankizumab group and followed up to 52 weeks. PASI 90 and PASI 100 responses significantly improved than the placebo observed earlier ($p < 0.001$) with a group Risankizumab dose of 150 mg compared with a dose of 75 mg. In Risankizumab 75-mg group, PASI 90 and 100 responses are 86.2% and 43.1%, respectively, and in Risankizumab 150-mg group, 92.7% and 41.8%, respectively. In subjects, who are re-randomized from the placebo group to Risankizumab 75 mg or Risankizumab 150 mg, PASI index was significantly increased from the 16th week to 52nd week of the treatment.

In the case of the phase 3 IMMHANCE trial, the primary efficacy point was the improvement of score of sPGA with clear or nearly almost clear (0/1) at 52nd week. In this study, the patients in the Risankizumab group underwent

Table 2 Efficacy and quality of life results at week 16 in adults with moderate to severe plaque psoriasis in ULTIMMA-1, ULTIMMA-2, SustaIMM, and IMMVENT trials

Study group endpoint	PASI 90	sPGA0/1	PASI 100	DLQI
ULTIMMA-1				
Risankizumab (150 mg) ($n = 304$)	75.3%	87.8%	35.9%	65.8%
Placebo ($n = 102$)	4.2%	6.3%	0%	7.8%
Ustekinuzumab 45 or 90 mg ($n = 100$)	42%	63%	12%	
ULTIMMA-2				
Risankizumab (150 mg) ($n = 294$)	74.8%	83.7%	50.7%	66.7%
Placebo ($n = 98$)	2.0%	5.1%	2.0%	4.1%
Ustekinuzumab 45 or 90 mg ($n = 99$)	47.5%	61.7%	24.2%	46.5%
SustaIMM phase 2/3 trial				
Risankizumab 75 mg ($n = 58$)	75.9%	86.2%	22.4%	62.1%
Risankizumab 150 mg ($n = 55$)	74.5%	92.7%	32.7%	58.2%
Placebo ($n = 58$)	1.7%	10.3%	0%	5.2%
SustaIMM phase 2/3 trial (sub-group analysis of patients with psoriatic arthritis)				
Risankizumab 75 mg ($n = 11$)	72.7%	NA	NA	NA
Risankizumab 150 mg ($n = 5$)	100%	NA	NA	NA
Placebo ($n = 7$)	0%	NA	NA	NA
IMMVENT				
Risankizumab 150 mg (n %, $n = 301$)	72.4%	83.7%	39.9%	65.8%
Adalimumab (n %, $n = 304$)	47.4%	60.2%	23.0%	48.7%

randomization to Risankizumab and the placebo group after 28 weeks of therapy with Risankizumab for assessment of the long-term effectiveness of Risankizumab. The results after 52 weeks is described below in Table 4.

The difference between the two groups was significantly higher in the Risankizumab group than the placebo group; this implies that patients with a severity scale of moderate to the severe type psoriasis consistently show good clinical response with Risankizumab.

The Tolerability of the Risankizumab

Risankizumab, a humanized monoclonal antibody IgG that targets the protein p19 subunit of interleukin IL-23, was developed by the AbbVie in collaboration with the Boehringer Ingelheim for the management and the treatment of various immunological and inflammatory disorders. Risankizumab received its first global approval in March 2019 in Japan, for the treatment of adults with various forms of psoriasis like psoriasis vulgaris, generalized pustular psoriasis, erythrodermic psoriasis, and psoriatic arthritis [17].

The Risankizumab was generally well tolerated in adults with a severity scale of moderate to severe type plaque psoriasis as in the above trials [21]. There was no new safety signal developed in the above trials. In IMMHANCE trial, the most and frequently reported adverse effects were viral causing the upper respiratory tract infections. Other drug-related adverse effects are similar in both placebo and Risankizumab group.

Table 3 Comparison of different indicators in ULTIMMA-1 and ULTIMMA-2 at 52nd week

Study group endpoint	PASI 90	sPGA0/1	PASI 100
ULTIMMA-1			
Risankizumab (150 mg) ($n = 304$)	81.9%	57.6%	56.3%
Ustekinuzumab 45 or 90 mg ($n = 100$)	44%	21%	21%
Placebo to Risankizumab ($n = 97$)	78.4%	54.6%	54.6%
ULTIMMA-2			
Risankizumab (150 mg) ($n = 294$)	80.6%	59.5%	59.5%
Ustekinuzumab 45 or 90 mg ($n = 99$)	50.5%	30.3%	30.3%
Placebo to Risankizumab ($n = 94$)	85.1%	67.0%	67.0%

Table 4 Comparison of patients on Risankizumab and placebo at 52 weeks

Endpoints	sPGA	PASI 90	PASI 100
Risankizumab ($n = 111$)	87.4%	85.6%	64.0%
Placebo ($n = 225$)	61.3%	52.4%	30.2%

In SustaIMM trial also, treatment-related few adverse events were actually comparable across the treatment groups. The serious adverse event that was reported in this study is acute myocardial infarction (AMI) in one of the patient in Risankizumab group, and in placebo group, one developed a serious infection; both these events are not related to the intervention. One patient who shifted from placebo to Risankizumab 75-mg group developed treatment emergent rectal carcinoma, and one patient from placebo to Risankizumab 150 mg experienced severe dermatitis which lead to discontinuation of drug.

URTI and back pain were the most frequently reported adverse effects in this study. Few patients developed metabolic derangement especially with respect to glucose and lipids. Rise of γ-glutamyl transferase is seen in one patient.

In both ULTIMMA trials, safety profiles were similar among the groups treated with Risankizumab, Ustekinumab, and placebo. Infections due to treatment have been the most frequently noted in patients in the Risankizumab and the Ustekinumab than the placebo group. Two cases with skin cancer of nonmelanoma origin are reported in Risankizumab group and in the placebo group. At the end of 52 weeks, 2 major events related to cardiovascular were reported in the group with Risankizumab in ULTIMMA-2 trial of which one suffered sudden cardiac arrest. It is observed that both these patients have high risk towards cardiovascular events. One case of breast cancer is reported in the placebo group who shifted to the Risankizumab treatment group, and a case of prostate cancer was reported in the Ustekinumab group.

This review has made the content easily readable, and the new references have been added for better understanding. Even though few reviews have been already published, we tried to take the readers by comparing as many trials under single content.

Summary and Conclusion

Risankizumab is an effective drug in controlling the pathogenesis behind the psoriasis by binding to p19 subtype of IL-23 and inhibiting its activity in preventing the progression of disease and recovery from the lesions (Table 5). Efficacy and quality of life results at week 16 in adults with the moderate to severe type of plaque psoriasis in ULTIMMA-1 and ULTIMMA-2, SustaIMM, and IMMVENT trials [23] prove that it is better than currently available therapy in the management and treatment of moderate to severe type of psoriasis. All these studies also proved that there was no reduced efficacy of the long-term use of this drug with minimal change as there is possibility because of production of auto antibodies. Drug is well tolerated, and most commonly and frequently reported adverse effects are URTI and pain.

In conclusion, this is an effective drug that can be used as the monotherapy in the psoriasis with the severity scale ranging from moderate to severe type.

Table 5 Summary and clinical consideration

Summary
Risankizumab: clinical consideration in moderate to severe psoriasis
• Risankizumab is a fully humanized monoclonal antibody that belongs to IgG group target subtype 19 of IL-23. • Risankizumab is primarily indicated as monotherapy in moderate to severe plaque psoriasis. • Risankizumab is effective in preventing the disease progression and regression of disease-related disorders. • Risankizumab can maintain the therapeutic efficacy for long term. • This drug in general is well tolerated. Most frequently reported adverse events are upper respiratory tract infection including viral and bacterial origin.

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Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

References

1. Boehncke W-H, Schön MP. Psoriasis. Lancet. 2015;386(9997):983–94.
2. 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):1–8.
3. Kaplon H, Reichert JM. Antibodies to watch in 2019. InMAbs. 2019;11(2):219–38.
4. Menter A, Strober BE, Kaplan DH, Kivelevitch D, Prater EF, Stoff B, et al. Joint AAD-NPF guidelines of care for the management and treatment of psoriasis with biologics. J Am Acad Dermatol. 2019;80(4):1029–72.
5. Hawkes JE, Chan TC, Krueger JG. Psoriasis pathogenesis and the development of novel targeted immune therapies. J Allergy Clin Immunol. 2017;140(3):645–53.
6. Fotiadou C, Lazaridou E, Sotiriou E, Ioannides D. Targeting IL-23 in psoriasis: current perspectives. Psoriasis (Auckl). 2018;8:1–5.
7. Machado Á, Torres T. Spotlight on risankizumab and its potential in the treatment of plaque psoriasis: evidence to date. Psoriasis (Auckl). 2018;8:83–92.

8. Krueger JG, Ferris LK, Menter A, Wagner F, White A, Visvanathan S, et al. Anti-IL-23A mAb BI 655066 for treatment of moderate-to-severe psoriasis: safety, efficacy, pharmacokinetics, and biomarker results of a single-rising-dose, randomized, double-blind, placebo-controlled trial. J Allergy Clin Immunol. 2015;136(1):116–24.
9. Gordon KB, Strober B, Lebwohl M, Augustin M, Blauvelt A, Poulin Y, 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(10148):650–61.
10. Khatri A, Cheng L, Camez A, Ignatenko S, Pang Y, Othman AA. Lack of effect of 12-week treatment with risankizumab on the pharmacokinetics of cytochrome P450 probe substrates in patients with moderate to severe chronic plaque psoriasis. Clin Pharmacokinet. 2019;58(6):805–14.
11. Drugs and Lactation Database (LactMed) [Internet]. Bethesda (MD): National Library of Medicine (US);2006. Risankizumab.[Updated 2019 May 1].
12. Ohtsuki M, Fujita H, Watanabe M, Suzaki K, Flack M, Huang X, et al. Efficacy and safety of risankizumab in Japanese patients with moderate to severe plaque psoriasis: results from the SustaIMM phase 2/3 trial. J Dermatol. 2019;46(8):686–94.
13. Zhang TT, Ma J, Durbin KR, Montavon T, Lacy SE, Jenkins GJ, et al. Determination of IL-23 pharmacokinetics by highly sensitive accelerator mass spectrometry and subsequent modeling to project IL-23 suppression in psoriasis patients treated with anti-IL-23 antibodies. AAPS J. 2019;21(5):82.
14. Feldman SR, Krueger GG. Psoriasis assessment tools in clinical trials. Ann Rheum Dis. 2005;64:ii 65–8.
15. Papp KA, Blauvelt A, Bukhalo M, Gooderham M, Krueger JG, Lacour JP, et al. Risankizumab versus ustekinumab for moderate-to-severe plaque psoriasis. N Engl J Med. 2017;376(16):1551–60.
16. Blauvelt A, Papp KA, Gooderham M, Langley RG, Leonardi C, Lacour JP, et al. Risankizumab efficacy/safety in moderate-to-severe plaque psoriasis: 16-week results from immhance. Acta Dermatol Venereol. 2018;98(Supplement 219):30. https://doi.org/10.2340/00015555-2978.
17. McKeage K, Duggan S. Risankizumab: first global approval. Drugs. 2019;79(8):893–900.
18. Suleiman AA, Minocha M, Khatri A, Pang Y, Othman AA. Population pharmacokinetics of Risankizumab in healthy volunteers and subjects with moderate to severe plaque psoriasis: integrated analyses of phase I-III clinical trials. Clin Pharmacokinet. 2019;58(10):1309–21.
19. Khatri A, Eckert D, Oberoi R, Suleiman A, Pang Y, Cheng L, et al. Pharmacokinetics of Risankizumab in Asian healthy subjects and patients with moderate to severe plaque psoriasis, generalized pustular psoriasis, and erythrodermic psoriasis. J Clin Pharmacol. 2019;59(12):1656–68.
20. Puig L. The role of IL 23 in the treatment of psoriasis. Expert Rev Clin Immunol. 2017;13(6):525–34.
21. Crowley JJ, Warren RB, Cather JC. Safety of selective IL-23p19 inhibitors for the treatment of psoriasis. J Eur Acad Dermatol Venereol. 2019;33(9):1676–84.
22. Gaspari AA, Tyring S. New and emerging biologic therapies for moderate-to-severe plaque psoriasis: mechanistic rationales and recent clinical data for IL-17 and IL-23 inhibitors. Dermatol Ther. 2015;28(4):179–93.
23. Reich K, Gooderham M, Thaçi D, Crowley JJ, Ryan C, Krueger JG, 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(10198):576–86.