



Risankizumab: First Global Approval

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Abstract

Risankizumab (Skyrizi[®]), a humanised IgG monoclonal antibody that targets the p19 subunit of IL-23, was developed by AbbVie in collaboration with Boehringer Ingelheim for the treatment of immunological and inflammatory disorders. In March 2019, risankizumab received its first global approval in Japan for the treatment of adults with psoriasis vulgaris, psoriatic arthritis, generalized pustular psoriasis and erythrodermic psoriasis. Risankizumab has also received approval in the USA, Canada and the EU for the treatment of moderate-to-severe plaque psoriasis, and is in phase 3 development for this indication as well as psoriatic arthritis in several countries worldwide. Phase 2 and 3 clinical evaluation of risankizumab is ongoing in several countries in the treatment of Crohn's disease and ulcerative colitis. Risankizumab is also in phase 2 development for the treatment of atopic dermatitis globally. This article summarizes the milestones in the development of risankizumab leading to this first approval for psoriasis vulgaris, psoriatic arthritis, generalized pustular psoriasis and erythrodermic psoriasis.

1 Introduction

Interleukin (IL)-23 has a pivotal role in the pathogenesis of plaque psoriasis, and various biologics that target IL-23 have been developed in order to improve treatment outcomes [1, 2]. Ustekinumab, which targets the p40 subunit common to both IL-12 and -23 has demonstrated efficacy in the treatment of moderate-to-severe plaque psoriasis. More recently, agents that target the p19 subunit specific to IL-23 have been effective in the treatment of this chronic condition.

Risankizumab (Skyrizi[®]) is a humanised IgG monoclonal antibody that was developed by AbbVie in collaboration with Boehringer Ingelheim for the treatment of immunological and inflammatory disorders. The drug binds to and neutralises the p19 subunit of IL-23, thereby inhibiting the proinflammatory effects of IL-23 [1]. Risankizumab is available for intravenous and subcutaneous administration.

On March 26 2019, risankizumab received its first global approval in Japan for the treatment of adults with psoriasis

vulgaris, psoriatic arthritis, generalized pustular psoriasis and erythrodermic psoriasis [3, 4]. Risankizumab also received approval in Canada [5], the USA [6] and the EU [7] (on April 18, 23 and 30, respectively) for moderate-to-severe plaque psoriasis in adults who are candidates for systemic therapy or phototherapy. The recommended dosage of risankizumab is 150 mg (two 75 mg subcutaneous injections) at weeks 0 and 4, then once every 12 weeks [3, 8, 9]. The manufacturer's prescribing information carries a warning regarding the risk of infections, including the activation of tuberculosis (TB) in patients with a history of TB.

Risankizumab is in preregistration for the treatment of plaque psoriasis in Canada, and in phase 3 development for this indication and psoriatic arthritis in several countries worldwide. Phase 3 clinical evaluation of risankizumab is ongoing in the treatment of Crohn's disease (for which the drug has orphan status for paediatric patients in the USA) and ulcerative colitis. Risankizumab is also in phase 2/3 development for the treatment of atopic dermatitis globally. The development of risankizumab for the treatment of asthma and ankylosing spondylitis was discontinued.

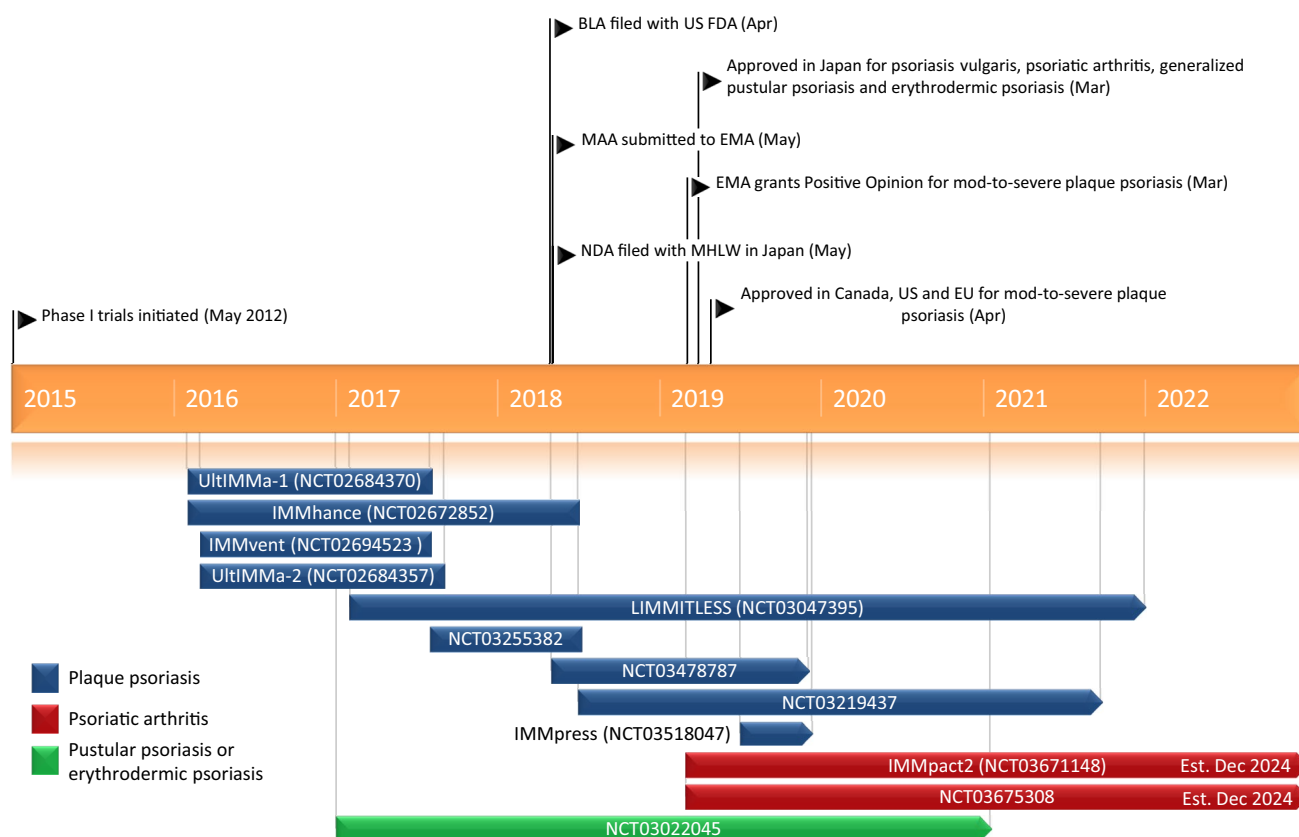
This profile has been extracted and modified from the *AdisInsight* database. *AdisInsight* tracks drug development worldwide through the entire development process, from discovery, through pre-clinical and clinical studies to market launch and beyond.

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1.1 Company Agreements

AbbVie acquired all rights to risankizumab from Boehringer Ingelheim in April 2016, with both companies sharing the responsibility for phase 3 development [6, 10, 11]. Under the terms of the agreement, AbbVie



Key milestones in the development of risankizumab in moderate-to-severe plaque psoriasis or psoriatic arthritis and generalized pustular or erythrodermic psoriasis. *BLA* Biologics Licence Application, *EMA*

European Medicine's Agency, *Est.* estimated, *MAA* marketing authorization application, *MHLW* Ministry of Health, Labour and Welfare, *mod* moderate, *NDA* New Drug Application

made an upfront payment of \$US 595 million. In addition, AbbVie may make additional contingent payments upon the achievement of defined development, regulatory and commercial milestones, as well as royalty payments based on net revenues of licensed products.

2 Scientific Summary

2.1 Pharmacodynamics

Risankizumab is a humanised IgG monoclonal antibody that binds to and neutralises the p19 subunit of IL-23, thereby preventing IL-23 receptor activation and disrupting the IL-23/Th17 axis, which plays an important role in the development of chronic inflammation [1, 2]. In vitro, risankizumab inhibited IL-23-dependent phosphorylation of STAT3 in human B-lymphoblastoid cell lines derived from human diffuse large cell lymphoma [3]. Risankizumab inhibited the induction of IL-17 production from human IL-23 stimulation in mouse splenocytes.

2.2 Pharmacokinetics

The pharmacokinetics of risankizumab were characterized using a two-compartment model with linear absorption, distribution and elimination in patients with moderate-to-severe psoriasis in an integrated analysis of phase 1–3 clinical trials [12]. Data were available from healthy subjects and moderate-to-severe plaque psoriasis patients (n = 1899) who had received single doses of 0.01–5 and 200–1200 mg/kg intravenously, 0.25–1 mg/kg and 18–300 mg subcutaneously, and multiple doses of 90 and 180 mg subcutaneously at weeks 0, 4 and 16 and at the recommended dose of 150 mg subcutaneously at weeks 0, 4 and every 12 weeks thereafter [12]. Risankizumab clearance, steady-state volume of distribution, and terminal-phase elimination half-life were estimated to be 0.31 L/day, 11.2 L and 28 days, respectively, in a 90 kg patient with psoriasis and a baseline albumin level of 44 g/L. The absolute bioavailability of risankizumab administered subcutaneously was 89%, and inter-individual variability for clearance was 24%. Pharmacokinetics

Features and properties of risankizumab

Alternative names	Skyrizi™, ABBV 066, BI-655066
Class	Anti-inflammatories, antipsoriatics, antirheumatics, monoclonal antibodies, skin disorder therapies
Mechanism of action	Interleukin-23 subunit p19 inhibitors
Route of administration	Intravenous, subcutaneous
Pharmacodynamics	Binds to and neutralizes the p19 subunit of IL-23 thereby inhibiting its interaction with the IL-23 receptor
Pharmacokinetics	Characterized by a two-compartment model with linear absorption, distribution and elimination in patients with psoriasis and Crohn's disease
Adverse events	
Most frequent	Viral upper respiratory tract infection
Occasional	Upper respiratory tract infection, arthralgia, headache
Rare	Serious infection
ATC codes	
WHO ATC code	L04A-C18 (risankizumab)
EphMRA ATC code	L4C (interleukin inhibitors)

were typical of those of other IgG1 monoclonal antibodies, with no apparent target mediated disposition.

The risankizumab regimen of 150 mg administered subcutaneously at weeks 0 and 4, then every 12 weeks thereafter was shown to maximize short- (week 16) and long-term (week 52) efficacy in patients with moderate-to-severe chronic plaque psoriasis in an exposure-response analysis using data from phase 2 and 3 clinical trials [13]. There was no apparent relationship between exposure and adverse events, including serious events or infection.

Risankizumab does not have the potential to cause drug interactions via cytochrome P450 (CYP) enzymes, as in vivo activity of CYP1A2, CYP2C9, CYP2C19, CYP2D6 and CYP3A enzymes was not affected by subcutaneous risankizumab 150 mg once every 4 weeks in patients with moderate-or-severe plaque psoriasis [14].

2.3 Therapeutic Trials

2.3.1 Psoriasis

2.3.1.1 Phase 3 Trials Skin clearance rates in patients with moderate-to-severe plaque psoriasis were significantly higher with risankizumab than ustekinumab and placebo administered subcutaneously in two randomized, double-blind, one-year trials (ultIMMA-1 and ultIMMA-2) [15]. In groups receiving risankizumab ($n=304$), ustekinumab ($n=100$) or placebo ($n=102$) in ultIMMA-1 (NCT02684370), the proportion of patients achieving a 90% improvement in the psoriasis area severity index (PASI 90) at week 16 (coprimary endpoint) was 75.3% versus 42.0% [treatment difference 33.5% (22.7–44.3); $p<0.0001$] and 4.9%, respectively [15]. In corresponding groups, the static Physician's Global Assessment (sPGA) score of 0 or

1 (clear or almost clear) at week 16 (coprimary endpoint), was achieved by 87.8% versus 63.0% [treatment difference 25.1% (15.2–35.0); $p<0.0001$] and 7.8%. In ultIMMA-2 (NCT02684357), the proportion of patients in risankizumab ($n=294$), ustekinumab ($n=99$) or placebo ($n=98$) groups achieving PASI 90 at week 16 was 74.8% versus 47.5% [treatment difference 27.6% (16.7–38.5); $p<0.0001$] and 2.0% [15]. In corresponding groups, an sPGA score of 0 or 1 at week 16 was achieved by 83.7% versus 61.6% [treatment difference 22.3% (12.0–32.5); $p<0.0001$] and 5.1%.

In both the ultIMMA-1 and -2 trials, at one year, after a further 36 weeks' treatment with risankizumab or ustekinumab (patients who initially received placebo were switched in a blinded fashion to risankizumab at week 16), the proportion of patients achieving PASI 90 or a sPGA score of 0 was significantly ($p<0.0001$ for both endpoints) higher with risankizumab than ustekinumab in both trials. In both trials, the dose of risankizumab was 150 mg and the dose of ustekinumab was based on weight (45 mg for patients with a body weight of ≤ 100 kg or 90 mg for patients with a body weight of >100 kg), with both treatments given subcutaneously at weeks 0 and 4 and then every 12 weeks [15].

In an integrated analysis of the ultIMMA-1 and ultIMMA-2 trials, risankizumab was more effective in achieving skin clearance than ustekinumab, regardless of baseline demographics, disease characteristics, or prior treatment history [16].

In the randomized, double-blind withdrawal trial in patients with moderate-to-severe plaque psoriasis (IMMhance; NCT02672852), risankizumab ($n=407$) was more effective than placebo ($n=100$) [both subcutaneous] at week 16, with PASI 90 scores achieved by 73.2% versus 2.0%, and sPGA scores of 0 or 1 achieved by 83.5% versus 7.0% [17]. At week 16, all patients received a dose

of risankizumab, and at week 28, patients who were initially randomized to risankizumab and who had a sPGA of 0 or 1 were re-randomized to risankizumab or placebo every 12 weeks. At week 52, 87.4% of patients in the risankizumab maintenance group ($n = 111$) versus 61.3% of patients in the withdrawal group ($n = 225$) achieved sPGA scores of 0 or 1 at one year ($p < 0.001$) [primary endpoint] [18]. Similar results were observed in other efficacy endpoints, including PASI 90 and 100. Significant ($p < 0.01$) differences in sPGA 0/1 and PASI 90 in favour of continuous risankizumab versus treatment withdrawal were observed from week 40 (i.e. after one missed dose).

In the randomized, double-blind, double-dummy IMMvent trial (NCT02694523), skin clearance rates were significantly greater with risankizumab than adalimumab (both subcutaneous), and patients with moderate-to-severe plaque psoriasis with an early intermediate response to adalimumab treatment had an improved response after switching to risankizumab [19]. At week 16, PASI 90 scores were achieved by 72.4% of patients receiving the approved dosage regimen of risankizumab ($n = 301$) compared with 47.4% receiving adalimumab 80 mg at week 0 and 40 mg every other week from week 1 ($n = 304$), and sPGA scores of 0 or 1 were achieved by 83.7% versus 60.2% ($p < 0.001$ for both coprimary endpoints). Patients with an intermediate response to adalimumab (PASI 50 and $<$ PASI 90) at week 16 were re-randomized to continue adalimumab (40 mg every other week) [$n = 56$] or switch to risankizumab ($n = 53$). At week 44, 66.0% of patients re-randomized from adalimumab to risankizumab achieved PASI 90 compared with only 21.4% who were re-randomized to adalimumab ($p < 0.001$). In corresponding groups, the proportion of patients with a Dermatology Life Quality Index (DLQI) score of 0 or 1 at week 44 was 66.0% versus 28.6% ($p < 0.001$) [19].

2.3.1.2 Phase 2 Trials Clinical response rates with risankizumab were superior to those with ustekinumab in a randomized, dose-ranging trial in patients with moderate-to-severe plaque psoriasis (NCT02054481) [20]. Patients received subcutaneous injections of either risankizumab (90 or 180 mg at weeks 0, 4 and 16) or ustekinumab [45 mg (bodyweight ≤ 100 kg) or 90 mg (bodyweight > 100 kg) at week 0, 4 or 16]; a further treatment group received a single dose of risankizumab 18 mg week 0 (results not discussed here). At week 12, 77% of patients receiving risankizumab 90 or 180 mg ($n = 83$) versus 40% of patients receiving ustekinumab ($n = 40$) achieved PASI 90 (primary endpoint) [$p < 0.001$]. After the final dose of risankizumab, efficacy was generally maintained up to 20 weeks.

Two different dosages of risankizumab (75 or 150 mg administered at weeks 0 and 4 and then every 12 weeks)

were associated with significantly higher rates of response than placebo in a randomized, double-blind, phase 2/3 trial in Japanese patients ($n = 171$) with moderate-to-severe plaque psoriasis (NCT03000075) [3]. The proportion of patients achieving PASI 90 at week 16 in the risankizumab 75 mg, 150 mg and placebo groups was 75.9%, 74.5% and 1.7%, respectively ($p < 0.001$ vs placebo for both dosages). After a further 36 weeks of active treatment, PASI 90 was achieved in 86.2% of patients receiving risankizumab 75 mg and 92.7% receiving risankizumab 150 mg.

2.3.2 Psoriatic Arthritis

Subcutaneously administered risankizumab improved joint and skin symptoms significantly more than placebo in a phase 2, randomized, double-blind, 24-week, dose-ranging study in patients with active psoriatic arthritis ($n = 185$) [NCT02719171] [21, 22]. An improvement of $\geq 20\%$ in American College of Rheumatology criteria (ACR20) at week 16 (primary endpoint) among risankizumab dosage groups (150 mg at weeks 0, 4, 8, 12, and 16; 150 mg at weeks 0, 4, and 16; 150 mg at weeks 0 and 12; and a 75 mg single dose at week 0) was achieved in 57.1%, 61.9%, 59.0% and 65.0% of patients, respectively, compared with 35.7% in the placebo group ($p < 0.05$ for all dosages) [22]. In an analysis of data pooled from all dosage groups at week 24, ACR20 ($p < 0.05$), ACR50 ($p < 0.01$) and ACR70 ($p < 0.01$) responses were significantly higher in patients receiving risankizumab than placebo [21]. At week 24, risankizumab recipients (pooled across all risankizumab dosage arms) demonstrated significant improvement from baseline in the modified total Sharps Score (mTSS), a measure of joint damage progression, compared with placebo.

In an open-label extension of the phase 2 trial, improvements in joint and skin symptoms were maintained with continued 12-weekly administration of risankizumab 150 mg (NCT02986373) [23]. At week 52, ACR and PASI response rates were generally similar to corresponding response rates for pooled risankizumab data at the completion of the NCT02719171 trial (week 24). Similar results were observed in improvements in short-form 36 scores at week 52 compared with week 24 as a result of decreasing pain and functional disability.

2.3.3 Crohn's Disease

The proportion of patients achieving clinical remission was significantly higher with risankizumab than with placebo in a randomized, double-blind, short-term, phase 2 trial in adults with moderate-to-severe Crohn's disease (NCT02031276) [24]. At week 12, clinical remission [Crohn's Disease Activity Index (CDAI) < 150 ; primary endpoint] was achieved in 31% of patients receiving risankizumab (200 or 600 mg

intravenously every 4 weeks, data pooled) [$n = 82$] compared with 15% of patients receiving placebo ($n = 39$) [$p < 0.05$]. Most (93%) patients had been treated previously with ≥ 1 tumour necrosis factor antagonist. In individual risankizumab 200 and 600 treatment groups ($n = 41$ for each), clinical remission was achieved in 24% (not statistically significant) and 37% ($p < 0.025$), respectively versus placebo. In pooled results for risankizumab 200 or 600 mg recipients ($n = 82$), clinical response, endoscopic remission and endoscopic response rates in risankizumab recipients (39%, 17% and 32%, respectively) were significantly ($p < 0.05$) greater than with placebo (21%, 3% and 13%).

In Period 2 ($n = 107$), the 12-week open-label induction or washout portion of the phase 2 trial, extended induction treatment with risankizumab increased clinical response and remission rates [25]. Patients who had not achieved deep remission (CDAI < 150 and endoscopic remission) at week 12 received risankizumab 600 mg intravenously every 4 weeks for 12 weeks starting at week 14, and patients who had achieved deep remission at week 12 underwent a 14-week washout. Among the 101 patients who received risankizumab intravenously during Period 2, 53% were in clinical remission at week 26. Patients in clinical remission at week 26 were given the option to receive risankizumab 180 mg subcutaneously every 8 weeks during the 26-week period 3 portion of the phase 2 trial. At week 52 ($n = 62$), clinical remission was maintained in 71% of patients, 81% had a clinical response (CDAI < 150 or a reduction from baseline of ≥ 100 points), 35% had endoscopic remission [Crohn's Disease Endoscopic Index of Severity (CDEIS) ≤ 4 or ≤ 2 for patients with baseline-isolated ileitis] and 55% had endoscopic response ($> 50\%$ reduction from baseline in CDEIS).

According to interim results from a longer-term, open-label extension (NCT02513459) [26] of the earlier trial (NCT02031276), clinical and endoscopic remission were maintained at week 48 in patients receiving risankizumab. The trial enrolled risankizumab recipients who had achieved clinical response after period 2 (week 26) or clinical response and/or remission after Period 3 (week 52) in the preceding trial; patients were enrolled to receive risankizumab 180 mg subcutaneously every 8 weeks for up to 216 weeks [26].

2.4 Adverse Events

In phase 2 and 3 clinical trials in patients with plaque psoriasis described in Sect. 2.3.1, the overall incidence of adverse events was generally similar across treatment groups, with most events being mild to moderate in severity [27]. Over the short-term (16 weeks), the overall incidence of

adverse events in groups receiving risankizumab ($n = 1306$), ustekinumab ($n = 239$), adalimumab ($n = 304$), or placebo ($n = 300$) subcutaneously was 48.9%, 52.3%, 56.9% and 48.3%, respectively. Serious adverse events occurred in 2.4% of risankizumab recipients compared with 5.0%, 3.0% and 4.0% in ustekinumab, adalimumab and placebo recipients, respectively. The most frequently reported (occurring in ≥ 2 patients) serious adverse events among risankizumab recipients during this period were cellulitis and squamous cell carcinoma. During long-term risankizumab treatment (up to 40 months) [$n = 2234$], the most common treatment-emergent adverse events were viral upper respiratory tract infection (21.5 events per 100 patient years), upper respiratory tract infection (12.8), arthralgia (5.7), and headache (5.3) [27]. The rate of serious adverse events per 100 patient years was 9.8 over the long term compared with 9.9 over the 16-week period. The long-term discontinuation rate of risankizumab due to adverse events was low (2.1) and no patterns were identified. Injection-site reactions (most commonly erythema, pain, pruritus, reaction, swelling, hematoma and hemorrhage) occurred in 3.1% of patients, and all were mild to moderate in severity. There were no cases of serious hypersensitivity reactions related to risankizumab.

The rate of infection (most events were mild to moderate in severity) in risankizumab recipients over short- and long-term therapy was 90.8 and 75.5 events per 100 patient years, respectively, in the pooled analysis of phase 2 and 3 trials in patients with plaque psoriasis ($n = 2234$; up to 40 months' treatment duration) [28]. The rate of serious infection was 1.7 events per 100 patient years during short- and long-term treatment. The most common (≥ 0.2 events per 100 patient years) serious infections in the long-term analysis were sepsis, cellulitis and pneumonia. There were no cases of active TB [28]. Among patients with latent TB at screening ($n = 72$), none developed active TB during concurrent treatment with risankizumab and appropriate TB prophylaxis (mean follow-up was 61 weeks of treatment with risankizumab). Among patients with latent TB who did not receive prophylaxis during risankizumab treatment ($n = 31$), none developed active TB (mean follow-up 55 weeks).

Over long-term treatment with risankizumab in phase 2 and 3 psoriasis trials, the event rate of any malignant tumor (including non-melanoma skin cancer) was 1.3 events per 100 patient years [i.e. generally similar to rates observed with ustekinumab, ixekizumab, secukinumab, guselkumab and brodalumab in clinical trials (0.81–1.3 events per 100 patient years)] [29].

Risankizumab was generally well tolerated in patients with Crohn's disease, according to results from a randomised, phase 2 trial [24] and its open-label extensions [25, 26]. In the 12-week randomized study [24], the most

Key clinical trials of risankizumab (AbbVie/Boehringer Ingelheim)

Drug(s)	Indication	Phase	Status	Location(s)	Identifier	Sponsor
Risankizumab	Generalized pustular psoriasis or erythrodermic psoriasis	3	Active	Japan	NCT03022045	AbbVie
Risankizumab	Moderate-to-severe plaque psoriasis (maintenance over long term)	3	Active	Multinational	NCT03047395 (LIMMITLESS)	AbbVie
Risankizumab, secukinumab	Moderate-to-severe plaque psoriasis	3	Active	Multinational	NCT03478787	AbbVie
Risankizumab, placebo	Moderate-to-severe plaque psoriasis	3	Active	Russia	NCT03518047 (IMMpress)	AbbVie
Risankizumab, methotrexate	Moderate-to-severe plaque psoriasis	3	Recruiting	Brazil	NCT03219437	AbbVie
Risankizumab, fumaric acid	Moderate-to-severe plaque psoriasis	3	Complete	Germany	NCT03255382	AbbVie
Risankizumab, ustekinumab, placebo	Moderate-to-severe plaque psoriasis	3	Complete	Multinational	NCT02684370 (ultIMMA-1)	AbbVie, BI
Risankizumab, ustekinumab, placebo	Moderate-to-severe plaque psoriasis	3	Complete	Multinational	NCT02684357 (ultIMMA-2)	AbbVie, BI
Risankizumab, adalimumab, placebo	Moderate-to-severe plaque psoriasis	3	Complete	Multinational	NCT02694523	AbbVie, BI
Risankizumab, placebo	Moderate-to-severe plaque psoriasis	3	Complete	Multinational	NCT02672852 (IMMhance)	AbbVie, BI
Risankizumab, placebo	Moderate-to-severe plaque psoriasis	2/3	Complete	Japan	NCT03000075	AbbVie, BI
Risankizumab	Moderate-to-severe plaque psoriasis	2	Complete	Multinational	NCT02203851	AbbVie, BI
Risankizumab, ustekinumab	Plaque psoriasis	2	Complete	Multinational	NCT02054481	BI
Risankizumab, placebo	Psoriatic arthritis	3	Recruiting	Multinational	NCT03671148	AbbVie
Risankizumab, placebo	Psoriatic arthritis	3	Recruiting	Multinational	NCT03675308	AbbVie
Risankizumab	Psoriatic arthritis	2	Complete	Multinational	NCT02986373	AbbVie
Risankizumab, placebo	Psoriatic arthritis	2	Complete	Multinational	NCT02719171	AbbVie, BI
Risankizumab, placebo	Moderate-to-severe active Crohn's disease	3	Recruiting	Multinational	NCT03105128	AbbVie
Risankizumab, placebo	Moderate-to-severe active Crohn's disease (patients who responded to induction with IV risankizumab)	3	Recruiting	Multinational	NCT03105102	AbbVie
Risankizumab, placebo	Moderate-to-severe active Crohn's disease (patients who failed prior biologic)	3	Recruiting	Multinational	NCT03104413	AbbVie
Risankizumab	Moderate-to-severe active Crohn's disease	2	Active	Multinational	NCT02513459	AbbVie, BI
Risankizumab, placebo	Moderate-to-severe active Crohn's disease	2	Complete	Multinational	NCT02031276	AbbVie, BI
Risankizumab, placebo	Ulcerative colitis (patients who responded to induction with IV risankizumab)	3	Recruiting	Multinational	NCT03398135	AbbVie
Risankizumab, placebo	Moderate-to-severe active ulcerative colitis (patients who failed prior biologic)	2/3	Recruiting	Multinational	NCT03398148	AbbVie
Risankizumab	Atopic dermatitis	2	Recruiting	Multinational	NCT03706040	AbbVie

common adverse events observed with risankizumab were associated with the GI tract (nausea, abdominal pain), and arthralgia and headache. No new safety signals were

detected during the extended treatment periods, with no deaths, malignancies or cases of tuberculosis reported [25, 26].

2.5 Ongoing Clinical Trials

There are several ongoing trials of risankizumab in various indications. In the treatment of moderate-to-severe plaque psoriasis, four phase 3 trials are active, including a multinational trial comparing efficacy with secukinumab (NCT03478787), a multinational trial evaluating long-term safety and efficacy in patients completing phase 2 and 3 studies (NCT03047395; LIMMITLESS), a trial in Brazil that will compare efficacy with methotrexate (NCT03219437), and a trial in Russia comparing safety and efficacy with placebo (NCT03518047; IMMpress). A phase 3 trial in Japan is evaluating the efficacy and safety of two dosage regimens of risankizumab in Japanese patients with generalized pustular psoriasis or erythrodermic psoriasis (NCT0322045).

Risankizumab trials are also active or recruiting in psoriatic arthritis [two phase 3 (NCT03671148 and NCT03675308)], Crohn's disease [a phase 2 long-term extension (NCT02513459) and three phase 3 (NCT03104413, NCT03105128 and NCT03105102), including a long-term extension], ulcerative colitis [one phase 2/3 (NCT03398148) and a phase 3 (NCT03398135)], and atopic dermatitis [one phase 2 (NCT03706040)].

3 Current Status

Risankizumab received its first global approval on March 26, 2019 for the treatment of adults with psoriasis vulgaris, psoriatic arthritis, generalized pustular psoriasis and erythrodermic psoriasis in Japan, and received approval in Canada, the USA and the EU (on April 18, 23 and 30, respectively) for moderate-to-severe plaque psoriasis in adults who are candidates for systemic therapy or phototherapy.

Compliance with Ethical Standards

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Conflict of interest During the peer review process the manufacturer of the agent under review was offered an opportunity to comment on the article. Changes resulting from any comments received were made by the authors on the basis of scientific completeness and accuracy. Kate McKeage and Sean Duggan are contracted employees of Adis/Springer, are responsible for the article content and declare no relevant conflicts of interest.

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