



Risankizumab

Updated: June 9, 2021.

OVERVIEW

Introduction

Risankizumab is a humanized monoclonal antibody to IL-23 which is used to treat moderate-to-severe plaque psoriasis. Risankizumab is generally well tolerated and is associated with a low rate of serum aminotransferase elevations during therapy, but has not been linked to instances of clinically apparent liver injury.

Background

Risankizumab (ris' an kiz' ue mab) is a humanized monoclonal IgG1 antibody directed against the p19 subunit of IL-23, which results in inhibition of IL-23 signaling and decrease in synthesis of proinflammatory cytokines such as IL-17. Risankizumab has been evaluated as therapy of several immune and inflammatory conditions, most extensively in plaque psoriasis. In several large, preregistration randomized controlled trials, 48 weeks of risankizumab therapy resulted in a significant improvement in psoriatic skin lesions in more than 70% of patients. Clinical responses were generally maintained with long term therapy. Risankizumab was approved in the United States in 2019 as therapy for moderate-to-severe plaque psoriasis in adult candidates for systemic therapy. It is also being evaluated in patients with psoriatic arthritis, inflammatory bowel disease and atopic dermatitis. Risankizumab is available in single dose pre-filled syringes of 75 mg in 0.83 mL under the brand name Skyrizi. The recommended dose is 150 mg (two syringes) administered subcutaneously at weeks 0 and 4 followed by every 12 weeks thereafter. Common side effects include mild local injection reactions, nasopharyngitis, fatigue, headache, arthralgia and skin rashes. Uncommon, potentially severe adverse reactions include severe infections, reactivation of tuberculosis and skin cancer.

Hepatotoxicity

Mild-to-moderate serum aminotransferase elevations arise in up to 10% of patients treated with risankizumab, but the abnormalities are generally transient and asymptomatic, rarely necessitating drug discontinuation. In large, preregistration trials there were no instances clinically apparent liver injury or severe hepatic adverse events attributed to risankizumab. Since its approval and more general use, there have been no reports of clinically significant liver injury attributed to risankizumab.

Likelihood score: E (unlikely cause of clinically apparent acute liver injury).

Mechanism of Injury

The possible mechanisms of liver injury due to risankizumab are unclear. Monoclonal antibodies and immunoglobulins are generally taken up and metabolized intracellularly to short peptides and amino acids.

There is no evidence to suggest that inhibition of IL23 signaling would trigger liver injury or autoimmune liver conditions.

Drug Class: [Monoclonal Antibodies, Psoriasis Agents](#)

PRODUCT INFORMATION

REPRESENTATIVE TRADE NAMES

Risankizumab – Skyrizi®

DRUG CLASS

Psoriasis Agents

COMPLETE LABELING

Product labeling at DailyMed, National Library of Medicine, NIH

CHEMICAL FORMULA AND STRUCTURE

DRUG	CAS REGISTRY NO.	MOLECULAR FORMULA	STRUCTURE
Risankizumab	1612838-76-2	Monoclonal Antibody	Not Available

ANNOTATED BIBLIOGRAPHY

References updated: 09 June 2021

Sewell MJ, Burkhart CN, Morrell DS. Dermatology pharmacology. In: Brunton LL, Hilal-Danan R, Knollman BC, eds. Goodman & Gilman's the pharmacological basis of therapeutics. 13th ed. New York: McGraw-Hill, 2018, pp. 1271-96.

(Textbook of pharmacology and therapeutics).

FDA. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/nda/2019/761105Orig1s000MultidisciplineR.pdf

(Multidisciplinary FDA review of risankizumab in support of its approval for use in moderate-to-severe plaque psoriasis in the US with discussion of safety, which mentions that there were no serious hepatic adverse events attributed to risankizumab and that evaluation of changes in "...clinical chemistry values did not identify any significant safety concerns").

Papp KA, Blauvelt A, Bukhalo M, Gooderham M, Krueger JG, Lacour JP, Menter A, et al. Risankizumab versus ustekinumab for moderate-to-severe plaque psoriasis. *N Engl J Med.* 2017;376:1551–60. PubMed PMID: 28423301.

(Among 166 patients with moderate-to-severe plaque psoriasis treated with risankizumab or ustekinumab for 16 weeks, clinical response rates were higher with risankizumab [77% vs 40%], while total adverse event rates were similar 81% vs 80% and there were no serious adverse events attributed to either medication).

Gordon KB, Strober B, Lebwohl M, Augustin M, Blauvelt A, Poulin Y, Papp KA, 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. PubMed PMID: 30097359.

(Among 997 patients with moderate-to-severe plaque psoriasis treated in two controlled trials, clinical response rates were highest with risankizumab [75%], than with ustekinumab [42-48%] or placebo [2-5%], while adverse event rates were similar in all three groups and there were no episodes of reactivation of tuberculosis, severe hypersensitivity reactions, cancer [other than non-melanoma skin cancer] or major cardiovascular events attributed to therapy; no mention of ALT elevations or hepatotoxicity).

Risankizumab (Skyrizi) for psoriasis. *Med Lett Drugs Ther.* 2019;61(1573):81–3. PubMed PMID: 31170118.

(Concise review of the mechanism of action, clinical efficacy, safety and costs of risankizumab shortly after its approval for use in the US for plaque psoriasis, mentions side effects of nasopharyngitis, headache and arthralgia; no mention of ALT elevations or hepatotoxicity).

Drugs for psoriasis. *Med Lett Drugs Ther.* 2019;61(1574):89–96. PubMed PMID: 31381544.

(Concise review of drugs approved for therapy of psoriasis in the US including calcipotriene, tazarotene, phototherapy, methotrexate, cyclosporine, acitretin, apremistat, tumor necrosis factor inhibitors, IL-17A antagonists and IL-23 inhibitors).

McKeage K, Duggan S. Risankizumab: first global approval. *Drugs.* 2019;79:893–900. PubMed PMID: 31098898.

(Review of the chemical structure, mechanism of action, pharmacology, clinical efficacy and safety of risankizumab mentions that common adverse events include injection site reactions, headache, arthralgia and upper respiratory infection symptoms, and uncommon potential severe adverse reactions include infections, reactivation of tuberculosis and cancer).

Reich K, Gooderham M, Thaçi D, Crowley JJ, Ryan C, Krueger JG, Tsai TF, 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. PubMed PMID: 31280967.

(Among 605 patients with moderate-to-severe plaque psoriasis treated with Risankizumab vs adalimumab for 16 weeks, clinical response rates were higher with risankizumab [84% vs 60%] while adverse event rates were similar [56% vs 57%, severe in 3% vs 3%, and hepatic in 2% vs 1%], one person developing a severe hepatitis that was attributed to isoniazid therapy of latent tuberculosis).

Blauvelt A, Leonardi CL, Gooderham M, Papp KA, Philipp S, Wu JJ, Igarashi A, 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;156:649–58. PubMed PMID: 32267471.

(Among 507 patients with moderate-to-severe plaque psoriasis treated with risankizumab vs placebo for 16 weeks, clinical response rates were higher with risankizumab while total and severe adverse event rates were similar [46% vs 49% and 2% vs 4%], although hepatic adverse events occurred in 7% vs 2% including ALT elevations in 1.8% vs 0.4%).

Warren RB, Blauvelt A, Poulin Y, Beeck S, Kelly M, Wu T, Geng Z, et al. Efficacy and safety of risankizumab vs. secukinumab in patients with moderate-to-severe plaque psoriasis (IMMerge): results from a phase III, randomized, open-label, efficacy-assessor-blinded clinical trial. *Br J Dermatol.* 2021;184:50–9. PubMed PMID: 32594522.

(Among 327 patients with moderate-to-severe plaque psoriasis treated with risankizumab or secukinumab for one year, clinical response rates were higher with risankizumab [74% vs 66% at week 16 and 87% vs 57% at week 52], while total and severe adverse event rates were similar [71% vs 71% and 5.5% vs 4%]; no mention of ALT elevations or hepatotoxicity).

Papp KA, de Vente S, Zeng J, Flack M, Padilla B, Tyring SK. Long-term safety and efficacy of risankizumab in patients with moderate-to-severe chronic plaque psoriasis: results from a phase 2 open-label extension trial. *Dermatol Ther (Heidelb).* 2021;11:487–97. PubMed PMID: 33512666.

(Among 110 patients with moderate-to-severe plaque psoriasis enrolled in an one year open label extension study of risankizumab after a randomized controlled trial, 74% achieved a clinical response by week 48 and adverse events arose in 77%, which were considered “hepatic” in 4.5%).

Ferrante M, Feagan BG, Panés J, Baert F, Louis E, Dewit O, Kaser A, et al. Long-term safety and efficacy of risankizumab treatment in patients with Crohn's disease: results from the phase 2 open-label extension study. *J Crohns Colitis* 2021 Jun 2: jjab093. Epub ahead of print.

(Among 65 patients with Crohn's disease treated with risankizumab [180mg every 8 weeks] in an open label extension study for a median of 33 months, the adverse event rate was 25 per 100 patient-years including hepatic events [mostly ALT or AST elevations above 5 times ULN] of 10 per 100 patient years).