2021

Is Risankizumab Effective in Decreasing Scaling and Percentage of Body Surface Area Affected Amongst Adults with Moderate-Severe Plaque Psoriasis?

Angel L. Berry
Philadelphia College of Osteopathic Medicine

Is Risankizumab Effective in Decreasing Scaling and Percentage of Body Surface Area Affected Amongst Adults with Moderate-Severe Plaque Psoriasis?

Angel L. Berry, PA-S

A SELECTIVE EVIDENCE BASED MEDICINE REVIEW

In Partial Fulfillment of the Requirements For

The Degree of Master of Science

In

Health Sciences – Physician Assistant

Department of Physician Assistant Studies
Philadelphia College of Osteopathic Medicine
Philadelphia, Pennsylvania

December 17, 2020

ABSTRACT

OBJECTIVE: The objective of this selective EBM review is to assess if risankizumab is effective in decreasing the percentage of scaling and body surface area affected amongst those with moderate to severe plaque psoriasis.

STUDY DESIGN: A review of three peer-reviewed randomized controlled trials published between 2015-2018.

DATA SOURCES: The three randomized controlled trials were located using the PubMed database. The studies were selected based upon patient-oriented evidence that matters (POEMs) in correlation to answering the question proposed.

OUTCOMES MEASURED: Outcomes were measured through the Psoriasis Area Severity Index Score.

RESULTS: The studies done by Gordon et al., Krueger et al., and Papp et al., all found statistically significant results (p values < 0.0001, 0.05, and 0.001) when assessing the efficacy of risankizumab vs comparison groups in decreasing the percentage of scaling and body surface area affected in patients with moderate to severe plaque psoriasis.

CONCLUSIONS: The evidence presented within the three randomized control trials demonstrate a statistically significant relationship between risankizumab and its proficiency in treating the symptoms associated with moderate to severe plaque psoriasis.

KEYWORDS: moderate to severe plaque psoriasis and Risankizumab

Introduction

One potentially debilitating dermatologic condition that affects many individuals worldwide is psoriasis. It is a chronic inflammatory dermatologic disease that has both genetic and autoimmune traits.[1] It affects 7.6 million Americans.[2] There are several subtypes of the disease, which are known as psoriasis vulgaris, inverse psoriasis, guttate psoriasis, pustular psoriasis, and erythrodermic psoriasis. The most prevalent is psoriasis vulgaris, synonymously called the plaque-type psoriasis. Approximately 90% of psoriasis cases diagnosed are of the chronic plaque psoriasis type.[1] Chronic plaque psoriasis often clinically manifests as sharply demarcated, erythematous pruritic plaques covered in silvery scales which can coalesce and cover a vast percentage of body surface area.

Although psoriasis primarily presents as skin manifestations of plaques, there are also comorbidities associated with the condition due to its inflammatory autoimmune pathophysiology. There is still much to be learned about psoriasis, but it is thought to be caused by a defect in the body's TNFα-IL23-Th17 axis which regulates immune and inflammatory processes. This axis plays an important role in T cell mediated plaque psoriasis.[1] It has been hypothesized that overexpression of the inflammatory process leads to chronicity of plaque psoriasis and systemic comorbidities.[1]

Those who are diagnosed with psoriasis have a 40% chance of developing psoriatic arthritis, this is due to psoriatic inflammation of the joints.[1] Studies have also revealed that patients with severe chronic psoriasis are also at an increased risk of myocardial infarctions, coronary artery disease, and renal disease.[1] There has also been evidence that demonstrates a higher prevalence of suicidal ideation amongst those with severe chronic plaque psoriasis due to the silvery scales covering large portions of a patient's skin, diminishing their self-confidence.[1]

There is medication available to treat moderate to severe plaque psoriasis and to help improve the patient's quality of life but they can be quite expensive. The monoclonal antibodies and biologics that are often prescribed are estimated to be $95,000-100,000 per person annually.[3] Patients who have less severe cases of plaque psoriasis only requiring phototherapy are estimated to spend $3,000-7,200 per year.[4]

This skin condition affects many Americans and one study found that 50% of their survey respondents who had plaque psoriasis reported going to their dermatologist annually and 3% reported going to an ambulatory clinic annually.[5] It is possible that because the disease has no cure patients who have plaque psoriasis may visit their providers less frequently. It has been demonstrated how disabling the condition can be and though there are medications such as biologics, furamic acid esters, phosphodiesterase-4 inhibitors, TNFα inhibitors, and monoclonal antibodies used to treat the condition, there has been a proposal of a new monoclonal antibody that may be more efficacious than other therapeutics in treating the symptoms associated with moderate to severe plaque psoriasis.

The new monoclonal antibody is risankizumab. There have been three randomized controlled trials (RCTs) conducted that assess the medication's proficiency in relation to comparison groups in treating symptoms of moderate to severe plaque psoriasis such as scaling, and percentage of body surface area affected.[6,7,8] If this medication is deemed to be more efficacious in alleviating the patient's symptoms in comparison to others, then this may ultimately lead to the patient having an increased quality of life and it could also improve rapport within the patient-provider relationship. Therefore, these trials will be further discussed to evaluate this possibility.

Objective

The objective of this selective EBM review is to determine whether risankizumab efficiently decreases scaling and percentage of body surface area affected within adults who have moderate to severe plaque psoriasis.

Methods

Criteria used for selection of studies:

The population specifically focused on within this review is adults older than 18 with moderate to severe plaque psoriasis who have a high percentage of body surface area affected by the disease. The three peer-reviewed randomized controlled trials being discussed conducted their studies amongst this population.[6,7,8] Risankizumab is the monoclonal antibody that is being assessed as an intervention regarding it's efficacy in reducing scaling and the percentage of body surface area affected amongst those with moderate to severe plaque psoriasis. The randomized controlled trials used the Psoriasis Area Severity Index (PASI) Score, which can measure the reduction of total body surface area involvement, to assess the drug's effectiveness in decreasing symptoms.[6,7,8]

Gordon et al. compared 150 mg of risankizumab to 45 or 90 mg of ustekinumab and 150 mg of risankizumab to a placebo for 52 weeks to further determine this.[6] Krueger et al. compared a single dose of risankizumab at 0.01, 0.05, 0.25, 1, 3, or 5mg/kg IV or subcutaneous to a placebo within their study to assess the drug's proficiency.[7] Papp et al. compared subcutaneous injections of risankizumab of 18 mg – 180 mg (dependent upon the week of the study) vs. 45 – 90 mg (according to body weight) of ustekinumab to evaluate risankizumab's potential in reducing symptoms.[8] The participants of studies began with a PASI baseline of 12 or greater and percentage of body surface area affected of 10% or greater.[6,7,8]

Table 1. - Demographics and Characteristics of Included Studies

Study	Type	# Pts	Age(yrs)	Inclusion Criteria	Exclusion Criteria	W/D	Interventions
Gordon et al. 2018 (6)	RCT	506	>18 yrs	Patients older than 18 with stable chronic moderate to severe plaque psoriasis	Individuals who could not undergo systemic or phototherapy and were ineligible for treatment with ustekinumab	29	150 mg of risankizumab vs. 45 or 90 mg of ustekinumab 150 mg of risankizumab vs. placebo
Krueger et al. 2015 (7)	RCT	39	18-75 yrs	Patients with moderate to severe chronic plaque psoriasis for at least 6 months.	Female subjects of childbearing potential or if they had received prior treatment with ustekinumab within 24 weeks, other biologic agents, or psoralen, and UVA within 12 weeks.	1	Single dose of risankizumab 0.01, 0.05, 0.25, 1, 3, or 5mg/kg IV or subcutaneous vs placebo
Papp et al. 2017 (8)	RCT	166	18-75 years	Patients between the ages of 18-75 who were stable with moderate to severe chronic plaque.	Patients who previously had ustekinumab or any other agent targeting interleukin-12 or interleukin-23.	11	Subcutaneous injections of risankizumab 18 mg – 180 mg dose (dependent upon the week of the study) vs. 45 – 90 mg (according to body weight) of ustekinumab

Data Sources:

The three peer-reviewed randomized controlled trials were found using PubMed and Google Scholar databases. They were all originally published in English. The keywords that were used when searching for the RCTs were risankizumab and moderate to severe plaque psoriasis. Studies that were not peer-reviewed and had a substantial number of confounding variables were disqualified from selection. Studies were selected based upon if they were published within the past five years and also if they included patient-oriented evidence that matters (POEMs) in correlation to if risankizumab is an effective treatment compared to other monoclonal antibodies in reducing percentage of body surface area affected by moderate to severe plaque psoriasis. The summary of the statistics used within the RCTs to accurately assess this were NNT, CER, EER, RBI, ABI, and p-value.[6,7,8]

Outcomes Measured

The Psoriasis Area Severity Index Score was how the patient-oriented outcomes were measured within the randomized controlled trials.[6,7,8] Papp et al. states that the PASI score is ultimately a comprehensive assessment relating to erythema, induration, scaling and percentage of body surface area affected.[8] A reduction in the PASI score was documented as PASI100, PASI90, PASI75, and PASI50 throughout the studies pertaining to the participant's outcomes after the RCTs were complete.[6,7,8] The number after PASI demonstrates the total reduction in erythema, induration, scaling, and percentage compared to the participant's baseline PASI score.[6,7,8] For example, if one of the participants within the studies had a baseline PASI score of 15 and they completed the study as PASI90 this demonstrates a 90% reduction in their original score. We will go on to further review the studies and discuss how they display risankizumab's role relating to the reduction of the PASI score.

Results

In the double-blind, randomized, placebo-controlled trial conducted by Gordon et al. there were two groups that were involved. The first group included patients who were randomly assigned to receive 150 mg of risankizumab or 45 or 90 mg of ustekinumab.[6] The second group included patients who were randomly assigned to receive 150 mg of risankizumab or 45 mg or 90 mg of ustekinumab.[6] The trial ended at 52 weeks and was conducted at 139 sites which included hospitals, university medical centers, clinical research units, and private practices.[6] The mean baseline PASI score was 20.[6]

At 16 weeks within both groups PASI90 was achieved by 75.3% of patients treated with risankizumab, compared to 42% treated with ustekinumab.[6] Dermatologic presentations of psoriasis were also found to completely resolve (PASI100) among some patients taking risankizumab when compared to ustekinumab.[6] Among the patients that were taking risankizumab 35.9% achieved PASI100 compared to 12% of those taking ustekinumab.[6] Between the groups there was a statistically significant difference found regarding the efficacy of risankizumab compared to ustekinumab in reducing symptoms of patients with moderate to severe plaque psoriasis; p value of < 0.0001 was determined.[6]

The study conducted by Krueger et al. was also a double-blind, randomized, placebo-controlled trial. There was a total of 39 patients included in this 24 week study which took place in 8 different centers.[7] Patients were given 0.01, 0.05, 0.25, 1, 3, or 5 mg/kg of risankizumab intravenously (n=18), 0.25 or 1mg/kg of risankizumab subcutaneously (n=13), or placebo (n=8).[7] Mean PASI score was between 15.7-22.8.[7] The PASI reduction score was shown to be higher in those receiving risankizumab subcutaneously compared to those receiving it intravenously.[7] According to Kruger et al., at 24 weeks among patients who were receiving risankizumab

intravenously or subcutaneously at doses of 0.25mg/kg and higher 84%, 60%, and 36% achieved PASI75, PASI90, or PASI100 when compared to placebo.[7] The study demonstrated that the placebo had no effect on the PASI score.[7] Between risankizumab and the placebo there was statistically significant difference regarding the aptitude of risankizumab compared to the placebo in reducing scaling, erythema, induration, and percentage of body surface area affected within patients who had moderate to severe plaque psoriasis; p value of <0.05 was determined.[7]

The study conducted by Papp et al. included 166 patients who received either 18-180 mg per week of risankizumab subcutaneously or 45-90 mg of ustekinumab.[8] The study was conducted at 32 sites and was over the course of 48 weeks.[8] The mean PASI score was 12 within the sample.[8] Risankizumab was shown to be more efficient than ustekinumab at week 12 where PASI90 was achieved in 77% of patients being treated with risankizumab, whereas only 40% of those being treated with ustekinumab achieved PASI90 at week 12.[8] In the study Papp et al. also displayed how risankizumab was more efficacious than ustekinumab even in lower doses.[8] Also, patients who were receiving risankizumab were demonstrating a superior ability compared to those receiving ustekinumab to achieve PASI100 at week 12.[8] This was shown by 45% of patients receiving risankizumab achieving PASI100 compared to 18% amongst those taking ustekinumab.[8] Ultimately, statistical significance was found between risankizumab and ustekinumab regarding risankizumab's superiority in reducing symptoms of patients with moderate to severe plaque psoriasis; p value of < 0.001 was found.[8]

Although the studies reviewed exhibit substantial evidence regarding risankizumab's effectiveness in treating symptoms related to moderate to severe plaque psoriasis, there is still much to be learned about the drug. Krueger et al. revealed that four participants with predisposing health risks had severe adverse reactions after taking the drug.[7] According to Papp

et al. some participants developed serious adverse reactions as well after taking the drug, which included basal cell carcinoma, myocardial infarction, and cerebrovascular accidents.[8] These patients accounted for 5/166 participants.[8] It is possible that safety may be of concern within certain populations after taking the drug. Table 2 demonstrates the experimental event rate (EER), relative benefit increase (RBI), absolute benefit increase (ABI), numbers needed to treat (NNT), control event rate (CER), and p-value of all three studies.

Table 2 – Summary of Statistics Reported

Study	EER	RBI	ABI	NNT	CER	P-value
Gordon et al. 2018 (6)	.753	.79	.333	4	.42	<0.0001
Krueger et al. 2015 (7)	.85	undefined	.85	2	0	<0.05
Papp et al. 2017 (8)	.73	.83	.33	4	.42	<0.001

Discussion

Although risankizumab was approved by the FDA in 2019, it is a still a very new monoclonal antibody and there is still much to be learned about it. While researching the monoclonal antibody, there were articles discovered pertaining to the possibility of risankizumab treating inflammatory bowel disease, hidradenitis suppurativa, as well as moderate to severe plaque psoriasis. Due to the drug being in its infancy this allows for limitations within this

review. As mentioned previously, a small number of patients who have taken the drug have developed severe adverse reaction.[7,8] It has not been well-established as to whether these adverse reactions are something to critically be concerned about. Ultimately, being unable to provide proper information regarding the safety of consuming the medication in certain populations provides opportunity for limitations of the review.

Conclusion

Overall, the randomized controlled trials that were reviewed allowed for much clarification regarding the question originally proposed. Individuals affected by moderate to severe plaque psoriasis live through tumultuous circumstances each day. The monoclonal antibody risankizumab has demonstrated much proficiency in being able to provide relief to individuals suffering from the disease. The evidence discussed from the RCTs provide an answer to the question of if risankizumab is effective in decreasing symptoms associate with moderate to severe plaque psoriasis. The answer has been shown to be “yes”. The three randomized controlled trials discussed display risankizumab’s dominance over ustekinumab in treating moderate to severe plaque psoriasis. There was statistically significant data revealed in each study reviewed. Risankizumab is a drug by which individuals affected by moderate to severe psoriasis can look to to provide them with relief of their symptoms which ultimately include erythema, induration, scaling, and percentage of body surface area affect. Risankizumab has been demonstrated to be a promising treatment for those who have be debilitated by moderate to severe plaque psoriasis and it can be looked to as a source of hope within this population.

References

1. Rendon A, Schäkel K. Psoriasis pathogenesis and treatment. *Int J Mol Sci*. 2019;20(6):1475. doi:10.3390/ijms20061475

2. Langley RGB, Krueger GG, Griffiths CEM. Psoriasis: epidemiology, clinical features, and quality of life. *Ann Rheum Dis* 2005;64**:**ii18-ii23

3. San-Juan-Rodriguez A, Parekh N, Newman T, Hernandez I; Pricing of monoclonal antibodies in the United States. *Glob J Health Sci* 1 August 2018; 1 (1): 4–5.

4. Beyer V, Wolverton SE. Recent trends in systemic psoriasis treatment costs. *Arch Dermatol.* 2010;146(1):46–54. doi:10.1001/archdermatol.2009.319

5. Fischer AH, Shin DB, Gelfand JM, Takeshita J. Health care utilization for psoriasis in the United States differs by race: An analysis of the 2001-2013 medical expenditure panel surveys. *J Am Acad Dermatol*. 2018;78(1):200-203. doi:10.1016/j.jaad.2017.07.052

6. Gordon KB, Puig L, Foley P, 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 North American Edition (10148):650-661. doi: 10.1016/S0140-6736(18)31713-6.

7. Krueger JG, Ferris LK, Menter A, 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 Jul;136(1):116-124.e7. doi: 10.1016/j.jaci.2015.01.018.

8. Papp KA, Blauvelt A, Bukhalo M, et al. Risankizumab versus Ustekinumab for Moderate-to-severe plaque psoriasis. *N Engl J Med*. 2017 Apr 20;376(16):1551-1560. doi: 10.1056/NEJMoa1607017.