

# Risankizumab effectiveness and safety in psoriasis patients who failed other biologics: Real-life case series

Sir,

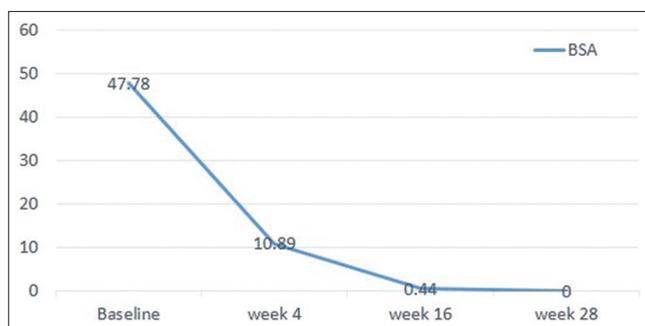
Psoriasis is a chronic relapsing immune-mediated inflammatory disease. Individuals show variable response to different biologics. Risankizumab is one of the most recently approved biologic agents for treating psoriasis which is a humanised immunoglobulin G1 monoclonal antibody that targets the p19 subunit of IL-23.<sup>1</sup> Real-life reports regarding its effectiveness are still limited.

This study was conducted at Al Hada Armed Forces Hospital, Saudi Arabia on nine adult psoriasis patients who showed failure, intolerance and/or side effects to one or more biologic agent and were shifted to risankizumab to document its effectiveness and safety in different clinical types of psoriasis. They were prescribed risankizumab 150 mg subcutaneous injection at baseline, four weeks then every 12 weeks for at least 28 weeks. It was performed

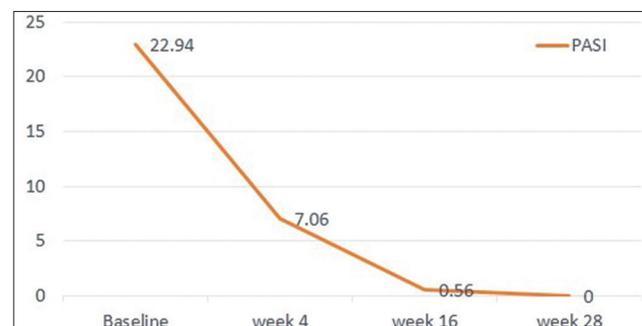
in line with the principles of the Declaration of Helsinki of 1975 (revised in 2000). Approval was granted by the regional research and ethics committee at Al Hada Armed Forces Hospital.

Clinical, demographic and treatment data were collected retrospectively from patients' files at baseline [Table 1], four weeks of risankizumab injection and every 12 weeks thereafter. Psoriatic arthritis and its type were recorded. Severity assessment using body surface area affected, psoriasis area and severity index (PASI), physician global assessment and dermatology life quality index were analysed.

Following risankizumab, all measured parameters showed significant improvement over time [Figures 1a-1d]. Finally at week 28, all patients showed PASI 100 response [Figure 2].



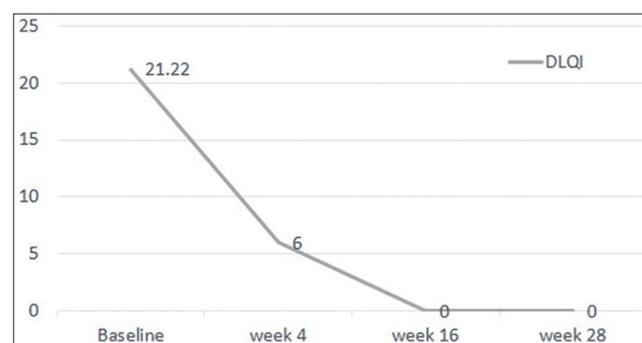
**Figure 1a:** Body surface area improvement over 28 weeks of risankizumab therapy



**Figure 1b:** Absolute PASI significant decline over 28 weeks of risankizumab therapy



**Figure 1c:** Physician global assessment 0/1 achievement at 16/28 weeks of risankizumab therapy



**Figure 1d:** Dermatology life quality index scores improvement over 28 weeks

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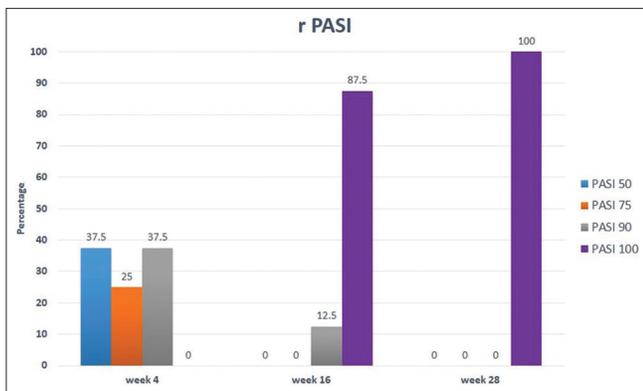
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**Table 1: Clinical data and previous treatment details of the studied cases**

Cases	Age (year)/ sex	BMI (kg/m <sup>2</sup> )	Clinical variant	Special sites			PsA	Phototherapy	Conventional therapy	Biologics and others	Cause of biologic switch
				Nail	Scalp	Genital					
1	26/f	21	Plaque	-	-	-	-	+	MTX	Adalimumab Etanercept	Failure
2	35/f	24	Plaque	+	+	+	-	+	MTX	Adalimumab Etanercept	Failure
3	30/f	27	Plaque	-	+	+	-	+	MTX acitretin	Adalimumab Etanercept	Failure
4	43/m	24	Plaque	-	-	-	Enthesitis	+	MTX acitretin	Adalimumab Etanercept	Failure
5	48/m	29	Plaque	-	+	+	-	+	MTX acitretin	Adalimumab Etanercept	Failure
6	49/f	54.6	Plaque	-	+	+	Peripheral joints (Small IP)	+	MTX acitretin cyclosporine	Adalimumab Etanercept Secukinumab Combination	- Failure to anti TNF- $\alpha$ , - Failure to secukinumab - Severe injection site reaction to ixekizumab
7	55/f	34	Plaque	-	+	-	Peripheral joints (Shoulder, hip)	-		Adalimumab Tofacitinib	-Failure to anti TNF- $\alpha$ -Failure to JAK inhibitors
8	42/m	25	Pustular				-		MTX acitretin cyclosporine	Adalimumab Etanercept Infliximab secukinumab	Failure
9	37/f	27.2	Plaque	-	+	-	Peripheral joint (Small IP) Dactylitis	+		Etanercept	-Rising ANA titer -Limited efficacy

PsA: Psoriatic arthritis, TNF: Tumour necrosis factor, MTX: Methotrexate, JAK inhibitor: Janus kinase inhibitor, IP: Interphalangeal



**Figure 2:** Percentage of patients showing improvement of relative PASI throughout study time (28 weeks)

Clinical improvement was clearly identified in various psoriasis types and localisations. Furthermore, no adverse events or relapse were reported during the study period (28 weeks) or thereafter (9-18 months follow-up period).

Switching therapies have become more emphasized on achieving greatest possible skin clearance (clear or almost

clear), least side effects, improved quality of life and patient satisfaction. In the present study, although 90% of patients showed failure to one or more TNF- $\alpha$  inhibitors, they had an excellent response to risankizumab. This was in concordance with IMMvent study of Reich *et al.*<sup>2</sup> who proved significant efficacy of risankizumab compared to adalimumab in achieving skin clearance for moderate-to-severe psoriasis. Furthermore, two (22.2%) patients showed failure to IL-17 antagonists following proper response on the loading dose. This was reported in IMMerge randomised clinical trial which showed that risankizumab and secukinumab efficacy was nearly similar at 16 weeks but risankizumab was superior at 52 weeks of therapy.<sup>3</sup>

In the current study, risankizumab showed excellent effectiveness among plaque psoriasis patients irrespective of their body mass index. These results are in agreement with Ruiz-Villaverde *et al.*<sup>1</sup> who showed a significant decline of all scales in 100% of patients regardless of their body mass index. This was higher than what was reported in clinical trials UltIMMa-1 and UltIMMa-2 in which results achieved PASAI 90 at week 16 in 75.3% and 74.8% of patients, respectively.<sup>4</sup> Furthermore, an Italian multicentre study



**Figure 3a:** Baseline psoriasis lesions (abdomen) in morbid obese patient



**Figure 3b:** Baseline psoriasis lesions (back) in morbid obese patient



**Figure 3c:** Baseline psoriasis lesions (leg) in morbid obese patient



**Figure 3d:** Psoriasis lesions (right arm) after 4 weeks of risankizumab



**Figure 3e:** Psoriasis lesions (left arm) after 4 weeks of risankizumab

showed PASI 100 improvement in 49.1% of their patients (87.5% in the present study) at week 16 with better results in females with less than 25 body mass index.<sup>5</sup>

Among our plaque psoriasis patients, 3/8 (37.5%) experienced PASI 90 response at week four which signifies rapidity of action of risankizumab. This is in agreement with Singh *et al.*<sup>6</sup> meta-analysis which reported rapid response to risankizumab similar to ixekizumab and brodalumab with a better safety profile and maintenance of response. It has a faster response than guselkumab and tildrakizumab, possibly due to its stronger affinity and higher selective inhibition of the IL23-IL17 axis.

Among our patients, a morbid obese female (body mass index=54.6) [Figure 3a-c] who has shown failure to escalated doses of anti-tumour necrosis factor (TNF)- $\alpha$  drugs, IL-17 antagonists and combinations has demonstrated an excellent relatively fast response with PSAI75 improvement at week four [Figure 3d-f], PSAI 90 at week 16 [Figure 3g] and PASI 100 at week 28 [Figure 3h] with a sustained response up to 52 weeks. Obesity is known to be a negative prognostic marker being a risk factor to altered pharmacokinetics and higher clearance of all anti-TNF drugs, resulting in lower serum trough drug concentrations.<sup>7</sup> This may explain why obese patients treated even with weight-based regimens such as infliximab, had lower response to treatment.<sup>8</sup>



**Figure 3f:** Psoriasis lesions (back) after 4 weeks of risankizumab

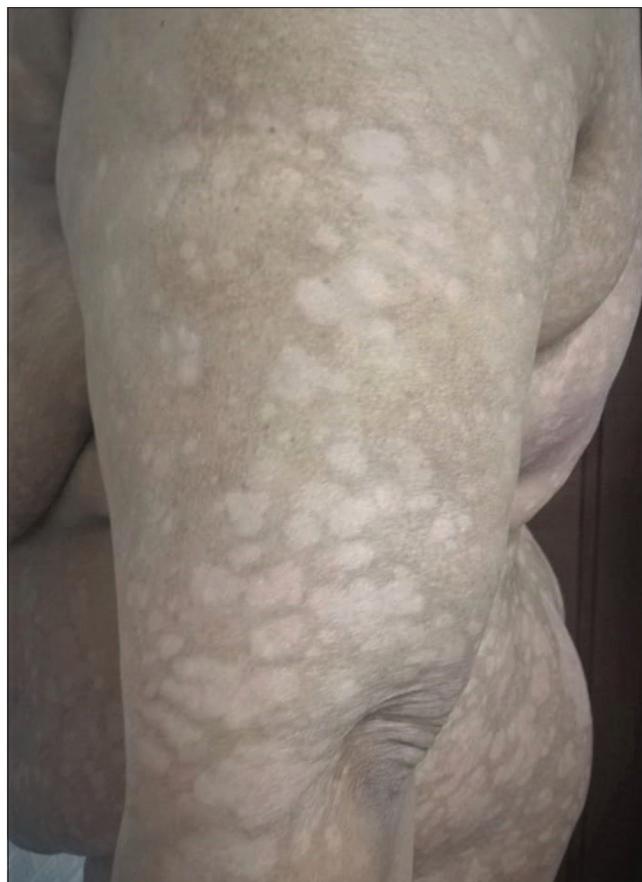
Data from risankizumab Phase II and III clinical trials showed that although its blood levels are 30% lower in patients of weight >100 kg than those of patients with less weight, the levels reached are still within the therapeutic range. Hence, the usual recommended dose of risankizumab seems to remain optimal in obese patients.<sup>9</sup>

One of the presented cases had generalised pustular psoriasis. With risankizumab, the patient showed progressive improvement of body surface area affected with sustainability of that excellent response till 52 weeks. Anti-TNF- $\alpha$  drugs showed some efficacious results in treating pustular psoriasis, but this efficacy was dose-dependent since the majority of patients required escalating doses or reduced intervals between the doses.<sup>10</sup> On the other hand, TNF- $\alpha$  inhibitors were considered as one of the drugs triggering pustular psoriasis (paradoxical reaction) and substitution of these agents by anti-p40 or anti-IL-17A may be greatly helpful.<sup>11</sup> In Japan (March 2019), risankizumab gained its first global approval for treatment of adults with plaque psoriasis, its severe forms (pustular and erythrodermic psoriasis) and psoriatic arthritis.<sup>12</sup> Worldwide clinical trials and placebo-controlled studies investigating different ethnic groups and taking in consideration mutations of *IL-36RN* are recommended to examine risankizumab effectiveness in pustular psoriasis patients.

Among the studied cases, 4 (44.4%) patients suffered from psoriatic arthritis of different types with inadequate response to non-biologic disease modifying anti-rheumatic drugs, anti TNF- $\alpha$ , methotrexate or JAK inhibitor (tofacitinib).



**Figure 3g:** Psoriasis area severity index 90 response (mild erythema) at week 16 of risankizumab therapy



**Figure 3h:** Psoriasis area severity index 100 response in morbid obese female at week 28 of risankizumab therapy

Risankizumab proved to be effective in all reported types of psoriatic arthritis at the standard dose approved for skin psoriasis. The Phase III studies, KEEPSAKE-1 and KEEPSAKE-2, has shown favourable clinical and radiological outcome in adult psoriatic arthritis patients treated with risankizumab versus placebo (unpublished data).<sup>12</sup>

Regarding safety, none of the patients developed any serious adverse events. Although, one of the patients had latent tuberculosis at baseline, she did not develop any symptoms of active tuberculosis till week 40 and continued safely in the study. She received prophylactic dose of once daily 300 mg isoniazid and 20 mg pyridoxine for three months, and then started risankizumab after one month of receiving the antitubercular medications. One of the patients acquired COVID-19 infection with mild symptoms denoting possible safety of risankizumab in COVID-19 patients. However, long-term safety data needs to be assessed.

Localised psoriasis were also reported; scalp in 6 (66.7%) patients, genital in 4 (44.4%) patients, and nail in one (11.1%) patient. These difficult to treat subtypes showed excellent response to risankizumab; as also stated by Dattola *et al.*<sup>13</sup> However, it was noted that nail psoriasis in

the form of oil drops, pitting and thickening started to recur shortly before the scheduled next dose. Further clinical studies are needed to confirm the most effective dosing for nail psoriasis.

In conclusion, risankizumab proved to be effective, safe and tolerable biologic agent for treatment of different types of psoriasis including severe form (pustular psoriasis), difficult to treat areas (nail and scalp) and psoriatic arthritis with sustainable and durable response. It might be an excellent choice for psoriasis patients who failed other biologics. However, the limited number of patients and short duration of the study make it difficult to generalise its results to all settings.

#### **Declaration of patient consent**

The authors certify that they have obtained all appropriate patient consent.

#### **Financial support and sponsorship**

Nil.

#### **Conflicts of interest**

There are no conflicts of interest.

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### References

- Ruiz-Villaverde R, Ayén-Rodríguez A, Llamas-Molina JM, Ruiz-Carrascosa JC. Risankizumab as a promising therapeutic approach in obese patients. *Dermatol Ther* 2020;33:e13323.
- 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;394:576-86.
- Warren RB, Blauvelt A, Poulin Y, Beeck S, Kelly M, Wu T, *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.
- Ruiz-Villaverde R, Ruiz-Carrascosa JC, Galán-Gutierrez M, Armario-Hita JC. Risankizumab: A pilot study of short-term effectiveness and safety in real clinical practice. *Dermatol Ther* 2021;34:e14711.
- Hansel K, Zangrilli A, Bianchi L, Peris K, Chiricozzi A, Offidani A, *et al.* A multicenter study on effectiveness and safety of risankizumab in psoriasis: An Italian 16-week real-life experience during the COVID-19 pandemic. *J Eur Acad Dermatol Venereol* 2021;35:e169-70.
- Singh S, Singh S, Thangaswamy A, Thangaraju P, Varthya SB. Efficacy and safety of Risankizumab in moderate to severe psoriasis: A systematic review and meta-analysis. *Dermatol Ther* 2021;34:e14487.
- Mostafa NM, Nader AM, Noertersheuser P, Okun M, Awni WM. Impact of immunogenicity on pharmacokinetics, efficacy and safety of adalimumab in adult patients with moderate to severe chronic plaque psoriasis. *J Eur Acad Dermatol Venereol* 2017;31:490-7.
- Singh S, Facciorusso A, Singh AG, Castele NV, Zarrinpar A, Prokop LJ, *et al.* Obesity and response to anti-tumor necrosis factor- $\alpha$  agents in patients with select immune-mediated inflammatory diseases: A systematic review and meta-analysis. *PLoS One* 2018;13:e0195123.
- Khatri A, Suleiman AA, Polepally AR, Othman AA. Exposure/Response Relationships for Efficacy and Safety of Risankizumab in Patients with Moderate to Severe Plaque Psoriasis: Integrated Analyses of Phase 2 and 3 Clinical Trials. Poster Presented at: The American Academy of Dermatology Annual Meeting, Washington, DC; 2019.
- Wang WM, Jin HZ. Biologics in the treatment of pustular psoriasis. *Expert Opin Drug Saf* 2020;19:969-80.
- Puig L. Paradoxical reactions: Anti-tumor necrosis factor alpha agents, ustekinumab, secukinumab, ixekizumab, and others. *Curr Probl Dermatol* 2018;53:49-63.
- McKeage K, Duggan S. Risankizumab: First global approval. *Drugs* 2019;79:893-900.
- Dattola A, Silvestri M, Tamburi F, Amoroso GF, Bennardo L, Nisticò SP. Emerging role of anti-IL23 in the treatment of psoriasis: When humanized is very promising. *Dermatol Ther* 2020;33:e14504.

## Transungual penetration of fractional CO<sub>2</sub> laser: A histopathological evaluation

Sir,

Lasers are one of the most promising device-based adjunctive therapies for onychomycosis.<sup>1</sup> Despite many lasers being used, there is a lack of clarity regarding their mechanism of action or expected outcomes, especially regarding their extent of penetration in the nail plate, or optimum energy to be used. Ablative lasers work by increasing permeability of an otherwise impervious nail plate to topical drugs.<sup>2</sup> However, the extent of penetration is unclear. Regarding their clinical efficacy, there are mostly uncontrolled data.<sup>2</sup> As of now, lasers are approved for 'cosmetic improvement in affected nails', whereas, for cure, more rigorous trials are required, aided by microscopically visualising laser effects on the nail plate.

We attempted histopathological correlation of energy delivered and the depth of penetration achieved in toenail specimens obtained from patients operated for ingrown nail. We used a 40 watts fractional carbon dioxide (CO<sub>2</sub>) laser, (REX CO<sub>2</sub> Model from AMI Laser Company), to assess the microscopic effects of fractional CO<sub>2</sub> laser on the nail plate. Nails, with a water content of 15–18%, should ideally respond to the wavelength of fractional CO<sub>2</sub> laser (10,600 nm). Fresh slivers of lateral nail plate removed during ingrown nail surgery were cleaned of surrounding tissue and irradiated with two passes of one of the four energy levels (50 mJ, 100 mJ, 150 mJ or 200 mJ) [Figures 1a and 1b]. Only one energy was delivered on one nail sliver. Two passes were given to increase the depth

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