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REVIEW

Risankizumab for the Treatment of Moderate to Severe Psoriasis: Impact on Health-Related Quality of Life and Psychological Wellbeing

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Abstract: Biologic treatments are increasingly being used in the management of moderate to severe plaque psoriasis (PSO). Risankizumab (RZB) is a humanized monoclonal antibody that specifically blocks the p19 subunit of interleukin 23, which in turn regulates the activation, differentiation, and survival of Th17. RZB has proved their efficacy and their safety compared to anti-TNF. However, studies that assess and compare the improvement in other secondary PROs such as the patient's quality of life are still scarce. Health-related quality of life (HRQoL) is the sum of physical health, well-being, and participation; it defines the functional effect of a disease or its treatment and how it is perceived by the patient. The objective of this paper is to analyze the literature on the impact of treatment with RZB on the quality of life of patients with PSO and their psychological well-being. A bibliographic search was carried out to identify all the papers published from July 2015 to June 1, 2022, on RZB treatment in psoriasis and its impact on health-related quality of life and psychological well-being, finally twenty articles have been evaluated in full text, of which 8 were excluded because they did not meet the inclusion criteria. Risankizumab has shown not only to have very relevant data on effectiveness and safety, but all of this is associated with an improvement in quality of life related to health and psychological well-being measured on generic and specific quality of life scales, both in pivotal trials, ad hoc analysis, and data in real clinical practice.

Keywords: Risankizumab, health related quality of life, psoriasis

Introduction

Psoriasis is a chronic immune-mediated inflammatory disease the predominantly affects the skin, but also encompasses a significant list of comorbidities such as an increased risk of mortality, cardiovascular disease, diabetes, hyperlipidemia, or diabetes.[1,2]

In addition to all of the above is its chronic nature and the feeling of therapeutic failure that often causes a sense of hopelessness and frustration, with an increased risk of suicide compared to the general population. In short, there is the effect of psoriasis at a physical level (due to the psoriasis itself, comorbidities and iatrogenesis), and also at a psychosocial level due to the limitation in social interaction and behavioural changes in daily life. Health-related quality of life (HRQoL) is the sum of physical health, well-being, and participation; it defines the functional effect of a disease or its treatment and how it is perceived by the patient.

The degree of HRQoL alteration is associated with psoriasis-dependent factors, but there are also personal factors that condition the patient's vulnerability to the disease.[3]

Due to the profound systemic and emotional impact of this disease, improvements in severity scales such as PASI are not sufficient for assessing the overall effectiveness of treatment, but other scales such as quality of life indices (DLQI, HRQoL, SKINDEX-29, etc.) must be taken into account.[4]

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With the advent of biological drugs, the psoriasis treatment paradigm has changed radically, taking into consideration PASI 90–100 therapeutic goals, and thus improvements in health-related quality of life.[5] Risankizumab (RZB) is a humanized monoclonal antibody that specifically blocks the p19 subunit of interleukin 23, which in turn regulates the activation, differentiation, and survival of Th17. The IL23/Th17 pathway is activated in psoriasis, being responsible for the chronic inflammation and skin manifestations of the disease. In this sense, numerous molecules have proved their efficacy, their safety compared to anti-TNF[6] however, studies that assess and compare the improvement in other secondary PROs such as the patient's quality of life are still scarce. It has been observed that low levels of absolute PASI have been related to improvements in the quality of life related to the patient's health and that even minimal residual disease has been related to a negative impact on the life of patients.[7]

The objective of this paper is to analyze the literature on the impact of treatment with risankizumab on the quality of life of patients and their psychological well-being.

Materials and Methods

A bibliographic search was carried out to identify all the papers published from July 2015 to June 1, 2022, on risankizumab treatment in psoriasis and its impact on health-related quality of life and psychological well-being. The results have been limited to studies conducted in humans and published in Spanish or English.

The studies were identified by searching the following databases: MEDLINE via PubMed, EMBASE, Centre of Review and Dissemination via University of York, Cochrane Library via Cochrane Database of Systematic Reviews, Cochrane Skin Group, Centre of Evidence Based Dermatology at the University of Nottingham, and the TESEO database of doctoral theses.

Additionally, the search has been expanded with the following websites: ClinicalTrials.gov, reec.aemps.es, Clinicaltrialsregister.eu.

Finally, with the aim of identifying the systematic reviews on quality of life related to health and psychological well-being in psoriasis, and more specifically on treatment with risankizumab, which are currently being carried out, an electronic search was conducted in PROSPERO, the International Prospective Register of Systematic Reviews.

The search terms that have been entered to conduct the definitive search for articles, according to the MeSH and DeSC dictionaries, have been: psoriasis, risankizumab, Health-Related Quality Of Life, quality of life.

Inclusion Criteria for the Studies

- Types of studies: Randomized controlled clinical trials; systematic reviews; observational studies with n greater than or equal to 20.
- Population: Psoriasis patients of legal age, regardless of gender, ethnicity, comorbidity, and prior treatment.
- For studies to be considered, they had to include psoriasis patients treated with risankizumab, at any dose for psoriasis.
- They were restricted to the following languages: Spanish and English.

Exclusion Criteria for the Studies

- Studies published outside the established time range.
- Studies that did not use accepted and validated assessment measures to evaluate health-related quality of life and psychological well-being.
- Case series with less than 20 patients.
- Studies in which risankizumab treatment was for psoriatic arthritis.
- Editorials and narrative reviews.

Management, Data Extraction, Data Synthesis, and Analysis of Methodological Quality

The results obtained by the searches were downloaded to a bibliographic reference manager (Mendeley®), where the papers were filtered based on the title and abstract. During this process, all the duplicate, discarded, and selected

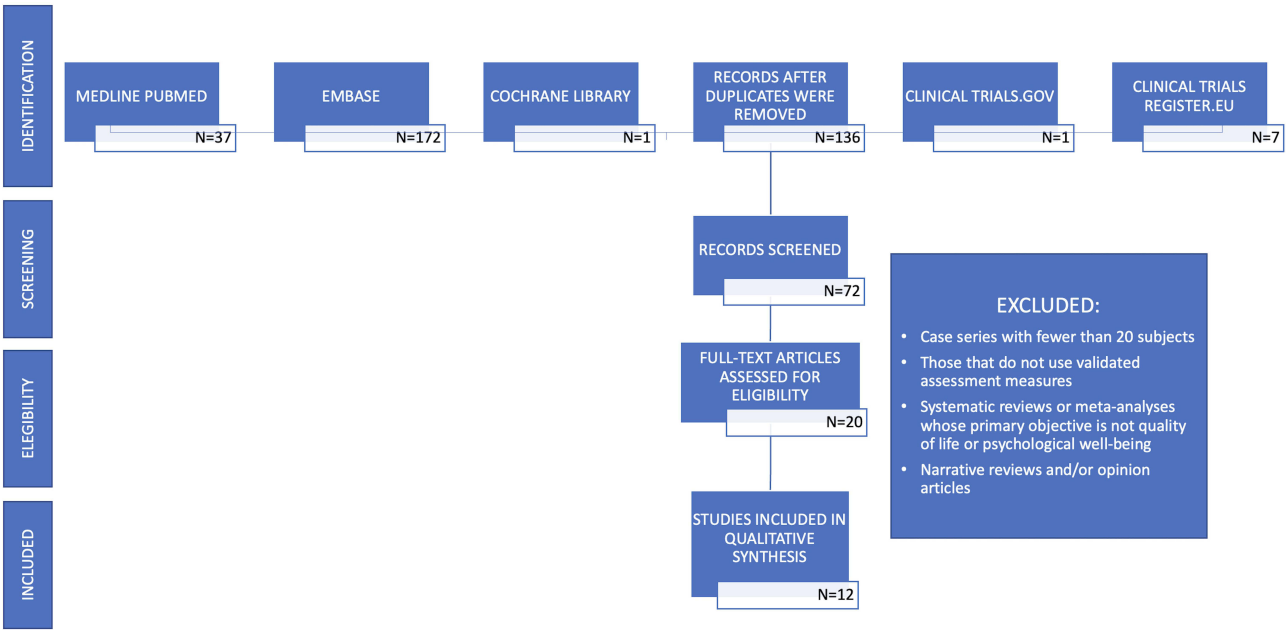

Figure 1 Flowchart of the bibliographic search carried out in the systematic review.

references have been recorded in a flow chart (Figure 1). The search was not blind in terms of authors, journal, or institution.

The Jadad scale for randomized trials[8] has been consulted, and the critical analysis has been based on the CONSORT guide.[9] To synthesize the data, the OSTEBA tool has been used, since it allows the quality of the evidence from the various types of studies to be assessed, in addition to preparing summary tables of results.[10]

Results

Included and Excluded Studies

Of the 218 records obtained, 198 were excluded after evaluating the title and abstract, and due to duplication in the search databases. Twenty articles have been evaluated in full text, of which 8 were excluded because they did not meet the inclusion criteria or had a small number of patients, as well as the systematic reviews whose primary objective was to evaluate only efficacy and safety, (Figure 1).[11–18]

Given the small number of clinical trials and systematic reviews, case series have been included, despite the fact that the evaluation of efficacy and effectiveness in them is very limited.[19–30] The studies that have been evaluated are: 8 clinical trials with high evidence,[19,20,23–26,28,29] 3 case series, one prospective,[21] and 2 retrospective,[22,27] of which the evidence is of low quality, and a cohort study of medium evidence quality.[30]

The studies have been carried out in Europe, the United States, and Japan. The follow-up period, the number of patients, the characteristics of the study population, and the applied intervention in the included studies are summarized in Table 1.

Sample Size

The number of participants in the included studies varied considerably, with a maximum of 1276[25] and a minimum of 20[21,30] with a total of 5035 patients analyzed. The mean number of participants was 419.5.

Participants

All studies included adults over 18 years old with moderate to severe chronic plaque psoriasis, both men and women.[19–29] One study only included patients with genital psoriasis.[30]

Table 1 Summary of the Articles Included in the Review, Number of Patients, Intervention, Type of Study, Results, and Level of Evidence

Reference	Type of Study	Number of Participants	Intervention and Monitoring	Results	Quality of the Evidence
Augustin et al[19]	**Design: Clinical Trial** **Aim**: To compare patient-reported outcomes (PROs) with RZB vs UST and PBO in psoriasis symptoms, health-related quality of life (HRQL), and mental health among patients with moderate to severe psoriasis. **Pivotal trial patients**:[31] *UltIMMa-1 Design: multinational, multicenter, randomized, double-blind, placebo controlled study. Phase III *UltIMMa-2 Design: multinational, multicenter, randomized, double-blind, placebo controlled study. Phase III **Primary endpoints**: PASI 90 and sPGA 0/1 at week 16	**UltIMMa-1 (N=**506) **UltIMMa-1 (N=**491) (RZB= 598)	**UltIMMa-1** Randomised 3:1:1 to either RZB 150 mg, UST 45 mg or 90 mg (weight-based per label) for 52 weeks, or PBO for 16 weeks followed by RZB through to 52 weeks. **UltIMMa-2** Randomised 3:1:1 to either RZB 150 mg, UST 45 mg or 90 mg (weight-based per label) for 52 weeks, or PBO for 16 weeks followed by RZB through to 52 weeks.	At week 16, a significantly greater proportion of patients treated with RZB than those treated with UST or PBO achieved: • **PSS** = 0, indicating no psoriasis symptoms (RZB: 30.3%, UST 15.1%, PBO 1.0%, *P* <.001). • **DLQI** = 0 or 1 indicating no impact on skin- HRQL (RZB 66.2%, UST 44.7%, PBO 6.0%, *P* <.001). • **MCID for DLQI** (RZB 94.5%, UST 85.1%, PBO 35.6%; both *P* <.001). • **EQ-5D-5L** (RZB 41.7% vs UST 31.5%, *P* =.01; vs PBO 19.0%, *P* <.001) • **HADS** (anxiety: RZB 69.1% vs UST 57.1%, *P* =.004; vs PBO 35.9%, *P* <.001; depression: RZB 71.1% vs UST 60.4%, *P* =.01; vs PBO 37.1%, *P* <.001). At week 52, improvements in patients treated with RZB compared with those treated with UST were sustained for PSS, DLQI, and EQ-5D-5L.	High
Papp et al[20]	**Design: Clinical Trial** **Aim**: To evaluate the impact of RZB withdrawal on HRQL measured by DLQI. Because DLQI was not measured beyond week 16 in IMMhance, a machine learning predictive model for DLQI was developed. **Pivotal trial patients**:[31–33] UltIMMa-1, UltIMMa-2, IMMvent, and IMMhance *IMMhance Design: multinational, multicenter, randomized, double-blind, placebo controlled study. Phase III **Endpoints**: PASI 90 and sPGA 0/1 (clear/almost clear) at week 16. *IMMvent Design: multinational, multicenter, randomized, double-blind, placebo controlled study. Phase III **Endpoints**: PASI 90 and sPGA 0/1 at week 16 (Part A) and PASI 90 at week 44 (Part B; for re-randomised patients only).	**UltIMMa-1** 506 **UltIMMa-1** 491 **IMMvent** 605 **IMMhance** 507 (Sample used for DLQI, RZB=111)	**IMMhance** Randomised 4:1 to either RZB 150 mg or PBO, followed by RZB starting at week 16. At week 28, patients randomised to RZB achieving sPGA 0/1 were re-randomised 1:2 to continue RZB or PBO. **IMMvent** Randomised 1:1 to either RZB 150 mg or Humira 40 mg EOW. At week 16, Humira-treated intermediate responders (PASI 50 to PASI <90) were re-randomised 1:1 to continue Humira or RZB, and Humira-treated non-responders (<PASI 50) switched to RZB.	The machine learning predictive model demonstrated good statistical fit during tenfold cross-validation and external validation against observed **DLQI** at weeks 0–16 of IMMhance (N = 507). Predicted improvements in DLQI from baseline were lower in the withdrawal versus the continuation cohort (mean DLQI change at week 104, −5.9 versus −11.5, difference [95% CI] = 5.6 [4.1, 7.3]). Predicted DLQI deteriorated more extensively than PASI (49.7% versus 36.4%) after treatment withdrawal.	High
Ruiz-Villaverde et al[21]	**Design: Case Series** **Aim**: To assess the effectiveness and safety results of risankizumab to control patients with moderate-to-severe psoriasis. **Endpoints**: PASI, BSA, VAS pruritus score, DLQI	RZB=20	An observational, longitudinal, retrospective study of real clinical practice from May to November 2020 in patients with psoriasis undergoing treatment with RZB.	The mean DLQI score at baseline was 13.64 ± 4.80 and at week 16 the mean DLQI was less than 1.	Low
Mastorino et al[22]	**Design: Case Series** **Aim**: The objectives were to evaluate the effectiveness and safety of Risankizumab and to investigate on possible predictor factors response as previous biologic experience. **Endpoints**: PASI, DLQI	RZB =236	A retrospective multicentre study with the aim of analysing the efficacy and safety of RZB at 16, 28, 40 and 52 weeks in adult psoriatic patients.	**DLQI** fell from a mean of 19.4 at baseline to 1 and 0.8, at 40 and 52 weeks respectively (p<0.001), with a DLQI 0/1 response of 78% and 83%.	Low
Lebwohl. et al[23]	**Design: Clinical Trial** **Aim**: This study aimed to estimate the duration of PASI 90 and DLQI 0/1 among patients with moderate to severe psoriasis receiving RZB and other treatments. **Endpoints**: PASI 90, DLQI 0/1 **Pivotal trial patients**: *UltIMMa-1, UltIMMa-2, IMMvent, and IMMhance	Overall population: =2101 RZB only=895 RZB and RZB/PBO=406 ADA and ADA/RZB=303 PBO/RZB=300	UltIMMa-1, UltIMMa-2, IMMvent, and IMMhance	Patients treated with only RZB throughout the study period experienced the longest **DLQI** 0/1 duration from baseline to week 52 [213.7 days (59% over 1 year)], followed by patients who received ADA and ADA/RZB [159.1 days (44% over 1 year)], and only UST [144.3 days (40% over 1 year)]. Patients who received PBO/RZB had the shortest DLQI 0/1 duration during the 52-week study period [90.5 days (25% over 1 year)].	High

(*Continued*)

Table 1 (Continued).

Reference	Type of Study	Number of Participants	Intervention and Monitoring	Results	Quality of the Evidence
Papp et al[24]	**Design: Clinical Trial** **Aim**: This study aimed to evaluate the long-term efficacy and safety of RZB for the treatment of psoriasis among patients who have participated in multiple phase 2/3 studies. **Pivotal trial patients**: *LIMMitless is an ongoing, phase 3, single-arm, global, multicentre, open-label extension study. **Endpoints**: PASI 90 and PASI 100, sPGA 0/1, and DLQI 0/1.	RZB=97	The LIMMitless study is designed for all patients to receive RZB 150 mg subcutaneously every 12 weeks for 252 weeks.	After 16 weeks of RZB treatment, >66% of patients achieved **DLQI 0/1**; this percentage increased to > 77% after 52 weeks of treatment and >78% after 172 weeks of treatment. More than half of patients (56.9%) achieved both PASI 90 and DLQI 0/1 after 16 weeks of treatment; this percentage increased to ≥70% in the LIMMitless study and remained stable through 172 weeks of treatment.	High
Lebhow et al[25]	**Design: Clinical Trial** **Aim**: To assess the impact of PASI response on total work productivity impairment (TWPI) in patients with moderate to severe psoriasis; to compare TWPI and associated indirect costs among patients treated with RZB, ADA, UST, and PBO. A machine learning model used REVEAL data to predict TWPI for patients in the RZB trials. **Endpoint**: Work loss hours and work impairment-related indirect costs for each treatment cohort. **Pivotal trial patients**: This study utilised data from one phase III, randomised clinical trial of adalimumab (REVEAL)[34] and four phase III, randomised clinical trials of risankizumab (UltIMMa-1, UltIMMa-2, IMMvent, IMMhance for the treatment of moderate to severe psoriasis.	UltIMMa, IMMvent, and IMMhance=2046 REVEAL=741 RZB=1276	Data from REVEAL (adalimumab Phase III trial) was used to assess differences in trial-observed TWPI across PASI response cohorts.	TWPI was measured at baseline and week 16 by **WPAI** questionnaire. In the RZB trials (N.2046), incremental TWPI relative to RZB was 3.4%/week for UST/ADA, and 17.1%/week for placebo; incremental indirect cost savings for RZB were $2179/year vs adalimumab, $2321/year vs UST, and $11,284/year vs placebo.	High
Ohtsuki et al[26]	**Design: Clinical Trial** **Aim**: The SustaIMM study conducted in Japan evaluated the efficacy and safety of two different dose regimens of RZB in patients with moderate to severe chronic plaque psoriasis. It is a phase 2/3, double-blinded, placebo-controlled study. **Endpoint**: PASI-90 at 16 weeks.	RZB=171	SustaIMM: Patients were randomised 2:2:1:1 to receive RZB 75 mg, RZB 150 mg, placebo with cross-over to RZB 75 mg or PBO with cross over to RZB 150 mg. The results are up to week 52 of treatment.	Significantly higher proportions of patients achieved a **DLQI** of 0 or 1 with RZB 75 mg and 150 mg versus placebo at week 16 (62.1% and 58.2% vs 5.2%, respectively; $P < 0.001$. At week 52, DLQI 0/1 response rates among patients continuously receiving RZB 75 mg and 150 mg were 75.9% and 80.0%, respectively. DLQI 0/1 response rates among patients previously receiving placebo who were switched to RZB 75 and 150 mg increased from week 16 to 52, reaching 66.7% and 81.5%, respectively, at week 52.	High
Gkalpakiotis et al[27]	**Design: Case Series**, a retrospective multicentre study. **Aim**: To analyse data on adult patients treated with RZB for moderate to severe psoriasis at 18 centres in the Czech Republic compiled in the BIOREP registry. **Endpoints**: Baseline characteristics included data on comorbidities, demographics, previous therapies, DLQI score, and PASI 90 and 100 after 16, 28, and 52 weeks.	RZB=154	Patients who received at least one dose of RZB 150 mg administered subcutaneously.	The mean (± SD) **DLQI** score at baseline was 14.9 ± 6.5, which decreased to 2.1 ± 3.2 after 16 weeks, to 1.0 ± 1.9 after 28 weeks, and to 0.5 ± 1.1 after 52 weeks of therapy. At week 16, patients who achieved a PASI 100 response had a greater reduction in the DLQI than those with a PASI 90 response. In the PASI 100 group, DLQI decreased by 15.9 points compared to 11.8 in the PASI 90 group ($P = 0.033$).	Moderate
Thaçi et al[28]	**Design: Clinical Trial** **Aim**: To evaluate PROs in patients treated with RZB compared with FAEs. Clinical trial, 3 phase 3, randomised, active-controlled and open label study with blinded efficacy assessment conducted at 21 sites in Germany. **Endpoints**: PSS, DLQI, SF-36v2, PBI, HADS, Patient Global, PtGA, and EQ-5D-5L. PROs were assessed at weeks 0, 16, and 24.	RZB=59 FAE=55	Patients were randomised 1:1 to receive either RZB 150 mg subcutaneous at weeks 0, 4, and 16 or FAEs (oral Fumaderm, initial 30 mg per tablet or Fumaderm 120 mg per tablet). Patients with severe plaque psoriasis, defined as BSA>10%, PASI score >10 DLQI score >10.	A significant **PSS** improvement was observed with RZB vs FAEs at weeks 16 and 24 for total and psoriasis-associated redness, itching, and burning scores ($P < 0.001$). **DLQI** scores were significantly lower with RZB vs FAEs, with least squares (LS) mean differences of 7.4 and 7.6 at weeks 16 and 24, respectively (both $P < 0.001$). Patients randomised to RZB also had larger improvements in **SF-36, HADS, PtGA, and EQ-5D-5L** index (all $P \leq 0.002$) at weeks 16 and 24 compared with FAEs. **PBI** was significantly higher, indicating greater benefit, with RZB vs FAEs, with an LS mean difference of 1.1 and 1.3 at weeks 16 and 24, respectively (both $P < 0.001$).	High

(*Continued*)

Table 1 (Continued).

Reference	Type of Study	Number of Participants	Intervention and Monitoring	Results	Quality of the Evidence
Gooderham et al[29]	**Design: Clinical Trial Post-Hoc Analysis**. **Aim**: To assess the achievement of absolute PASI thresholds and related improvements in HRQoL in patients with moderate to severe plaque psoriasis treated with RZB compared with UST, and long-term (>52 weeks to 172 weeks) RZB. Data from patients randomised to 150 mg RZB, or 45 mg or 90 mg UST in replicate randomised controlled trials UltIMMa-1 and UltIMMa-2 and LIMMitless. **Endpoints**: Absolute PASI levels, mean DLQI scores, and DLQI 0/1.	UltiMMa1 and UltiMMa 2 RZB=598 LIMMitless RZB=598	Data from patients randomised to 150 mg RZB, or 45 mg or 90 mg UST in replicate randomised controlled trials UltIMMa-1 and UltIMMa-2 and LIMMitless.	A significantly greater proportion of RZB treated patients achieved combined absolute PASI ≤ 3 and DLQI ≤ 5 at week 16 and 52 compared with UST patients, the adjusted difference between the 2 treatments was 26.2% [18.6, 33.8 (95% CI)] and 27.2% [19.8, 34.6 (95% CI)] for week 16 and week 52, respectively. Similarly, combined absolute PASI ≤ 1 and DLQI 0/1 was achieved by a greater proportion of RZB patients than UST patients (with adjusted differences between the 2 treatments of 22.1% [15.2, 29.1 (95% CI)] and 30.3% [23.1, 37.6 (95% CI)] for week 16 and week 52, respectively. Low absolute PASI scores corresponded with low mean absolute DLQI scores through to week 172 of continuous RZB treatment.	High
Sotiriou et al[30]	**Design: Cohort Study** **Aim**: To compare the efficacy and safety of RZB and IXE in genital psoriasis. **Endpoints**: sPGA-G, PASI, Itch-NRS, DLQI, and AEs.	RZB =20 IXE =16	Patients were assigned by the stratified randomisation process either to RZB or the IXE arm and received treatment at the standard dosing schemes.	Mean percentage decrease from baseline to week 24 was 92.1% and 91.8% for DLQI in the IXE and RZB group, respectively.	Moderate

Abbreviations: ADA, adalimumab; AEs, adverse effects; BSA, body surface area; DLQI, Dermatology Life Quality Index; FAEs, fumaric acid ester; HADS, Hospital Anxiety and Depression Scale; HRQL, health-related quality of life; IXE, ixekizumab; MCID, minimally clinically important difference; NRS, Numerical Rating Scale; PASI, Psoriasis Area Severity Index; PBI, Patient Benefit Index; PBO, placebo; PRO, Patient Reported Outcomes; PSS, Psoriasis Symptoms Scale; PtGA, Patient Global Assessment of Disease Activity; RZB, risankizumab; sPGA, static Physician's Global Assessment; TWPI, Total Work Productivity Impairment; UST, ustekinumab; VAS, Visual Analogue Scale; WPAI, Work Productivity and Activity Impairment questionnaire.

Design

Eight of the twelve included studies are clinical trials,[2,19,20,23–26,28] and the rest are case series,[21,22,27] and a cohort study.[30]

Of the studies included, five of them analyze data from the pivotal trials[31] UltIMMa-1, UltIMMa-2, which include active comparator with ustekinumab (UST) and placebo (PBO).[19,20,23,25,29]

In addition, Papp et al[20] and Lebwohl et al[23,25] use data from the IMMvent and IMMhance clinical trials, with active comparator with PBO and adalimumab (ADA).[32,33] Two studies analyze data from the LIMMitless extension clinical trial.[24,29] Ohtsuki et al[26] evaluated data from the SustaIMM trial comparing RZB 75 mg, 150 mg, and placebo. All these trials have a high level of evidence.

Of the studies with a case series design, one of them is based on the BIOREP registry,[27] and analyses patients with moderate-severe psoriasis in the Czech cohort treated with RZB; another article from a real clinical practice carried out in Spain analyses the effectiveness and safety of RZB.[21] Mastorino et al[22] studied whether there are differences in response to risankizumab in patients with bio-naive psoriasis versus bio-experience.

Finally, a cohort of patients with genital psoriasis has been included in which the efficacy and safety of risankizumab versus ixekizumab in genital psoriasis has been evaluated.[30]

Outcome Measures

The results, as well as the methodology and the quality of the evidence, are represented in Table 1. In the included studies, there was some variation in the method of evaluating the outcomes.

Since there are many tools for measuring the quality of life of people with psoriasis and other skin disorders, studies that have used psoriasis-specific measures have been taken into account. These measures can be categorized as psoriasis-specific (Psoriasis Symptoms Scale [PSS];[19,28] skin-specific (Dermatology Life Quality Index [DLQI];[19–24,26–30] and generic quality of life measures (SF-36),[28] (EQ-5D-5L),[19,28] Hospital Anxiety and Depression Scale (HADS),[19,28] Work Productivity and Activity Impairment Questionnaire (WPAI),[25] Patient Global Assessment of Disease Activity (PtGA),[28] and Patient Benefit Index (PBI).[28]

Discussion

Through the analyzed studies, RZB has shown to achieve a very significant improvement in the quality of life of patients compared to other drugs analyzed, especially in those who have not previously received any biological treatment.[22] Compared to UST, at week 16, 66.2% of patients achieved a DLQI 0/1 versus 44.7% with UST.[19] In the IMMvent and LIMMitless studies, these improvements were shown to increase to 77% and 78% at weeks 57 and 172, respectively.[24] Similar improvements were found when evaluating other scales related to quality of life, such as EQ-5D-5L or HADS.[19]

In addition, psoriasis-specific PROs (patient reported outcomes) such as PSS 0, indicating that there are no symptoms of psoriasis, is obtained in 30.3% of patients treated with RZB, compared to 15.1% with UST and 1% with PBO.[19]

When compared with fumaric acid esters (FAEs),[28] the most frequently prescribed first-line systemic treatment in Germany, patients treated with RZB had a lower PSS score compared to those treated with AEDs, which translates into less redness, itching, and burning associated with psoriasis.

On the other hand, patients randomized to RZB showed significant improvements in SF-36, HADS, PtGA, and EQ-5D-5L (<0.002); the benefit of treatment was even assessed from the patient's perspective based on the PBI questionnaire on the patient's therapeutic needs and another on the benefit achieved by the treatment. In this last questionnaire, RZB presented a better score than the FAEs.[28]

In real clinical practice, similar results have been observed; Ruiz-Villaverde et al[21] analyzed the effectiveness and safety of risankizumab in an observational and retrospective study, where they showed that the mean DLQI score at the start of treatment was 13.64 ± 4.80 and at week 16 the mean DLQI was less than 1, correlating with both improvements in PASI, BSA, and the visual analogue scale of pruritus.

Another very important piece of information is job productivity and the indirect costs associated with this disease. Lebwohl et al[25] through the Work Productivity and Activity Impairment Questionnaire (WPAI). The total work productivity impairment (TWPI) in the RZB trials (N.2046), incremental TWPI relative to RZB was 3.4%/week for UST/ADA, and 17.1%/week for placebo; incremental indirect cost savings for risankizumab were $2179/year vs adalimumab, $2321/year vs ustekinumab, and $11,284/year vs placebo.

Due to the systemic and psychological implications of psoriasis, it is necessary to analyse various PROs, both psoriasis-specific and general, in a combined manner, relating them to efficacy data, which allows us to obtain a global vision of the patient's situation. Thus, absolute PASI<1 and DLQI 0/1 were compared, showing adjusted differences of 22.1% [15.2, 29.1 (95% CI)] in patients treated with RZB versus those treated with UST at week 16, and 30.3% [23.1, 37.6 (95% CI)] at week 52.[29] Similarly, the LiMMItless study showed that more than half of patients achieved both PASI 90 and DLQI 0/1 at 16 weeks of treatment (56.9%), and this percentage increased to 70% at week 172.[24]

Lebwohl et al[23] in a Post Hoc Analysis of Four Phase 3 Clinical Trials (UltIMMa-1, UltIMMa-2, IMMvent, and IMMhance) agreed with the LiMMItless study; patients treated with risankizumab during the study period experienced the longest duration of DLQI 0/1: 215.7 days (59% over one year) followed by patients receiving adalimumab, adalimumab/risankizumab, 159.1 days (44% over one year) and ustekinumab, 144.3 days (40% over one year). The patients who received PBO/risankizumab maintained the DLQI 0/1 for less time, 90.5 days (25% over one year).

Even small differences in PASI can be significant when assessing the implications for patients' quality of life. In a Czech cohort of patients with moderate-severe psoriasis treated with RZB at week 16, patients with a PASI 100 response achieved greater reductions in DLQI compared with those who achieved a PASI 90 response (15.9 points vs 11.8 p<0.033).[27,34]

In addition, the DLQI deteriorates more rapidly than the PASI when treatment is discontinued (49.7% versus 36.4%) based on predictive models.[20]

Regarding the RZB dose, the DLQI 0/1 response rate is very good with both RZB 75 mg and 150 mg, both being much higher than the placebo (62.1% and 58.2% versus 5.2%, respectively). However, when the placebo group of patients was re-randomized to receive risankizumab 75 mg and 150 mg, the DLQI 0/1 response rates increased from week 16 to week 52 to 66.7% and 81.5%, respectively.[26]

On the other hand, the impact of RZB on special areas, such as the genitals, has also been studied. Sotiriou et al[30] compared the efficacy and safety of risankizumab vs ixekizumab in this area, demonstrating a reduction in DLQI from

baseline to week 24 of 91.8% and 92.1%, respectively, obtaining similar rates for PGA-G, falling to 0.3 and 0.4, respectively.

Limitations

The lack of SCOPUS database search and practical limitations when assessing the risk of bias in non-randomized studies.

In conclusion, risankizumab has shown not only to have very relevant data on effectiveness and safety, but all of this is associated with an improvement in quality of life related to health and psychological well-being measured on generic and specific quality of life scales, both in pivotal trials, ad hoc analysis, and data in real clinical practice.

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Disclosure

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