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Research Article

2-Year Experience with Risankizumab in the Treatment of Plaque Psoriasis in Lazio Region, Italy

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Background. Given the chronic relapsing, remitting course of psoriasis, data about long-term effectiveness may be useful to assess the maintenance of clinical response over time. *Objective*. To evaluate 2-year drug survival of risankizumab and identify any predictive factor of discontinuation for ineffectiveness. *Materials and Methods*. A multicenter retrospective study was conducted in patients who initiated risankizumab between July 2019 and December 2020. PASI was measured at baseline and after 104 weeks. Any adverse event was registered during visits. Univariable and multivariable logistic regressions were used to assess baseline patients' characteristics that predicted clinical response. The drug survival analysis was descriptively performed using the Kaplan–Meier survival curve. *Results*. 112 patients with moderate-to-severe plaque psoriasis were included. The overall median observation time was 35.3 months (26.7–37.3); the estimated survivor cumulative function at months 12 and 24 was 93.6% and 90.6%, respectively. No differences in BMI, disease duration, disease severity, or previous biological therapies were observed in patients who responded or did not respond to treatment. No significant adverse events were reported, but there was relapse of psoriatic arthritis and ulcerative colitis in a patient. *Conclusions*. We found that risankizumab was associated with long-term effectiveness, and a favorable safety profile in a population of psoriatic patients was observed, over a period of 2 years.

1. Introduction

Psoriasis is an immune-mediated inflammatory disease with a chronic course, which requires a long-term management. The progress in the knowledge of psoriasis pathogenesis enabled the development of new biologic therapies that target interleukins (ILs) with a specific role in the inflammatory cascade. IL-23 is a cytokine, produced by dendritic cells and composed by the p40 and p19 subunits, inducing the differentiation of Th17 cells and therefore the production of IL-17A, a key effector of psoriatic inflammation [1, 2]. IL-23 inhibitors (risankizumab, guselkumab, and tildrakizumab) are highly effective drugs with a favorable safety profile [1]. In particular, risankizumab is a humanized immunoglobulin G1 (IgG1) monoclonal antibody which binds the p19 subunit of IL-23 and approved by FDA and EMA in April 2019 for the treatment of moderate-severe psoriasis. Risankizumab has shown high levels of efficacy in 17-phase I–III clinical trials [3, 4], with about 75% of patients with moderate-to-severe psoriasis achieving PASI90 at week 16. These data have been confirmed by several real-world studies [5, 6]. However, the majority of these reports described the short-term effectiveness of risankizumab, and to date, data about the long term are scarce [7–9].

Therefore, additional data may be useful to assess the maintenance of clinical response over time with this drug.

We performed a retrospective, Italian multicenter study with the primary objective to evaluate the 2-year drug survival of risankizumab in the treatment of moderate-to-severe plaque-type psoriasis in a real-world setting in the Lazio region.

2. Materials and Methods

We performed a multicenter, retrospective, observational analysis in patients with chronic plaque psoriasis who started treatment with risankizumab between July 2019 and December 2020.

We included adult male and female patients (>18 years) with psoriasis attending the outpatient psoriasis clinics of nine Italian referral centers (Policlinico Universitario Fondazione A. Gemelli IRCCS; IFO San Gallicano; Ospedale Sant'Andrea, Università di Roma La Sapienza—Polo Pontino; Università Campus Biomedico; Policlinico Umberto I; Ospedale Nuovo Regina Margherita; Istituto Dermopatico dell'Immacolata—IDI; Policlinico Tor Vergata; and Ospedale di Belcolle, Viterbo) in Lazio, Italy. Exclusion criteria were as follows: generalized, erythrodermic, or palmoplantar pustular psoriasis; use of systemic therapies for psoriasis in addition to risankizumab; and participation in clinical trials. All patients were treated with risankizumab at the EMA approved dosage (150 mg administered by subcutaneous injection at week 0, week 4, and every 12 weeks thereafter).

We collected data related to the characteristics of the patients (age, sex, and BMI) and of the disease (age at onset, duration of psoriasis, and previous treatments). The severity of psoriasis was measured with the Psoriasis Area and Severity Index (PASI) score at baseline and after 104 weeks of treatment. Any adverse event that occurred during treatment with risankizumab was recorded.

Descriptive data were summarized using means and standard deviations (SDs) or medians and interquartile ranges (IRs) for continuous variables after testing for their normal distribution; categorical variables were described using absolute and relative (%) frequencies. Univariable and multivariable logistic regressions were used to assess baseline patients' characteristics that predicted clinical response. The drug survival analysis was descriptively performed using the Kaplan–Meier survival curve. The event considered for discontinuation was the main reason of discontinuation, ineffectiveness, and adverse events or other reasons. Patients were censored when lost to follow-up or when the database was extracted and patients were actively undergoing their treatment. Statistical significance was set at p value <0.05. Analyses were performed by using Stata 13.0 Software (StataCorp, Texas).

The Institutional Review Board's approval was not required for this study because all the procedures did not deviate from routine clinical practice. The study was performed following the principles of the Declaration of Helsinki.

3. Results

Data regarding 112 patients with moderate-to-severe psoriasis were analyzed. The mean age of the patients was 47.7 years (SD 13.8), and the majority of patients (63.4%) were males. The median PASI score at baseline was 15.2 (IR 10.0–20.0). The demographic and clinical characteristics of the study population are reported in Table 1. Data about the first 52 weeks of treatment have been already reported [10], and PASI90 response was achieved by 95.24% of patients at the last follow-up visit (as observed by the analysis). At week 104, 93 of 112 (83.0%) patients were still on treatment, with median PASI and DLQI scores of 0.0 (IR 0.0-0.0). The overall median observation time was 35.3 months (26.7–37.3); the estimated survivor cumulative function at months 12 and 24 was 93.6% and 90.6%, respectively. The Kaplan–Meier estimated drug survival curve is depicted in Figure 1.

In detail, the reasons for discontinuation were as follows: ineffectiveness in 5 (4.5%) patients, remission of psoriasis in 3 (2.7%) patients, arthroplasty surgery in 1 (0.9%) patient, relapse of psoriatic arthritis and ulcerative colitis in 1 (0.9%) patient, and loss to follow-up in 9 patients (8.0%). The median time for discontinuation was 25.0 (IR 16.5–52.0) weeks after the starting of treatment.

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Table 1: Clinical and demographic characteristics of the study population.

Characteristics (total $n = 112$)	N (%); median (IQR)
Gender	
Male	71 (63.4)
Female	41 (36.6)
Age	48 (39.5–57.0)
BMI	27.0 (24.0–29.4)
Arthropathy	
No	83 (74.1)
Yes	29 (25.9)
Family history	
No	54 (54.5)
Yes	45 (45.4)
Age of onset	24 (16.0–35.0)
Treatment duration (mo) with risankizumab	15.2 (8.5–17.2)
Previous treatment	
Phototherapy	37 (33.6)
Cyclosporine	79 (71.2)
Methotrexate	61 (54.9)
Acitretin	29 (26.4)
Apremilast	8 (7.3)
Infliximab	9 (8.2)
Etanercept	35 (8.2)
Adalimumab	41 (36.9)
Golimumab	2 (1.8)
Certolizumab	1 (0.9)
Ustekinumab	21 (19.1)
Secukinumab	17 (15.6)
Ixekizumab	6 (5.4)
Guselkumab	7 (6.4)
Brodalumab	3 (2.7)
Last biologics prior to risankizumab	
Naïve	47 (42.0)
Anti-TNFα	35 (31.2)
Anti-IL17	15 (13.4)
Anti-IL23 or anti-IL12/23	15 (13.3)
Treatment suspension	
No	93 (83.0)
Yes	19 (17.0)
PASI at baseline	15.2 (10–20)
PASI at week 104	0.51 (0.0–0.8)

In Table 2, we reported the baseline clinical and demographic characteristics of patients who have withdrawn the drug because of ineffectiveness. The mean age of the patients was 54 years (SD 16.86), and 60% were males. The median age at the diagnosis of psoriasis was 23 years (IR 20.00–31.00), with a median disease duration of 37 years (IR 11.00–38.00). The majority (60%) had a family history of psoriasis. The median PASI score at baseline was 8.1 (IR 6.50–10.20), the median BMI was 26.78 (IR 26.12–27.68), and 80% of patients were bioexperienced. No significant differences in BMI ($p = 0.221$), disease duration ($p = 0.251$), severity ($p = 0.058$), or previous biological therapies ($p = 0.161$) were observed in patients who responded compared to those who did not respond to treatment.

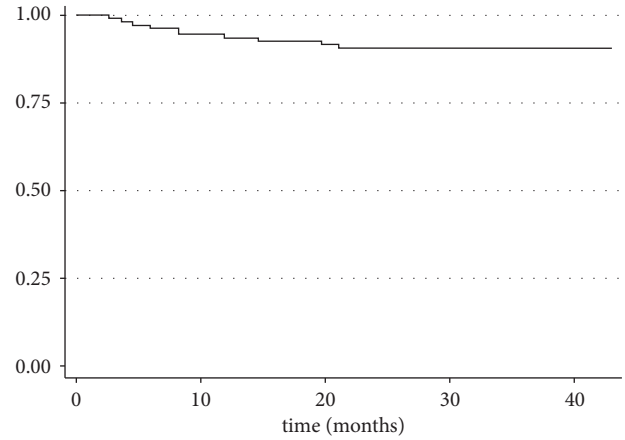

Figure 1: Kaplan–Meier survival curve (ineffectiveness, adverse events, and other reasons for drug discontinuation).

No serious adverse events were reported, but there was relapse of psoriatic arthritis and ulcerative colitis in one patient.

One patient suspended temporarily the administration of risankizumab due to SARS-CoV-2 infection, resuming the therapy after testing negative.

4. Discussion

A wide variety of systemic treatments is currently available for moderate-to-severe psoriasis. Drug survival is a real-life indicator of effectiveness and safety of a drug in the long term, representing an important parameter in the management of a chronic condition such as psoriasis. In this study, we evaluated the drug survival of risankizumab, an anti-IL-23 agent approved for the treatment of moderate-to-severe plaque psoriasis. The estimated survivor cumulative function after 2 years was 90.6%, confirming the high rate of persistence in treatment with this drug for patients with plaque psoriasis [4]. In line with our study, Torres et al. reported a retrospective, multinational, multicenter cohort study evaluating drug survival of IL-17 and IL-23 inhibitors for the treatment of psoriasis. Treatment courses included in the study were 4,866 (4178 patients), 1,702 of which with an IL-23 inhibitor. After 24 months of therapy, the drug survival rate of risankizumab was 0.92 (95% confidence interval (CI): 0.89–0.95), which was higher than that of other biologic therapies [11]. Some authors suggested that this remarkable long-term effectiveness may be due to the inhibition of tissue resident memory cells, involved in psoriasis pathogenesis and responsible for recurrences in clinically resolved psoriatic lesions [12]. One recent study focusing on another IL-23 inhibitor, guselkumab, showed its ability to modify the phenotype of immune cells in psoriatic skin lesions. Indeed, it reduced memory T cells and maintained regulatory T cells, exerting a disease modification effect, which could prevent disease recurrences [13]. Although there is no evidence on the impact of risankizumab

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Table 2: Characteristics of the study population who discontinued the treatment.

Patients who discontinued the drug for ineffectiveness	Sex	Age (years)	BMI	Comorbidities	Disease duration (years)	PASI at baseline	Previous biological therapies	Time of suspension (weeks)
#1	M	69	26.12	Abdominal aortic aneurysm and hypercholesterolemia	38	10.2	Ustekinumab	86
#2	F	60	28.52	—	51	8.1	Secukinumab	64
#3	M	59	27.68	—	11	25.0	Ustekinumab	92
#4	F	57	25.39	Psoriatic arthritis and hypertension	37	6.5	Secukinumab	20
#5	M	25	26.78	—	2	6.4	None	12

M: male; F: female.

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on the immune phenotype of skin lesions, we may assume that it might have an effect similar to guselkumab on the basis of similarities between the two drugs. Another reason for the high persistence in treatment with risankizumab may be the high level of tolerability of this drug [4–6], as confirmed in our patients.

On the other hand, approximately 10% of patients lost to follow-up in our population might be due to the concurrent SARS-CoV-2 pandemic and its impact on the outpatient visits and access to hospitals during 2019-2020. No adverse events were observed in our patients, except for a relapse of psoriatic arthritis and ulcerative colitis in one patient, which occurred 16 weeks after starting risankizumab. However, this patient had previously been treated with adalimumab, an antitumor necrosis factor (TNF) alpha monoclonal antibody approved for both psoriatic arthritis and ulcerative colitis. Therefore, it is likely that the disease relapse was caused by the discontinuation of adalimumab rather than the initiation of the new therapy. Despite the limitation of the small sample size of our study, we did not find any factor that significantly impacted treatment discontinuation. There were no significant differences in terms of BMI, disease duration, severity, or previous biological therapies in patients who responded or not responded to the treatment. The current real-life literature only partially aligns with our findings. Several real-life studies have reported that BMI, psoriatic arthritis, and previous biologic failure may be associated with a reduced treatment response [7, 14–16]. In contrast, other studies did not find this correlation [8, 17, 18], which confirms our data and suggests that risankizumab could be used also in special categories of patients with unfavorable characteristics, such as obese, multitreated ones, or those with very severe disease.

Other limitations of the study are (a) the patient population that is confined to the Lazio Region and might not be the representative of the entire Italian population and (b) the small number of patients that discontinued risankizumab because of ineffectiveness, thus preventing more robust analysis of predictive factors.

In conclusion, we found that risankizumab was associated with long-term effectiveness and a favorable safety profile in a population of psoriatic patients, over a period of 2 years. We consider this datum worthy of note based on the chronic relapsing-remittent course of psoriasis.

Data Availability

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Conflicts of Interest

G Caldarola has received consulting fees, honoraria, and support for attending meetings from Abbvie, Lilly, Janssen, UCB, Novartis, and Leo Pharma. A Zangrilli has received support for consulting fees, honoraria, and support for attending meetings from Abbvie. L Bianchi has received support for consulting fees, honoraria, and support for attending meetings and taken part in advisory boards for Amgen, Abbvie, Novartis, Janssen-Cilag, Pfizer, UCB, Sanofi, and Leo Pharma. C De Simone has received support for consulting fees, honoraria, and support for attending meetings from Abbvie, Lilly, Janssen, UCB, Novartis, Leo Pharma, Sanofi, and Almirall. K Peris has received support for consulting fees and honoraria from Abbvie, Almirall, Biogen, Celgene, Janssen Galderma, Novartis, Lilly, Novartis, Pierre Fabre, Sandoz, Sanofi, and Sun Pharma. A. Dattola has received support for consulting fees and honoraria from Amgen, Abbvie, Novartis, Janssen, UCB, Leo Pharma, Ely Lilly, and Almirall. G. Pellacani has received support for consulting fees and honoraria from Amgen, Abbvie, Novartis, Janssen-Cilag, UCB, Leo Pharma, Sanofi, Almirall, Eli Lilly, and Galderma. D. Giordano has received consulting fees, honoraria, and support for attending meetings from Abbvie, Almirall, Amgen, Eli Lilly, Fresenius Kabi, Janssen-Cilag, Novartis, and Sanofi. All other authors declare that they have no conflicts of interest relevant to this manuscript.

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