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LETTER TO THE EDITOR

A risankizumab super responder profile identified by long-term real-life observation-IL PSO (ITALIAN LANDSCAPE PSORIASIS)

Dear Editor,

Risankizumab is a humanized monoclonal antibody that targets interleukin (IL-)23, approved for the treatment of moderate-to-severe plaque psoriasis, which has shown efficacy in both clinical trials and real-world experiences.[1–4] However, there is still limited knowledge regarding which patients could benefit the most from the therapy with risankizumab.

We report the results of a 156-week multicentre, retrospective, real-world study designed to assess the effectiveness of risankizumab and to identify a possible profile of 'super-responder' patients. Among 1572 patients who received at least one injection of risankizumab at 17 Italian Dermatology Units, we enrolled 1047 patients who had completed at least one follow-up visit. The effectiveness endpoints were the improvement of 75%, 90% and 100% in Psoriasis Area and Severity Index (PASI) compared with baseline (PASI75, PASI90 and PASI100, respectively) and an absolute PASI ≤ 2.[5] The effectiveness of risankizumab was evaluated according to body mass index, comorbidities, previous treatments, involvement of difficult-to-treat areas and disease duration at Weeks 52, 104 and 156. The chi-square and Fisher's exact tests were used to analyse categorical variables, while continuous data were compared using Student's *t*-test and Mann–Whitney *U*-tests, when appropriate. Subsequently, a multivariate logistic regression analysis was performed for all variables with a probability value (*p*-value) of less than 0.2 in the univariate analysis. Odds ratios (ORs) and 95% confidence intervals (CIs) were reported. A p-value < 0.05 was considered significant. All analyses were performed using STATA/SE 17.0 software. The demographic characteristics of our cohort at baseline are shown in Table 1.

We observed the continuous effectiveness of risankizumab throughout the study, as PASI90 was reached by 81.44% of the patients at Week 52, 88.99% at Week 104 and 99.07% at Week 156. Complete skin clearance was achieved by 65.72%, 73.73% and 74.77% of patients at the same time points (Figure 1a). After 1 year, bio-naive patients were more likely to achieve PASI90 (OR 2.38, CI 1.65–3.44, $p < 0.001$) and PASI100 (OR 1.91, CI 1.40–2.62, $p < 0.001$). Similarly, patients with a short disease history (less than 2 years) had significantly better responses in terms of PASI90 (OR 1.88, CI 1.11–3.18, $p < 0.05$), PASI100 (OR 2.05, CI 1.32–3.19, $p = 0.001$) and PASI ≤ 2 (OR 2.94, CI 1.23–7.05, $p < 0.05$).

TABLE 1 Characteristics of the patients at baseline.

Number of total patients	1572
Number of patients enrolled	1047
	Mean ± SD
Age (years)	51.37 ± 14.95
BMI	28.05 ± 5.66
mPASI at baseline	15.73 ± 7.62
Disease duration (years)	16.03 ± 12.25
	***N* (%)**
Males	705 (67.34)
Obese (BMI ≥ 30)	256 (24.45)
PsA	127 (12.13)
Difficult-site involvement	623 (59.50)
Cardiometabolic comorbidities	535 (51.10)
Viral hepatitis	14 (1.34)
HIV infections	1 (0.10)
TB infections	10 (0.96)
Bio-experienced	446 (42.60)
Anti-TNF-α	283 (27.03)
Adalimumab	183 (17.48)
Etanercept	77 (7.35)
Infliximab	22 (2.10)
Certolizumab	1 (0.10)
Anti-IL-17	289 (27.60)
Secukinumab	153 (14.61)
Ixekizumab	98 (9.36)
Brodalumab	38 (3.63)
Anti-IL-23	15 (2.48)
Guselkumab	24 (2.29)
Tildrakizumab	15 (1.43)
Ustekinumab	126 (12.03)
Apremilast	19 (1.81)

Abbreviations: BMI, body mass index; mPASI, mean PASI; PASI, psoriasis area and severity index; PsA, psoriatic arthritis; SD, standard deviation.

Additional negative predictors of PASI100 were the involvement of at least one difficult-to-treat area and the presence of cardiometabolic diseases (OR 0.66, CI 0.48–0.90, $p = 0.01$; OR 0.60, CI 0.42–0.85, $p < 0.01$). The bio-naive status was a

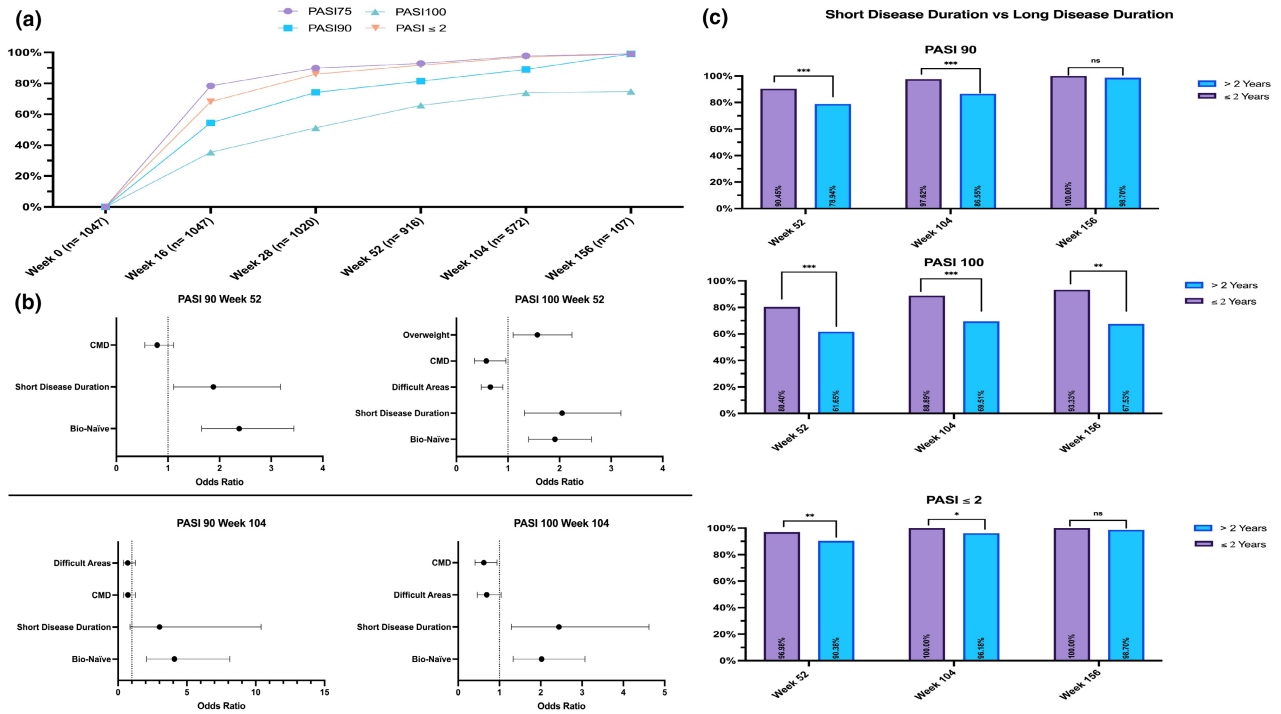

FIGURE 1 Effectiveness of risankizumab throughout 156 weeks in terms of PASI 75, PASI 90, PASI 100 and absolute PASI ≤ 2 (a). Forest plot of variables associated with the likelihood of reaching PASI 90 and PASI 100 at Week 52 and Week 104 (b). Effectiveness of risankizumab according to the disease duration (less than 2 years vs. more than 2 years) (c). CMD, Cardiometabolic Diseases; PASI, Psoriasis Area and Severity Index. **p*-value < 0.05; ***p*-value ≤ 0.01; ****p*-value ≤ 0.001; ns, not significant.

predictor of both PASI90 (OR 4.09, CI 2.06–8.12, $p < 0.001$) and PASI100 (OR 2.02, CI 1.33–3.07, $p = 0.001$) at Week 104, and a predictor of PASI100 at Week 156 (OR 6.31, CI 1.86–21.40, $p < 0.01$). A short history of psoriasis was also a predictor of PASI100 at Week 104 (OR 2.44, CI 1.29–4.62, $p < 0.01$). A graphical representation of the predictors of 'super response' to risankizumab is shown in Figure 1b.

In our experience, patients with shorter disease duration (≤2 years) achieved higher rates of PASI90 and PASI100 after 52 weeks (Figure 1c), supporting preliminary data from the GUIDE trial that showed better responses to guselkumab in this subpopulation.[6] It has been hypothesized[6] that early intervention with anti-IL-23 drugs could promote a balancing in Th17/regulatory T-lymphocytes and control the concentration of tissue-resident memory cells in psoriatic skin. In this way, the IL-23 inhibition could promote a potentially disease-modifying effect.[6] Moreover, patients with longer disease duration are more likely to have previously received more therapies for psoriasis.[7] In our experience, the bio-naive status was independently associated with better responses throughout the study period, consistent with other experiences on IL-23 inhibitors.[8–10]

This study has a few limitations, being its retrospective nature and the heterogeneity of clinical evaluations from different clinicians. However, its main strengths are the large sample size and the extended follow-up, along with the analysis of the subpopulations of patients with a recent history of psoriasis. These initial findings are consistent with preliminary analyses of ongoing clinical trials and need to be further assessed to identify whether selective IL-23 blockade exerts significant modifying effects on disease pathophysiology.

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None.

CONFLICT OF INTEREST STATEMENT

L. Gargiulo has been a consultant for Almirall. P. Malagoli has been a speaker for AbbVie, Lilly, Novartis, Janssen-Cilag, Celgene, Leopharma and Almirall. A. Balato has received honoraria for participation in advisory boards, meetings or as speaker for AbbVie, Celgene, Janssen-Cilag, Eli Lilly, Novartis Pharma, Pfizer, Sanofi-Genzyme and UCB Pharma. F. Bardazzi has been a consultant advisor and clinical study investigator for Eli Lilly, Abbvie, Novartis, Leo Pharma, Sandoz, Bristol Myers, Abiogen-Pharma, Celgene and Janssen. M. Burlando has acted as a speaker and consultant for AbbVie, Janssen, Amgen, Novartis, Eli Lilly and UCB Pharma. C. G. Carrera has served as a board participant or speaker for Abbvie, Lilly, Janssen, Novartis, Celgene, Almirall and Leopharma. G. Damiani served as consultant and/or speaker for AbbVie, Almirall, Bristol-Meyers Squibb, LeoPharma, Novartis, Pfizer, Sanofi and UCB and received unrestricted grants from Pfizer and Almirall. P. Dapavo has been a speaker for Novartis,

Abbvie, Sanofi, UCB, Janssen, Lilly and LeoPharma. G. Fabbrocini acted as a speaker or consultant for Abbvie, Amgen, Eli Lilly, Janssen, Leo-Pharma, Almirall, Novartis, Sanofi and UCB. F. M. Gaiani acted as a speaker or consultant for Novartis, Abbvie, Eli Lilly, Celgene, LeoPharma and Almirall. G. Girolomoni served as consultant and/or speaker for AbbVie, Almirall, Amgen, Biogen, Boehringer-Ingelheim, Bristol-Meyers Squibb, Eli-Lilly, LeoPharma, Novartis, Pfizer, Samsung, Sanofi and UCB. C. Guarneri has been a scientific consultant/speaker/clinical study investigator for Abbvie, Celgene, Janssen, Eli Lilly, Novartis, Pfizer, Sanofi, Almirall and LEO Pharma. C. Lasagni declares a conflict of interest with Abbvie, Novartis, Lilly and Almirall. F. Loconsole served on advisory boards and/or received honoraria for lectures from Abbvie, Janssen-Cilag, Novartis, Lilly and Sanofi. A. V. Marzano reports consultancy/advisory boards disease-relevant honoraria from AbbVie, Boehringer-Ingelheim, Novartis, Pfizer, Sanofi and UCB. M. Megna acted as a speaker or consultant for Abbvie, Eli Lilly, Janssen, Leo-Pharma, UCB and Novartis. F. Sampogna has served as consultant for AbbVie. M. Valenti has been a consultant and/or speaker for Sanofi, Leo Pharma, Eli Lilly, Novartis, Janssen, AbbVie and Boehringer Ingelheim. A. Costanzo has served as an advisory board member, consultant and has received fees and speaker's honoraria or has participated in clinical trials for Abbvie, Almirall, Biogen, LEO Pharma, Lilly, Janssen, Novartis, Pfizer, Sanofi Genzyme and UCB-Pharma. A. Narcisi has served on advisory boards, received honoraria for lectures and research grants from Almirall, Abbvie, Leo Pharma, Celgene, Eli Lilly, Janssen, Novartis, Sanofi-Genzyme, Amgen and Boehringer Ingelheim. L. Ibba, F. Amoruso, G. Argenziano, V. Dini, C. Franchi, M. Maurelli, D. Orsini and M. Travaglini have nothing to declare.

DATA AVAILABILITY STATEMENT

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

ETHICS STATEMENT

Institutional review board approval was exempted, as the study procedures did not deviate from standard clinical practice. All included patients had provided written informed consent for the retrospective analysis of their clinical data. The study was conducted in accordance with the Helsinki Declaration of 1964 and its later amendments.

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