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ORIGINAL RESEARCH

Real-world analysis of IL-23 inhibitors in patients with moderate-to-severe psoriasis and early musculoskeletal symptoms

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Abstract

Background: Psoriasis is a chronic inflammatory condition that may develop into psoriatic arthritis (PsA) in a significant number of patients. Clinical signs such as enthesitis and nail involvement have been suggested as early indicators of this progression. IL-23 inhibitors have demonstrated effectiveness in psoriasis and, more recently, in PsA. This article aims to evaluate the effect of IL-23 inhibitors on clinical outcomes and progression of PsA in patients with moderate-to-severe psoriasis and early musculoskeletal involvement.

Methods: This was a retrospective, multicentre observational study conducted in Italy. Data were collected from 207 adult patients who had already started treatment with guselkumab, risankizumab or tildrakizumab prior to inclusion. All clinical data, including baseline characteristics and follow-up outcomes, were retrieved retrospectively from medical records across eight dermatology centres.

Results: Enthesitis was observed in 44.8% of patients with joint involvement. Guselkumab was the most commonly used treatment (57%) and demonstrated sustained improvements in Psoriasis Area and Severity Index, Visual Analogue Scale pain and Dermatology Life Quality Index scores. Importantly, no patients with enthesitis treated with guselkumab progressed to overt PsA. At 52 weeks, the average Psoriasis Area and Severity Index score was 0.61, Visual Analogue Scale pain score was 0.59 and Dermatology Life Quality Index score was 0.91.

Conclusion: IL-23 inhibitors have proven effective in managing both skin and joint symptoms in patients with psoriasis at risk for PsA. Whilst the findings suggest that IL-23 inhibitors may help control early musculoskeletal symptoms in patients with psoriasis at risk of PsA, the absence of systematic rheumatological evaluation and the retrospective design preclude definitive conclusions about their disease-modifying potential. These results suggest a potential disease-modifying role that warrants further prospective validation.

Keywords: guselkumab, IL-23, psoriasis, psoriatic arthritis.

Citation

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Introduction

Psoriasis is a chronic, immune-mediated skin condition affecting approximately 3% of people worldwide. Amongst those with psoriasis, one-third may eventually develop psoriatic arthritis (PsA), a systemic inflammatory disease that involves the musculoskeletal system. PsA is a significant health concern linked to psoriasis and is known for its varied clinical presentation. The incidence of PsA amongst patients with psoriasis ranges from 0.27 to 2.7 per 100 person-years. Epidemiological research shows that most patients with PsA initially display skin symptoms before developing arthritis. The prevalence of PsA is highest amongst people aged 30–60 and affects both genders equally.[1,2]

Despite extensive research, the relationship between psoriasis and PsA remains only partially understood. Multiple factors are believed to contribute to the transition from psoriasis to PsA, including comorbidities (e.g. obesity, hyperlipidaemia, uveitis, depression, thyroid disease and hyperuricaemia),[1] environmental exposures (such as alcohol consumption or smoking)[3] and genetic predispositions (like polymorphisms in the genes encoding the IL-23 receptor (IL-23R) and TNF-induced protein 3 (TNFAIP3)).[1] Additionally, psoriasis-related factors, such as disease location, nail involvement, psoriasis sub-type and severity, may also influence the risk of developing PsA.[4]

Both psoriasis and PsA significantly affect health-related quality of life. Psoriasis severity is closely linked to symptoms like fatigue, itch and pain, which contribute to functional impairment and decreased work productivity. Patients with PsA face a wide range of issues that affect their physical and emotional health, negatively impacting daily activities, work, leisure and social life.[5,6]

Currently, three IL-23 inhibitors, namely guselkumab, tildrakizumab and risankizumab, have been approved for the treatment of moderate-to-severe psoriasis.[7] Moreover, guselkumab and risankizumab have been demonstrated to be effective for PsA in pivotal phase III trials, specifically DISCOVER-1 and DISCOVER-2 and the KEEPsAKE programmes, and have received regulatory approval for this indication.[8,9]

Numerous studies have previously shown that patients with psoriasis, especially those with nail involvement, involvement of difficult-to-treat areas and a high BMI, are more likely to experience the transition from psoriasis to PsA.[10] This study aims to investigate whether clinical features, such as enthesitis and involvement of difficult-to-treat areas, often seen as early signs of PsA, are linked to disease progression in patients treated with IL-23 inhibitors. We hypothesize that guselkumab might offer a protective effect against progression to PsA.

Methods

Study design, study population and data collection

This was a retrospective, multicentre observational study carried out in real-world clinical practice across eight Italian dermatology centres. Data were gathered from adult patients with moderate-to-severe psoriasis who had already started treatment with IL-23 inhibitors guselkumab, risankizumab or tildrakizumab before entering the study. Baseline characteristics, treatment information and clinical outcomes were retrospectively obtained from patient medical records, beginning from the date they started IL-23 therapy. Importantly, these patients did not have a formal diagnosis of PsA at the time of enrolment because PsA diagnosis was an exclusion criterion at baseline. During follow-up, patients were clinically evaluated for musculoskeletal symptoms by dermatologists; however, no formal rheumatological assessment (e.g. CASPAR criteria) was performed, and no new PsA diagnoses were documented during the study period.

The study population included bio-naive patients (those who had never received biologic treatments) and bio-experienced patients (those who had prior biologic therapy).

Inclusion criteria are detailed in Table 1 and include the following: age ≥18 years; moderate-to-severe psoriasis confirmed by the Psoriasis Area and Severity Index (PASI) score, involvement of difficult-to-treat areas (e.g. scalp, nails, pretibial region or genital area), a Dermatology Life Quality Index (DLQI) assessment, and at least 6 months of prior therapy. The average duration of ongoing treatment at the time of inclusion was 7.3 months (standard deviation (SD) 3.4), with a range from 1 to 14 months. The study period spanned from January 2023 to October 2024 and was carried out across eight centres in Italy (Table 2).

Quantitative and qualitative data were collected using a customized tool that included variables such as treatments (IL-23 inhibitor, specifying guselkumab, risankizumab, or tildrakizumab and treatment duration), demographic information (age, sex, weight, height, age at psoriasis onset, duration in years, and family history of PsA), clinical details (comorbidities and previous treatments), and psoriasis indicators (PASI at 0, 4, 8 and 12 weeks, difficult-to-treat areas, Nail Psoriasis Severity Index (NAPSI), Visual Analogue Scale (VAS) for pain at 0, 4, 8 and 12 weeks, Dermatology Life Quality Index (DLQI) at 0 and 12 weeks, VAS itch scale, presence of fatigue, joints involved, enthesitis and C-reactive protein levels). Ultrasound examination for enthesitis

Table 1. Study inclusion criteria.

	Characteristics
Age	≥18 years
Evaluation of psoriasis according to different parameters:	
Body surface area involvement	≥10%
Physician's Global Assessment score	≥3
Involvement of difficult-to-treat areas (scalp, nails, pretibial and genital area)	
Therapy duration	≥6 months
Diagnosis	Moderate to severe psoriasis without a diagnosis of psoriatic arthritis
Therapeutic history	Bio-naive or bio-experienced
Therapy	Treatment with IL-23 inhibitors (guselkumab, risankizumab or tildrakizumab) ongoing or in the initiation phase
Imaging diagnostics (if available)	Ultrasonographic signs of musculoskeletal inflammation (enthesitis)

Table 2. Centres involved in the study.

Centre
UOC of Dermatology Polo Pontino, Sapienza University of Rome
UOC of Dermatology, Policlinico Umberto I, Sapienza University of Rome
Dermatology Clinic, University of Cagliari
Dermatological Institute San Gallicano Institute, Rome
Dermopatic Institute of Immaculate (IDI) IRCCS, Rome
Dermatology Clinic, Azienda Ospedaliero-Universitaria Ospedali Riuniti di Ancona
Dermatology clinic, AO Santa Maria of Terni
UOC of Dermatology, AO Sant' Andrea, Sapienza University of Rome

was performed only in patients with clinical suspicion of musculoskeletal involvement (e.g. localized pain or swelling at tendon insertions) and was not systematically applied to the entire cohort. Diagnosis of enthesitis was based on sonographic features following current rheumatological imaging criteria. According to the radiology reports, enthesitis was identified based on standard sonographic features, including enthesophyte formation, calcifications, enthesal thickening, and bony erosions, in line with general clinical practice. However, a formal scoring system, such as OMERACT, was not uniformly applied across centres. Patients receiving guselkumab had further follow-up assessments at 24 and 52 weeks.

Outcome measures

Primary end point

The primary end point was to evaluate clinical characteristics and disease features over time, as well as the potential impact of the investigated pharmacological treatments in patients with moderate-to-severe psoriasis.

Secondary end point

The secondary end point was to determine whether the disease progressed under the study treatments (guselkumab, risankizumab or tildrakizumab) in patients diagnosed with enthesitis or with involvement of difficult-to-treat areas, especially nails.

Statistical analysis

Descriptive statistics summarized the data. Continuous variables are presented as the mean (SD), and categorical variables as proportions. All statistical analyses and figures were generated using GraphPad Prism 4.0 (GraphPad Software Inc., La Jolla, CA, USA). Multivariate analyses were performed using R, version 4.0.5 (phyloseq package).

Ethics statement

The Ethics Committee waived the requirement for ethics approval and informed consent for collecting, analysing and publishing the retrospectively obtained and anonymized data in this non-interventional study.

Results

Patient population

Table 3 summarizes the characteristics of the patients. The study involved 207 adult patients with moderate-to-severe psoriasis. The average age was 51.9 years (SD 14.6) and 60% were male. Difficult-to-treat areas were affected in 85% of patients, most commonly the scalp (58.4%), nails (35.7%) and pretibial area

Table 3. Patient baseline characteristics.

Patient characteristics	
Demographic data	
Male	125 (60%)
Age, mean (SD)	51.9 (14.55)
Weight, mean (SD)	74.33 (14.56)
Height, mean (SD)	170.43 (8.66)
Age of onset of psoriasis in years, mean (SD)	31.7 (15.61)
Family history of psoriatic arthritis	85 (41.0%)
Clinical information	
Bio-experienced	90 (52%)
Any comorbidity	115 (55.5%)
• Cardiometabolic	97 (74.7%)
• Gastrointestinal	11 (8.6%)
• Other	47 (16.7%)
Psoriasis indicators	
Baseline PASI index (T0), mean (SD)	13.18 (6.9)
Difficult-to-treat areas (defined as lesions in at least one of the listed areas)	176 (85.0%)
• Scalp	121 (58.4%)
• Nails	74 (35.7%)
• Genital area	66 (31.8%)
• Pretibial area	106 (51.2%)
Baseline VAS pain scale (T0), mean (SD)	3.7 (3.12)
Baseline DLQi, mean (SD)	11 (6.8)
Fatigue	67 (32.4%)
• Years, mean (SD)	5.8 (SD)
Joints involved, mean (SD)	78 (37.7%)
Ultrasound-diagnosed enthesitis	35 (44.8%)
Treatment	
Guselkumab	117 (57.0%)
Tildrakizumab	29 (14.0%)
Risankizumab	61 (29.0%)

DLQI, Dermatology Life Quality Index; PASI, Psoriasis Area Severity Index; SD, standard deviation; VAS, Visual Analogue Scale.

(51.2%). A total of 115 (55.5%) patients had at least one comorbidity, mainly of cardiometabolic type. All patients had already started IL-23 inhibitor therapy at the time of inclusion, with an average treatment duration of 7.3 months (SD 3.4).

Skin response (PASI)

Overall, the average PASI index of the examined population was 13.18 at baseline, 3.86 after 4 weeks, 2.01 after 8 weeks and 0.99 after 12 weeks.

Variation in the average PASI score was similar across the three treatment types: patients treated with guselkumab had an initial PASI of 13.29, which decreased to 4.58 after 4 weeks, then dropped to 2.28 after 8 weeks and reached 0.93 after 12 weeks; patients treated with risankizumab started with an average PASI of 12.72, decreasing to 2.52 after 4 weeks, then dropping to 1.45 after 8 weeks, and finally reaching 0.68 after 12 weeks; patients treated with tildrakizumab had an initial PASI of 13.71, which decreased to 3.75 after 4 weeks, then to 2.11 after 8 weeks, and ultimately reached 1.89 after 12 weeks (Figure 1).

In terms of standard efficacy thresholds, PASI-75, PASI-90 and PASI-100 were reached by a progressively greater proportion of patients at each follow-up visit. At week 4 (T4), PASI-75, PASI-90 and PASI-100 were achieved by 52.5%, 28.5% and 20.7% of patients, respectively. These rates increased to 74.3% (PASI-75), 53.6% (PASI-90) and 42.5% (PASI-100) at week 8 (T8), and further improved at week 12 (T12), when 79.7% of patients achieved PASI-75, 63.2% achieved PASI-90 and 52.1% achieved complete clearance (PASI-100).

In total, 43 patients achieved PASI-0 after only 4 weeks, starting from an average baseline PASI of 13.2. Amongst these, 21 patients were treated with guselkumab, 14 with risankizumab and 8 with tildrakizumab (Figure 2).

Patient-reported outcomes

Overall, the analysed patients had an average VAS pain score of 3.7 at baseline, 1.7 after 4 weeks, 1.0 after 8 weeks, and 0.7 after 12 weeks.

The average DLQI values were 11.05 at baseline and 1.97 after 12 weeks. Amongst patients with challenging-to-treat localizations, DLQI values varied depending on the site. In patients with nail involvement, the mean DLQI at baseline was 11.15 (6.73 SD) and decreased to 2.04 (3.07 SD) after 12 weeks. In patients without nail involvement, these values were 11.81 (7.16 SD) and 1.92 (2.86 SD), respectively.

In patients with scalp involvement, the mean DLQI at baseline was 11.01 (7.87 SD) and decreased to 2.03 (2.86 SD) after 12 weeks. In patients without scalp involvement, these values were 12.41 (6.67 SD) and 1.85 (3.05 SD), respectively.

In patients with genital area involvement, the mean DLQI at baseline was 10.87 (6.22 SD) and decreased to 1.51 (1.90 SD) after 12 weeks. In patients without involvement of the genital area, these values were 11.9 (7.36 SD) and 2.18 (3.31 SD), respectively.

Figure 1. Psoriasis Area and Severity Index (PASI) reduction over time by treatment group. Mean PASI scores at baseline (T0), week 4 (T4), week 8 (T8) and week 12 (T12) for patients treated with guselkumab (GUS), risankizumab (RIS) or tildrakizumab (TIL). PASI is scored on a 0–72 scale. Values are means ± SD. Sample sizes per group: GUS (*n*=117), RIS (*n*=61), TIL (*n*=29).

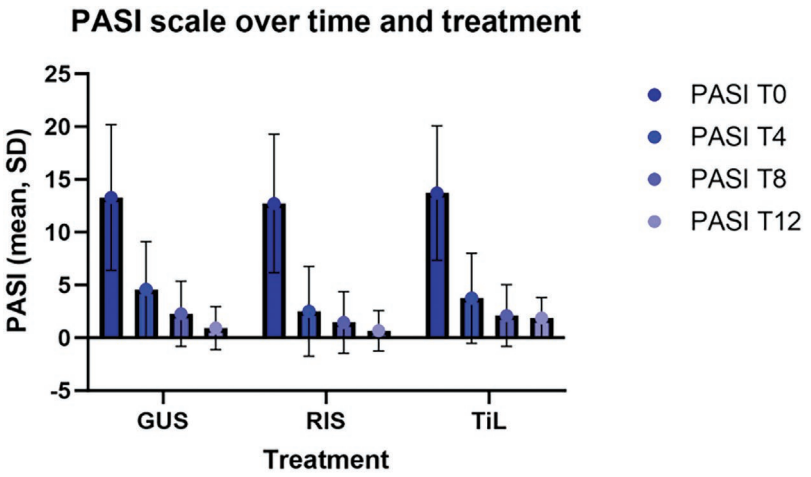
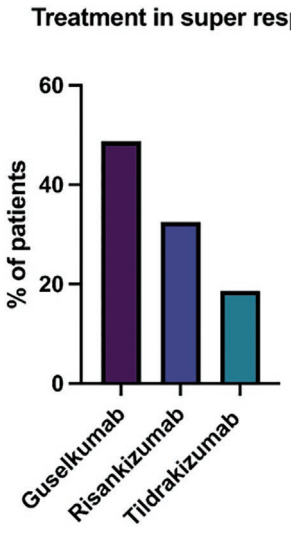


Figure 2. Super-responders (Psoriasis Area and Severity Index (PASI) 0 at week 4) by treatment. Number of patients achieving PASI 0 at week 4 (T4) stratified by treatment. PASI 0 is defined as complete skin clearance. Super-responders were those achieving PASI 0 starting from a baseline PASI of ≥10. Total super responder group: *n*=43.



In patients with pretibial involvement, the mean DLQI at baseline was 11.21 (6.51 SD) and decreased to 2.15 (2.67 SD) after 12 weeks. In patients without pretibial involvement, these values were 11.94 (7.5 SD) and 2.15 (3.20 SD), respectively.

Joint involvement and enthesitis

In this study, at least one joint was involved in 78 patients, with the majority (57%) receiving treatment with guselkumab. The wrists were the most commonly affected joints, followed by the knees, interphalangeal joints, ankles and elbows, in decreasing order of frequency. Interestingly, the analysis did not show a significant increase in the number of affected joints in the presence of comorbidities. Specifically, the average number of affected joints in patients with comorbidities was 2.9, compared to 2.5 in those without comorbidities.

No cases of incident PsA were reported or formally diagnosed during the follow-up period.

Enthesitis was diagnosed in 35 patients (44.8% of those with joint involvement) using ultrasound imaging. Notably, ultrasound was performed only in patients with clinical suspicion of entheseal involvement based on symptoms such as localized pain or reduced function. Amongst the patients with ultrasound-confirmed enthesitis, 66% were bio-experienced.

In patients diagnosed with enthesitis and treated with guselkumab, the average PASI at baseline was 10.51 (*versus* 4.04 in patients without enthesitis); at 4 weeks, it was 3.17 (*versus* 4.62 in patients without enthesitis), at 8 weeks it was 1.78 (*versus* 2.61 in patients without enthesitis), and at 12 weeks, it was 0.83 (*versus* 0.86 in patients without enthesitis).

The decrease in the VAS pain scale confirmed the absence of disease progression, serving as a colouri-

metric indicator of pain sensitivity. Indeed, in this specific group, the mean VAS pain score reported at the start of the study was 5.4. This measure then decreased, reaching 2.88, 1.94 and 1.4 after 4, 8 and 12 weeks, respectively.

Long-term outcomes with guselkumab

In the follow-up analysis of 104 patients with moderate-to-severe psoriasis treated with guselkumab, significant improvements in disease measures were observed at 24 and 52 weeks. At week 24 (T24), PASI was available for 94 patients, with a mean score of 0.58 (SD 1.20), whilst the VAS pain score was recorded for 93 patients, averaging 0.68 (SD 1.63). By week 52 (T52), PASI data were available for 92 patients (only two of whom had T24 data), with a mean score of 0.61 (SD 1.07). Meanwhile, VAS pain was documented in 91 patients, showing a reduced mean score of 0.59 (SD 1.42). Additionally, the mean DLQI score at T52, available for 86 patients, was of 0.91 (SD 2.07).

Safety

No serious adverse events were reported during the study period. All IL-23 inhibitors were well tolerated, and there were no treatment discontinuations due to safety concerns.

Discussion

Our findings support the hypothesis that IL-23 inhibitors not only improve skin symptoms in patients with moderate-to-severe psoriasis but may also help prevent the progression to PsA. In this real-world, multicentre cohort, patients with enthesitis or involvement of difficult-to-treat areas – particularly the nails – responded well to guselkumab, with no evidence of transition to overt PsA during the 12–52-week follow-up. Whilst the lack of PsA diagnoses in patients with enthesitis treated with guselkumab is noteworthy, the study design does not allow us to confirm disease-modifying effects or prevention of PsA onset. Instead, these findings should be seen as supporting the role of IL-23 inhibitors in managing musculoskeletal symptoms that may indicate an increased risk of PsA.

Psoriasis and PsA are chronic autoimmune inflammatory diseases, with the latter being closely linked to skin involvement, which usually precedes joint symptoms by a decade.[1,2] Following significant progress in psoriasis treatment, more efforts have been directed towards understanding PsA and developing more targeted therapies, especially for patients affected by both conditions. Early diagnosis of PsA is crucial to initiate treatment and quickly prevent irreversible joint damage.[11–14] Although there is currently no definitive method to determine the best treatment strategy, our results suggest that early intervention with guselkumab could be key in preventing PsA progression. Additionally, the signs and symptoms of early PsA are so varied and similar to other arthropathies, with non-specific serological biomarkers, that clinical diagnosis and treatment remain challenging. PsA typically involves painful inflammation in the joints and connective tissues, often affecting the finger and toe joints. This inflammation can also impact the hips, knees, spine and sacroiliac joints.[15]

In our study, ultrasound-confirmed enthesitis was observed in 44.8% of patients with joint involvement. Amongst these, those treated with guselkumab experienced significant reductions in PASI and VAS pain scores, indicating improvements in both skin and musculoskeletal areas. Notably, none of these patients developed obvious arthritis during follow-up, suggesting that IL-23 inhibitors may help regulate sub-clinical inflammation and delay or prevent the onset of PsA. The most frequently reported joints include (in descending order) wrists, knees, interphalangeal joints, ankles and elbows. This distribution aligns with existing literature, which indicates that PsA typically affects peripheral joints and can severely impact physical function if left untreated.

Comorbidities were present in over half of the study population, mainly cardiometabolic (74.7%), gastrointestinal or psychiatric conditions such as depression and mood disorders. However, the presence of comorbidities was not linked to a higher number of affected joints, indicating that whilst they increase overall disease burden, they may not directly contribute to musculoskeletal progression in this context. These findings are supported by existing literature, which shows that psoriasis can be associated with various metabolic disturbances, including hypertension, obesity, dyslipidaemia, type 2 diabetes, insulin resistance and non-alcoholic fatty liver disease.[16] Specifically, meta-analyses have demonstrated a strong association between psoriatic disease and metabolic syndrome.[17] This relationship may result from shared inflammatory mechanisms involved in both conditions.[18] Other comorbidities include gastrointestinal issues and psychiatric conditions, such as depression or mood disorders, as reported in the literature.[19–22]

Our data indicate that anti-IL-23 therapies effectively improve skin symptoms. Additionally, although preliminary, some findings suggest that these agents might also influence sub-clinical enthesitis, potentially helping to prevent its progression to arthritis. Patients treated with guselkumab experienced significant decreases in PASI and VAS pain scores, highlighting the therapy's dual benefits for skin and joint symptoms. The study also showed that clinical signs like pain, fatigue and involvement of difficult areas (e.g. scalp, nails) could serve as additional markers for clinicians to evaluate the risk of PsA development.

In the era of biological treatments, the most recent approved options for moderate-to-severe psoriasis include anti-IL-23 agents such as guselkumab, risankizumab and tildrakizumab. These IL-23 inhibitors show similar and notable drug survival and effectiveness, especially in patients with difficult-to-treat psoriasis and PsA.[23,24] Our treatment approach varied based on whether patients were biologically naive or had prior exposure to biologics. Tildrakizumab was used by 18% of biologically naive patients and 10% of those with previous biologic therapy. Risankizumab was administered to 33% of biologically naive patients and 26% of those with prior biologic experience. Guselkumab remained the most commonly used drug in both biologically naive (49%) and biologically experienced patients (64%). The high use of guselkumab (57%) in our cohort reflects typical prescribing patterns observed in real-world settings across the participating centres. This pattern likely results from a combination of factors such as prescriber familiarity, earlier market availability, and institutional or regional prescribing protocols. These factors may introduce selection bias, so comparisons between IL-23 inhibitors should be interpreted cautiously.

Psoriasis often affects difficult-to-treat areas, including the genital region (14–43%), the scalp (43–65%), the face (30–49%), nails (23–60%), and hands and/or feet (12–16%). This can lead to underestimating disease severity when using standard tools and measurements. These specific areas need customized and targeted treatment because of their significant impact on the lives of patients, along with the frequent challenge of accessing some of these regions with conventional treatments.[25–27]

The nail and scalp are the most affected areas in psoriasis.[28,29] Nail involvement commonly occurs in specific sites affected by psoriasis, leading to pitting, irregular nail growth and discolouration. This condition greatly impacts the quality of life of patients and may serve as a predictive risk factor for clinical features associated with an increased risk of PsA.[28] The locations in difficult-to-treat areas appear similar between biologically experienced and biologically naive patients: for instance, psoriasis on the nails was present in 61% of biologically naive patients and 68% of biologically experienced patients; the scalp was affected in 60% of biologically naive patients and 57% of biologically experienced patients; psoriatic lesions in the genital area were found in 29% of biologically naive patients and 34% of biologically experienced patients; finally, psoriasis on the pretibial area was seen in 48% of biologically naive patients and 54% of biologically experienced patients.

Overall, the average PASI index of the examined population was 13.18 at baseline, 3.86 after 4 weeks, 2.01 after 8 weeks, and 0.99 after 12 weeks.

Biologically experienced individuals achieved PASI of 0 in a slightly longer time (T8 and T12) compared to naive individuals. A reduction in the PASI index was observed with all treatments, although guselkumab seemed to show a more rapid decline. Overall, 48.8% of our patients achieved PASI of 0 after 4 weeks of guselkumab treatment and remained in long-term remission, qualifying as super responders. These results align with the GUIDE study, which enrolled 880 patients treated with guselkumab and defined super responders as those achieving complete skin clearance at weeks 20 and 28.[30] Our clinical cohort's consistent and favourable response reinforces the potential benefits of early intervention with guselkumab in managing moderate-to-severe psoriasis. At the same 4-week time point, 14 super responder patients achieved PASI of 0 in the cohort treated with risankizumab. Gargiulo et al. conducted a retrospective study on 1047 patients to evaluate the efficacy of risankizumab and identified a potential super-responder profile (65.72%) who maintained complete skin clearance at 52 weeks.[31] Finally, only eight patients treated with tildrakizumab reached a PASI close to zero at the same time point.

In patients diagnosed with enthesitis and treated with guselkumab, the average PASI at baseline was 10.51 (*versus* 14.04 in patients without enthesitis); at 4 weeks, it was 3.17 (*versus* 4.62 in patients without enthesitis), at 8 weeks it was 1.78 (*versus* 2.61 in patients without enthesitis), and at 12 weeks, it was 0.83 (*versus* 0.86 in patients without enthesitis).

The absence of disease progression was confirmed by the observed decrease in VAS pain. This clinometric indicator specifically measures pain sensitivity. Notably, in patients with enthesitis, the participants' initial average VAS pain score was 5.4. Over time, this score significantly decreased, reaching 2.88, 1.94 and 1.4 after 4, 8 and 12 weeks, respectively. This notable decline in pain highlights the positive effect of the intervention on managing pain in this group.

Since guselkumab was the most frequently prescribed IL-23 inhibitor in our cohort, long-term follow-up data were primarily available for this sub-group. Overall, 104 patients underwent long-term follow-up assessments at 24 and 52 weeks. Patients monitored at weeks 24 and 52 maintained low PASI, VAS pain and DLQI scores, highlighting durable disease control and quality of life improvements. These findings are consistent with previous real-world studies confirming the sustained efficacy of IL-23 inhibitors in both skin and joint domains.

Nevertheless, this study has limitations. First, it was retrospective and based on clinical records, which may have caused reporting inconsistencies. Second, though guselkumab was the most used agent in this cohort,

comparisons amongst IL-23 inhibitors were not a formal objective of this study, and no statistical head-to-head analysis was conducted. Therefore, all efficacy considerations should be interpreted as descriptive and not comparative. The predominant use of guselkumab (57% of patients) might reflect prescriber preference, earlier drug availability or site-specific protocols, leading to selection bias. Additionally, long-term follow-up data (24 and 52 weeks) were available only for patients treated with guselkumab due to its earlier availability in Italy and its greater adoption at the time of data collection. Consequently, our long-term results cannot be generalized to the entire IL-23 inhibitor class, and future research should include extended outcomes for all agents.

Third, joint involvement and inflammatory markers were only measured at baseline and were not systematically tracked over time, which limits our ability to assess dynamic musculoskeletal changes. Finally, the lack of formal rheumatological evaluation means that PsA progression could neither be confirmed nor ruled out with validated criteria. Future prospective studies should include standardized imaging, biomarker monitoring and collaboration with rheumatologists.

Conclusion

These real-world data suggest that IL-23 inhibitors may offer dual benefits for patients with psoriasis at high risk of PsA, improving skin symptoms and potentially preventing joint disease progression. Although guselkumab was the most frequently used IL-23 inhibitor in our cohort, the retrospective design, lack of comparator analysis, and absence of standardized rheumatological evaluation limit the ability to assess potential disease-modifying effects. Enthesitis, especially when identified through imaging, serves as a key clinical indicator of PsA risk. Future prospective research should aim to identify predictive markers and treatment strategies that support early intervention in PsA development.

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