Check for updates

THERAPEUTIC ADVANCES in
Musculoskeletal Disease

Original Research

IMPACT study: large real-world evaluation of guselkumab in psoriatic arthritis integrating clinical response and treatment persistence

Ther Adv Musculoskelet Dis

2026, Vol. 18: 1–20

DOI: 10.1177/1759720X261460108

© The Author(s), 2026.
Article reuse guidelines: sagepub.com/journals-permissions

Valentino Paci*, Roberta Foti*, Ilenia Pantano, Antonio Carletto, Eleonora Celletti, Giovanni Francesco Miceli, Ignazio Cangemi, Giuseppe Lopalco, Simona Montalbano, Maria Sole Chimenti, Andrea Picchianti Diamanti, Umberto Massafra, Emilio Filippucci, Anna Parisi, Pietro Leccese, Anna Panaccione, Ilaria Puca, Giorgio Amato, Sabrina Marrone, Myriam Di Penta, Salvatore Corrao, Eneida Cela, Alessandra Rai, Enrico Tirri, Florenzo Iannone, Fabiola Atzeni, Maurizio Rossini, Francesco Ciccia, Rosario Foti§, Gianluca Moroncini§ and Michele Maria Luchetti Gentiloni§; on behalf of the IMPACT Study Group

Abstract

Background: In psoriatic arthritis (PsA), real-world evidence complements randomised controlled trials by evaluating treatment effectiveness in routine care. Guselkumab (GUS), a selective interleukin-23p19 inhibitor, has demonstrated efficacy in phase-III trials, but real-world data remain limited.

Objectives: To assess the real-world effectiveness, treatment persistence and safety of GUS in a large, multicentre PsA cohort.

Design: IMPACT (Italian Multicentric PAtient-Centred assessment of Guselkumab Treatment) is a multicentre, observational, longitudinal study including consecutive adult patients with PsA treated with GUS.

Methods: Clinical assessments were conducted at baseline and at 3, 6, 9 and 12 months. Effectiveness outcomes included the change from baseline in Disease Activity in Psoriatic Arthritis (DAPSA), Axial Spondyloarthritis Disease Activity Score (ASDAS) and Psoriasis Area Severity Index (PASI) scores, as well as the resolution of enthesitis and dactylitis, and treatment persistence. Predictors of DAPSA remission and treatment discontinuation were analysed using multivariable Cox regression models.

Results: A total of 389 patients were included (245 (63.0%) female; median age 56.0 years), with moderate-to-high baseline disease burden and prevalent prior biologic (b-)/targeted synthetic disease-modifying anti-rheumatic drugs (DMARD) exposure (86.4%). Median DAPSA decreased from 24.2 at baseline to 10.5 at 12 months, with significant improvements from 3 months onward. The proportion of patients achieving DAPSA-low disease activity, or -remission increased progressively, reaching up to 58.6% (187/319) and 14.1% (45/319), respectively, at 12 months. Improvements were observed across multiple disease domains, including skin involvement (PASI-100 in 123/182 (67.6%) at 12 months), enthesitis and dactylitis (12-month resolution in 118/186 (63.4%) and 57/60 (95.0%), respectively) and axial disease (ΔASDAS −1.7 at 12 months). Treatment persistence was 78.7% at 12 months, with discontinuations mainly due to ineffectiveness; age, sex, fibromyalgia, baseline disease activity, prior b/tsDMARD exposure and corticosteroid use were associated with remission and/or discontinuation. Few adverse events were recorded, with no unexpected safety signals.

Correspondence to:
Michele Maria Luchetti Gentiloni
Clinica Medica, Department of Internal Medicine, Marche University Hospital and Department of Clinical and Molecular Sciences, Marche Polytechnic University, via Tronto 10/A, Ancona 60020, Italy
m.luchetti@staff.univpm.it

Valentino Paci
Gianluca Moroncini
Clinica Medica, Department of Internal Medicine, Marche University Hospital and Department of Clinical and Molecular Sciences, Marche Polytechnic University, Ancona, Italy

Roberta Foti
Giorgio Amato
Rosario Foti
Rheumatology Unit, Policlinico San Marco Hospital, Catania, Italy

Ilenia Pantano
Sabrina Marrone
Francesco Ciccia
Rheumatology Section, Department of Precision Medicine, University of Campania Luigi Vanvitelli, Naples, Italy

Antonio Carletto
Maurizio Rossini
Rheumatology Unit, University of Verona, Verona, Italy

Creative Commons Non Commercial CC BY-NC: This article is distributed under the terms of the Creative Commons Attribution-NonCommercial 4.0 License (https://creativecommons.org/licenses/by-nc/4.0/) which permits non-commercial use, reproduction and distribution of the work without further permission provided the original work is attributed as specified on the Sage and Open Access pages (https://us.sagepub.com/en-us/nam/open-access-at-sage).

Eleonora Celletti
Myriam Di Penta
Department of Medicine and Science of Aging, Medical Clinic, SS. Annunziata Hospital of Chieti, 'G. D'Annunzio' University of Chieti-Pescara, Chieti, Italy

Giovanni Francesco Miceli
Fabiola Atzeni
Rheumatology Unit, AOU G. Martino, University of Messina, Messina, Italy

Ignazio Cangemi
Salvatore Corrao
Department of Clinical Medicine, Internal Medicine Unit with Rheumatology, Dermatology, Diabetology and Tertiary Diabetic Foot Health Care, National Relevance and High Specialization Hospital Trust ARNAS Civico Di Cristina Benfratelli, Palermo, Italy

Giuseppe Lopalco
Florenzo Iannone
Department of Precision and Regenerative Medicine and Ionian Area (DiMePRe-J), University of Bari 'Aldo Moro', Bari, Italy

Simona Montalbano
Enrico Tirri
Rheumatology Unit, Department of Medicine, Ospedale del Mare, Naples, Italy

Maria Sole Chimenti
Eneida Cela
Rheumatology, Allergology and Clinical Immunology, Department of Systems Medicine, University of Rome Tor Vergata, Rome, Italy

Andrea Picchianti Diamanti
Alessandra Rai
Department of Clinical and Molecular Medicine, S. Andrea University Hospital, 'Sapienza' University of Rome, Rome, Italy

Umberto Massafra
Rheumatology Service, S. Pietro Fatebenefratelli Hospital, Rome, Italy

Emilio Filippucci
Rheumatology Unit, Department of Clinical and Molecular Sciences, 'Carlo Urbani' Hospital, Polytechnic University of Marche, Ancona, Italy

Anna Parisi
Rheumatology Unit, AORN Cardarelli, Naples, Italy

Pietro Leccese
Rheumatology Department of Basilicata, San Carlo Hospital, Potenza, Italy

Conclusion: In this large real-world cohort, GUS demonstrated sustained effectiveness in several disease domains, favourable treatment persistence and no unexpected safety signals, supporting its use in routine care of complex and b/tsDMARD-experienced PsA patients.

Keywords: biologic DMARD, clinical effectiveness, guselkumab, interleukin-23 inhibitors, psoriatic arthritis, real-world evidence

Received: 23 February 2026; revised manuscript accepted: 21 May 2026.

Introduction

Psoriatic arthritis (PsA) is a chronic, immune-mediated inflammatory disease characterised by a complex intersection of musculoskeletal and cutaneous manifestations. In routine care, PsA rarely occurs in isolation: articular and skin inflammation coexist with cardiovascular, metabolic and psychosocial comorbidities, identified under the broader spectrum of 'Psoriatic Disease'.[1–3] The resulting clinical complexity translates into a substantial disease burden and warrants a personalised treatment strategy, which takes into consideration not only the objective measures of disease activity but also patients' priorities, comorbidity constraints and the overall impact of PsA on daily life.[4,5]

Over the past years, the therapeutic armamentarium for PsA has expanded beyond tumour necrosis factor inhibitors (TNFi) to include agents targeting and inhibiting the interleukin-23 (IL-23i) and -17 (IL-17i) pathways.[6] Guselkumab (GUS), a monoclonal antibody targeting the p19 subunit of IL-23, demonstrated efficacy and an excellent safety profile in several phase III studies.[7–12]

Nevertheless, translating trial efficacy into real-world effectiveness remains challenging. Randomised controlled trials (RCTs) are designed to maximise internal validity, but their controlled setting and selected populations only partially capture the complexity of real-life PsA.[13,14]

In real-world settings, treatment effectiveness is influenced not only by disease activity across different domains but also by comorbidity burden, patient and physician perceptions, treatment accessibility and organisational factors. Therefore, pragmatic real-world studies are necessary to better understand the range of GUS effectiveness under routine-care conditions.

The IMPACT (Italian Multicentric PAtient-Centred assessment of Guselkumab Treatment) study aimed to evaluate the real-world effectiveness of GUS in a large, multicentre, routine-care cohort of patients with PsA, combining validated clinical outcomes with treatment persistence to provide a more comprehensive picture of treatment performance in everyday clinical practice.

Secondary aims included characterising the study cohort, identifying clinical predictors of remission and treatment discontinuation, and describing the safety profile of GUS in the real-life setting.

Methods

Study design and population

The IMPACT study had a multicentre, observational, longitudinal design and was conducted across 17 tertiary rheumatology centres in Italy. From January 2022 to December 2024, consecutive adult patients with PsA fulfilling the inclusion criteria were enrolled after providing informed consent and were followed for up to 12 months.

The main inclusion criteria were: (a) diagnosis of PsA, based on the rheumatologist assessment of the clinical picture and in accordance with the Classification Criteria for Psoriatic Arthritis; (b) age greater than 18 years and (c) initiation of treatment with GUS according to clinical indication and in compliance with authorised Italian reimbursement criteria. No exclusion criteria were applied. Clinical data were collected until completion of follow-up or treatment discontinuation for any reason.

The study was designed, conducted and reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines.

The study protocol was approved by the Lazio Regional Ethics Committee (Protocol Number 0022902/2024 – Comitato Etico Territoriale

Anna Panaccione
Rheumatology, Santa Maria General Hospital, Terni, Italy

Ilaria Puca
Rheumatology Unit, S.G. Moscati Hospital, Avellino, Italy

*These authors are first co-authors

§These authors are senior co-authors

Lazio Area 2) and was accepted by all participating centres. The study was conducted in accordance with the principles of the Declaration of Helsinki and Good Clinical Practice guidelines.

Global clinical assessment

Data on demographic and baseline clinical features were collected for all patients, including sex, age, comorbidities, disease domains and the type and number of prior biologic (b-) and/or targeted synthetic (ts-) disease-modifying anti-rheumatic drugs (DMARDs).

Clinical assessment of disease activity was performed at baseline and at 12, 24, 36 and 52 weeks. These included tender joint count (68 joints – TJC) and swollen joint count (66 joints – SJC), visual analogue scale for pain (VAS pain), patient and physician global assessment (PtGA and PhGA). Laboratory data, including complete blood count, liver and renal function tests and C-reactive protein (CRP), were collected at the same timepoints.

Enthesitis was evaluated both categorically (presence vs absence at any peripheral entheseal site) and using the Leeds Enthesitis Index, whereas dactylitis was assessed categorically only.

Skin involvement was assessed at each timepoint in patients with psoriasis, using the proportion of body surface area affected by psoriasis (BSA-PSO) and the Psoriasis Area Severity Index (PASI).

The Disease Activity in Psoriatic Arthritis (DAPSA) score and the Axial Spondyloarthritis Disease Activity Score (ASDAS) based on CRP were calculated at each visit in patients with peripheral and axial involvement, respectively. Axial involvement was defined based on rheumatologist evaluation of the clinical picture and confirmed by imaging of the spine and sacroiliac joints. Specifically, the diagnosis of axial PsA was supported by magnetic resonance imaging (MRI) findings consistent with active inflammatory and/or structural post-inflammatory lesions according to the rheumatologist and radiologist assessment and in line with the Assessment of Spondyloarthritis International Society and Outcome Measures in Rheumatology definitions for a positive MRI.[15–17]

MRI imaging was interpreted locally at each participating centre, without central reading or formal inter-reader reliability assessment. No patient was classified as having axial involvement based on clinical assessment alone.

Fibromyalgia was recorded based on clinical assessment by the treating rheumatologist during routine care. Systematic application of American College of Rheumatology (ACR) classification criteria for fibromyalgia was not part of the study protocol.

All patients received GUS according to one of the two approved dosing regimens for PsA: 100 mg administered subcutaneously (s.c.) at baseline, week 4 and every 8 weeks thereafter (q8w), or at baseline and every 4 weeks thereafter (q4w). At each visit, the dosing regimen was assessed, and any modification was recorded. Concomitant therapies, including conventional synthetic (cs) DMARD, corticosteroids and non-steroidal anti-inflammatory drugs (NSAIDs), were also recorded at each timepoint.

All adverse events (AEs) occurring during the study period were recorded and classified according to the Common Terminology Criteria for Adverse Events (CTCAE), version 5.0.

Outcomes

The primary outcomes of the study were the change from baseline in the DAPSA score and the proportion of patients achieving low disease activity (LDA) and remission at each time point, defined according to validated DAPSA thresholds, namely DAPSA remission (i.e. a DAPSA score $\leqslant 4$) and DAPSA LDA (i.e. a DAPSA score >4 and $\leqslant 14$), respectively.

The secondary outcomes included: (i) the change from baseline in the ASDAS score among patients with axial involvement; (ii) the treatment persistence and its difference across clinically relevant subgroups; (iii) the clinical predictors of DAPSA remission and treatment discontinuation and (iv) the proportion, type and severity of AEs recorded in the study cohort.

Data analysis

Baseline characteristics were described for the overall cohort. Continuous variables were summarised as median and interquartile range (1st–3rd quartile), whereas categorical variables were reported as absolute frequencies and percentages.

Missing data were limited to skin-related assessments and post-discontinuation follow-up assessments, with no additional missing data. Skin-related analyses were conducted using a complete-case approach, excluding patients with unavailable dermatological assessments. Post-discontinuation missing data were addressed through sensitivity analyses for the main outcomes: for continuous outcomes, a last observation carried forward approach was applied; for categorical outcomes, non-responder imputation (NRI) was performed, considering patients with missing data as non-responders. In addition, LUNDEX-adjusted response rates were calculated for key binary outcomes.

Longitudinal changes in disease activity outcomes were analysed using mixed-effects models. Specifically, linear mixed-effects models were fitted for continuous outcomes, while generalised linear mixed-effects models were used for categorical outcomes. In all mixed-effects models, timepoint was included as a fixed effect and a patient-level random intercept was added to account for within-subject correlation. No additional covariates were included in these models. Pairwise comparisons versus baseline were estimated using marginal means with Holm adjustment for multiple comparisons. Subjects who discontinued treatment were considered up to the last observation point, including all patients in the analyses. Model estimates were reported with corresponding 95% confidence intervals (CI).

Treatment persistence was defined as time from the study drug initiation to treatment discontinuation for any reason. Drug retention was analysed using Kaplan–Meier survival curves, and differences between clinically relevant subgroups were assessed using the log-rank test. The retention rates and corresponding 95% CIs were reported. Drug retention used for LUNDEX calculations was defined consistently with the Kaplan–Meier analysis, in which discontinuations occurring at a given timepoint were counted as events at that timepoint.

Predictors of DAPSA remission and treatment discontinuation were explored using multivariable Cox proportional hazards regression models. For the remission analysis, the event was defined as the first follow-up visit meeting the DAPSA remission threshold; patients already in DAPSA remission at baseline were excluded, and those not achieving remission were censored at the last available assessment. Covariates were selected based on expert opinion and clinical relevance, avoiding collinearity. The model stability was assessed by calculating the events-per-variable (EPV) ratio and the proportional hazards assumption was assessed using Schoenfeld residuals. A sensitivity analysis was performed with reduced Cox models including a smaller set of clinically selected covariates. Results were reported as hazard ratios (HRs) with 95% CIs.

All statistical analyses and figures were produced using the R software, version 4.4.2 (R Foundation for Statistical Computing, Vienna, Austria), with a two-sided p-value < 0.05 considered statistically significant.

Results

Cohort characteristics

Cohort characteristics at baseline are reported in Table 1. A total of 389 patients, mostly female (245/389, 63.0%), were included. The median age was 56.0 years (47.0–63.0) and the median BMI was 26.3 kg/m^2 (23.4–30.4). Comorbidities were frequent, particularly overweight (166/389, 42.7%), cardiovascular disease (162/389, 41.7%) and metabolic disease (121/389, 31.1%); fibromyalgia was reported in 92/389 patients (23.7%). Regarding disease domains, most patients presented peripheral arthritis (373/389, 95.9%); enthesitis and dactylitis were reported in 227/389 (58.4%) and 79/389 (20.3%), respectively, while axial involvement was present in 81/389 (20.8%) patients.

Patients showed a high overall disease activity at baseline (Table 2). The median DAPSA score was 24.2 (18.5–32.6), whereas patients with axial involvement showed a median ASDAS score of 3.3 (2.5–3.7). A small proportion of patients (3/389, 0.8%) were already in DAPSA remission at baseline, and these patients were treated with GUS primarily due to high psoriasis severity and/or AEs to previous b/tsDMARDs.

Data on baseline skin involvement were available for 354 out of 389 patients (91.0%), while 35 (9.0%) had missing data about skin severity. Given the limited proportion of missing values, skin-related analyses were conducted using a complete-case approach. Among these patients,

Table 1. Cohort characteristics at baseline.

Cohort characteristics	Total patients	Missing data
	389	
Sex, female	245 (63.0%)	/
Age, years	56.0 (47.0–63.0)	/
BMI (kg/m^2)	26.3 (23.4–30.4)	/
Comorbidities		
Cardiovascular disease	162 (41.7%)	/
Metabolic disease	121 (31.1%)	/
Overweight	166 (42.7%)	/
Chronic infections	23 (5.9%)	/
Fibromyalgia	92 (23.7%)	/
Psychiatric disorders	24 (6.2%)	/
Disease domains		
Axial involvement	81 (20.8%)	/
Peripheral arthritis	373 (95.9%)	/
Enthesitis	227 (58.4%)	/
Dactylitis	79 (20.3%)	/
Skin involvement (active)	219 (61.9%)	35 (9.0%)
IBD	25 (6.4%)	/
Uveitis	5 (1.3%)	/
Treatment		
b/tsDMARD-experienced	336 (86.4%)	/
Previous b/tsDMARD lines	2.0 (1.0–3.0)	/

Continuous variables are reported as median (IQR), categorical variables as absolute number (%). For categorical variables, percentages are computed on non-missing values; missing values are reported as absolute number.
BMI, body mass index; b/tsDMARD, biologic/targeted synthetic disease-modifying anti-rheumatic drugs; IBD, inflammatory bowel disease; IQR, interquartile range.

219/354 (61.9%) presented with active psoriasis at baseline. The median BSA-PSO and PASI scores were 4.0% (1.0%–7.5%) and 4.4 (1.2–10.0), respectively.

Baseline laboratory data showed a median CRP level of 0.35 (0.20–0.80) mg/dl, and 150 out of 389 (38.6%) patients had CRP levels above the upper normal limit (u.l.n.; 0.5 mg/dl).

Most patients were b/tsDMARD-experienced (336/389, 86.4%), with a median of 2.0 (1.0–3.0) prior b/tsDMARD lines. The majority of patients (370/389, 95.1%) initiated GUS with the q8w dosing regimen. A considerable proportion of patients were receiving csDMARDs, corticosteroids and/or NSAIDs as concomitant therapy at baseline, specifically 165/389 (42.4%), 79/389 (20.3%) and 117/389 (30.1%), respectively.

Table 2. Longitudinal assessment of disease activity, inflammatory markers and patients/physician-reported outcomes over 52 wks.

Number of patients	Baseline	12 wks	*p*-Value	24 wks	*p*-Value	36 wks	*p*-Value	52 wks	*p*-Value
	389 (100%)	389 (100%)	12 wks vs bsl	367 (94.3%)	24 wks vs bsl	329 (84.6%)	36 wks vs bsl	319 (82.0%)	52 wks vs bsl
Tender joint count	7.0 (3.0–12.0)	4.0 (1.0–8.0)	<0.0001	2.0 (0.0–6.0)	<0.0001	2.0 (0.0–5.0)	<0.0001	2.0 (0.0–4.0)	<0.0001
Swollen joint count	2.0 (0.0–4.0)	0.0 (0.0–2.0)	<0.0001	0.0 (0.0–1.0)	<0.0001	0.0 (0.0–0.0)	<0.0001	0.0 (0.0–0.0)	<0.0001
DAPSA	24.2 (18.5–32.6)	15.8 (10.5–22.1)	<0.0001	13.2 (8.2–18.1)	<0.0001	11.1 (6.3–15.2)	<0.0001	10.5 (6.2–14.2)	<0.0001
DAPSA: LOCF	/	/		*14.1 (8.3–18.9)*	*<0.0001*	*12.4 (7.2–18.1)*	*<0.0001*	*12.1 (7.2–18.1)*	*<0.0001*
DAPSA remission	3 (0.8%)	20 (5.1%)	<0.0001	27 (7.4%)	<0.0001	43 (13.1%)	<0.0001	45 (14.1%)	<0.0001
DAPSA remission: NRI	/	/		*27 (6.9%)*		*43 (11.1%)*		*45 (11.6%)*	
DAPSA remission: LUNDEX	/	*(4.9%)*		*(6.2%)*		*(10.7%)*		*(11.1%)*	
DAPSA LDA	43 (11.1%)	140 (36.0%)	<0.0001	166 (45.2%)	<0.0001	174 (52.9%)	<0.0001	187 (58.6%)	<0.0001
DAPSA LDA: NRI	/	/		*166 (42.7%)*		*174 (44.7%)*		*187 (48.1%)*	
DAPSA LDA: LUNDEX	/	*(34.0%)*		*(38.3%)*		*(43.4%)*		*(46.1%)*	
ASDAS	3.3 (2.5–3.7)	2.1 (1.7–2.7)	<0.0001	1.9 (1.5–2.4)	<0.0001	1.7 (1.4–2.3)	<0.0001	1.6 (1.3–2.1)	<0.0001
ASDAS: LOCF	/	/		*1.9 (1.5–2.4)*	*<0.0001*	*1.8 (1.4–2.4)*	*<0.0001*	*1.8 (1.3–2.4)*	*<0.0001*
BSA-PSO	4.0 (1.0–7.5)	1.0 (0.0–2.0)	<0.0001	0.0 (0.0–1.0)	<0.0001	0.0 (0.0–1.0)	<0.0001	0.0 (0.0–1.0)	<0.0001
PASI	4.4 (1.2–10.0)	0.4 (0.0–2.2)	<0.0001	0.0 (0.0–1.2)	<0.0001	0.0 (0.0–0.3)	<0.0001	0.0 (0.0–0.4)	<0.0001
PASI: LOCF	/	/		*0.0 (0.0–1.2)*	*<0.0001*	*0.0 (0.0–0.6)*	*<0.0001*	*0.0 (0.0–0.6)*	*<0.0001*
CRP (mg/dL)	0.35 (0.20–0.80)	0.32 (0.20–0.61)	0.0657	0.28 (0.20–0.45)	0.0016	0.22 (0.17–0.41)	<0.0001	0.20 (0.14–0.40)	<0.0001
CRP above u.l.n.	150 (38.6%)	115 (29.6%)	0.0007	82 (22.3%)	<0.0001	53 (16.1%)	<0.0001	49 (15.6%)	<0.0001
PhGA (0–10)	6.0 (5.0–7.4)	4.0 (2.0–5.0)	<0.0001	3.0 (2.0–5.0)	<0.0001	2.5 (1.0–4.0)	<0.0001	2.0 (1.0–3.5)	<0.0001
PtGA (0–10)	7.0 (6.0–9.0)	5.0 (3.0–7.0)	<0.0001	4.5 (3.0–6.0)	<0.0001	4.0 (2.0–5.0)	<0.0001	3.7 (2.0–5.0)	<0.0001
VAS pain (0–10)	7.1 (6.0–8.0)	5.0 (4.0–7.0)	<0.0001	4.2 (3.0–6.0)	<0.0001	4.0 (2.0–5.0)	<0.0001	3.5 (2.0–5.0)	<0.0001

Continuous variables are reported as median (IQR), while categorical variables are reported as absolute number (%). The first line shows the available observations at each timepoint. For each follow-up timepoint, changes from baseline were analysed using mixed-effects models accounting for repeated measurements within patients, with adjustment for multiple comparisons. Sensitivity analyses are provided for the main outcomes: for continuous outcomes, a LOCF approach is reported; for categorical outcomes, both NRI and LUNDEX approaches are reported.
Italic text indicates sensitivity analyses performed using NRI, LUNDEX or LOCF approaches.
ASDAS, Axial Spondyloarthritis Disease Activity Score; BSA-PSO, body surface area affected by psoriasis; bsl, baseline; CRP, C-reactive protein; DAPSA, Disease Activity in Psoriatic Arthritis; LDA, Low Disease Activity; LOCF, last observation carried forward; NRI, non-responder imputation; PASI, Psoriasis Area and Severity Index; PhGA, Physician Global Assessment; PtGA, Patient Global Assessment; u.l.n., upper limit of normal; VAS, Visual Analogue Scale; wks, weeks.

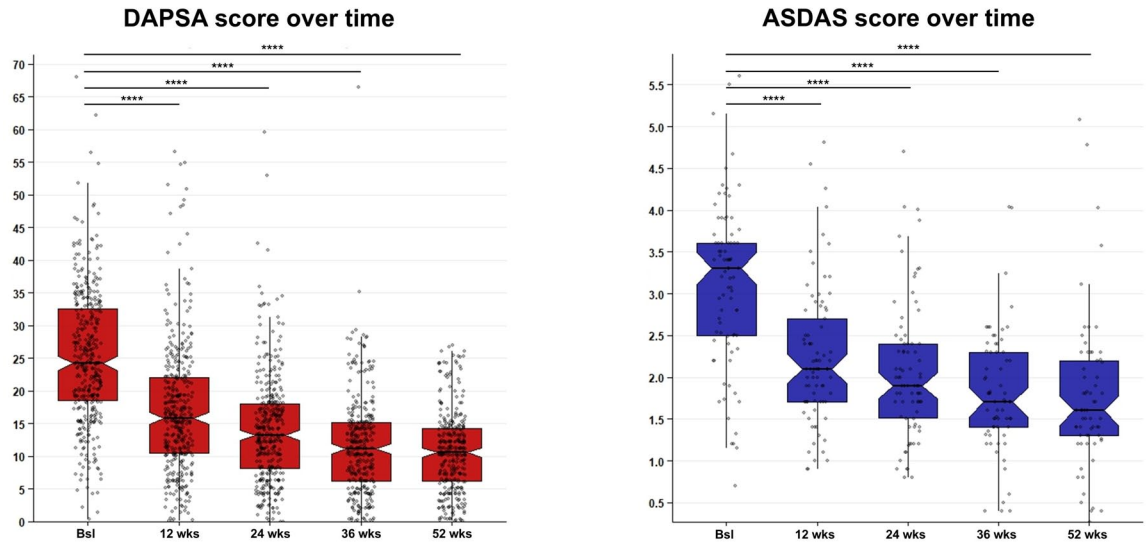


Figure 1. Longitudinal changes in DAPSA and ASDAS scores over 12 months. Box-and-whisker plots showing the distribution of DAPSA and ASDAS at baseline and at 12, 24, 36 and 52 weeks. Individual dots correspond to single patient values. Asterisks indicate statistically significant differences compared with baseline according to mixed-effects models (****$p < 0.0001$).
ASDAS, Axial Spondyloarthritis Disease Activity Score; bsl, baseline; DAPSA, Disease Activity in Psoriatic Arthritis; wks, weeks.

Longitudinal analysis

The results of the mixed-effects models showing longitudinal changes in disease activity scores are reported in Table 2 and Figure 1. Disease activity improved early and was maintained over time. The median DAPSA significantly decreased to 15.8 (10.5-22.1) (Δ −8.4) at 12 weeks, further improving to 13.2 (8.2–18.1) (Δ −11.0) at 24 weeks, 11.1 (6.3–15.2) (Δ −13.1) at 36 weeks and 10.5 (6.2–14.2) (Δ −13.7) at 52 weeks, mirrored by consistent reductions in TJC and SJC ($p < 0.0001$ for all comparisons vs baseline).

Furthermore, Figure 2 provides a patient-level visual representation of the longitudinal shift in DAPSA categories over time, showing the progressive transition from predominantly moderate/high disease activity at baseline toward LDA and remission during follow-up.

Specifically, among evaluable patients at each timepoint, the proportion of patients in DAPSA-remission and -LDA significantly increased from 3/389 (0.8%) and 43/389 (11.1%) at baseline to 20/389 (5.1%) and 140/389 (36.0%) at 12 weeks, 27/367 (7.4%) and 166/367 (45.2%) at 24 weeks, 43/329 (13.1%) and 174/329 (52.9%) at 36 weeks and 45/319 (14.1%) and 187/319 (58.6%) at 52 weeks, respectively (Table 2). Improvements were also observed in patients with axial involvement of PsA, with ASDAS scores significantly decreasing from 3.3 (2.5–3.7) at baseline to 1.6 (1.3–2.1) at 52 weeks (Δ −1.7; Table 2).

Data regarding effectiveness on enthesitis and dactylitis are reported in Table 3, Figure 3 and Supplemental Figure 1. Among evaluable patients with baseline enthesitis, resolution rates progressively increased from 99/227 (43.6%) at 12 weeks to 116/211 (55.0%) at 24 weeks, 120/191 (62.8%) at 36 weeks and 118/186 (63.4%) at 52 weeks. Resolution rates for baseline dactylitis were higher, starting from 66/79 (83.5%) at 12 weeks, increasing to 65/68 (95.6%) at 24 weeks and remaining stable thereafter. During follow-up, among patients without enthesitis or dactylitis at baseline, 32 new cases of enthesitis and 2 new cases of dactylitis were observed. Half the cases (16/32; 50%) of new enthesitis resolved without discontinuation of the study drug, whereas both cases of incident dactylitis discontinued GUS due to ineffectiveness.

Improvements in psoriasis severity among patients with active skin involvement are shown in Tables 2 and 3 and Figure 4. A significant improvement was observed in both BSA-PSO and PASI scores, which decreased from baseline to 0.0% (0.0%–1.0%) and 0.0 (0.0–0.4) at 52 weeks, respectively.



Figure 2. Patient-level heatmap of DAPSA categories distribution over time. Heatmap illustrating the longitudinal distribution of DAPSA categories at baseline and at 12, 24, 36 and 52 wks. Each row represents an individual patient and each column a study timepoint, allowing visualisation of individual trajectories and overall shift toward lower disease activity states over follow-up. Colours indicate DAPSA categories: REM (⩽4), LDA (>4–⩽14), MDA (>14–⩽28) and HDA (>28); grey indicates missing data.
bsl, baseline; DAPSA, Disease Activity in Psoriatic Arthritis; HDA, high disease activity; LDA, low disease activity; MDA, moderate disease activity; NA, missing data (due to treatment discontinuation); REM, remission; wks, weeks.

Table 3. Resolution of enthesitis, dactylitis and psoriasis (PASI-100) over follow-up among patients with baseline involvement and available assessments at each visit.

Resolution	12 wks	24 wks	36 wks	52 wks
Enthesitis	99/**227** (43.6%)	116/**211** (55.0%)	120/**191** (62.8%)	118/**186** (63.4%)
Enthesitis: NRI	/	*116/**227** (51.1%)*	*120/**227** (52.9%)*	*118/**227** (52.0%)*
Enthesitis: LUNDEX	*(40.5%)*	*(46.3%)*	*(51.5%)*	*(50.3%)*
Dactylitis	66/**79** (83.5%)	65/**68** (95.6%)	59/**62** (95.2%)	57/**60** (95.0%)
Dactylitis: NRI	/	*65/**79** (82.3%)*	*59/**79** (74.7%)*	*57/**79** (72.2%)*
Dactylitis: LUNDEX	*(71.9%)*	*(75.0%)*	*(72.3%)*	*(70.9%)*
PASI-100	78/**219** (35.6%)	115/**208** (55.3%)	132/**187** (70.6%)	123/**182** (67.6%)
PASI-100: NRI	/	*115/**219** (52.5%)*	*132/**219** (60.3%)*	*123/**219** (56.2%)*
PASI-100: LUNDEX	*(34.3%)*	*(47.5%)*	*(59.3%)*	*(54.9%)*

Resolution analyses were restricted to patients presenting with active enthesitis, dactylitis or psoriasis at baseline. For each visit, proportions were calculated among patients with available data (i.e. not discontinuing the study drug) which had enthesitis, dactylitis or psoriasis at baseline. Patients who developed enthesitis, dactylitis or psoriasis after baseline were not included in this table. Results are reported as number (%) of patients achieving resolution over the number of evaluable patients at each timepoint. Sensitivity analyses with both NRI and LUNDEX approaches are reported.
Italic text indicates sensitivity analyses performed using NRI or LUNDEX approaches. Bold text indicates denominators for ease of interpretation.
NRI, non-responder imputation; PASI, Psoriasis Area Severity Index; wks, weeks.

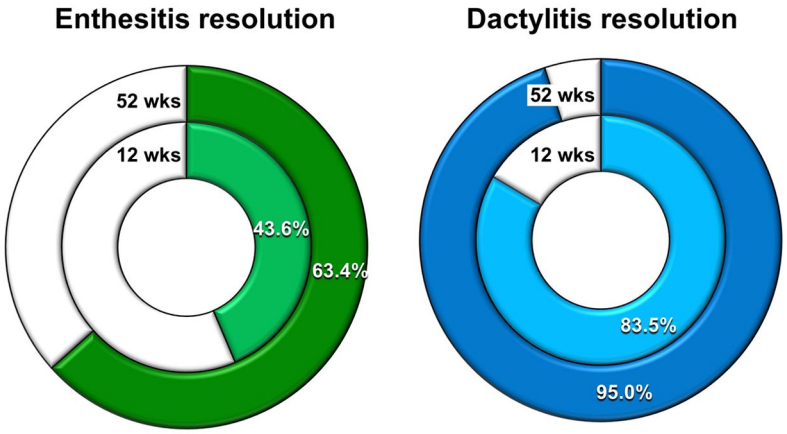


Figure 3. Resolution of enthesitis and dactylitis at 3 and 12 months. Donut charts illustrating the proportion of patients achieving resolution of enthesitis and dactylitis at 12 and 52 wks among those with baseline involvement.
wks, weeks.

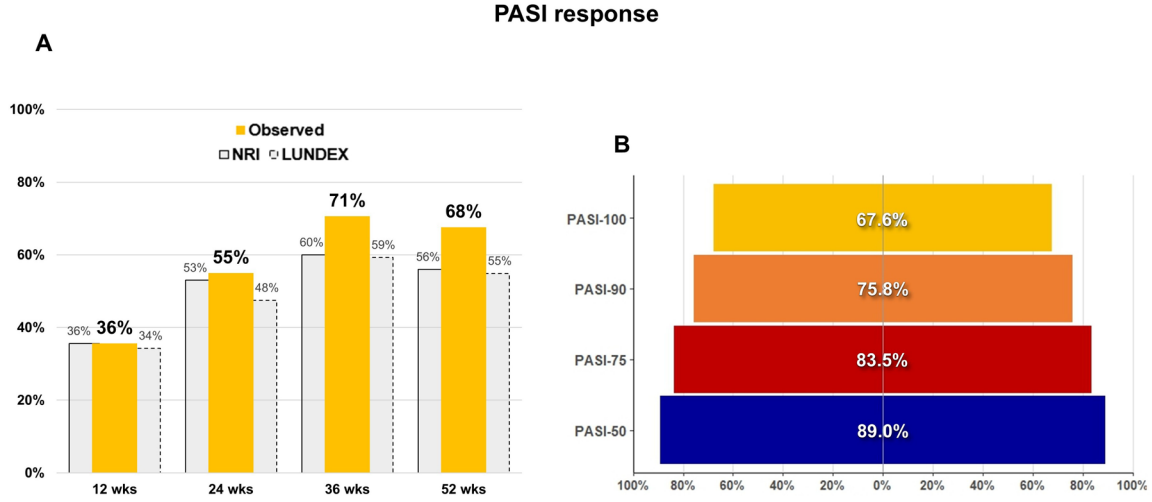


Figure 4. Skin response to GUS over time. Panel (a), on the left, shows proportion of patients with active psoriasis at baseline achieving PASI-100 at 12, 24, 36 and 52 wks. Panel (b), on the right, shows distribution of PASI response rates at 52 wks, showing the proportions of patients achieving PASI-50, PASI-75, PASI-90 and PASI-100. Percentages were calculated among patients with active skin involvement at baseline.
GUS, guselkumab; PASI, Psoriasis Area and Severity Index; PASI-50/75/90/100, ⩾50%, ⩾75%, ⩾90% and 100% improvement from baseline PASI score; wks, weeks.

In this regard, a considerable proportion of patients achieved PASI-90 (i.e. a 90% improvement in PASI score) and PASI-100 (i.e. a complete resolution of psoriasis) at 52 weeks, specifically 138/182 (75.8%) and 123/182 (67.6%), respectively.

Regarding inflammatory markers, median CRP levels significantly decreased from 0.35 (0.20–0.80) to 0.20 (0.14–0.40) mg/dl by 52 weeks, and the proportion of patients with CRP above u.l.n. decreased from 38.6% to 15.6% over the same period (Table 2).

PtGA and PhGA showed a parallel improvement over time, and the VAS pain decreased rapidly from 7.1 (6.0–8.0) at baseline to 5.0 (4.0–7.0) at 12 weeks, with further reductions to 4.2 (3.0–6.0), 4.0 (2.0–5.0) and 3.5 (2.0–5.0) at 24, 36 and 52 weeks, respectively (Table 2).

Sensitivity analyses showed consistent results across outcomes. NRI and LUNDEX-adjusted analyses demonstrated lower resolution rates for enthesitis and dactylitis compared with the main analysis. Furthermore, a sensitivity analysis on

Table 4. Key week-52 effectiveness outcomes stratified by prior b/tsDMARD exposure.

Outcomes	Bio-naïve	1 prior b/tsDMARD	⩾2 prior b/tsDMARDs
DAPSA remission	11/**53** (20.8%)	16/**110** (14.5%)	18/**226** (8.0%)
DAPSA LDA	29/**53** (54.7%)	61/**110** (55.5%)	97/**226** (42.9%)
PASI-90	26/**37** (70.3%)	50/**66** (75.8%)	62/**116** (53.4%)
PASI-100	22/**37** (59.5%)	46/**66** (69.7%)	55/**116** (47.4%)
Enthesitis resolution	17/**30** (56.7%)	35/**65** (53.8%)	66/**132** (50.0%)
Dactylitis resolution	8/**10** (80.0%)	20/**28** (71.4%)	29/**41** (70.7%)

Patients were stratified according to prior b/tsDMARD exposure. A NRI approach was used. DAPSA outcomes were calculated out of the total number of patients in each subgroup. PASI, enthesitis and dactylitis outcomes were calculated among patients with baseline involvement in each subgroup.
Bold text indicates denominators for ease of interpretation.
b/tsDMARD, biologic/targeted synthetic disease-modifying anti-rheumatic drug; DAPSA, Disease Activity in Psoriatic Arthritis; LDA, low disease activity; NRI, non-responder imputation; PASI, Psoriasis Area and Severity Index.

DAPSA outcomes excluding patients with fibromyalgia is shown in Supplemental Table 1.

Finally, additional analyses stratified by prior b/tsDMARD exposure (bio-naïve, one previous b/tsDMARD and ⩾2 previous b/tsDMARDs) were performed. Longitudinal mixed-effects modelling showed significant DAPSA improvement over time across all subgroups (all within-group $p < 0.0001$). Although patients with ⩾2 prior b/tsDMARDs showed slightly attenuated improvement, overall DAPSA trajectories remained broadly comparable. In addition, a descriptive week-52 subgroup analysis showed numerically lower DAPSA remission/LDA and PASI-90/100 rates among patients with ⩾2 prior b/tsDMARDs, whereas enthesitis and dactylitis resolution rates were broadly comparable across subgroups (Table 4).

Drug analysis and persistence

Drug persistence was estimated using the Kaplan–Meier method and is shown in Supplemental Figure 2. The estimated retention rate was 84.6% (95% CI 81.1%–88.2%) at 6 months and 78.7% (95% CI 74.7%–82.8%) at 12 months. Subgroup analysis demonstrated that treatment retention differed significantly according to prior b/tsDMARD exposure, with higher persistence in b/tsDMARD-naïve patients and lower persistence among patients with ⩾2 prior b/tsDMARDs (log-rank $p = 0.0001$).

During follow-up, 22 (5.7%), 38 (9.8%), 10 (2.6%) and 13 (3.3%) patients discontinued GUS after the visit at 12, 24, 36 and 52 weeks, respectively, resulting in an overall discontinuation rate of 83/389 (21.3%) over 1 year. Among these, 77/83 patients discontinued treatment due to lack of effectiveness, specifically 68 due to musculoskeletal ineffectiveness, 4 due to cutaneous ineffectiveness and 5 due to both. Across the entire follow-up period, only nine AEs were recorded, six of which led to treatment discontinuation (Supplemental Table 3). Over a total exposure of 351 patient-years, this corresponded to an exposure-adjusted incidence rate of 2.56 events per 100 patient-years. Two AEs were classified as severe (grade 3, according to CTCAE v5.0), namely one case of cholangiocarcinoma, not considered drug-related by the treating physician, and one case of prostatic adenocarcinoma, corresponding to a malignancy incidence rate of 0.57 events per 100 patient-years. One death (grade 5, CTCAE v.5.0) occurred during follow-up in a 72-year-old patient with severe comorbidities, including stage 5 chronic kidney disease requiring haemodialysis, overweight and dyslipidaemia; death occurred as a complication of pre-existing conditions and, therefore, was not considered related to the study drug, and corresponded to an incidence rate of 0.29 events per 100 patient-years. The remaining mild-to-moderate AEs (grade 1–2, CTCAE v.5.0) included three cases of urticaria, one prostate infection, one recurrent bladder infection and one case of creatine phosphokinase elevation. No life-threatening AEs (grade 4, CTCAE v.5.0) were observed.

Most patients were treated with the q8w GUS dosing regimen throughout follow-up, although

Table 5. Concomitant treatments and GUS dosing regimen during follow-up.

Number of patients	Baseline	12 wks	24 wks	36 wks	52 wks
	389 (100%)	**389 (100%)**	**367 (94.3%)**	**329 (84.6%)**	**319 (82.0%)**
Guselkumab q8w*	370 (95.1%)	343 (88.2%)	308 (83.9%)	292 (88.8%)	274 (85.9%)
Corticosteroids	79 (20.3%)	56 (14.4%)	38 (10.4%)	25 (7.6%)	26 (8.2%)
csDMARD	165 (42.4%)	111 (28.5%)	83 (22.6%)	75 (22.8%)	82 (25.7%)
MTX	114 (29.3%)	84 (21.6%)	62 (16.9%)	55 (16.7%)	58 (18.2%)
SSZ	33 (8.5%)	19 (4.9%)	16 (4.4%)	14 (4.3%)	17 (5.3%)
NSAID	117 (30.1%)	88 (22.6%)	60 (16.4%)	51 (15.5%)	42 (13.2%)

The table summarises the distribution of GUS dosing regimens and the use of concomitant therapies at baseline and during follow-up. Data are reported as number of patients (%). Percentages are calculated on the number of patients observed at each timepoint.
*q8w indicates the standard guselkumab dosing regimen, administered at baseline and week 4, followed by maintenance dosing every 8 weeks (as opposed to the every-4-week [q4w] regimen).
csDMARD, conventional synthetic disease-modifying anti-rheumatic drug; GUS, guselkumab; MTX, methotrexate; NSAID, non-steroidal anti-inflammatory drug; SSZ, sulfasalazine; wks, weeks.

the q4w regimen prescription increased from 4.9% at baseline to 14.1% at 52 weeks (Table 5).

Finally, the use of concomitant treatments decreased over time, with corticosteroid use reducing from 20.3% at baseline to 8.2% at 52 weeks, NSAIDs use from 30.1% to 13.2% and csDMARD use from 42.4% to 25.7% (Table 5).

Predictors of remission and discontinuation

The results of the exploratory multivariable Cox regression analyses are reported in Table 6 and Supplemental Figure 3. Female sex was associated with a 46% lower likelihood of achieving DAPSA remission compared with males (HR 0.54; $p = 0.031$). Older age was also inversely associated with remission, with each additional year reducing the hazard of remission by approximately 3% (HR per year 0.97; $p = 0.034$).

The presence of fibromyalgia was associated with a markedly lower likelihood of achieving DAPSA remission over time (HR 0.08; $p = 0.017$), as well as a lower risk of treatment discontinuation (HR 0.47; $p = 0.024$), likely reflecting the persistently high disease activity scores in the absence of objective inflammatory findings. Each additional point in the baseline DAPSA score was associated with a 6% reduction in the probability of DAPSA remission and a 3% increase in the risk of discontinuation. Regarding treatment-related factors, prior exposure to b/tsDMARDs and concomitant corticosteroid use at baseline were associated with approximately threefold and twofold increases in the risk of discontinuation, respectively (HR 3.06; $p = 0.029$ and HR 2.14; $p = 0.0039$), whereas neither factor significantly influenced the probability of achieving remission.

In the full models, the EPV ratio was 3.33 and 4.61 for predictors of DAPSA remission and treatment discontinuation, respectively. Therefore, reduced clinically driven Cox models were fitted as sensitivity analyses and are shown in Supplemental Table 2, yielding results consistent with the full models. The global Schoenfeld test did not indicate violation of the proportional hazards assumption in the reduced remission model, whereas a borderline deviation was observed in the reduced discontinuation model.

Discussion

The management of PsA in routine practice is challenged by its clinical complexity, where musculoskeletal and cutaneous manifestations coexist with cardiometabolic and psychosocial comorbidities. In everyday care, treatment decisions and outcomes are further influenced by factors only partially captured in RCTs, including patient and physician perception of disease control, treatment tolerability, access constraints and, in some settings, cost-related considerations. Consequently, in real-world cohorts, treatment response may not be fully captured by a single disease activity index,

Table 6. Predictors of DAPSA remission and treatment discontinuation.

Variable	Remission		Discontinuation	
	HR (95% CI)	*p*-Value	HR (95% CI)	*p*-Value
Sex, female vs male	0.54 (0.31–0.94)	***0.0306***	0.84 (0.52–1.37)	0.4892
Age, year	0.97 (0.95–1.00)	***0.0340***	0.99 (0.97–1.01)	0.4213
BMI, kg/m^2	0.96 (0.90–1.03)	0.2789	1.01 (0.96–1.06)	0.8015
CVD, present vs absent	1.03 (0.53–2.01)	0.9254	1.28 (0.76–2.16)	0.3460
MTB, present vs absent	1.47 (0.80–2.70)	0.2092	1.45 (0.84–2.50)	0.1829
Fibromyalgia, present vs absent	0.08 (0.01–0.64)	***0.0166***	0.47 (0.25–0.91)	***0.0242***
Axial involvement, present vs absent	1.06 (0.56–2.01)	0.8602	1.22 (0.71–2.09)	0.4730
Enthesitis, present vs absent	1.60 (0.87–2.93)	0.1298	0.91 (0.56–1.46)	0.6914
Dactylitis, present vs absent	0.91 (0.43–1.95)	0.8227	1.12 (0.63–2.01)	0.6981
Psoriasis, present vs absent	1.34 (0.70–2.57)	0.3701	0.72 (0.43–1.21)	0.2149
Psoriasis: missing data vs present	0.78 (0.10–6.22)	0.8124	1.33 (0.52–3.37)	0.5477
DAPSA score	0.94 (0.91–0.97)	***0.0005***	1.03 (1.00–1.05)	***0.0411***
CRP, mg/d	0.98 (0.62–1.54)	0.9332	1.11 (0.85–1.45)	0.4495
Prescription year	1.05 (0.74–1.51)	0.7782	1.14 (0.82–1.60)	0.4313
GUS dose, q8w vs q4w	2.08 (0.56–7.73)	0.2729	0.65 (0.18–2.31)	0.5020
Prior b/tsDMARDs, present vs absent	0.67 (0.32–1.39)	0.2788	3.06 (1.12–8.36)	***0.0290***
csDMARD use, present vs absent	0.93 (0.53–1.62)	0.7862	0.95 (0.59–1.52)	0.8341
Corticosteroids use, present vs absent	0.57 (0.22–1.50)	0.2552	2.14 (1.28–3.58)	***0.0039***
EPV	*3.33*		*4.61*	
Global Schoenfeld p-value	*0.2169*		*0.0003*	

Exploratory multivariable Cox proportional hazards models were used to identify baseline predictors of DAPSA remission and treatment discontinuation. For the remission analysis, patients in DAPSA remission at baseline were excluded, and the event was defined as the first follow-up visit meeting the DAPSA remission threshold. For the discontinuation analysis, the event was defined as treatment discontinuation, with patients censored at the end of follow-up if still on treatment. Continuous variables were modelled per unit increase. Events per variable and the global Schoenfeld test *p*-value are reported to assess model stability and the proportional hazards assumption. Results are reported as HRs with 95% CIs. *p*-Values were reported in bold italics if <0.05.
Italics text reports model diagnostics, including events per variable (EPV) and the global Schoenfeld test p-value for assessment of the proportional hazards assumption.
b/tsDMARD, biologic/targeted synthetic disease-modifying anti-rheumatic drug; BMI, body mass index; CI, confidence interval; CRP, C-reactive protein; csDMARD, conventional synthetic disease-modifying anti-rheumatic drug; CVD, cardiovascular diseases; DAPSA, Disease Activity in Psoriatic Arthritis; EPV, event-per-variable ratio; GUS, guselkumab; HR, hazard ratio; MTB, metabolic diseases; q4w, every 4 weeks; q8w, every 8 weeks.

and 'effectiveness' should integrate domain-specific measures with broader outcomes such as treatment persistence, reduction of concomitant therapies and symptoms resolution.

In this context, robust real-world evidence (RWE) is essential to complement RCTs and to clarify how newer mechanisms of action, in our case IL-23p19 blockade, perform under routine-care

conditions in heterogeneous and comorbidity-rich populations.

In the IMPACT study, four main messages emerge.

First, GUS was associated with sustained improvement in musculoskeletal disease activity in a large, multicentre, real-life cohort of patients with PsA, with early DAPSA reduction maintained through 12 months and paralleled by improvements in pain perception.

Second, GUS demonstrated effectiveness in several disease domains, with marked skin improvement, exploratory evidence of ASDAS improvement among patients diagnosed with axial PsA and progressive reduction in concomitant therapy use, particularly corticosteroids, providing a clinically intuitive, real-world picture of effectiveness extending beyond improvements in disease activity scores.

Third, patient-related factors, including sex, age, fibromyalgia, baseline disease activity, prior b/ts DMARDs exposure and corticosteroid use, were associated with the probability of achieving remission and/or treatment discontinuation, highlighting the relevance of clinical context in achieving stringent targets.

Fourth, despite high baseline disease burden and prevalent prior b/tsDMARD exposure, GUS showed favourable persistence and a reassuring safety profile, while acknowledging the potential for incomplete AE capture in real-world studies.

The primary aim of this study was to assess the real-world effectiveness on peripheral disease activity. We observed an early improvement in the DAPSA score, sustained through 12 months. In addition, the distribution of DAPSA categories shifted from predominately moderate-to-high disease activity toward LDA and remission, with DAPSA-LDA becoming the dominant category by 12 months.

Consistent improvements in pain and PtGA support the patient's perceived clinical benefit, and the reduction of CRP levels suggests an overall anti-inflammatory effect.

Enthesitis and dactylitis, difficult domains in the management of PsA therapy, also significantly improved over follow-up. Enthesitis resolution increased progressively, whereas dactylitis showed high resolution rates from early timepoints, with few incident cases observed during follow-up.

Peripheral musculoskeletal efficacy of GUS has been established in phase III RCTs, including both bDMARD-naïve and bDMARD-experienced patients.[7–12] In these trials, ACR response criteria, less commonly used in RWE, were the primary endpoints, limiting comparisons with our outcomes. Nevertheless, a pooled post hoc analysis from DISCOVER-1 and DISCOVER-2 trial reported 1-year DAPSA LDA and remission rates closely comparable to our findings, specifically of ~53% and ~18% for LDA and remission, respectively.[18]

The 1-year enthesitis and dactylitis resolution rates in other pooled RCT analyses (~58% and ~75%, respectively) were also consistent with our results.[19,20] Notably, lower resolution rates have been reported in RCTs focusing on bDMARD-experienced populations (~56% and ~67% for enthesitis and dactylitis, respectively),[21] which is notable given the high proportion of such patients in our cohort.

RWE from Italian and European cohorts confirms similar trends. Data from the Italian GISEA registry, including 170 patients treated with GUS, reported a numerically superior 1-year DAPSA improvement compared to our findings, with approximately 70% of patients achieving DAPSA LDA, and a 12-month drug retention of ~76%, with bDMARD-naïve status associated with a higher likelihood of achieving minimal disease activity.[22] A separate analysis of 111 patients by Ruscitti et al.[23] reported a 6-month DAPSA LDA rate of ~40%, with an 18-month drug retention of ~67%, without significant differences between clinical subgroups. Additional Italian and European real-world studies with smaller sample sizes have reported broadly comparable effectiveness and persistence outcomes.[24–27]

Although peripheral domains dominated the clinical phenotype, axial involvement was identified in a relevant subset of patients, in whom a reduction in the ASDAS score was observed over follow-up. However, interpretation of this outcome warrants caution for several reasons. First, MRI assessment was performed and interpreted locally, potentially introducing inter-centre variability. Second, imaging follow-up was not systematically available. Third, ASDAS score has not been

specifically validated for axial PsA and includes patient-reported components that may be influenced by peripheral disease activity, pain perception and comorbid conditions. Growing data support the clinical effectiveness of GUS, and IL-23 axis inhibition, in the axial domain of PsA, both in post hoc analyses[28] and in dedicated RWE studies,[29–31] showing outcomes comparable to those reported in our cohort. However, our findings regarding axial involvement are exploratory and should not be interpreted as clear evidence of axial effectiveness, but rather as a clinically relevant real-world signal, consistent with emerging literature and requiring confirmation in dedicated studies with appropriate classification of axial PsA. In this regard, a dedicated RCT is currently ongoing.[32]

Cutaneous efficacy represents a well-established strength of IL-23 inhibition, and our real-world data confirm the high rates of PASI-90 and PASI-100 responses available in the literature,[33,34] supporting the effective musculoskeletal and cutaneous control in routine clinical practice.

Treatment persistence is a real-world outcome reflecting not only clinical response but also safety, patient perception and healthcare-system factors. In this cohort, 12-month persistence was 78.7%, with clinically plausible lower retention among patients with multiple prior b/tsDMARDs.

In the absence of an internal comparator, treatment persistence may provide a useful contextual benchmark across real-world cohorts, although indirect comparisons across mechanisms should be interpreted very cautiously. Large RWE comparing multiple b/tsDMARDs persistence in PsA were mostly conducted before the availability of IL-23 inhibitors. In the PsABio study, the 1-year persistence was 80% for TNFi and 83.6% for ustekinumab,[35] whereas a French nationwide cohort reported substantially lower retention, with 1-year persistence of 36.8%, 46.3% and 56.0% for TNFi, IL-17i and ustekinumab, respectively.[36]

More recent Italian and Spanish data are available for IL-17i, reporting 12-month retention rates of 77.5% and 81.0%, respectively.[37,38] Large persistence data on JAK inhibitors are more limited; in the BIOBADASER registry, 1-year persistence in PsA was 60.6% for JAKi, compared with 69.3% for TNFi.[39]

Regarding GUS persistence, comparable findings have been reported in the CorEvitas PsA/SpA Registry and in an Italian real-world analysis, which respectively reported 6-month and 1-year persistence of 79% and 80%.[40,41] In addition, comparative observational studies reported long-term retention rate for GUS higher than other bDMARD classes, such as TNFi or IL-17i.[42,43] Taken together, these data place the persistence observed in IMPACT within the range of available RWE benchmarks, without implying comparative superiority.

In our study, most patients remained on the standard q8w regimen; however, the proportion receiving q4w dosing increased from 4.9% at baseline to 14.1% at 12 months. Although the study was not designed to formally analyse the dosing regimen variation, this finding reflects the pragmatic use of dose escalation as a real-world strategy to manage partial or incomplete response. However, patients escalated to q4w likely represent a subgroup with more difficult-to-treat disease, and therefore no comparative interpretation between dosing regimens should be inferred.

The use of concomitant therapies, including csDMARDs, corticosteroids and NSAIDs, decreased over time. Although tapering decisions in observational cohorts are not standardised and may be influenced by multiple factors, including physician preference and local clinical practice, this overall reduction may still represent an indirect indicator of improved disease control in routine care.

Exploratory multivariable analyses provided useful insights into clinical factors associated with treatment outcomes. Female sex and older age were associated with a lower likelihood of achieving DAPSA remission, consistent with previous reports.[41] Higher baseline DAPSA was also inversely associated with remission, suggesting that a greater initial disease burden makes stringent remission targets more difficult to achieve. Fibromyalgia emerged as a strong negative predictor of remission, while also being associated with a lower risk of discontinuation. This apparently paradoxical finding is clinically coherent: fibromyalgia may inflate subjective components of DAPSA. In sensitivity analyses excluding patients with fibromyalgia, the absolute number of patients achieving DAPSA remission remained essentially unchanged despite the smaller cohort size, suggesting that very few patients with

concomitant fibromyalgia achieved remission. This finding emphasises the potential limitations of treat-to-target strategies based on composite scores in patients with central sensitisation and the importance of careful interpretation of clinical scores in this context.

Regarding treatment discontinuation, prior b/tsDMARD exposure and baseline corticosteroid use were associated with a higher discontinuation risk, probably reflecting more severe or treatment-refractory disease.

Collectively, these predictors may help identify patients requiring closer monitoring and support a more realistic expectation of achievable targets within the first year of therapy. However, Cox regression analyses were exploratory, and they could be affected by model instability due to the limited number of events relative to covariates; sensitivity analysis with reduced models yielded consistent results, although a borderline deviation from the proportional hazards assumption was observed for the predictors of discontinuation, further supporting a cautious interpretation of these analyses.

Compared with previous real-world studies on GUS in PsA, IMPACT adds evidence from a large multicentre cohort enriched with patients previously exposed to b/tsDMARDs. This population likely reflects the Italian reimbursement criteria for GUS, which mainly restrict its use to patients with prior b/tsDMARD exposure, and therefore extrapolation of these findings to different healthcare systems should be performed cautiously. This study integrates longitudinal disease activity outcomes, treatment retention, predictors of remission and discontinuation, conservative sensitivity analyses accounting for attrition and stratified analyses according to prior b/tsDMARD exposure. This provides a pragmatic assessment of GUS performance in a heavily pretreated routine-care population, complementing available registry and multicentre evidence.

Limitations

Limitations are inherent to the observational design, including potential missing data, limited capture of granular variables, such as NSAID dosing or the assessment of nail psoriasis, and probable underreporting of minor AEs. In addition, post-discontinuation missing data over follow-up represent a common challenge in real-world studies and may have introduced attrition bias, potentially leading to some overestimation of observed response rates. To mitigate this issue, additional sensitivity analyses were performed, showing overall consistent results across outcomes, although a residual overestimation of effectiveness cannot be excluded. Furthermore, missing data regarding skin-related outcomes were handled with a complete-case approach, and this may have introduced selection bias. In this cohort, the real-world observational design limited the systematic collection of functional capacity data, precluding a reliable assessment of a comprehensive multidomain outcome such as minimal disease activity. This represents a relevant limitation, as reliance on individual disease activity measures, such as DAPSA, may not fully capture the multidomain nature of PsA.

Additional limitations concern both the assessment of axial involvement, for which axial outcomes should be considered exploratory as stated above, and the assessment of fibromyalgia, which was based on routine clinical evaluation rather than systematic application of formal classification criteria, potentially introducing inter-centre variability. Finally, the study was conducted in tertiary referral rheumatology centres, which may limit the generalisability of the findings to other clinical settings.

Conclusion

In this large multicentre real-world cohort, GUS was associated with early and sustained improvement in several disease domains, favourable treatment persistence and no unexpected safety signals in a real-life PsA population, supporting its role as an effective option for psoriatic disease management in routine care.

Declarations

Ethics approval and consent to participate

The study protocol was approved by the Lazio Regional Ethics Committee (Protocol Number 0022902/2024 – Comitato Etico Territoriale Lazio Area 2) and was conducted in accordance with the principles of the Declaration of Helsinki and Good Clinical Practice guidelines. Consent to participate: Written informed consent was obtained from all participants in accordance with the Declaration of Helsinki and as required by the approving Ethics Committee.

Consent for publication
Not applicable.

Author contributions

Valentino Paci: Conceptualisation; Data curation; Formal analysis; Investigation; Methodology; Resources; Software; Validation; Visualisation; Writing – original draft.

Roberta Foti: Conceptualisation; Data curation; Formal analysis; Investigation; Methodology; Resources; Validation; Visualisation; Writing – original draft.

Ilenia Pantano: Data curation; Investigation; Resources.

Antonio Carletto: Data curation; Investigation; Resources.

Eleonora Celletti: Data curation; Investigation; Resources.

Giovanni Francesco Miceli: Data curation; Investigation; Resources.

Ignazio Cangemi: Data curation; Investigation; Resources.

Giuseppe Lopalco: Data curation; Investigation; Resources.

Simona Montalbano: Data curation; Investigation; Resources.

Maria Sole Chimenti: Data curation; Investigation; Resources.

Andrea Picchianti Diamanti: Data curation; Investigation; Resources.

Umberto Massafra: Data curation; Investigation; Resources.

Emilio Filippucci: Data curation; Investigation; Resources.

Anna Parisi: Data curation; Investigation; Resources.

Pietro Leccese: Data curation; Investigation; Resources.

Anna Panaccione: Data curation; Investigation; Resources.

Ilaria Puca: Data curation; Investigation; Resources.

Giorgio Amato: Data curation; Investigation; Resources.

Sabrina Marrone: Data curation; Investigation; Resources.

Myriam Di Penta: Data curation; Investigation; Resources.

Salvatore Corrao: Data curation; Investigation; Resources.

Eneida Cela: Data curation; Investigation; Resources.

Alessandra Rai: Data curation; Investigation; Resources.

Enrico Tirri: Data curation; Investigation; Resources.

Florenzo Iannone: Data curation; Investigation; Resources.

Fabiola Atzeni: Data curation; Investigation; Resources.

Maurizio Rossini: Data curation; Investigation; Resources.

Francesco Ciccia: Data curation; Investigation; Resources.

Rosario Foti: Data curation; Investigation; Resources.

Gianluca Moroncini: Conceptualisation; Investigation; Methodology; Project administration; Resources; Supervision; Validation; Writing – review & editing.

Michele Maria Luchetti Gentiloni: Conceptualisation; Funding acquisition; Investigation; Methodology; Project administration; Resources; Supervision; Validation; Writing – review & editing.

Acknowledgments
The following members of the IMPACT study group contributed to patient recruitment and data collection: Giulia Marchionni – Clinical Medicine, Department of Clinical and Molecular Sciences and Internal Medicine Department, Polytechnic University of Marche, Azienda Ospedaliero Universitaria delle Marche, Ancona, Italy; Rosanna Somma – Rheumatology Unit, University of Verona, Verona, Italy; Riccardo Maria Ricciardi – Department of Medicine and Science of Aging, Medical Clinic, SS. Annunziata Hospital of Chieti, 'G. D'Annunzio' University of Chieti-Pescara, Chieti, Italy; Cesare Siragusano – Rheumatology Unit, AOU G. Martino, University of Messina, Messina, Italy; Salvatore Scibetta – Department of Clinical Medicine, Internal Medicine Unit with Rheumatology, Dermatology, Diabetology and Tertiary Diabetic

Foot Health Care, National Relevance and High Specialization Hospital Trust ARNAS Civico Di Cristina Benfratelli, Palermo, Italy; Vincenzo Venerito – Department of Precision and Regenerative Medicine and Ionian Area (DiMePRe-J), University of Bari 'Aldo Moro', Bari, Italy; Arianna D'Antonio – Rheumatology, Allergology and Clinical Immunology, Department of Systems Medicine, University of Rome Tor Vergata, Rome, Italy; Emanuele Tesoriere – Department of Clinical and Molecular Medicine, S. Andrea University Hospital, 'Sapienza' University of Rome, Rome, Italy; Andrea Di Matteo – Leeds Institute of Rheumatic and Musculoskeletal Medicine, Faculty of Medicine and Health, University of Leeds, Leeds, UK; Ilenia De Andres – Rheumatology, ARNAS 'Garibaldi' Hospital, Catania, Italy; Luca Navarini – Rheumatology and Clinical Immunology, University of Rome 'Campus Bio-Medico', Rome, Italy; Luca Di Cato – Rheumatology, Santa Maria General Hospital, Terni, Italy.

Funding

The authors disclosed receipt of the following financial support for the research, authorship and/or publication of this article: Valentino Paci received an unconditional grant from Johnson & Johnson for medical writing related to this manuscript. Journal fees (Article Processing Charges) for this manuscript were unconditionally funded by Johnson & Johnson. Johnson & Johnson had no influence on the manuscript content or the authors' decision to publish. This research did not receive any other specific grant from funding agencies in the public, commercial or not-for-profit sectors.

Competing interests

The authors declared the following potential conflicts of interest with respect to the research, authorship and/or publication of this article: V.P. received an unconditional grant from Johnson & Johnson for medical writing related to this manuscript, speaking and/or consulting fees from AbbVie, Eli Lilly and Johnson & Johnson. G.M. reports speaking and/or consulting fees from AbbVie, Johnson & Johnson, Novartis and Pfizer. M.M.L.G. reports research support from AbbVie, speaking and/or consulting fees from AbbVie, Amgen, Eli-Lilly, Johnson & Johnson, Novartis and Pfizer. The remaining authors declared no potential conflicts of interest with respect to the research, authorship and/or publication of this article.

ORCID iDs

Valentino Paci https://orcid.org/0000-0002-9466-8460

Roberta Foti https://orcid.org/0000-0002-3074-4508

Eleonora Celletti https://orcid.org/0009-0007-5301-9900

Giuseppe Lopalco https://orcid.org/0000-0003-4524-9566

Maria Sole Chimenti https://orcid.org/0000-0002-1343-1729

Andrea Picchianti Diamanti https://orcid.org/0000-0002-8552-4641

Alessandra Rai https://orcid.org/0000-0001-8102-7421

Florenzo Iannone https://orcid.org/0000-0003-0474-5344

Maurizio Rossini https://orcid.org/0000-0001-9692-2293

Francesco Ciccia https://orcid.org/0000-0002-9352-1264

Rosario Foti https://orcid.org/0000-0002-7301-8362

Availability of data and materials

The individual participant data that underlie the results reported in this article will be made available upon reasonable request to the corresponding author. Requests for data sharing outside the European Union will be evaluated in accordance with the EU General Data Protection Regulation (Regulation (EU) 2016/679, GDPR) and applicable Italian privacy laws, to ensure appropriate safeguards for international data transfer.

Artificial intelligence disclosure

Generative artificial intelligence was not used to create text, references, images or other content in this article.

Supplemental material

Supplemental material for this article is available online.

References

1. FitzGerald O, Ogdie A, Chandran V, et al. Psoriatic arthritis. *Nat Rev Dis Primers* 2021; 7: 1–17.
2. Armstrong A, Bohannan B, Mburu S, et al. Impact of psoriatic disease on quality of life: interim results of a global survey. *Dermatol Ther (Heidelb)* 2022; 12: 1055–1064.
3. Gupta S, Syrimi Z, Hughes DM, et al. Comorbidities in psoriatic arthritis: a systematic review and meta-analysis. *Rheumatol Int* 2021; 41: 275.
4. James L, Hailey LH, Suribhatla R, et al. The impact of psoriatic arthritis on quality of life: a systematic review. *Ther Adv Musculoskelet Dis* 2024; 16: 1759720X241295920.
5. Kavanaugh A, Helliwell P and Ritchlin CT. Psoriatic arthritis and burden of disease: patient perspectives from the population-based multinational assessment of psoriasis and psoriatic arthritis (MAPP) survey. *Rheumatol Ther* 2016; 3: 91–102.
6. Benfaremo D, Paci V, Luchetti MM, et al. Novel therapeutic approaches and treatment targets for psoriatic arthritis. *Curr Pharm Biotechnol* 2021; 22: 85–98.
7. Deodhar A, Helliwell PS, Boehncke WH, et al. Guselkumab in patients with active psoriatic arthritis who were biologic-naive or had previously received TNFα inhibitor treatment (DISCOVER-1): a double-blind, randomised, placebo-controlled phase 3 trial. *Lancet* 2020; 395: 1115–1125.
8. Mease PJ, Rahman P, Gottlieb AB, et al. Guselkumab in biologic-naive patients with active psoriatic arthritis (DISCOVER-2): a double-blind, randomised, placebo-controlled phase 3 trial. *Lancet* 2020; 395: 1126–1136.
9. Coates LC, Gossec L, Theander E, et al. Efficacy and safety of guselkumab in patients with active psoriatic arthritis who are inadequate responders to tumour necrosis factor inhibitors: results through one year of a phase IIIb, randomised, controlled study (COSMOS). *Ann Rheum Dis* 2021; 81: 359–369.
10. McInnes IB, Rahman P, Gottlieb AB, et al. Efficacy and safety of guselkumab, an interleukin-23p19-specific monoclonal antibody, through one year in biologic-naive patients with psoriatic arthritis. *Arthritis Rheumatol* 2021; 73: 604–616.
11. McInnes IB, Rahman P, Gottlieb AB, et al. Long-term efficacy and safety of guselkumab, a monoclonal antibody specific to the p19 subunit of interleukin-23, through two years: results from a phase III, randomized, double-blind, placebo-controlled study conducted in biologic-naive patients with active psoriatic arthritis. *Arthritis Rheumatol* 2022; 74: 475–485.
12. Ritchlin CT, Mease PJ, Boehncke WH, et al. Durable control of psoriatic arthritis with guselkumab across domains and patient characteristics: post hoc analysis of a phase 3 study. *Clin Rheumatol* 2024; 43: 2551–2563.
13. Eichler HG, Pignatti F, Schwarzer-Daum B, et al. Randomized controlled trials versus real world evidence: neither magic nor myth. *Clin Pharmacol Ther* 2020; 109: 1212.
14. Wilson BE and Booth CM. Real-world data: bridging the gap between clinical trials and practice. *EClinicalMedicine* 2024; 78: 102915.
15. Rudwaleit M, Jurik AG, Hermann KGA, et al. Defining active sacroiliitis on magnetic resonance imaging (MRI) for classification of axial spondyloarthritis: a consensual approach by the ASAS/OMERACT MRI group. *Ann Rheum Dis* 2009; 68: 1520–1527.
16. Lambert RGW, Bakker PAC, Van Der Heijde D, et al. Defining active sacroiliitis on MRI for classification of axial spondyloarthritis: update by the ASAS MRI working group. *Ann Rheum Dis* 2016; 75: 1958–1963.
17. Baraliakos X, Østergaard M, Lambert RGW, et al. MRI lesions of the spine in patients with axial spondyloarthritis: an update of lesion definitions and validation by the ASAS MRI working group. *Ann Rheum Dis* 2022; 81: 1243–1251.
18. Coates LC, Ritchlin CT, Gossec L, et al. Guselkumab provides sustained domain-specific and comprehensive efficacy using composite indices in patients with active psoriatic arthritis. *Rheumatology (Oxford)* 2023; 62: 606–616.
19. Mcgonagle D, Mcinnes IB, Deodhar A, et al. Resolution of enthesitis by guselkumab and relationships to disease burden: 1-year results of two phase 3 psoriatic arthritis studies. *Rheumatology (Oxford)* 2021; 60: 5337–5350.
20. McGonagle D, McInnes IB, Deodhar A, et al. Guselkumab, a selective interleukin-23 p19 subunit inhibitor, resolves dactylitis in patients with active psoriatic arthritis: pooled results through week 52 from two phase 3 studies. *ACR Open Rheumatol* 2023; 5: 227–240.
21. Marzo-Ortega H, McInnes IB, Sharaf M, et al. Impact of dactylitis and enthesitis resolution on disease control in guselkumab-treated psoriatic arthritis patients with TNFi-IR: COSMOS post

hoc analysis. *Rheumatology (Oxford)* 2026; 65(1): keaf490.

22. Atzeni F, Rotondo C, Siragusano C, et al. Italian multicenter real-world study on the twelve-month effectiveness, safety, and retention rate of guselkumab in psoriatic arthritis patients. *J Clin Med* 2025; 14: 4111.
23. Ruscitti P, Cataldi G, Gentile M, et al. The evaluation of effectiveness and safety of guselkumab in patients with psoriatic arthritis in a prospective multicentre 'real-life' cohort study. *Rheumatol Ther* 2024; 11: 539.
24. Farina N, Boffini N, Adinolfi A, et al. Real-world efficacy and retention of guselkumab in psoriatic arthritis: insights from a 12-month multicenter study. *ARP Rheumatol* 2025; 4(3): 215–220.
25. Pantano I, Mauro D, Romano F, et al. Real-life efficacy of guselkumab in patients with early psoriatic arthritis. *Rheumatology (Oxford)* 2022; 61: 1217–1221.
26. Ak T, Temiz SNY, Taner M, et al. Effectiveness of anti-interleukin-23 therapy in psoriatic arthritis: a pilot prospective real-world study. *Int J Rheum Dis* 2023; 26: 878–884.
27. Rocamora V, Crespi L, Ferran M, et al. Guselkumab effectiveness and survival in patients with psoriasis and psoriatic arthritis: multicenter analysis in daily clinical practice by the Spanish Psoriasis Group. *Dermatol Ther* 2022; 35: e15865.
28. Mease PJ, Gladman DD, Poddubnyy D, et al. Efficacy of guselkumab on axial-related symptoms through up to 2 years in adults with active psoriatic arthritis in the phase 3, randomized, placebo-controlled DISCOVER-2 study. *Rheumatol Ther* 2023; 10: 1637–1653.
29. Tonutti A, Abacar K, Macleod T, et al. Time to lift the moratorium on IL-23 inhibitors for axial psoriatic arthritis. *Lancet Rheumatol* 2025; 8: e144–e156.
30. Ruscitti P, Pantano I, Cataldi G, et al. Short-term effectiveness of guselkumab in psoriatic arthritis patients and axial involvement: results from a real-life multicentre cohort. *Rheumatology* 2025; 64: 1122–1130.
31. Foti R, Amato G, Visalli E, et al. Guselkumab in psoriatic arthritis: therapeutic impact on axial and peripheral involvement – monocentric real-world evidence. *J Clin Med* 2025; 14: 3151.
32. Gladman DD, Mease PJ, Bird P, et al. Efficacy and safety of guselkumab in biologic-naïve patients with active axial psoriatic arthritis: study protocol for STAR, a phase 4, randomized, double-blinded, placebo-controlled trial. *Trials* 2022; 23: 743.
33. Blauvelt A, Papp KA, Griffiths CEM, et al. Efficacy and safety of guselkumab, an anti-interleukin-23 monoclonal antibody, compared with adalimumab for the continuous treatment of patients with moderate to severe psoriasis: results from the phase III, double-blinded, placebo- and active comparator-controlled VOYAGE 1 trial. *J Am Acad Dermatol* 2017; 76: 405–417.
34. Reich K, Armstrong AW, Foley P, et al. Efficacy and safety of guselkumab, an anti-interleukin-23 monoclonal antibody, compared with adalimumab for the treatment of patients with moderate to severe psoriasis with randomized withdrawal and retreatment: results from the phase III, double-blind, placebo- and active comparator-controlled VOYAGE 2 trial. *J Am Acad Dermatol* 2017; 76: 418–431.
35. Gossec L, Siebert S, Bergmans P, et al. Long-term effectiveness and persistence of ustekinumab and TNF inhibitors in patients with psoriatic arthritis: final 3-year results from the PsABio real-world study. *Ann Rheum Dis* 2023; 82: 496–506.
36. Pina Vegas L, Hoisnard L, Bastard L, et al. Long-term persistence of second-line biologics in psoriatic arthritis patients with prior TNF inhibitor exposure: a nationwide cohort study from the French health insurance database (SNDS). *RMD Open* 2022; 8: e002681.
37. Paci V, Ariani A, Celletti E, et al. Does prior exposure affect retention? A real-world, multicentre assessment of IL-17 inhibitor cycling in psoriatic arthritis. *Rheumatol Ther* 2026; 13(3): 629–643.
38. Joven B, Manteca CF, Rubio E, et al. Real-world persistence and treatment patterns in patients with psoriatic arthritis treated with anti-IL17 therapy in Spain: the PerfIL-17 study. *Adv Ther* 2023; 40: 5415.
39. Hernández-Cruz B, Otero-Varela L, Freire-González M, et al. Janus kinase inhibitors and tumour necrosis factor inhibitors show a favourable safety profile and similar persistence in rheumatoid arthritis, psoriatic arthritis and spondyloarthritis: real-world data from the BIOBADASER registry. *Ann Rheum Dis* 2024; 83: 1189–1199.
40. Mease PJ, Ogdie A, Tesser J, et al. Six-month persistence and multi-domain effectiveness of guselkumab in adults with psoriatic arthritis: real-world data from the CorEvitas Psoriatic Arthritis/Spondyloarthritis Registry. *Rheumatol Ther* 2023; 10: 1479.

Visit Sage journals online
journals.sagepub.com/
home/tab

Sage journals

41. Becciolini A, Marchesoni A, Parisi S, et al. Guselkumab effectiveness in real-world settings: observations from an Italian multicentre study. *Rheumatol Adv Pract* 2025; 9: rkaf094.

42. Mease PJ, Walsh JA, Fitzgerald TP, et al. On-label treatment persistence through 24 months among patients with active psoriatic arthritis initiating guselkumab or subcutaneous tumor necrosis factor inhibitors. *Rheumatol Ther* 2025; 13: 115.

43. Mease PJ, Ferrante SA, Shiff NJ, et al. Comparison of on-label treatment persistence in real-world patients with psoriatic arthritis receiving guselkumab versus subcutaneous interleukin-17A inhibitors. *Adv Ther* 2025; 42: 734–751.