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Concise report

Real-life efficacy of guselkumab in patients with early psoriatic arthritis

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Abstract

Objectives. To assess the efficacy of the novel anti-IL-23 monoclonal antibody guselkumab in a real-life observational cohort of patients with early PsA.

Methods. We conducted an observational study on patients with early PsA followed by the joint dermatology-rheumatology clinics of two Italian centres starting therapy with guselkumab for severe skin involvement. Each patient was evaluated at baseline and every 24 weeks for one year, recording Disease Activity Index for PsA (DAPSA), PASI, VAS Pain, VAS Prutitus, Patient's Global Assessment (PtGA) and assessing DAPSA response.

Results. Twenty-four patients were recruited (16 women). The mean duration of skin disease was 12.5 years (CI 8; 17), but all patients had a shorter articular disease duration, 21.29 months (CI 15.9; 26.68). At baseline, all patients displayed a moderate cutaneous disease with a mean PASI of 15.2 (CI 11.7–18.6) and high disease activity, characterized by mean DAPSA of 26.84 (CI 22.49–31.19). An inflammatory low back pain was reported by five patients (20%) with a mean BASDAI 5.1 (CI 4,38–5,85) at baseline. The majority of guselkumab-treated patients ($n = 18$; 75%) reached DAPSA remission or DAPSA low disease activity after six months. Seventeen out of 24 patients completed 12 months of treatment, 11 of them (65%) in low disease activity, six (35%) in remission. All patients with axial disease reported improvement of inflammatory low back pain at week 24 with a mean BASDAI 2.98 (CI 2,18– 3,77). No significant side effects were reported.

Conclusions. Real-life data on a cohort of early PsA patients confirm the efficacy and safety of guselkumab on peripheral and axial manifestations.

Key words: PsA, spondyloarthritis, psoriasis, guselkumab, IL-23

Rheumatology key messages

- Guselkumab is safe and effective for the treatment of early PsA in a real-life setting.
- Real-life data on larger cohorts are, however, warranted.

Introduction

Guselkumab is a fully human IgG1 lambda monoclonal antibody that binds to the p19 subunit of IL-23. Blocking IL-23 with guselkumab is an effective therapeutic strategy in patients with psoriasis (PsO) [1], and more recently, two randomized clinical trials (RCTs) have also demonstrated its efficacy in patients with PsA [2, 3]. Although not yet approved in Italy for PsA, guselkumab is widely used for the treatment of PsO.

The evidence that ~30% of PsO patients develop chronic inflammatory joint disease makes PsO the most sensible clinical biomarker of PsA predictive for the development. In Italy, one year after the diagnosis of severe PsO, the incidence rate of PsA has been estimated to be 8.4% [4]. Therefore, the dermatological clinics are privileged settings to observe and treat patients with early PsA [5].

This study aimed to investigate the efficacy of guselkumab on articular inflammatory manifestations, satisfying criteria for PsA, in PsO patients in a real-life setting.

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CLINICAL SCIENCE

Patients and methods

From January 2019, 24 consecutive patients with early active PsA (less than two years of joint involvement), diagnosed according to CASPAR criteria [6], admitted to the joint dermatologist-rheumatologist outpatient clinics of the University della Campania L. Vanvitelli and Humanitas University, Italy, were considered for the study. The study was observational, and the patients were treated according to current medical practice. The study was performed according to the Helsinki declaration, and patients provided written informed consent for data collection and analysis. The study was performed following the approval of the ethical committee of the University of Campania 'L. Vanvitelli' university hospital (20200027743/i).

For each patient, information on sex, age, BMI, disease duration, time of diagnosis of PsA and smoking status were retrieved at baseline. All the PsA patients started therapy with guselkumab after performing screening for TB and hepatitis for the dermatological indication, and PASI score, VAS pruritus, PtGA and DAPSA were assessed at baseline and then after 6 and 12 months. At both baseline and at 3 and 6 months, patients were classified in remission (REM), low (LDA), moderate (MDA) or high (HDA) disease activity according to DAPSA criteria [7]. Statistical analysis was performed by using GraphPad Prism comparing the baseline values with the assessment at week 24 and 52 by one-way ANOVA and Dunnet's test for multiple comparisons.

Results

Baseline characteristics

Eight males and 16 females PsA patients started therapy with guselkumab, the mean age was 51.4 years and the mean duration of skin disease was 12.5 years (8–17). Detailed information on the baseline characteristics of PsA patients is shown in Table 1.

The Dermatology Unit already followed these patients for skin involvement, and only subsequently, they developed joint involvement as assessed during the joint dermatology-rheumatology clinic.

All the patients had a shorter joint disease duration $\leq$2 years, mean 21.29 months (15.9; 26.68). Most patients ($n = 14$) had already undergone therapy with other biological drugs (eight patients were on the third line of treatment, four patients on the second line, one patient on the fourth and one patient on the fifth line). Ten out of 24 patients (42%) were bDMARDs naive. Five out of 24 patients were also taking methotrexate at baseline and continued the same dose of methotrexate throughout the observation period. At baseline, all the patients displayed a moderate cutaneous disease with a mean PASI of 15.2 (11.7–18.6) and a mean VAS pruritus of 7.09 (5.06–9.13). An oligoarticular peripheral pattern of joint involvement was observed in 70%, whereas a polyarticular pattern was observed in 30%. At baseline, all the patients with peripheral joint involvement showed a high disease activity, characterized by a mean PtGA of 7.12 (6.09–8.15) and mean DAPSA of 26.84 (22.49–31.19). A clinician-diagnosed axial involvement, defined as inflammatory back pain in the absence of other cause, was also present in five PsA patients (20%); all of them showed a BASDAI $>$4 [mean BASDAI 5.1 (4.38–5.85)].

Response to guselkumab

After 24 weeks of guselkumab treatment, joint and skin disease activity was assessed. The majority of guselkumab-treated patients ($n = 18$; 75%) reached a remission or DAPSA-low disease activity (LDA) after six months of guselkumab treatment. In particular, 13 of these patients were in LDA (72%), 5 out of 18 patients achieved remission. As shown in Fig. 1, in comparison to baseline, VAS-Pain was also significantly reduced after treatment with guselkumab:

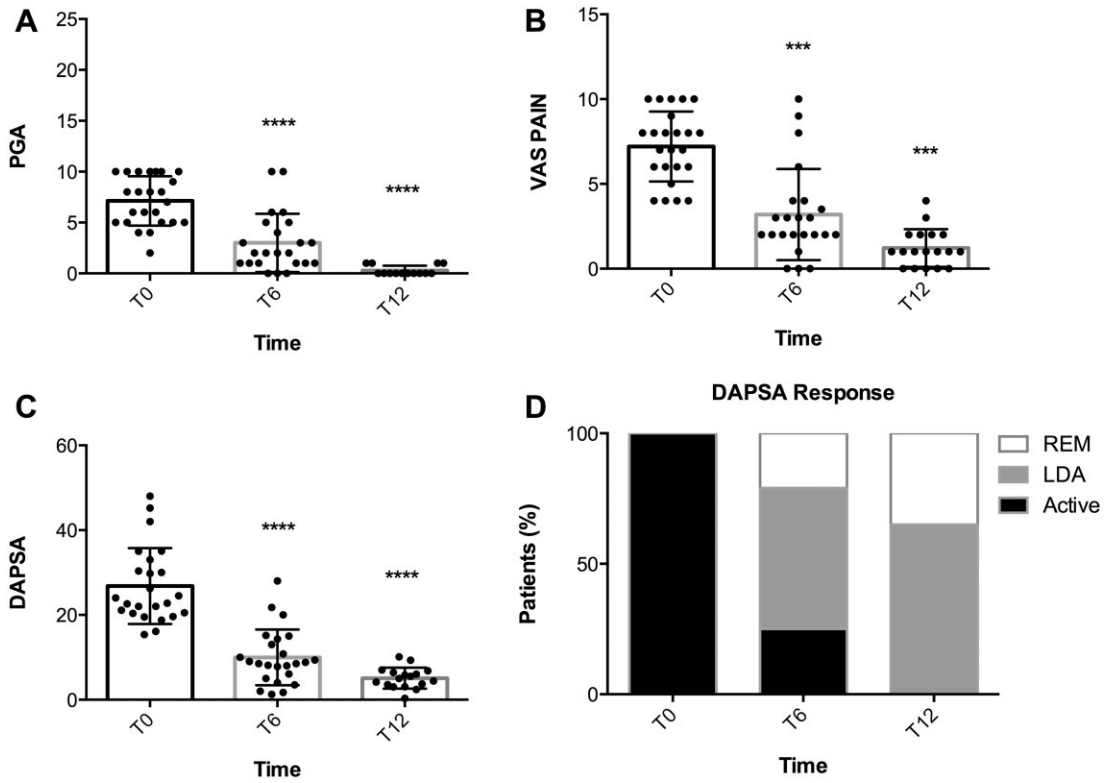
Table 1 Baseline characteristics of the 24 patients included in the study

Age at inclusion, mean (95% CI), years	51.4 [45.7, 57.16]
Sex, women, *n* (%)	16 (66,7)
BMI, median [95% CI]	26.83 [22.55, 28.18]
Smoker, *n* (%)	10 (42)
Disease duration of PsO mean [95% CI], years	12.5 [8, 17]
Disease duration of PsA mean [95% CI], months	21.29 [15.9, 26.68]
Axial involvement, *n* (%)	5 (20)
Peripheral involvement, *n* (%)	22 (91)
MTX use, *n* (%)	5 (20%)
Line of treatment:	
First, *n* (%)	10 (42)
Second, *n* (%)	4 (16.6)
Third, *n* (%)	8 (33.2)
Fourth, *n* (%)	1 (4.1)
Fifth, *n* (%)	1 (4.1)
PASI mean [95% CI]	15.2 [11.7, 18.6]
DAPSA mean [95% CI]	26.84 [22.49, 31.19]

DAPSA: Disease Activity Index for PsA; PASI: Psoriasis Area and Severity Index; PsO: psoriasis.

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FIG. 1 Clinical articular response to guselkumab therapy.



The mean value of Patient Global Assessment (**A**), Visual Analogue Scale of Pain (VAS Pain) (**B**), Disease Activity Score of PsA (**C**) are shown before the therapy with guselkumab (T0) and after 6 (T6) and 12 months (T12) of therapy. The Disease Activity Index for PsA response is reported in (**D**). ***P <0.001, ****P <0.0001 (one-way ANOVA with Dunnet's test for post-hoc analysis).

T0 mean 7.1 (6.1–8), T6 3.2 (2–4.35) and T12 1.17 (0.59–1.75). Similarly, DAPSA reduced from T0 [mean 26.83 (23.05–30.62)] to T6 [mean 9.99 (7.22–12.76)] reaching the minimum in T12 [mean 5.09 (3.83–6.36)]. Patient Global Assessment values at baseline have a mean of 7.15 (6.07–8.15) and significantly reduced at T6 [mean 3.0 (1.76–4.24)] and at T12 [mean 0.29 (0.02–0.56)].

Seventeen out of 24 patients completed 12 months of treatment, 11 of them (65%) in LDA and six (35%) in remission. All five patients with concomitant axial disease reported the disappearance of inflammatory low back pain as early as 24 weeks with a significantly improvement of BASDAI [mean 2.98 (2.18–3.77)]. Guselkumab treatment also resulted in a significant reduction of the extension of skin involvement: 75% of patients attained PASI 90, and 42% attained even PASI 100 after 24 weeks of therapy with guselkumab. Finally, during the whole follow-up, no adverse events were recorded with guselkumab, including reactions at the injection site and severe infections related to the drug.

Discussion

Guselkumab binds to the p19 subunit of IL-23 and inhibits its intracellular and downstream signalling of IL-23, a key cytokine in the pathogenesis of PsO and of spondyloarthritis [8, 9]. The block of IL-23 is now an established therapy for the treatment of severe PsO. After the registration RCTs (VOYAGE-1 and VOYAGE-2 [10, 11]), a growing body of real-life data are emerging, paralleled with the diffusion of guselkumab in dermatology practices.

Only recently, the two randomized controlled trials Discover 1 and 2 demonstrated the efficacy of guselkumab also on the joint manifestations of patients with PsA, leading to its approval in PsA [2, 3]. Real-life data on the efficacy and safety of guselkumab are lacking.

Despite the extensive use of guselkumab in patients with PsO, the use of guselkumab in patients with PsA is still limited, and data are scarce. In addition, data on the efficacy of guselkumab in patients with early PsA are limited. The dermatological setting of the use of guselkumab allows the evaluation of its effectiveness in patients who have PsO and early joint involvement, and our study focussed on these patients. Although there is no universally accepted definition of 'early PsA' for PsA [12–14], enrolled patients had a disease duration of shorter than two years and severe skin involvement, which motivated the introduction of guselkumab therapy. Therefore, these data inform on the efficacy of guselkumab in the early phase of the disease.

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Conversely, the patients enrolled in the trials Discover-1 and Discover-2 had a mean disease duration of 6.5 years and 5.3 years, respectively [2, 3].

However, it remains challenging to compare the data of this study with the one coming from the Discover trials, where disease response was expressed in terms of ACR response; in our study, the response was evaluated by DAPSA response criteria [7]. In our patients with early PsA, guselkumab demonstrated remarkable efficacy to achieve DAPSA LDA in 65% and DAPSA remission in 35%. It is interesting to note how the efficacy of guselkumab was comparable both in naïve patients and in those already treated with biological drugs for the skin domain. A minority of the patients enrolled in the study also had an axial component since the reported inflammatory low back pain. Although these patients could not be evaluated with spinal radiological examinations, they had elevated BASDAI at the time of introduction of guselkumab, and after 24 weeks of treatment, all patients reported clinical improvement achieving a reduction in BASDAI below 4. During the study's entire duration, no patients reported drug-related adverse events: there were no anaphylactic shocks or injection site reactions. Furthermore, all patients reported good tolerability of the drug.

Our work has some of the limits found in a small observational study. Since its recent approval in Italy, the number of patients receiving guselkumab outside clinical trials is still limited. The study setting, performed in a dermatology unit, may represent both added value and a limitation. The enrolment of dermatologic patients allowed the identification of PsA patients in an early phase of the joint disease but a long-standing cutaneous disease; conversely, the cohort is skewed towards patients with severe skin involvement and may not fully represent the entire PsA population. Further, most of the patients were treated with multiple lines of treatment before commencing guselkumab. The recent approval of guselkumab offered a new therapeutic option for patients that did not respond to multiple previous lines of treatment. Therefore, initially most of the patients in our cohort experienced previous treatments.

The joint dermatologic-rheumatologic clinic guarantees the accurate clinical evaluation of the joint involvement performed by an experienced rheumatologist, which is not always possible in dermatologic settings. The rheumatologic evaluation is indeed often more focussed on the articular involvement and, at least in our experience, makes more use of imaging and serum inflammatory markers. Only a limited number of investigations were available at baseline before the involvement of the rheumatologic team.

In conclusion, to the best of our knowledge, this work is the first ever published demonstrating the efficacy of guselkumab on peripheral and axial manifestations of early PsA patients in a real-life setting. Further real-life data coming from registries are warranted to confirm the safety, efficacy and effectiveness of guselkumab on PsA in the real world.

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Data availability statement

The data underlying this article will be shared on reasonable request to the corresponding author.

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