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ORIGINAL RESEARCH

Real-world outcomes in patients with moderate-to-severe plaque psoriasis treated with guselkumab for up to 1 year

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ABSTRACT

Background: Real-world data on guselkumab, especially at times >6 months, are limited.

Research design and methods: We performed a longitudinal, retrospective analysis on 307 patients with moderate–severe chronic plaque psoriasis (Psoriasis Area Severity Index [PASI] >10) treated with guselkumab for up to 12 months.

Main outcome measures: PASI 75, PASI 90, and PASI 100 were assessed at baseline and at 4, 12, 20, 28, 36, 44, and 52 weeks.

Results: At 12 weeks, PASI 75, PASI 90, and PASI 100 were achieved in 56.4%, 33.6%, and 24.1% of patients, respectively. At 52 weeks, PASI 75, PASI 90, and PASI 100 were achieved in 82.7%, 68.7%, and 51.1% of patients, respectively. Patients without comorbidities and those naïve to previous biological therapy had better responses. The mean Dermatology Life Quality Index score decreased from 14.0 at baseline to 3.1 at 12 weeks and 1.6 at 6 months, which was maintained at later times. Similar improvements were seen in pruritus visual analog scale.

Conclusions: Guselkumab maintains its efficacy for up to 12 months among responders in a real-world cohort of patients with moderate–severe plaque psoriasis, confirming data from prior real-world studies with smaller cohorts and shorter duration of follow-up.

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Guselkumab; efficacy; plaque psoriasis; treatment; real-world

1. Introduction

Psoriasis is a chronic inflammatory immune skin condition that affects up to 3% of global population [1]. In recent years, biological therapies have drastically changed the management of moderate-to-severe psoriasis [2]. Indeed, as more effective therapies have become available, treatment goals have now become more rigorous, including achieving complete or nearly complete skin clearance [3]. This is especially true for patients with moderate-to-severe psoriasis, in whom it is highly desirable to attain adequate control of the disease in the long term through continued administration of a treatment that is both effective and well tolerated [4,5].

Among the newer biological therapies, the monoclonal antibody guselkumab targets interleukin (IL)-23 by binding to its p19 subunit, leading to selective inhibition of its intracellular and downstream signaling, which is required for terminal differentiation and survival of T helper (Th)17 cells [6]. Guselkumab was studied in two phase 3 studies, VOYAGE 1 and VOYAGE 2, which demonstrated significant improvements in efficacy vs. placebo and superiority over adalimumab [7,8]. The NAVIGATE trial reported that patients with inadequate response to ustekinumab who were switched to guselkumab had greater improvements in psoriasis severity compared to those who were maintained on ustekinumab at 1 year [9].

Long-term extensions of the VOYAGE trials have further demonstrated that continuous treatment with guselkumab maintains clinical responses for up to 4 and even 5 years [10–12]. At 5 years, guselkumab has also shown to have

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a consistent safety profile, with clear improvement in health-related quality of life [12,13].

The generalizability of findings from clinical trials to routine practice is potentially limited by factors such as the need for strict enrollment criteria that differ from patients being treated in a real-world setting. Indeed, in this regard, it is now well known that disparities may be present in biological therapy for treatment of psoriasis when comparing the results from clinical trials to those obtained in real-life practice [14–17]. Indeed, as one example, ustekinumab was reported to be more efficient in real-life analyses compared to randomized clinical trials [18].

Thus, greater understanding of real-world effectiveness is valuable for overall assessment of the efficacy and use of new biological therapies. For guselkumab, data on efficacy, and especially at times >6 months, is very limited. Herein, we present real-world outcomes on the efficacy of guselkumab in patients with moderate–severe chronic plaque psoriasis and treated with guselkumab for 12 months.

2. Patients and methods

2.1. Study design

This is a longitudinal, retrospective analysis that reviewed data from patients with moderate–severe chronic plaque psoriasis who were treated with guselkumab at 13 dermatologic clinics in Italy from September 2019 to February 2021, and thus mostly during the COVID-19 pandemic and related lockdowns. Guselkumab was administered according to the Summary of Product Characteristics (induction: 100 mg subcutaneously at weeks 0 and 4; maintenance: every 8 weeks) to patients with moderate-to-severe psoriasis who had failed to respond or had contraindications or side effects to at least one conventional systemic therapy according to Italian recommendations [4]. Moderate-to-severe psoriasis was considered as: i) those with Psoriasis Area Severity Index (PASI) >10); ii) patients with a PASI <10 at baseline and involvement of sensitive areas (i.e. face, scalp, soles of the feet, hands, nails, or genital areas); iii) patients with a PASI <10 at baseline and Dermatology Life Quality Index (DLQI) >10 (even if this last indication is not reimbursed anymore in Italy). Patients started treatment at different times during the study, with the result that the data represent only a cross-sectional 'snapshot' of our experience up to the end of February 2021.

Exclusion criteria included patients with other autoimmune/inflammatory diseases such as Crohn's disease, ulcerative colitis, rheumatoid arthritis, and ankylosing spondylitis; patients treated with a biologic within 4 weeks or patients who had received systemic treatment or phototherapy in combination with biologic agent within 4 weeks of the first visit; and patients with guttate, erythrodermic, or pustular psoriasis.

Diagnosis of psoriasis was based on clinical criteria. Data on demographics, clinical history, comorbidities, and PASI score at enrollment were collected. All patients gave written informed consent for their participation prior to enrollment. The study was in accordance with the ethical standards established in the 1975 Declaration of Helsinki. Safety and tolerability were evaluated over the duration of the study.

Clinical efficacy was evaluated using PASI 75, PASI 90, and PASI 100 (75%, 90%, 100% reduction in PASI score) at baseline and at 4, 12, 20, 28, 36, 44, and 52 weeks. Data were also collected on Dermatology Life Quality Index (DLQI) and pruritus visual analog scale (VAS) at the same time points.

2.2. Statistical analysis

Data are presented as mean ± standard deviation for continuous variables, and number and percentage for categorical variables. Multivariate logistic regression was performed to evaluate the association between dependent variables sex, age, disease duration, body mass index (BMI), PASI at baseline, number of comorbidities, and number of previous biologic treatments (PBT) on achieving of PASI 75, PASI 90, and PASI 100 at the different time points. Missing values for intermediate visits were imputed using the last observation carried forward (LOCF) method. A $p < 0.05$ was considered statistically significant. All analyses were carried out using SPSS (IBM SPSS Statistics for Windows, Version 27.0. Armonk, NY: IBM Corp).

3. Results

3.1. Study population

A total of 307 patients with moderate-to-severe plaque psoriasis were treated with guselkumab. All patients included were treated for at least 12 weeks. None of the patients were being administered combination therapy with systemic agents (as cyclosporine, methotrexate, or other conventional synthetic disease-modifying antirheumatic drugs (csDMARDs).

Among the 307 patients, 209 had PASI data at 6 months, 159 at 9 months, and 127 at 12 months. In all, 302 patients are still continuing the treatment. Two patients discontinued due to secondary loss of response (at 6 and 12 months, respectively), 1 self-suspended due to fear linked to COVID-19 pandemic, 1 suspended due to concurrent, unrelated, TB infection, and started prophylaxis (treatment resumed after 1 month).

3.2. Clinical characteristics

The main clinical characteristics at baseline of the cohort are presented in Table 1. Of these, 63.5% were male with a mean age of 50.2 years, mean disease duration of 20.1 years, mean BMI of 27.7 kg/m^2; 28.7% of patients were obese; 35.5% were biologic naïve and 34.2% had received 1 previous biologic agent; 6.8% of patients were biologic naïve and had received no prior systemic therapy. Regarding comorbidities, about 40% of patients had hypertension and almost one-third has hypercholesterolemia, with various other comorbidities present in <20% of patients. Mean PASI score at baseline was 14.9 ± 9.2. Data are also shown for patients with a PASI at baseline of <10 or ≥10 (Table 1). Comparable values of clinical characteristics are seen for both subgroups.

3.3. PASI response

Treatment with guselkumab was associated with a rapid decrease in mean PASI score, from 14.9 at baseline to 6.8

Table 1. Characteristics of patients with psoriasis.

Characteristic	Overalln = 307	PASI at baseline <10n = 88	PASI at baseline ≥10n = 219
General			
Male gender, n (%)	195 (63.5)	58 (65.9)	137 (62.6)
Age (years)	50.2 ± 15.2	48.8 ± 16.6	50.7 ± 14.5
BMI (kg/m^2)	27.7 ± 5.6	26.9 ± 5	28.1 ± 5.7
Disease characteristics			
Age at disease onset	31.1 ± 15.9	28.3 ± 15.8	32.3 ± 15.8
Disease duration	20.1 ± 13.6	21.6 ± 15.6	19.5 ± 12.7
PASI at baseline	14.9 ± 9.1	6.1 ± 2.2	18.5 ± 8.4
Biologic therapy, n (%)			
Biologic naïve	109 (35.5)	32	77
• Biologic naïve and no prior systemic therapy	21 (6.8)	3 (3.4%)	18 (8.2%)
1 biologic	105 (34.2)	31	74
2 biologics	44 (14.3)	12	32
≥ 3 biologics	49 (16.0)	13	36
Last therapy class, n (%)			
Anti-TNF	52 (16.9%)	16 (18.2%)	36 (16.4%)
Anti-IL17	68 (22.1%)	18 (20.5%)	50 (22.8%)
ANTI-IL12/23	69 (22.5%)	19 (21.6%)	50 (22.8%)
Conventional systemic therapy	97 (31.6%)	32 (36.4%)	65 (29.7%)
Biologic naïve and no prior systemic therapy	21 (6.8%)	3 (3.4%)	18 (8.2%)
Comorbidities, n (%)			
Hypertension	127 (41.4)	33 (37.5)	94 (42.9)
Hypercholesterolemia	84 (27.4)	21 (23.9)	63 (28.8)
PsA	69 (22.5)	20 (22.7)	49 (22.4)
Obesity (BMI ≥ 30 kg/m^2)	88 (28.7)	20 (22.7)	68 (31.1)
Hypertriglyceridemia	57 (18.6)	11 (12.5)	46 (21)
Diabetes*	34 (11.1)	5 (5.7)	29 (13.2)
Psychiatric illness	21 (6.8)	7 (8.0)	14 (6.4)
Cardiovascular disease	15 (4.9)	5 (5.7)	10 (4.6)
Thyroiditis, hypothyroidism or other thyroid disease	15 (4.9)	6 (6.8)	9 (4.1)
Asthma/COPD/rhinitis	9 (2.9)	4 (4.5)	5 (2.3)
Hepatitis B	9 (2.9)	4 (4.5)	5 (2.3)
Hepatitis C	8 (2.6)	3 (3.4)	5 (2.3)
IBD	8 (2.6)	2 (2.3)	6 (2.7)
Latent TB infection	8 (2.6)	5 (5.7)	3 (1.4)
Neoplasm	6 (2.0)	0 (0)	6 (2.7)
Hepatic steatosis	4 (1.3)	1 (1.1)	3 (1.4)
GERD/gastric ulcer/ previous gastric surgery	4 (1.3)	0 (0)	4 (1.8)
HIV infection	3 (1.0)	3 (3.4)	0 (0)
Other	31 (10.1)	7 (8.0)	24 (11.0)

*Both type 1 and type 2 diabetes.
BMI: body mass index; PASI: psoriasis area severity index; PsA: psoriatic arthritis; COPD: chronic obstructive pulmonary disease; IBD: inflammatory bowel disease; TB: tuberculosis; GERD: gastro-esophageal reflux disease

at 4 weeks and 1.4 at 6 months (Figure 1(a)). A PASI score ≤3 was achieved in 25.4% of patients at 4 weeks and 57.7% at 12 weeks, and improved throughout 52 weeks up to 85.3% of patients (Figure 1(b)). At 4 weeks, PASI 75, PASI 90, and PASI 100 was achieved in 23.5%, 9.8%, and 7.8% of patients, respectively, increasing to 56.4%, 33.6%, and 24.1% of patients, respectively, at 12 weeks (Figure 1(c)). At 52 weeks, PASI 75, PASI 90, and PASI 100 was achieved in 82.7%, 68.7%, and 51.1% of patients, respectively, which was maintained at the longer follow-up times (Figure 1(c)).

3.4. PASI response in different patient subgroups

PASI responses were also assessed according to the presence or absence of comorbidities and PBT (Figure 2). PASI 75 was achieved in 72.6% of patients without comorbidities and in 51.3% with comorbidities at 12 weeks, which improved at 6 months and then was generally maintained throughout the duration of follow-up (Figure 2(a)). PASI 90 was achieved in 72.6% of patients without comorbidities and in 47.4% with comorbidities at 6 months, which was maintained throughout the duration of follow-up (Figure 2(b)). PASI 100 was observed in 54.8% of patient without comorbidities and in 41.5% without comorbidities at 6 months, with similar responses during follow-up (Figure 2(c)).

Considering PBT, patients who were naïve to PBT had better responses overall. At 6 months, PASI 75 was achieved in 92.7% of patient who were naïve to PBT and in 71.2% with PBT (Figure 2(d)). Similar but lower responses were seen for PASI 90 and PASI 100 when dividing patient by history of PBT (Figure 2(e,f)).

3.5. Additional outcomes

We also evaluated patient-reported outcomes using the DLQI and pruritus VAS (Table 2). The DLQI score decreased from a mean of 14.0 at baseline to 6.9 at 4 weeks, 3.1 at 12 weeks, and 1.6 at 6 months, after which the decrease was maintained at 9 and 12 months. Similar improvements were seen in pruritus VAS: from a mean baseline value of 4.5, decreasing to 1.9 at 4 weeks, 0.6 at 12 weeks, 0.4 at 6 months, 0.2 at 9 months, and 0.3 at 12 months.

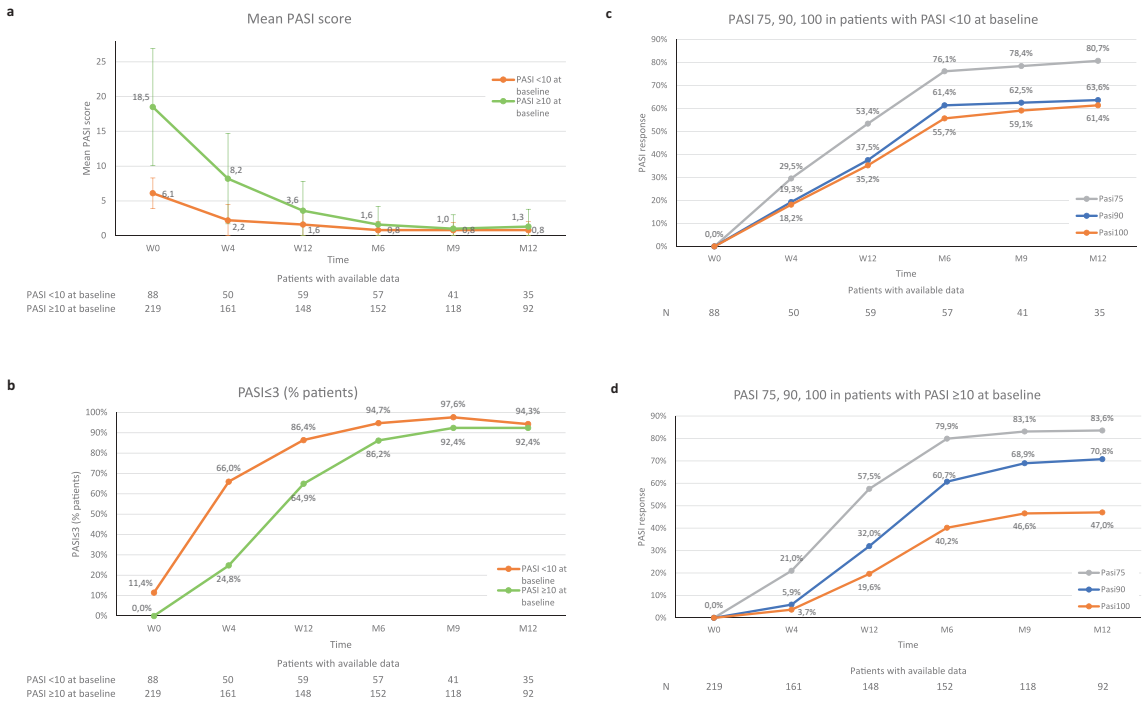

Figure 1. **Effect of guselkumab in psoriatic patients on Psoriasis Area and Severity Index (PASI) score and achievement of PASI 75, 90, and 100 responses over 1 year**. (a) PASI is presented as mean values and standard deviation. (b) % of patients achieving a PASI score ≤3. (c) % of patients with PASI <10 at baseline achieving PASI 75, 90, and 100 response (LOCF method). (d) % of patients with PASI ≥10 at baseline achieving PASI 75, 90, and 100 response (LOCF method).

3.6. Multivariate analysis

Multivariate logistic regression analysis was carried out using sex, age, disease duration, BMI, PASI at baseline, previous class of treatment received, presence of hypertension, psoriatic arthritis, hypertriglyceridemia, hypercholesterolemia, diabetes, cardiovascular disease, and psychiatric disorders on achieving PASI 75, PASI 90, and PASI 100 to assess possible predictors of improved PASI response to guselkumab (Table 3; Supplementary material). Among these, PASI at baseline showed a significant association at some time points and biologic-naïve patients experienced the best outcomes, as expected. For example, patients with PASI at baseline < 10 vs the ones with PASI ≥ 10 had significantly higher probability to achieve PASI 90 and PASI 100 at week 4 (OR 4.00, P = 0.002 and OR 6.59, P < 0.001 respectively). Regarding comorbidities the most recurring ones leading to reduced probability on achieving PASI outcomes were psoriatic arthritis (PASI 75 at month 9: OR 0.47, P = 0.040; PASI 90 at months 6 and 9: OR 0.52, P = 0.029 and 0.033 respectively) and diabetes (PASI 100 at months 6 and 12: OR 0.36, P = 0.034 and OR 0.39 P = 0.030, respectively).

3.7. Safety

Regarding the safety profile, 10 patients experienced adverse events. All were mild except for 1 transient ischemic attack which led to motor impairment (the patient is continuing treatment) and 2 adverse events which led to therapy discontinuation (one experienced erythroderma, the other general malaise with sudden sweating, fatigue, and muscle aches). There was no reactivation of Hep B or Hep C during the study.

4. Discussion

Herein, we present the real-world clinical outcomes of patients with moderate-to-severe plaque psoriasis treated with guselkumab for up to 52 weeks. Long-term extension studies of the VOYAGE trials reported that continuous treatment with guselkumab is associated with maintenance of clinical responses for even 5 years [10–12]. However, even if real-world evidence for guselkumab is accumulating, most evaluations have been carried out for shorter time periods. A previous report in a real-world setting followed patients for 52 weeks, but was based on a smaller cohort of 52 patients with moderate-to-severe psoriasis [19]. To our knowledge, the present cohort of 307 patients is the largest real-world study to date with the longest follow-up time on guselkumab for treatment of moderate-to-severe plaque psoriasis.

In the present real-world analysis, outcomes were broadly similar to those observed in that study, although somewhat lower rates of patients achieving PASI 90 and PASI 100 were seen [19]. In the previous study, at 12 months PASI 75, PASI 90, and PASI 100 response was achieved in 84.2%, 78.9%, and 63.2% of patients, respectively, compared to 82.7%, 68.7%, and 51.1% of patients, respectively. In line with that study, the presence of comorbidities was associated with poor response. Compared to the prior cohort of 52 patients, the present population had fewer patients who were biologic naïve (35.5% vs. 42.3%), which considering the PBT is associated with lower PASI responses as shown herein, this may at least partially explain the differences observed.

Notwithstanding, our results are largely in line with previous real-world evidence at shorter follow-up times. Snast et al. reported on a cohort of 33 patients followed for

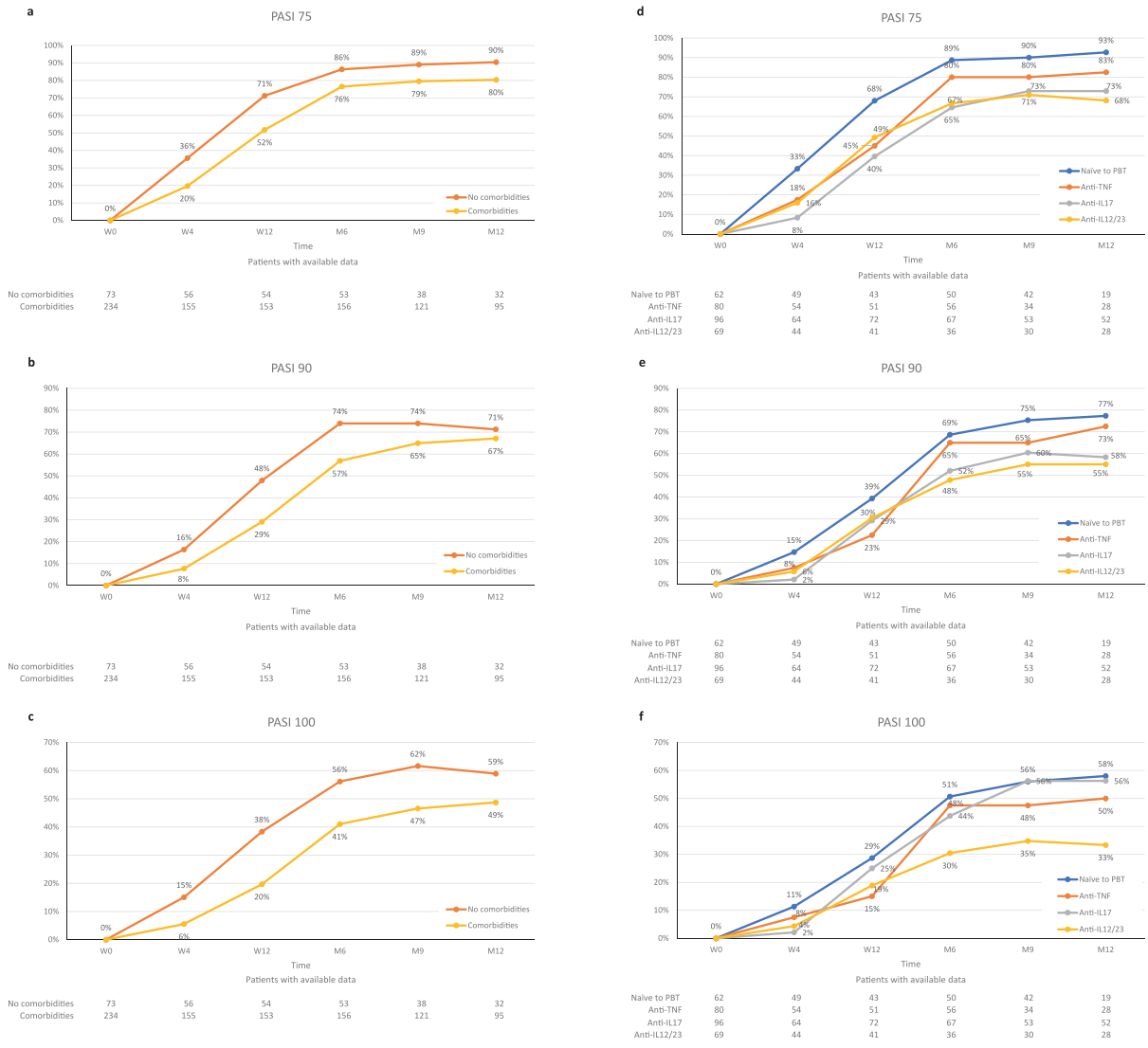

Figure 2. Effect of guselkumab in subgroups of psoriatic patients on achievement of PASI 75, 90, and 100 responses over 1 year (LOCF method). (a–c) The % of patients with comorbid diseases compared to those without comorbid diseases in achieving PASI 75 (a), 90 (b), and 100 (c) response are presented for each time point. (d–f) The % of patients naïve to previous biological treatment compared to those having previously received biological treatment in achieving PASI 75 (d), 90 (e), and 100 (f) response are presented for each time point. The % of patients at each time point is shown.

Table 2. DLQI and pruritus VAS at baseline and follow-up.

	Baseline	4 weeks	12 weeks	6 months	9 months	12 months
DLQI						
Overall	14.0 ± 6.7	6.9 ± 5.6	3.1 ± 4.1	1.6 ± 2.6	1.0 ± 2.1	0.9 ± 1.8
PASI at baseline <10	10.3 ± 5.9	3.1 ± 3.5	2.2 ± 3.1	0.9 ± 1.9	0.8 ± 1.6	0.7 ± 1.4
PASI at baseline ≥10	15.3 ± 6.5	7.8 ± 5.7	3.4 ± 4.4	1.8 ± 2.8	1.1 ± 2.2	0.9 ± 1.9
Pruritus VAS						
Overall	4.5 ± 3.1	1.9 ± 2.2	0.6 ± 1.4	0.4 ± 0.9	0.2 ± 0.7	0.3 ± 1.0
PASI at baseline <10	4.3 ± 3.2	1.8 ± 2.6	0.7 ± 1.6	0.4 ± 1.1	0.4 ± 1.0	0.4 ± 1.3
PASI at baseline ≥10	4.7 ± 3.1	1.9 ± 2.0	0.6 ± 1.4	0.3 ± 0.8	0.1 ± 0.5	0.2 ± 0.9

DLQI: dermatology life quality index; PASI: psoriasis area severity index; VAS: visual analogue scale.

a mean of 9.5 months, finding that 76% achieved PASI 75 or higher, 62% PASI 90 or higher, and 17% PASI 100 [20]. Schwensen et al. found in their cohort of 50 patients with moderate-to severe plaque psoriasis treated with guselkumab for 3 months that 68.6% had a PASI ≤3 and 36.4% achieved PASI 90 [21]. Similarly, in a real-world analysis of 44 patients with psoriasis receiving guselkumab, PASI 75, PASI 90 and PASI 100 were 95.5%, 59.1% and 16%, respectively, at 6 months [22]. Comparable results were also seen in a cohort of 68 patients in China followed for 20 weeks: PASI 90, 72.1% and PASI 100, 47.1% [23]. Megna et al. carried out a real-life analysis of 23 patients with moderate-to-severe psoriasis treated with guselkumab who were followed for 44 weeks, reporting that the mean PASI score decreased to 0.8 at study end from a baseline value of 15.1 [24]. The same group also carried out a real-life assessment of 44 psoriasis patients who had

Table 3. **Multivariate logistic regression analysis of PASI 75, PASI 90, and PASI 100**. Variables included in the model were sex, age, disease duration, BMI, PASI at baseline, previous class of treatment received, and the presence of hypertension, psoriatic arthritis, hypertriglyceridemia, hypercholesterolemia, diabetes, cardiovascular disease, psychiatric disorders. Only variables with P < 0.05 are shown.

			95% CI for OR		
Time	Variable	OR	Lower	Upper	P-value
PASI 75					
W4	Previous therapy: Anti-TNF vs Biologic-naïve	0.33	0.12	0.94	0.038
	Anti-IL17 vs Biologic-naïve	0.20	0.06	0.60	0.004
	Previous therapy: Anti-IL12/23 vs Biologic-naïve	0.41	0.19	0.89	0.025
W12	Age	1.02	1.01	1.04	0.011
	Hypertension	0.49	0.27	0.89	0.020
	Previous therapy: Anti-TNF vs Biologic-naïve	0.29	0.13	0.63	0.002
	Previous therapy: Anti-IL17 vs Biologic-naïve	0.32	0.15	0.66	0.002
	Previous therapy: Anti-IL12/23 vs Biologic-naïve	0.46	0.25	0.87	0.017
M6	PASI at baseline < 10	0.42	0.23	0.78	0.006
	Age	1.02	1.00	1.04	0.040
M9	PASI at baseline < 10	0.40	0.21	0.77	0.006
	Age	1.03	1.01	1.05	0.003
	Psoriatic arthritis	0.47	0.23	0.97	0.040
	Previous therapy: Anti-IL17 vs Biologic-naïve	0.32	0.13	0.79	0.014
	Previous therapy: Anti-IL12/23 vs Biologic-naïve	0.24	0.11	0.54	0.001
M12	PASI at baseline < 10	0.45	0.23	0.87	0.017
	Age	1.04	1.01	1.06	0.001
	Previous therapy: Anti-IL17 vs Biologic-naïve	0.28	0.11	0.69	0.006
	Previous therapy: Anti-IL12/23 vs Biologic-naïve	0.20	0.09	0.45	<0.001
PASI 90					
W4	PASI at baseline < 10	4.00	1.67	9.57	0.002
	Obesity (BMI ≥30 kg/m^2)	0.11	0.01	0.98	0.048
	Previous therapy: Anti-IL17 vs Biologic-naïve	0.11	0.01	0.91	0.041
W12	Previous therapy: Anti-IL17 vs Biologic-naïve	0.32	0.13	0.80	0.015
M6	Psoriatic arthritis	0.52	0.29	0.94	0.029
	Previous therapy: Anti-IL12/23 vs Biologic-naïve	0.43	0.23	0.81	0.009
M9	PASI at baseline < 10	0.52	0.30	0.90	0.020
	Psoriatic arthritis	0.52	0.28	0.95	0.033
	Previous therapy: Anti-IL12/23 vs Biologic-naïve	0.36	0.19	0.70	0.002
M12	PASI at baseline < 10	0.53	0.30	0.92	0.023
	Previous therapy: Anti-IL17 vs Biologic-naïve	0.46	0.22	0.96	0.039
	Previous therapy: Anti-IL12/23 vs Biologic-naïve	0.35	0.18	0.69	0.002
PASI 100					
W4	PASI at baseline < 10	6.59	2.45	17.70	<0.001
W12	PASI at baseline < 10	2.54	1.40	4.59	0.002
M6	Diabetes	0.36	0.14	0.93	0.034
	Previous therapy: Anti-IL12/23 vs Biologic-naïve	0.44	0.228	0.85	0.015
M9	Previous therapy: Anti-IL12/23 vs Biologic-naïve	0.41	0.21	0.77	0.006
M12	Diabetes	0.39	0.16	0.91	0.030
	Previous therapy: Anti-IL12/23 vs Biologic-naïve	0.36	0.19	0.69	0.002

PASI: Psoriasis Area and Severity Index; BMI: body mass index

failed anti-IL17 therapy in which mean PASI decreased from 13.9 to 0.9 at week 52 [25]. Considering patients who had failed prior ustekinumab and/or anti-IL17 therapy, Ruggiero et al. followed 13 patients for 52 weeks: mean PASI was 13.2 at baseline and decreased to 0.5 at study end [26].

In the German PERSIST trial in 155 patients, at week 28, PASI 90 response was observed in 55.3% patients [27]. In more recent real-world studies, 67% of 135 patients achieved PASI 75 at 36 weeks [28] and in 249 patients, 59.4% achieved a PASI 90 response and 49.0% a PASI 100 response at 24 weeks [29]. In this latter analysis, BMI ≥30 kg/m^2 and PBT were both associated with a lower probability of response [29]. Our results are in agreement, although for BMI we found a significant association (OR 0.11, P = 0.048) in our multivariate analysis herein only for PASI 90 at week 4.

Bardazzi et al. recently published the results of a 60-week real-life study, observing a decrease in mean PASI from 14.2 at baseline to 0 at weeks 36, 48, and 60 [30]. This appears to confirm the good long-term efficacy of guselkumab in real-life settings.

In the present multivariate analysis, among the variables evaluated, a lower PASI at baseline was significantly associated with greater early PASI response, especially PASI 100 (OR 6.59, P < 0.001). This result has been confirmed in a real-world analysis of 74 patients with moderate-to-severe plaque-type psoriasis treated with guselkumab for 12 weeks, wherein absolute PASI at baseline was found to be a predictor of clinical response [31]. Subgroup analysis also confirmed that similar to previous study [19], in addition to PBT as mentioned, the presence of comorbidities was also associated with lower PASI responses.

Taken together, our results confirm guselkumab as an effective treatment for moderate-to-severe plaque psoriasis, with results maintained for up to 12 months. This also helps to validate the results of the VOYAGE trials and long-term extensions [7,8,10–12].

In the VOYAGE 1 and VOYAGE 2 trials, greater improvement in the DLQI were seen with guselkumab compared to placebo or adalimumab [32], which were also maintained at 5-year follow-up [12]. However, few analyses have focused on

improvements in health-related quality of life with guselkumab. Ruiz-Villaverde et al reported the results of a real-life study of 87 patients with moderate-to-severe psoriasis receiving guselkumab [33]. In that analysis, DLQI decreased from a mean of 15.8 at baseline to 1.54 at 5 weeks, which is very similar to what we observed in the present cohort of patients. The improvements in quality of life are likely also related to the improvement in pain and itch seen herein.

Despite these positive aspects, the present study has some limitations that warrant mention. Firstly, the number of patients followed progressively decreased over time, but this was due to the design of the trial since patients started treatment at different times, so that the present analysis is a cross-sectional 'snapshot' of our experience up to the end of February 2021. However, given to its only recent availability, this limits the possibility for real-world data. These aspects highlight that longer follow-up in larger cohorts of patients is needed. Additionally, information on tobacco use was only available in a small minority of patients. Lastly, we are aware that guselkumab is approved in some countries also for psoriatic arthritis, in Italy it is only recently reimbursed for this indication. In some cases, the patients may have also had psoriatic arthritis, although for the above reason efficacy data on arthritis were not evaluated in this analysis.

5. Conclusions

In summary, our results show that guselkumab maintains its efficacy among responders in a real-world cohort of patients with moderate-to-severe plaque psoriasis. The results largely confirm data from previous real-world studies with smaller cohorts and shorter duration of follow-up. Further analyses are also needed to validate the use of PASI as a predictor or response, in addition to the presence of comorbidities and PBT. Additional studies are warranted to validate these positive results.

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Declaration of interest

The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

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A reviewer on this manuscript has disclosed that they have worked on clinical trials for ustekinumab and guselkumab but that they are not an advisor for the company. They have acted as an advisor for Abbvie, Bristol-Myers Squibb, Amgen and Eli Lilly and have worked on clinical trials for Abbvie, Bristol-Myers Squibb, Amgen, Eli Lilly and Union Chimique Belge. Peer reviewers on this manuscript have no other relevant financial relationships or otherwise to disclose.

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