Received: 7 June 2021 | Revised: 22 October 2021 | Accepted: 22 November 2021

DOI: 10.1111/dth.15231

DERMATOLOGIC THERAPY WILEY

ORIGINAL ARTICLE

Effectiveness and safety of guselkumab for the treatment of psoriasis in real-world settings at 24 weeks: A retrospective, observational, multicentre study by the Spanish Psoriasis Group

Elena del Alcázar[1] | Anna López-Ferrer[2] | Álvaro Martínez-Doménech[3] | Ricardo Ruiz-Villaverde[4] | Mª. del Mar Llamas-Velasco[5] | Vicenç Rocamora[6] | Marc Julià[7] | Jaime Notario[8] | Lourdes Rodríguez Fernández-Freire[9] | Antonio Sahuquillo-Torralba[10] | David Vidal[11] | Raquel Rivera[12] | Gregorio Carretero[13] | Almudena Mateu[14] | Pablo de la Cueva[15] | José Manuel Carrascosa[1]

[1]Department of Dermatology, Hospital Universitari Germans Trias i Pujol, Universitat Autònoma de Barcelona (UAB), Badalona, Spain

[2]Department of Dermatology, Hospital de la Santa Creu i Sant Pau, Barcelona, Spain

[3]Department of Dermatology, Hospital General Universitario de Valencia, Valencia, Spain

[4]Department of Dermatology, Hospital Clínico Universitario San Cecilio, Granada, Spain

[5]Department of Dermatology, Hospital Universitario de la Princesa, Madrid, Spain

[6]Department of Dermatology, Hospital de Manacor (Illes Balears), Manacor, Spain

[7]Department of Dermatology, Hospital Universitario de Basurto, Bilbao, Spain

[8]Department of Dermatology, Hospital Universitari de Bellvitge, L'Hospitalet de Llobregat, Barcelona, Spain

[9]Department of Dermatology, Hospital Universitario Virgen del Rocío, Sevilla, Spain

[10]Department of Dermatology, Hospital Universitario y Politécnico La Fe Valencia, Instituto de Investigación Sanitaria La Fe, Valencia, Spain

[11]Department of Dermatology, Complex Hospitalari Moisès Broggi, Sant Joan Despí (Barcelona), Barcelona, Spain

[12]Department of Dermatology, Hospital Universitario 12 de Octubre, Madrid, Spain

[13]Department of Dermatology, Hospital Universitario de Gran Canaria Dr. Negrín, Las Palmas de Gran Canaria, Las Palmas, Spain

[14]Department of Dermatology, Hospital Universitario Dr. Peset, Valencia, Spain

[15]Department of Dermatology, Hospital Infanta Leonor, Madrid, Spain

Correspondence
Elena del Alcázar, Department of Dermatology, Hospital Universitari Germans Trias i Pujol, Universitat Autònoma de Barcelona (UAB). Badalona, Spain.
Email: elenadelalcazarviladomiu@gmail.com

Abstract

Data on the effectiveness and safety of a drug in real-world clinical practice complement the evidence from clinical trials, which are carried out in a different setting. Little has been published on the effectiveness and safety of guselkumab in the treatment of psoriasis in clinical practice. The ojective of this study was to assess the effectiveness and safety of guselkumab at 24 weeks in patients with moderate to severe plaque psoriasis in routine clinical practice. A retrospective, multicentre study

of adult patients with moderate to severe plaque psoriasis treated with guselkumab for at least 24 weeks was carried out in Spain. We studied 343 patients, 249 of whom were followed for 24 weeks. By week 24, the mean (SD) psoriasis area severity index (PASI) had decreased from 11.1 (7.3) to 1.7 (2.8) (−9.3; [−10.2;-8.4]), 85.9% of the patients had achieved PASI score of 4 or less and 77.9% a PASI score of 2 or less. In terms of relative PASI response, 59.4% of the patients achieved a PASI-90 response and 49.0% a PASI-100 response. On multivariate analysis, two factors reduced the probability of a PASI of 2 or less at 24 weeks: a BMI ≥30 (OR, 0.44; 95% CI, 0.22–0.88) and a greater previous exposure to biologic therapy (OR, 0.69; 95% CI, [0.56–0.84]). Adverse events were rare (9.9%) and led to withdrawal from treatment in only nine patients (2.6%) by the end of the follow-up period. The results of this study confirm the high efficacy and safety of guselkumab indicated by the clinical trial data. In clinical practice, the absolute PASI score appears to be a better marker of response to treatment than the relative value.

KEYWORDS
guselkumab, psoriasis, real-world

1 | INTRODUCTION

Guselkumab is a fully human immunoglobulin G1 lambda monoclonal antibody to the interleukin (IL)-23 protein, which it inhibits by binding selectively to the p19 subunit with high specificity and affinity.[1]

The immune response of the IL-23/T17 axis is currently thought to be the main pathogenic pathway in psoriasis, which would explain why agents targeting this pathway achieve the best clinical response and are currently the drugs most often used to treat these patients.[2,3]

The Phase III clinical trials (VOYAGE 1 and 2) demonstrated the superiority of guselkumab over adalimumab in the treatment of moderate to severe plaque psoriasis.[4,5] In VOYAGE 1 and 2, respectively, 80.2% and 75.2% of patients treated with guselkumab achieved a psoriasis area and severity index (PASI)-90 response at week 24 as compared to 53.0% and 54.8% of those treated with adalimumab ($p < 0.001$). The results of the Phase III trials also showed that guselkumab has a good safety profile, similar to that of adalimumab[4,5] and ustekinumab,[6] with upper respiratory tract infections being the most commonly reported adverse event. Guselkumab also showed superior efficacy over secukinumab in the ECLIPSE study. In that study, a PASI 90 response at week 48 was achieved by 84% of the patients treated with guselkumab compared to 70% of those treated with secukinumab ($p < 0.0001$).[7]

In November 2017, guselkumab became the first IL-23 inhibitor to be approved by the EMA. Since February 2019, it has been available in Spain for the treatment of moderate to severe plaque psoriasis in patients who have had an inadequate response or a contraindication or intolerance to conventional systemic treatments and PUVA.[1] In accordance with the criteria of the treatment appraisal report issued by the Spanish Ministry of Health, guselkumab is only prescribed to patients who have previously received a biologic TNF inhibitor.

Clinical trial data are obtained under conditions distinct from those found in routine clinical practice. Authors studying the real-world use of various drugs have observed that the patient population in clinical practice has different characteristics to that of clinical trials[8,9] and, in some cases, the outcomes observed in registry data are different from those reported in clinical trials.[10] For this reason, data on the use of a drug in a real-world setting help clinicians to predict how it will work in the patients they attend in their practice. The objective of this study was to assess the effectiveness and safety of guselkumab at 24 weeks in patients with moderate to severe plaque psoriasis.

2 | MATERIAL AND METHODS

2.1 | Study design, patients, and data collected

The Spanish Psoriasis Group of the Spanish Academy of Dermatology and Venereology carried out a retrospective, observational, multicentre study with the participation of 35 Spanish hospitals. The patients included were adults (≥18 years) with a diagnosis of moderate to severe plaque psoriasis who had been treated with guselkumab between February 1, 2019 and June 30, 2020. Patients who completed at least 16 weeks of follow-up were deemed not to have withdrawn from treatment.

The following patient data were extracted from anonymized electronic medical records: age, sex, weight, height, body mass index (BMI; categorized as normal or overweight <30 or obesity ≥30), comorbidities, personal history of cancer, and previous treatment for psoriasis, including systemic and biologic therapies. Patients received guselkumab 100 mg at weeks 0 and 4 followed by a maintenance

dose every 8 weeks as indicated in the Summary of Product Characteristics, except in the case of 10.2% of the patients (35/343), who did not receive an induction dose.

The present study was conducted in accordance with the Declaration of Helsinki on Ethical Principles for Medical Research Involving Human Subjects and was approved by the local clinical research ethics committee at Hospital Universitari Germans Trias i Pujol (reference number: EDA-GUS-2019-01).

2.2 | Response assessment

The 35 dermatologists who took part in the study are all members of the Spanish Psoriasis Group. Data on the following variables were obtained from the patients' medical records: PASI, body surface area (BSA), physician global assessment (PGA) and dermatology life quality index (DLQI) at baseline and at weeks 16 and 24. The PGA was assessed on a 6-point scale (0 = clear, 1 = almost clear, 2 = mild, 3 = moderate, 4 = severe, and 5 = very severe).

The primary endpoints were improvement in mean PASI score and the percentage of patients who had achieved a PASI score of 2 or less (PASI ≤2) or of 4 or less (PASI ≤4) at week 24. The secondary endpoints were the percentage of patients who achieved a PASI ≤2 or PASI ≤4 at week 16 and a PASI-90, or PASI-100 at weeks 16 and 24. Other effectiveness variables analyzed were the mean reduction in BSA, PGA, and DLQI scores at weeks 16 and 24. Other objectives included describing the clinical characteristics of the patients, identifying variables that might condition the clinical response, and evaluating the clinical response according to prior treatments received.

2.3 | Safety

Data were collected on the frequency of adverse events and the percentage of patients who discontinued treatment due to such events. Reasons for discontinuation were also recorded and classified as follows: lack or loss of efficacy, serious adverse events, and others (lack of compliance, patient's decision, etc.).

2.4 | Statistical analysis

Qualitative variables were expressed in absolute (*n*) and relative (percentages) values and quantitative variables as mean and standard deviation (SD). Pearson's chi-square test was used to compare qualitative variables. For quantitative variables, Student's t test was used once the normality hypothesis had been tested. To compare the same variable over time at different time points, we used statistical tests for pairwise comparison and expressed the results as the difference in the mean and 95% confidence interval (difference; 95% CI). The clinical characteristics associated with the achievement of PASI-90 and PASI ≤2 were analyzed using simple and multiple logistic regression models and the forward method. The results were expressed as odds ratios (OR) and 95% CI. The statistical analysis was performed using the SPSS software package (version 22.0 for Windows). A *p* value of less than 0.05 was considered significant. The as observed method was used in the case of missing data as this is the most common method used in this type of study. We also performed a modified non-responder imputation (NRI) analysis of the data. A non-responder was defined as any patient in whom treatment was discontinued, whether due to treatment-related factors (lack of efficacy, adverse events) or other reasons (i.e., patient decision).

3 | RESULTS

3.1 | Demographic and clinical characteristics

The study included 343 patients with plaque psoriasis who received guselkumab in the 35 participating hospitals. The clinical and demographic characteristics of the study population are shown in Table 1.

TABLE 1 Baseline characteristics of study patients[a]

Characteristic	*n* = 343
Male	198 (57.7)
Age, mean (SD) years	48.3 (14.1)
Weight, mean (SD) kg	85.5 (20.7)
Height, mean (SD) cm	169.5 (10.1)
Body mass index, mean (SD) kg/m^2 (*n* = 331)	29.7 (6.5)
<30	192 (58.0)
≥30	139 (42.0)
Duration of psoriasis, mean (SD) years (*n* = 338)	22.4 (12.0)
Baseline PASI, mean (SD) (*n* = 343)	11.1 (7.3)
Baseline BSA, mean (SD) (*n* = 316)	13.7(13.8)
Baseline PGA, mean (SD) (*n* = 202)	3.2 (0.8)
Baseline DLQI, mean (SD) (*n* = 226)	11.9 (7.3)
Previous conventional systemic therapy	
Methotrexate	261(76.1)
Ciclosporin	187 (54.5)
Acitretin	129 (37.6)
Mean (SD) number prior to guselkumab	1.7 (0.9)
Phototherapy	191 (55.7)
Apremilast	28(8.2)
Number of prior biologic therapies	
0	28 (8.2)
1	105 (30.6)
2	80 (23.3)
3	54 (15.7)
≥4	76 (22.2)
Mean (SD) number prior to guselkumab	2.4 (1.7)
Previous biologic therapies	
Adalimumab	184 (53.6)
Etanercept	134 (39.1)

(Continues)

TABLE 1 (Continued)

Characteristic	$n = 343$
Infliximab	63 (18.4)
Certolizumab	6 (1.7)
Ustekinumab	186 (54.2)
Secukinumab	128 (37.3)
Ixekizumab	75 (21.9)
Brodalumab	6 (1.7)
Efalizumab	16 (4.7)
Comorbidities	
Psoriatic arthritis	55 (16)
Hypertension	105 (30.6)
Dyslipidaemia	126 (36.7)
Diabetes mellitus	51 (14.9)
Cardiovascular events	22 (6.4)
NAFLD	70 (20.4)
Bowel disease	7 (2.2)
Hepatitis	15 (4.4)
HIV	2 (0.6)
Cancer in personal history	18 (5.2)
Mental disorders	51 (14.9)

Abbreviations: BSA, body surface area; DLQI, dermatology life quality index; HIV, human immunodeficiency virus; NAFLD, non-alcoholic fatty liver disease; PASI, psoriasis area severity index; PGA, physician global assessment.
[a]Data expressed as number (%) of patients unless otherwise specified.

The mean (SD) values for the physical characteristics of the population (198 men and 145 women) were as follows: age, 48.3 (14.1) years; weight, 85.5 (20.7) kg; and BMI, 29.7 (6.5). At baseline, mean PASI was 11.1 (7.3), mean BSA was 13.7 (13.8), and mean DLQI was 11.9 (7.3). In total, 90.1% (309) of the patients had received conventional systemic therapy (ciclosporin, methotrexate, or acitretin), 55.7% (191) had undergone phototherapy, and 8.2% (28) had received apremilast. In all, 91.8% (315) had received biologic therapy and the mean number of biologic agents received was 2.4 (1.7). Of the patients included, 16% (55) had psoriatic arthritis, 5.2% (18) had a history of cancer, 4.4% (15) a history of hepatitis (four with hepatitis C, three of whom had been treated and cured prior to the administration of guselkumab, and 11 with hepatitis B), and 2.2% (7) a history of inflammatory bowel disease.

3.2 | Patient distribution over time

(Figure 1) Of the 343 patients included in the study, 249 completed 24-weeks follow-up. At week 16, eight patients had discontinued treatment (four due to adverse events and four for other reasons) and by week 24 a further 10 patients had discontinued (five due to adverse events, three due to lack of efficacy, and two for two lack of efficacy for joint symptoms). In addition, no data on effectiveness were collected at 24 weeks for 36 patients who were still receiving treatment but could not be assessed due to the COVID-19 pandemic, nor for 40 others, who were between weeks 16 and 24 of treatment.

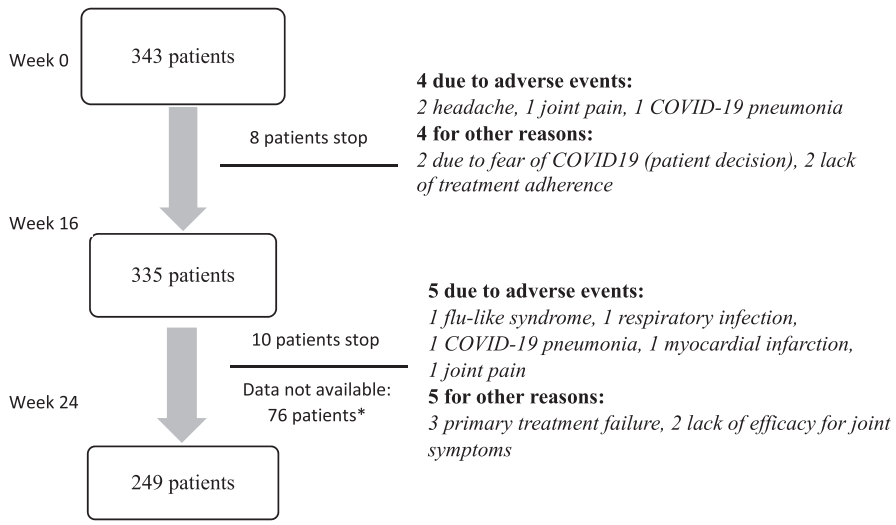

FIGURE 1 Distribution of patients over time (flow-chart)

*Reasons for missing data:
36 patients: COVID-19 pandemic
40 patients: between 16 and 24 weeks of treatment

3.3 | Effectiveness

Mean PASI, which was 11.1 (7.3) at baseline, decreased to 2.4 (3.2) (−8.8; [9.6; −8.0]) by week 16 and to 1.7 (2.8) (−9.3; [−10.2; −8.4]) at week 24, with statistically significant differences observed at both points (Figure 2). This represents a decline in mean PASI of 78.4% at week 16 and 84.7% at week 24. After 6 months of treatment, 85.9% (214/249) of the patients still receiving treatment had achieved PASI ≤4 and 77.9% (194/249) PASI ≤2 (Figure 3A). In terms of relative response, 59.4% (148/249) achieved a PASI-90 and 49.0% (122/249) a PASI-100 (Figure 4A). The analysis carried out using the modified NRI method produced slightly lower results: 80.1% (214/267) of the patients achieved PASI ≤4, 72.7% (194/267) achieved PASI ≤2, 55.4% (148/267) a PASI 90 response and 45.7% (122/267) a PASI 100 response (Figures 3B and 4B). Reductions at weeks 16 and 24 were also observed for the other variables studied (BSA, PGA, and DLQI) and significant differences were observed. The mean baseline BSA of 13.7 (13.8) decreased to 3.8 (7.0) (−9.8; [−11.1; −8.4]) by week 16 and to 2.3 (4.7) (−11.3; [−12.9; −9.7]) by week 24. The baseline PGA of 3.2 (0.8) fell to 1.1 (0.9) (−2.1; [−2.2; −1.9]) by the end of the fourth month and to 0.9 (0.9) (−2.2; [−2.5; −2.1]) by the end of the study. With respect to quality of life, the baseline mean DLQI of 11.9 (7.3) decreased to 2.7 (4.1) (−9.3; [−10.2; −8.4]) at week 16 and to 2.4 (4.3) (−9.9; [−11.1; −8.9]) by the end of the study.

To identify variables that might interfere with the PASI-90 and PASI ≤2 responses, we performed a bivariant analysis to observe the direct effect between variables complemented by a multivariate analysis to adjust for confounding variables (Table 2). On multivariate analysis the following factors decreased the probability of a PASI ≤2 at 24 weeks: BMI ≥30 (OR, 0.44; 95% CI, 0.22–0.88) and greater exposure to prior biologic therapy (OR, 0.69; 95% CI, 0.56–0.84). No significant differences were observed in the other variables analyzed: age, sex, psoriatic arthritis, initial severity of psoriasis (PASI >10 and PASI <10), and duration of disease.

Analysis of the clinical response according to the drug patients had received before guselkumab (Table 3) showed that PASI ≤2 at 24 weeks was achieved by 92.4% (61/66) of the patients treated with guselkumab after treatment with a TNF inhibitor, 84.9% (62/73) of those who switched from ustekinumab, and 60.8% (45/74) of those previously treated with an IL-17 inhibitor, with significant differences ($p < 0.001$).

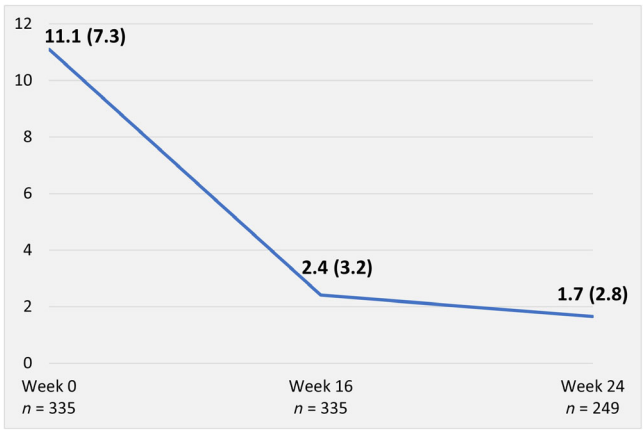

FIGURE 2 Mean (SD) PASI at weeks 16 and 24 according to as observed analysis. PASI, psoriasis area severity index

3.4 | Safety

Adverse events were reported by 9.9% (34/343) of patients, with infections being the most common (Table 4). Only nine patients (2.6%) discontinued treatment owing to adverse events: two headache, two joint pain, two COVID-19 pneumonia, one flu-like symptoms, one respiratory infection, and one acute myocardial infarction. Other reasons for stopping treatment were as follows: patient decision (2), poor adherence (2), primary treatment failure (3), and lack of efficacy on joint disease (2).

4 | DISCUSSION

We present a series of 343 patients with plaque psoriasis treated with guselkumab in clinical practice, the largest series reported in the literature to date.

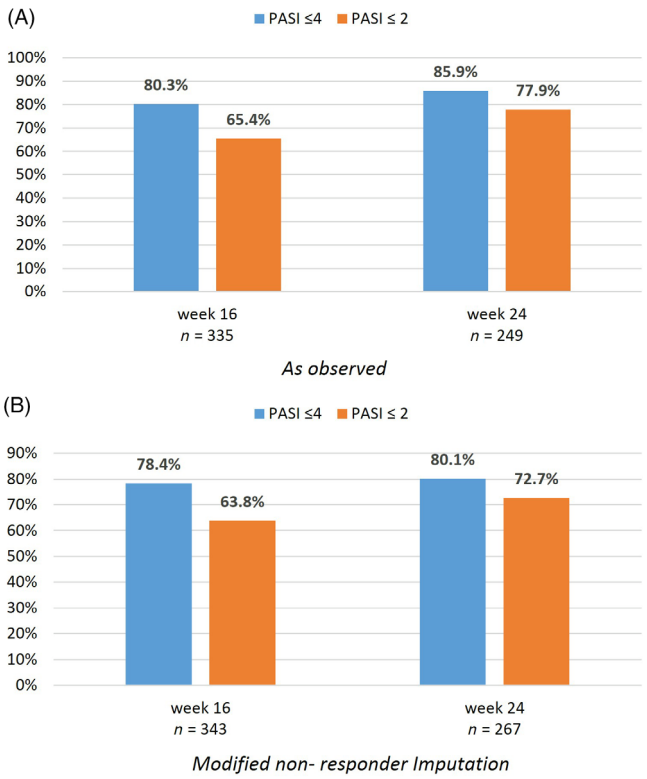

FIGURE 3 (A) Proportion of patients with PASI ≤4 and PASI ≤2 at weeks 16 and 24 according to the as observed analysis and (B) modified non-responder imputation analysis. PASI, psoriasis area severity index

Our clinical practice data reflect the effectiveness of guselkumab in a context different from that of clinical trials. It is well known that the profile of patients treated in a clinical practice is more complex than that of patients included in trials, with real-world patients having more comorbid conditions and greater exposure to previous biologic therapy.[11] In our study, over 90% of patients had received prior biologic therapy as compared to 20%–22% of the patients included in VOYAGE 1 and 2.[4,5] Furthermore, patients treated in real-world practice usually have a lower PASI score when they start treatment than participants in pivotal trials, mainly due to the absence of a washout period. In our study, the mean baseline PASI was 11, half that of the VOYAGE trials in which baseline PASI was around 22.[4,5] For this reason, the absolute PASI value is a better measure of the success of treatment than the relative values expressed as a 75% (PASI-75) or 90% (PASI-90) reduction over the baseline score. The advantage of using absolute PASI scores is that they are not dependent on baseline values, which are not thought to be clinically relevant 6 months after the start of treatment.[12] The British BADBIR group recently reported that an absolute PASI ≤2 corresponds to a PASI-90 response and that PASI ≤4 corresponds to a PASI-75 response.[13] These were the two absolute values used as primary endpoints in our study. At week 24, nearly 80% of our patients had a PASI ≤2, a percentage similar to that achieved for PASI-90 in VOYAGE 1 (80.2%) and VOYAGE 2 (75.2%). In addition, our results for complete clearing (PASI-100) at week 24 were slightly higher than those reported in the pivotal trials: 49% versus 44%.

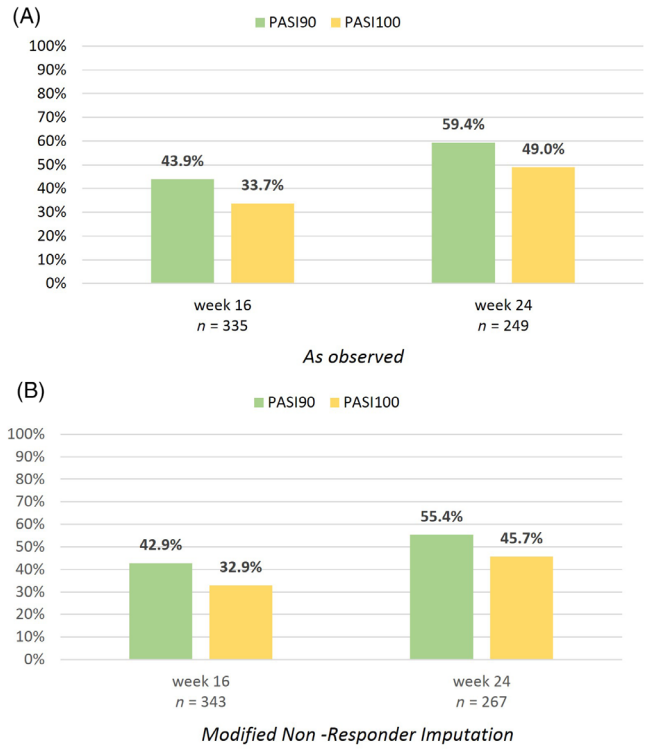

FIGURE 4 (A) Proportion of patients with PASI-90 and PASI-100 at weeks 16 and 24 according to the as observed analysis and (B) modified non-responder imputation analysis. PASI, psoriasis area severity index

Little evidence is available on the effectiveness of guselkumab in real-world clinical practice, with only nine series published in the literature[14–22] (Table 5).

Analysis of the baseline values in all of those series reveals that—in line with our findings—a higher proportion of the patients in clinical practice had received prior biologic therapy (59%–75.3%) than in the VOYAGE trials and that the mean baseline PASI was lower (12.7–15.1) in clinical practice than in the pivotal trials, with the exception of the series by Galluzzo et al.[19] with a mean baseline PASI of 20. In most of those series, effectiveness was expressed in relative PASI values and the response rates achieved for PASI-90 and PASI-100 in the two largest series are similar to those found in our study.[14,15] The only earlier study that assessed treatment response in terms of

TABLE 2 Factors associated with PASI-90 and PASI ≤2 at week 24 (bivariant and multivariant analysis). As observed analysis

		Bivariant analysis odds ratio (95% CI)		Multivariant analysis odds ratio (95% CI)	
Week 24		**PASI-90**	**PASI ≤2**	**PASI-90**	**PASI ≤2**
Age		0.99 (0.97–1.01)	0.99 (0.98–1.02)	0.99 (0.97–1.02)	1.00 (0.97–1.03)
Sex	Female	1	1	1	1
	Male	**0.55 (0.33–0.93)**	**0.49 (0.26–0.92)**	0.60 (0.35–1.06)	0.61 (0.30–1.24)
Obesity	BMI < 30	1	1	1	1
	BMI ≥ 30	**0.58 (0.34–0.99)**	**0.34 (0.18–0.64)**	0.73 (0.41–1.29)	**0.44 (0.22–0.88)**
Psoriatic arthritis	No	1	1	1	1
	Yes	0.81(0.41–1.59)	0.60 (0.28–1.29)	1.08 (0.50–2.32)	1.16 (0.46–2.92)
Severity psoriasis	PASI < 10	1	1	1	1
	PASI ≥ 10	1.07 (0.65–1.78)	0.45 (0.25–0.84)	1.16 (0.66–2.02)	0.50 (0.25–1.01)
Duration of psoriasis		1.0 (0.99–1.03)	1.01 (0.98–1.03)	1.02 (0.99–1.04)	1.01 (0.98–1.05)
Mean no. of prior biologic drugs		**0.77 (0.66–0.90)**	**0.66 (0.55–0.79)**	**0.78 (0.65–0.92)**	**0.69 (0.56–0.85)**

Note: The bold numbers mean these results show statistically significant difference.
Abbreviations: BMI, body mass index; PASI, psoriasis area severity index.

TABLE 3 Response to guselkumab at week 24 by prior biologic therapies. As observed analysis

Week 24	Mean (SD) N° of prior biologic treatments	Mean (SD) baseline PASI	Mean (SD) PASI	PASI-90	PASI ≤2
TNF inhibitors ($n = 92$)	2.0 (1.5)	10.6 (6.3)	0.8 (2.2)	77.3% (51/66)	92.4% (61/66)
IL-12/23 inhibitors ($n = 105$)	2.4 (1.4)	9.0 (5.5)[a]	1.4 (2.8)	58.9% (43/73)	84.9% (62/73)
IL-17 inhibitors ($n = 101$)	3.2 (1.7)	12.5 (9.1)[a]	2.7 (3.3)	43.2% (32/74)	60.8% (45/74)
p value	<0.001	0.003[a]	<0.001	<0.001	<0.001

Abbreviations: IL, interleukin; PASI, psoriasis area severity index.
[a]Statistically significant difference.

TABLE 4 Adverse events

Type of adverse event	No.	Description
Mild infections	8	Upper respiratory infection (3), flu-like syndrome (1), sty (1), boils (1), cystitis (1), herpes zoster affecting the first branch of the trigeminal nerve (1)
Serious infections	7	COVID-19 pneumonia (3), influenza A (1), acute bronchitis (1), viral pericarditis (1), salmonellosis (1)
Injection-site reactions	2	
Headache	2	
Joint pain	6	
Major adverse cardiac events (MACE)	1	Acute myocardial infarction
Laboratory test anomalies	2	Hyperuricemia (1), proteinuria (1), leukocytosis with neutrophilia (1)
Others	6	Mesenteric paniculitis (1), rosaceiform dermatitis (1), hypertension (1), hip fracture (1), airborne eczema (1), anxiety (1)

absolute PASI reported that 74.4% of the patients achieved a PASI ≤3 at week 20.[19] It appears, therefore, that guselkumab achieves high-efficacy rates in patients who have previously been treated with other biologic drugs.

It is known that certain variables or factors can negatively influence the efficacy of a drug: duration of the disease, obesity, a history of psoriatic arthritis, and prior treatment with multiple biologic agents.[23,24] In our series, the probability of achieving PASI ≤2 at 24 weeks decreased in the presence of obesity (BMI ≥30) and greater prior exposure to biologic therapy. Obesity has, in general, been associated with lower efficacy in biologic therapy, particularly in the case of drugs for which the dose is not weight adjusted.[25] There are a number of possible explanations for this effect, including the fact that body mass modifies the pharmacokinetics and clearance of biologic drugs, and that visceral fat triggers proinflammatory effects mediated by the release of adipokines. Although the dose of guselkumab is not adjusted to body weight, fat may interfere with pharmacokinetics (apparent clearance and volume of distribution).[26] Subgroup analyses of pooled data from the head-to-head Phase III trials that compared guselkumab, adalimumab and placebo showed that guselkumab provided superior sustained efficacy compared to adalimumab and placebo across all bodyweight classes.[27] The impact of prior biologic therapy has also been studied in other clinical practice series.[15,19] Galluzzo et al.[19] reported that lower prior exposure to biologic therapy was associated with a higher probability of achieving PASI-90, a finding similar to that of our study. Benhadou et al., by contrast, found no statistically significant differences in PASI-75, PASI-90, or PASI-100 response between biologic-naive patients and biologic-experienced patients, although those authors do not specify what the differences were.[15]

Our study reviewed the effectiveness of guselkumab as a function of prior biologic treatment. It is particularly interesting to evaluate the efficacy of guselkumab in patients who have failed to respond to treatment with ustekinumab because of the similar mechanism of action in the pathogenicity of psoriasis. In patients who have received IL-17 inhibitors, it is interesting because of the role of IL-23 in the positive regulation of IL-17 in the IL-23/IL-17 axis. In our study, almost 60% of the patients who switched from ustekinumab to guselkumab achieved PASI-90 at week 24, a result similar to that reported in the NAVIGATE trial,[6] reflecting that guselkumab may be an effective option for patients who do not achieve an optimal response with ustekinumab in clinical practice. In the group of patients who switched to guselkumab following failure with an IL-17 inhibitor, 43.2% achieved a PASI- 90 response by week 24. It should, however, be noted that the mean number of prior biologic treatments was higher in the IL-17 inhibitor group (3.2 [1.7]) than in the groups that received ustekinumab (2.4 [1.4]) or tumor necrosis factor inhibitors (2.0 [1.5]), and that this difference probably influenced the lower therapeutic response obtained.

With respect to safety, there were no serious adverse events during the follow-up period. Almost 10% (34/343) of the patients experienced some adverse effects, with infections being the most common. However, only 2.7% (9/343) discontinued treatment for this reason, a percentage similar to that observed in the VOYAGE 1 and 2 trials[4,5] and the series reported by Fougerousse et al.[14]

Our study has some limitations. Due to its retrospective design, some of the data or variables were missing or incomplete and the as observed assessment may have overestimated the effectiveness findings. However, the experience of the Spanish Psoriasis Group in

TABLE 5 Demographic characteristics of patients, effectiveness, and safety outcomes of guselkumab in real-world settings

	Our series ($n = 343$)	Fougerousse et al.[14] ($n = 180$)	Benhadou et al.[15] ($n = 112$)	Maliyar et al.[18] ($n = 89$)	Rodriguez Fernandez Freire et al.[17] (n = 55)	Galluzzo M et al.[19] ($n = 52$)	Snast et al.[22] ($n = 33$)	Megna et al.[16] ($n = 23$)
Age, mean (SD) years	48.3 (14.1)	45.2 (14.05)	48.9 (14.1)	54.0	49.8 (15.2)	51.3 (14.1)	60 (13)	49.7 (17.9)
Male, n (%)	198 (57.7%)	107 (59%)	63 (56.3%)	43 (48.3%)	37 (67.3%)	30 (57.7)	22 (67)	15 (65.2%)
Mean (SD) PASI	11.1 (7.3)	12.7 (8.95)	14.8 (6.5)	NA	13.7 (7.7)	20 (13.3)	14 (11)	15.1 (6.1)
Previous biologic therapy, n (%)	315 (91.8%)	128 (71.1%)	66 (59%)	67 (75.3%)	NA	30 (57.7%)	33 (100%)	15 (65.2%)
PASI 90 week 12–16 (%)	43.9% (week 16)	50.6% (week 16)	55.4% (week 16)	NA	69.1% (week 12)	36% (week 12)	NA	43.5% (week 12)
PASI 90 week 24 (%)	59.4%	NA	NA	NA	66.7%	62.8% (week 20)	62% (week 24)	69.6% (week 28)
PASI ≤2 or 3 week 20–24 (%)	77.9% PASI ≤2 (week 24)	NA	NA	NA	NA	74.4% PASI ≤3 (week 20)	NA	NA
Mean (SD) reduction in PASI week 12–16	2.4 (3.2) (week 16)	2.3 (3.62) (week 16)	2.03 (2.5) (week 16)	NA	1.5 (1.8) (week 12)	4.4 (4.7) (week 12)	NA	3.2 (1.9) (week12)
Mean (SD) reduction in PASI week 24–28	1.7 (2.8) (week 24)	NA	NA	NA	1.7 (3.3) (week 24)	1.9 (week 28)	2.9 (3.3)[c] (week 24)	1.1 (0.9) (week 28)
Adverse event, n (%)	34 (9.9%)	15 (8.3%)	3 (2.6%)	24 (30.4%)[a]	0	0[b]	0	6 (26%) 4 (17.4%)[d]
Withdrawal due to adverse event, n (%)	9 (2.6%)	5 (2.7%)	0	4 (5.1%)[a]	0	0	0	0
Withdrawal due to lack of efficacy, n (%)	3 (0.9%)	0	0	3 (3.8%)[a]	1 (1.8%)	0	2 (6.1%)	0

Abbreviations: NA, not available; PASI, psoriasis area severity index.
[a]Only 79 patients were included for efficacy and safety analyses.
[b]No evidence of cumulative or organ toxicity.
[c]Not including four patients with palmoplantar psoriasis.
[d]Mild blood alterations.

collaborative studies and the use of systematic data collection methods favor more homogeneous data collection in clinical practice than generally found in multicentre studies. Another limitation is that the COVID-19 pandemic may have led to a higher percentage of patients for whom data was missing at 24 weeks. Nonetheless, one of the strengths of the study is the large sample size (343 patients included and 249 with data collected up to 24 weeks) for a study of routine clinical practice.

5 | CONCLUSION

We present the largest series to date of patients treated with guselkumab in a clinical practice setting with data on effectiveness and safety at 24 weeks. Guselkumab achieved high response rates measured in terms of absolute PASI ≤2 and PASI ≤4 in a population with a more complex profile than that of the patients included in clinical trials. The drug also has a good safety profile and a very low withdrawal rate due to adverse effects. This is the first study in which response to treatment was evaluated using the absolute PASI score, which, in the authors' opinion, may be a more useful measure in clinical practice than relative response (PASI-75 or PASI-90). We therefore highlight the usefulness of using absolute PASI scores to assess response to treatment in real-world clinical practice.

ACKNOWLEDGMENTS

We would like to thank all the members of the Spanish Psoriasis Group who contributed patients to this series of patients treated in real-world clinical practice.

CONFLICT OF INTEREST

Elena del Alcázar has served as a consultant or paid speaker for or participated in clinical trials sponsored by companies, including AbbVie, Amgen, Leo Pharma, Almirall, Janssen-Cilag, Lilly, Novartis, Sanofi, and UCB. Anna López- Ferrer has perceived consultancy/educational support/speakers honoraria and/or participated in clinical trials sponsored by AbbVie, Almirall, Amgen, Boehringer Ingelheim, Celgene, Janssen, Leo Pharma, Lilly, MSD, Novartis, Pfizer, and UCB. Álvaro Martínez-Doménech has participated in clinical trials sponsored by companies that manufacture drugs used for the treatment of psoriasis, including Almirall and Janssen-Cilag. Ricardo Ruiz-Villaverde has received grants and research support, served as a consultant or received honoraria from Pfizer, Novartis, Lilly, Celgene, Almirall, and AbbVie. M. Llamas-Velasco has potential conflict of interests (advisory board member, consultant, research support, participation in clinical trials, and honorary for speaking) with the following pharmaceutical companies: AbbVie, Amgen, Janssen-Cilag, Leo Pharma, Novartis, Lilly and Celgene. Vinveç Rocamora has received grants and research support, served as a consultant or received honoraria from Novartis, Janssen-Cilag, AbbVie, Celgene, UCB i MSD. Marc Julià has served as a consultant or paid speaker for or participated in clinical trials sponsored by companies that manufacture drugs used for the treatment of psoriasis, including AbbVie, Amgen, Janssen-Cilag, LEO Pharma, Lilly, Novartis, and Pfizer. Jaime Notario has served as a consultant or paid speaker for and/or participated in clinical trials sponsored by AbbVie, Almirall, Celgene, Gebro, Janssen, Leo Pharma, Lilly, MSD, Novartis, and Pfizer. Lourdes Rodríguez Fernández-Freire has served as a consultant and speaker for AbbVie Laboratories, Janssen Pharmaceuticals Inc, MSD, Pfizer-Wyeth, Novartis, Celgene, Almirall SA, Lilly, and Leo-Pharma. Antonio Sahuquillo-Torralba has served as a consultant or paid speaker for or participated in clinical trials sponsored by companies that manufacture drugs used for the treatment of psoriasis, including AbbVie, Celgene, Janssen-Cilag, LEO Pharma, Lilly, Novartis, and Pfizer. Raquel Rivera-Diaz acted as a consultant and/or speaker for and/or participated in clinical trials sponsored by companies that manufacture drugs used for the treatment of psoriasis, including AbbVie/Abbott, Almirall, Amgen, Celgene, Janssen-Cilag, Leo Pharma, Lilly, MSD-Schering-Plow, Novartis, Pfizer, and UCB. David Vidal has participated in clinical trials and/or received honoraria as a consultant, investigator, speaker from AbbVie, Celgene, Janssen, Lilly, LeoPharma, and Novartis. Gregorio Carretero has participated as PI/SI and/or member of steering committee, and/or advisor and/or invited speaker for Celgene, Amgen, AbbVie, Almirall, Novartis, Leo-Pharma, Lilly, Sandoz, Mylan, Janssen. Almudena Mateu has potential conflict of interests (advisory board member, consultant, research support, participation in clinical trials, and honorary for speaking) with the following pharmaceutical companies AbbVie, Almirall SA, Celgene, Janssen-Cilag, Leo-Pharma, Lilly, Novartis y Pfizer. Pablo de la Cueva has served as a consultant or paid speaker for or participated in clinical trials sponsored by companies that manufacture drugs used for the treatment of psoriasis, including AbbVie, Almirall, Astellas, Biogen, Boehringer, Celgene, Janssen, LEO Pharma, Lilly, MSD, Novartis, Pfizer, Roche, Sanofi, UCB. José Manuel Carrascosa has participated as PI/SI, and/or member of steering committees and/or advisor and/or invited speaker for Celgene, Amgen, AbbVie, Almirall, Novartis, Leo-Pharma, Lilly, Sandoz, Mylan, and Janssen. PI/SI clinical trials Dermatology IGTP. None of the aforementioned has any relation to the present work.

AUTHOR CONTRIBUTIONS

All authors contributed to the design and implementation of the research. Elena del Alcázar contributed to collect data from the different centers, the analysis of the results and to the writing of the manuscript. José Manuel Carrascosa contributed to the supervision of the final manuscript.

DATA AVAILABILITY STATEMENT

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

ORCID

Elena del Alcázar https://orcid.org/0000-0002-5935-356X
Álvaro Martínez-Doménech https://orcid.org/0000-0002-1252-1001
Ricardo Ruiz-Villaverde https://orcid.org/0000-0002-0381-6174

Mª. del Mar Llamas-Velasco https://orcid.org/0000-0002-1187-1341
Raquel Rivera https://orcid.org/0000-0002-4604-0724
José Manuel Carrascosa https://orcid.org/0000-0003-4266-0771

REFERENCES

1. European Medicine Agency. Tremfya (Guselkumab): summary of product characteristics. 2019 https://www.ema.europa.eu/en/documents/product-information/tremfya-epar-product-information_es.pdf
2. Nograles KE, Davidovici B, Krueger JG. New insights in the immunologic basis of psoriasis. *Semin Cutan Med Surg*. 2010;29(1):3-9.
3. Puig L. The role of IL 23 in the treatment of psoriasis. *Expert Rev Clin Immunol*. 2017;13(6):525-534.
4. 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(3):405-417.
5. 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(3):418-431.
6. Langley RG, Tsai T-F, Flavin S, et al. Efficacy and safety of guselkumab in patients with psoriasis who have an inadequate response to ustekinumab: results of the randomized, double-blind, phase III navigate trial. *Br J Dermatol*. 2018;178(1):114-123.
7. Reich K, Armstrong AW, Langley RG, et al. Guselkumab versus secukinumab for the treatment of moderate-to-severe psoriasis (ECLIPSE): results from a phase 3, randomised controlled trial. *Lancet*. 2019;394(10201):831-839.
8. del Alcázar E, Suárez-Pérez JA, Armesto S, et al. Real-world effectiveness and safety of apremilast in psoriasis at 52 weeks: a retrospective, observational, multicentre study by the Spanish psoriasis group. *J Eur Acad Dermatol Venereol*. 2020;34(12):2821-2829.
9. Rivera R, Velasco M, Vidal D, et al. The effectiveness and safety of ixekizumab in psoriasis patients under clinical practice conditions: A Spanish multicentre retrospective study. *Dermatol Ther*. 2020;33(6):e14066.
10. Egeberg A, Bryld LE, Skov L. Drug survival of secukinumab and ixekizumab for moderate-to-severe plaque psoriasis. *J Am Acad Dermatol*. 2019;81(1):173-178.
11. Mason KJ, Barker J, Smith C, et al. Comparison of drug discontinuation, effectiveness, and safety between clinical trial eligible and ineligible patients in BADBIR. *JAMA Dermatol*. 2018;154(5):581-588.
12. Carretero G, Puig L, Carrascosa JM, et al. Redefining the therapeutic objective in psoriatic patients candidates for biological therapy. *J Dermatolog Treat*. 2018;29(4):334-346.
13. Mahil SK, Wilson N, Dand N, et al. Psoriasis treat to target: defining outcomes in psoriasis using data from a real-world, population-based cohort study (the British Association of Dermatologists biologics and Immunomodulators register, BADBIR). *Br J Dermatol*. 2020;182(5):1158-1166.
14. Fougerousse AC, Ghislain PD, Reguiai Z, et al. Effectiveness and short-term (16-week) tolerance of guselkumab for psoriasis under real-life conditions: a retrospective multicenter study. *J Eur Acad Dermatol Venereol*. 2020;34(10):e644-e646.
15. Benhadou F, Ghislain PD, Guiot F, et al. Real-life effectiveness and short-term (16-week) tolerance of guselkumab for psoriasis: a Belgian retrospective multicentre study. *J Eur Acad Dermatol Venereol*. 2020;34(12):e837-e839.
16. Megna M, Fabbrocini G, Cinelli E, Camela E, Ruggiero A. Guselkumab in moderate to severe psoriasis in routine clinical care: an Italian 44-week real-life experience. *J Dermatolog Treat*. 2020;4:1-5.
17. Rodriguez Fernandez-Freire L, Galán-Gutierrez M, Armario-Hita JC, Perez-Gil A, Ruiz-Villaverde R. Guselkumab: short-term effectiveness and safety in real clinical practice. *Dermatol Ther*. 2020;33(3):e13344.
18. Maliyar K, O'Toole A, Gooderham MJ. Long-term single center experience in treating plaque psoriasis with Guselkumab. *J Cutan Med Surg*. 2020;24(6):588-595.
19. Galluzzo M, Tofani L, Lombardo P, et al. Use of Guselkumab for the treatment of moderate-to-severe plaque psoriasis: a 1 year real-life study. *J Clin Med*. 2020;9(7):2170.
20. Lee EB, Reynolds KA, Pithadia DJ, Egeberg A, Wu JJ. Drug survival of guselkumab for psoriasis in a real-world setting: a single-center retrospective chart review. *J Dermatolog Treat*. 2020;31(4):342-343.
21. Ruggiero A, Fabbrocini G, Cinelli E, Megna M. Efficacy and safety of guselkumab in psoriasis patients who failed ustekinumab and/or anti-interleukin-17 treatment: a real-life 52-week retrospective study. *Dermatol Ther*. 2021;34(1):e14673.
22. Snast I, Sherman S, Holzman R, Hodak E, Pavlovsky L. Real-life experience of guselkumab in patients with psoriasis. *Dermatol Ther*. 2020;33(6):e13964.
23. Papp KA, Langley RG, Lebwohl M, et al. Efficacy and safety of ustekinumab, a human interleukin-12/23 monoclonal antibody, in patients with psoriasis: 52-week results from a randomised, double-blind, placebo-controlled trial (PHOENIX 2). *Lancet*. 2008;371(9625):1675-1684.
24. Mazzotta A, Esposito M, Costanzo A, Chimenti S. Efficacy and safety of etanercept in psoriasis after switching from other treatments: an observational study. *Am J Clin Dermatol*. 2009;10(5):319-324.
25. Chiricozzi A, Gisondi P, Girolomoni G. The pharmacological management of patients with comorbid psoriasis and obesity. *Expert Opin Pharmacother*. 2019;20(7):863-872.
26. Yao Z, Hu C, Zhu Y, et al. Population pharmacokinetic modeling of Guselkumab, a human IgG1λ monoclonal antibody targeting IL-23, in patients with moderate to severe plaque psoriasis. *J Clin Pharmacol*. 2018;58(5):613-627.
27. Gordon KB, Blauvelt A, Foley P, et al. Efficacy of guselkumab in subpopulations of patients with moderate-to-severe plaque psoriasis: a pooled analysis of the phase III VOYAGE 1 and VOYAGE 2 studies. *Br J Dermatol*. 2018;178(1):132-139.

How to cite this article: del Alcázar E, López-Ferrer A, Martínez-Doménech Á, et al. Effectiveness and safety of guselkumab for the treatment of psoriasis in real-world settings at 24 weeks: A retrospective, observational, multicentre study by the Spanish Psoriasis Group. *Dermatologic Therapy*. 2022;35(2):e15231. doi:10.1111/dth.15231