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ORIGINAL RESEARCH ARTICLE

Real-world Performance of a New Strategy for Off-Label Use of Guselkumab in Moderate to Severe Psoriasis: Super-Responder Patients as the Epitome of Efficacy and Optimisation

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Abstract

Background Guselkumab is a drug used to treat moderate to severe plaque psoriasis. However, real-life clinical data on its off-label use are limited, especially regarding the optimal drug dosage regimen for different patient profiles.

Objective The main objective of this real-world, single-centre, retrospective study was to identify the off-label guselkumab dosing regimen used in clinical practice. The study also aimed to evaluate the drug's efficacy, safety, and survival, as well as the proportion of super-responders (SR) based on a newly proposed definition.

Methods The study included 69 patients who started treatment with guselkumab between March 2019 and July 2021. Patients were followed up until April 2022, during which time their efficacy, safety, persistence, and use of guselkumab were recorded. Patients were aged $\geq$ 18 years and had moderate to severe plaque psoriasis.

Results The mean disease duration was 18.6 years, and 59% of patients had received at least one biologic treatment before guselkumab with a mean of 1.3 biologics per patient. The initial absolute Psoriasis Area and Severity Index (PASI) was 10.1 and decreased to 2.1 between Week 11–20 without significant changes in the PASI value throughout the 90 weeks of follow-up. The cumulative probability of drug survival was 93.5% at Week 52. No differences were found in terms of efficacy and survival associated with the off-label drug dosage regimens compared to the doses described in the Summary of Product Characteristics (SmPC). The greatest adjustments in the drug administration regimen were achieved in the subgroups of bio-naïve and SR patients, with a reduction in the number of administrations by 40% and 47% compared to the regimen described in the SmPC. Super-response to guselkumab was mainly associated with patients naïve to previous biologic treatment.

Conclusion The study demonstrated that off-label use of guselkumab was safe and effective in real-life clinical practice. The findings suggest that adjustments to the drug administration regimen may be necessary to optimise its use in different patient profiles, especially in SR and bio-naïve patients. Further studies are needed to confirm these findings.

1 Introduction

Psoriasis is a chronic immune-mediated inflammatory disease (IMID) that affects the skin, with a prevalence of 2–4% in Europe [1]. Moderate to severe psoriasis significantly impacts the quality of life (QoL) of affected patients [2].

Key Points

A new prescription pattern has been established for psoriasis patients who achieve complete response after three administrations of guselkumab.

Further administrations of the drug will occur on an as-needed basis, based on the reappearance of skin lesions.

This protocol has been shown to be safe and effective for long-term use, with results comparable to therapeutic guidelines. On-going research is focused on identifying patients who may benefit from new dosage optimisation strategies.

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Treatment for psoriasis is continuously evolving due to the development of new biological drugs that target the underlying disease mechanisms [3]. However, many questions remain unanswered, such as the best drug for each patient, genetic factors influencing treatment response, and ways in which to manage treatment suspension due to loss of efficacy or economic restrictions.

The key pathway in psoriasis is the IL-23/Th17 axis, and guselkumab is a fully human monoclonal antibody that specifically targets the p19 subunit of interleukin 23 (IL23). It has been approved for the treatment of moderate to severe psoriasis and psoriatic arthritis. Several Phase III clinical trials have shown its efficacy and safety [4–8]. Published results demonstrate satisfactory and stable responses up to 5 years of follow-up, with retention rates of 74.8% and Psoriasis Area and Severity Index (PASI) 90 values greater than 80% [5, 6, 9–14]. Real-world evidence studies from different countries have confirmed these findings, showing high short- and medium-term drug survival rates [15–24].

An interesting feature of IL-23 inhibitors like guselkumab is their durability of disease control even after drug discontinuation, compared to other biologic families [25]. Studies have shown that patients treated with IL-23 inhibitors can maintain disease control for a significant period after treatment withdrawal [6, 14, 26–28], which may be of particular importance in real-world settings where external factors like pandemics can disrupt treatment schedules [29–32]. Based on these findings, a new treatment strategy called 'on-demand treatment' has been proposed, where patients self-manage the intervals for drug administration under the supervision of a dermatologist.

The aim of the present study was to evaluate the effectiveness, safety, drug survival, and individual dosage of guselkumab on-demand treatment in routine clinical practice in Spain. The study also proposed and evaluated a new definition of "super-responder" (SR) – patients who may benefit from guselkumab on-demand treatment.

2 Methods

2.1 Study Design

A retrospective observational study was conducted at La Paz University Hospital, Madrid, Spain. The study included adult patients aged ≥ 18 years, with moderate to severe plaque psoriasis who received guselkumab treatment between March 2019 and July 2021. Patients who received less than three guselkumab administrations and/or had fewer than 150 days of follow-up were excluded from the on-demand strategy. Patient records were analysed to retrieve demographic data, comorbidities, concomitant treatments, prior therapies, disease severity PASI at guselkumab initiation and at the end of follow-up, and the number of drug administrations.

2.2 On-Demand Strategy Definition

Patients achieving a complete response after the first three guselkumab administrations (Weeks 0, 4 and 12) were offered on-demand follow-up. Further doses were administered when skin lesions reappeared (PASI ≥ 1).

2.2.1 Data Collection in Follow-up Visits

The on-demand treatment design made it impossible to analyse efficacy results using the standard fixed dosage regimen established in the Summary of Product Characteristics (SmPC). Instead, patients were grouped based on predefined time week ranges reflecting interval duration between doses to better evaluate efficacy (0, 4–10, 11–20, 21–30, 31–50, 51–70, 71–90).

2.3 Outcome Measures

The study evaluated the clinical efficacy of a guselkumab treatment in patients with reduction in the number of administrations, including both SR and nSR (no super-responder), as well as in patients who were bio-naïve and bio-experienced. The efficacy was measured by comparing the absolute PASI scores at the beginning of the study and at Weeks 11–20, 31–50, and 71–90. Additionally, a survival analysis was conducted to assess treatment discontinuation for any reason.

2.4 Dose-Reduction Analysis

Guselkumab dose analysis was analysed in two groups: SmPC, which followed the recommended dose of 100 mg administered subcutaneously at Weeks 0, 4, and 12, and every 8 weeks thereafter, and off-label treatment, which was defined as a variation greater than 20% from the recommended dose in the SmPC. Dose-reduction analysis was conducted by breaking down patients into four groups based on the percentage reduction in guselkumab administrations, ranging from patients who maintained similar dosage intervals to SmPC (green level) to patients who had a reduction > 20% and < 40% (blue level); > 40% and < 60% (orange level); or more than 60% (red level) (Fig 1).

2.5 Super-Responder Definition

Super-responder (SR) patients were defined as those who achieved a PASI $\leq$ 2 response after the third administration of guselkumab and maintained a PASI $\leq$ 1 response after subsequent doses for at least 52 weeks.

2.6 Safety and Drug Survival

Treatment safety was evaluated analysing serious adverse events (SAEs) that led to treatment discontinuation, and drug survival rates were defined as the period from the first dose of guselkumab to discontinuation due to loss of efficacy or SAEs.

2.7 Statistical Analysis

The analyses were performed on an "as observed" basis. The severity of the disease and treatment response were assessed by measuring the absolute PASI at baseline and between the interval of Weeks 11–20, 31–50, and 71–90. Continuous variables were presented as mean $\pm$ standard deviation (SD) and analysed using two-way analysis of variance (ANOVA). Drug survival rates were analysed using the Kaplan-Meier method and log-rank test, and statistical significance was set at $p < 0.05$.

3 Results

3.1 Baseline Characteristics

The study included 69 patients, with a mean age ($\pm$ SD) of 50.7 $\pm$ 14.6 years, of which 71% were men and 29% were women (Table 1). Most patients were overweight with a body mass index (BMI) of 28.3 $\pm$ 6.0. Among the patients, 48 (69%) had comorbidities, with 17 (24.6%) having 3 or more and 20 (29%) having none. The most common comorbidities were dyslipidaemia (58%), non-alcoholic fatty liver disease (38%), and psoriatic arthritis (35%). Of the patients, 41 (59%) had prior experience with at least one biological drug, with a median of 2.1 $\pm$ 1.3 biological drugs per patient. The most used biologics were ustekinumab (27.5%), adalimumab (21.7%), and etanercept (20.2%).

3.2 Overall Efficacy Analysis

At baseline, the complete cohort had an absolute PASI score of 10.1 $\pm$ 6.2 (Fig. 2). Between Weeks 11–20, absolute PASI decreased by 8 points, with a final score of 2.1 $\pm$ 2.7 ($p <$ 0.0001). The percentages of patients achieving PASI $\leq$ 5, PASI $\leq$ 3, and PASI $\leq$ 1 were 89.1%, 85.4%, and 52.7%, respectively (Fig. 3). During Weeks 31–50, mean absolute PASI was 2.6 $\pm$ 3.4 ($p = 0.38$), with 87.7%, 78.9%, and 54.4% achieving PASI $\leq$ 5, PASI $\leq$ 3, and PASI $\leq$ 1, respectively. Finally, between Weeks 71–90, mean absolute PASI was 2.4 $\pm$ 2.7 ($p = 0.99$), with 89.5%, 71.1%, and 52.6% achieving PASI $\leq$ 5, PASI $\leq$ 3, and PASI $\leq$ 1, respectively. In terms of guselkumab dosage, 68% of patients received an induction dose (Table 1), and the interval between subsequent doses was 12.2 $\pm$ 8.68 weeks, 4.2 weeks longer than expected according to the SmPC, resulting in a 33% decrease in the number of administrations.

3.3 Guselkumab Dosification Sub-analysis

To evaluate the real-world use of guselkumab, patients were grouped into four levels based on their dosage regimen (Fig. 1). The bottom level (green) had 24 patients (33%

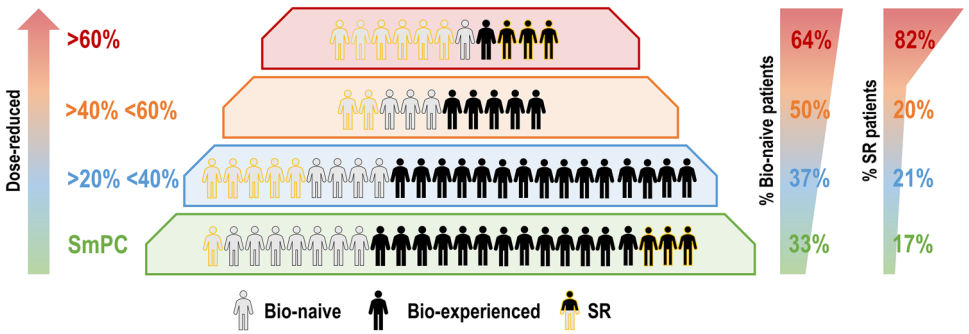

Fig. 1 Distribution of study patients according to the guselkumab dosage regimen used. Patients treated with guselkumab were categorised based on the reduction in the number of administrations compared to the recommended dosage stated in the SmPC. The patients were grouped into four categories: those who received the standard dosage as specified in the SmPC, those with a dose optimisation between 20 and 40% of the SmPC recommendation, those with a dose optimisation between 40 and 60%, and those with a dose optimisation above 60%. Within each group, patients were further classified as either bio-naïve or bio-experienced. The percentage of super-responder patients within each subgroup was also determined. *SmPC* Summary of Product Characteristics, *SR* super-responder

Table 1 Baseline characteristic in the different groups analysed in the study

Characteristics	Value	Dose-reduced groups			
		SmPC	> 20% < 40%	> 40% < 60%	> 60%
No. of patients	69	24	24	10	11
Mean age ± SD, (range), years	50.7 ± 14.6 (20–91)	48.9 ± 14 (20–81)	53.4 ± 14.9 (31–91)	50.5 ± 14.3 (30–72)	48.5 ± 16.6 (22–74)
Male, *n* (%)	49 (71)	18 (75)	17 (71)	7 (70)	7 (64)
Mean BMI ± SD, (range), kg/m^2	28.3 ± 6.0 (18–41)	28.4 ± 5.4 (21.1–41)	27.9 ± 4.6 (18–37.2)	29.3 ± 6.5 (20.5–40.7)	27.3 ± 4.2 (22.2–34.6)
Smoker, *n* (%)	18 (26)	9 (38)	4 (17)	2 (18)	3 (27)
Mean duration of psoriasis ± SD, (range), years	18.6 ± 11.7 (1–55)	16.9 ± 9.2 (2–33)	22.8 ± 12.5 (7–55)	12.6 ± 13.1 (2–40)	18.3 ± 13.0 (1–39)
Mean PASI at baseline ± SD, (range)	10.0 ± 6.0 (0–32)	9.5 ± 5.6 (0–24)	11.7 ± 6.8 (1–32)	9.5 ± 6 (0–16.2)	7.9 ± 5.3 (0–14.4)
Comorbidities, *n* (%)	48 (69)	18 (75)	16 (67)	7 (70)	7 (63)
Diabetes mellitus	6 (9)	2 (8)	3 (13)	1 (10)	1 (9)
Arterial hypertension	19 (28)	5 (21)	9 (38)	2 (20)	3 (27)
Dyslipidaemia	40 (58)	16 (67)	13 (54)	5 (50)	6 (55)
Fatty liver disease	26 (38)	10 (42)	10 (42)	3 (30)	3 (27)
Psoriatic arthritis	24 (35)	10 (42)	9 (38)	2 (20)	3 (30)
Super responders	20 (29)	4 (17)	5 (21)	2 (20)	9 (82)
Treatment					
Follow-up, weeks	88 ± 39	81 ± 37	88 ± 41	94 ± 45	95 ± 33
Conventional systemic, *n* (%)	55 (80)	18 (75)	20 (83)	9 (90)	8 (73)
Mean of previous systemic treatments ± SD	1.5 ± 0.94	1.5 ± 0.83	1.5 ± 0.96	1.3 ± 0.5	2 ± 1.4
Apremilast, *n* (%)	5 (7)	1 (4)	2 (8)	1 (10)	1 (9)
Biologic treatment, *n* (%)	41 (59)	17 (71)	15 (63)	5 (50)	4 (36)
1 biologic	18 (26)	7 (29)	4 (17)	6 (60)	0 (0)
2 biologics	10 (14)	3 (12)	6 (25)	0 (0)	1 (9)
≥ 3 biologics	13 (19)	5 (21)	5 (21)	0 (0)	3 (27)
Mean of previous biologic treatments ± SD	1.3 ± 1.5	1.5 ± 1.7	1.4 ± 1.4	0.5 ± 0.5	1.1 ± 1.6
Mean duration under biologic treatment ± SD, years	4.2 ± 3.4	4.0 ± 3.9	4.7 ± 4.5	2.4 ± 2.9	1.8 ± 3.1
Previous biologic therapies, *n* (%)					
Adalimumab	15 (22)	7 (29)	6 (25)	0 (0)	2 (18)
Etanercept	14 (20)	4 (17)	6 (25)	0 (0)	4 (36)
Infliximab	3 (4)	0 (0)	2 (8)	1 (10)	0 (0)
Ustekinumab	19 (28)	5 (21)	9 (38)	2 (20)	3 (27)
Secukinumab	10 (14)	6 (25)	3 (13)	1 (10)	0 (0)
Ixekizumab	8 (12)	4 (17)	3 (13)	0 (0)	1 (9)
Brodalumab	2 (3)	2 (8)	0 (0)	0 (0)	0 (0)
Efalizumab	2 (3)	1 (4)	1 (4)	0 (0)	0 (0)
Tildrakizumab	1 (1)	0 (0)	0 (0)	0 (0)	1 (9)
Dose adjustment					
No. of patients with induction dose, *n* (%)	46 (68)	17 (71)	15 (62)	8 (80)	6 (54)
Induction dose administration, mean ± SD, weeks	5.8 ± 2.7	5.5 ± 2.1	6.3 ± 3.7	4.9 ± 0.7	6.8 ± 3.6
Interval between administration doses, mean ± SD, weeks	12.2 ± 8.7	8.9 ± 2.9	11.0 ± 5.5	17.0 ± 12.7	27.1 ± 16.3

> 20% < 40%: patients who had a reduction >20% and < 40% respect to SmPC (blue level); > 40% < 60%: patients who had a reduction > 40% and <60% respect to SmPC (orange level); > 60%: patients who had a reduction more than 60% respect to SmPC (red level)

BMI body mass index, *PASI* Psoriasis Area and Severity Index, *SD* standard deviation, *SmPC* Summary of Product Characteristics

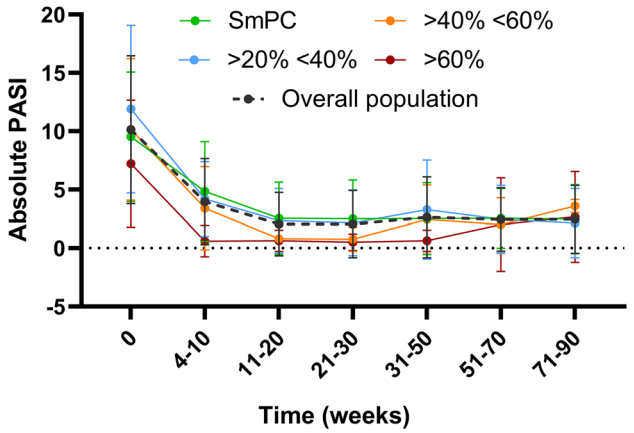

Fig. 2 Proportion of patients achieving absolute PASI scores. > 20% < 40%: patients who had a reduction > 20% and < 40% respect to SmPC (blue level); > 40% <60%: patients who had a reduction > 40% and < 60% respect to SmPC (orange level); >60%: patients who had a reduction more than 60% respect to SmPC (red level). *SmPC* Summary of Product Characteristics, *PASI* Psoriasis Area and Severity Index

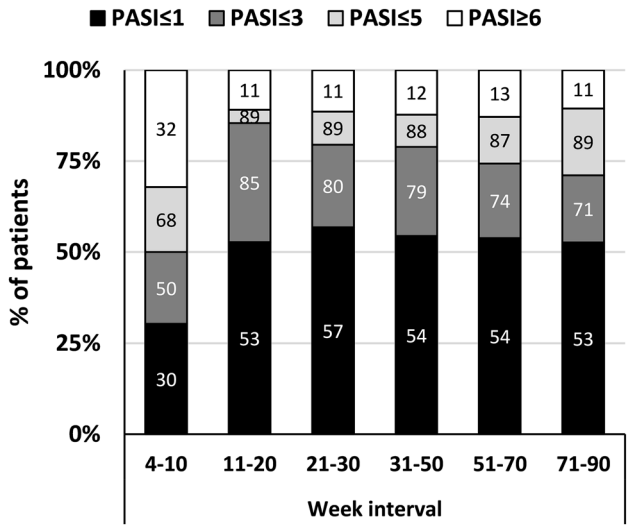

Fig. 3 Proportion of patients achieving absolute PASI ≤ 1, PASI ≤ 3, PASI ≤ 5 and PASI ≥ 6 in the overall population. The number within the columns indicates the percentage of patients reaching that range of efficacy. *PASI* Psoriasis Area and Severity Index

bio-naïve and 17% SR) who used a regimen comparable the one recommended in the SmPC, with an average reduction of 11% in dosification (8.9 ± 2.9 weeks). The next level (blue) had 24 patients (37% bio-naïve, 21% SR) with a 29% reduction (11.0 ± 5.5 weeks) in dosage compared to the SmPC. The third level (orange) had 10 patients (50% bio-naïve and 20% SR) with a 52% reduction (17.0 ± 12.7 weeks), and the fourth level (red) had 11 patients (64% bio-naïve and 82% SR) with a 71% reduction (27.1 ± 16.3 weeks).

3.4 Is the Efficacy Related to the Dosage of Use?

The efficacy of guselkumab over 90 weeks was analysed to determine whether reducing drug dosage affected disease control. No significant differences in efficacy were observed between the four groups analysed (Fig. 2). The mean baseline absolute PASI values for the different dosing regimens (from least to greatest reduction) were 9.5 ± 5.5, 11.9 ± 7.2, 10.2 ± 6, and 7.2 ± 5.4 (as presented in Fig. 1). Between Weeks 11 and 20, all groups showed a significant decrease in PASI compared to baseline, with values of 4.8 ± 4.3, 4.2 ± 3.2, 3.4 ± 3.6, and 0.6 ± 1.3 ($p < 0.0001$, $p < 0.0001$, $p = 0.002$, and $p = 0.003$, respectively). From Weeks 31 to 50, the mean absolute PASI reductions were 2.5 ± 3.1 ($p > 0.99$), 3.3 ± 4.2 ($p = 0.97$), 2.4 ± 3.0 ($p = 0.98$), and 0.6 ± 0.9 ($p > 0.99$). Finally, from Weeks 71 to 90, the absolute PASI values were 2.5 ± 3.0 ($p > 0.99$), 2.1 ± 3.0 ($p = 0.91$), 3.6 ± 0.5 ($p = 0.99$), and 2.7 ± 3.9 ($p = 0.95$).

3.5 Bio-Naïve Population Sub-analysis

At baseline, bio-naïve patients had a higher mean absolute PASI compared to bio-experienced patients (13.0 ± 5.3 vs 8.1 ± 6.2, respectively, $p < 0.0001$) (Suppl Fig. 1). However, both groups experienced significant reductions in absolute PASI scores compared to baseline between Weeks 11–20, with a reduction of 12.2 points in bio-naïve patients (0.8 ± 1.1, $p < 0.0001$) and 7.1 points in bio-experienced patients (1 ± 1, $p = 0.0008$). The percentages of patients achieving PASI ≤ 1 (bio-naïve vs bio-experienced) were 76.5% versus 41.7%, PASI ≤ 3 of 100% versus 77.8%, and PASI ≤ 5 of 100% versus 83.3%, respectively (Suppl Fig. 2). Between Weeks 31 to 50, similar values were found, with bio-naïve patients having an absolute PASI score of 1.3 ± 2.5 ($p = 0.99$) and bio-experienced patients having an absolute PASI score of 3.1 ± 3.6 ($p = 0.87$). The percentages of patients achieving PASI ≤ 1 was 68.4% versus 47.2%, PASI ≤ 3 was 94.7% versus 75.0%, and PASI ≤ 5 was 94.7% versus 80.5%. Finally, among Weeks 71 to 90, bio-naïve patients reached an absolute PASI score of 1.9 ± 2.6 ($p = 0.99$), paralleling with the bio-experienced population (2.8 ± 3.1, $p = 0.99$), with PASI ≤ 1 achieved in 61.5% versus 50.0%, PASI ≤ 3 in 76.9% versus 70.8%, and PASI ≤ 5 in 92.3% versus 83.3%. No statistically significant differences in efficacy were found between the two groups between Weeks 11 to 20 ($p > 0.99$), 31 to 50 ($p = 0.22$), and 71 to 90 ($p = 0.95$).

Among bio-naïve patients, 96% received the induction dose and maintenance doses were given every 14.7 ± 11.8 weeks (a 40% reduction from SmPC recommendations). In bio-experienced patients, guselkumab doses were administered every 11.0 ± 6.3 weeks (a 28% reduction from

established posology), and only 49% of patients had received the induction dose.

3.6 Responder Population Sub-Analysis

Super responder patients had a lower mean absolute PASI score at baseline compared to nSR. The difference was statistically significant (6.9 ± 6.2 vs 9.9 ± 6.6 (p = 0.0025) (Suppl Fig. 4). Both groups demonstrated statistically significant reductions in absolute PASI between Weeks 11 to 20. Super-responder patients achieved an absolute PASI of 0.4 ± 0.8 points ($p < 0.0001$) while patients with nSR had 2.7 ± 2.8 points ($p < 0.0001$). The percentage of patients reaching PASI ≤ 1 for SR versus nSR was 87.5% versus 36.8%, PASI ≤ 3 of 100% versus 78.9%, and PASI ≤ 5 of 100% versus 84.2% (Suppl Fig. 5).

These high levels of efficacy were maintained between Weeks 31 to 50 with SR patients maintaining an absolute PASI score of 0.1 ± 0.4 ($p > 0.99$) and nSR patients with 3.4 ± 3.6 (p = 0.99). The percentage of patients achieving PASI ≤ 1 for SR vs nSR was 100% versus 39.0%, PASI ≤ 3 of 100% versus 70.7%, and PASI ≤ 5 of 100% vs. 82.9%. Similar results were found between Weeks 71 to 90 with SR patients attaining an absolute PASI of 0.4 ± 1.1 ($p >$ 0.99) compared to 3.2 ± 3.1 ($p > 0.99$) in nSR patients. The percentage of patients achieving PASI ≤ 1 for SR versus nSR was 90% versus 38.5%, PASI ≤ 3 of 90% versus 65.4%, and PASI ≤ 5 of 100% versus 80.8%. Although there were significant differences in efficacy between Weeks 31 to 50 (p = 0.002), there were no significant differences at Weeks 11–20 (p = 0.17) and 71 to 90 (p = 0.10).

Furthermore, 75% of SR patients received induction dose (W4) compared to 65% of nSR patients (Suppl Table 2). The interval between maintenance doses in SR patients was the most extended over time for all analysed groups, settled at 15.3 ± 11.5 weeks, which meant a decrease of 47% in the total number of SmPC administrations. In contrast, nSR patients received drug administration every 11.3 ± 7.4 weeks with a mean decrease in the number of administrations of 27%.

3.7 Drug Survival and Safety

Guselkumab demonstrated a 52-week survival rate of 93.5% in the study population (Fig. 4). No significant difference in drug survival rates at 52 weeks were observed based on the differences in the range administration used (p = 0.48). Bio-naïve and bio-experienced patients had similar survival rates (Suppl Fig. 3), while statistically significant differences (p = 0.0358) were observed in SR patients (Suppl Fig. 6). Four patients were lost to follow-up, and no severe adverse effects or dropouts related to guselkumab safety profile were recorded.

4 Discussion

Real-world data complement the data obtained from randomised controlled clinical trials, which are considered the highest quality source of data in clinical research on biologic drugs. Real-world studies are useful to assess the influence of factors not considered in clinical trials, such as prior biologic exposure, disease duration, and comorbidities on the efficacy and safety of treatments. Managing biologic treatments in adverse, uncontrolled conditions can be challenging, and real-world studies can provide insights into how innovative biologic treatments, such as guselkumab, perform in these conditions.

This "forced" proof-of-concept study was based on an algorithm of patient monitoring, referred to as treatment on-demand. Patients who initially responded to guselkumab were allowed to self-adjust the intervals between doses during a long follow-up throughout the COVID-19 pandemic. This strategy, non-previously reported in real-world setting, was based on data previously collected in the retreatment studies after guselkumab controlled withdrawal, published by Reich et al in 2017 [6, 33]. Patients who achieved complete response after the first three administrations of guselkumab were offered on-demand guselkumab. The following administrations were given when skin lesions began to reappear (absolute PASI ≥ 1), and other considerations included clinical factors, organisational factors, as well as patient preferences and willingness to undergo this type of follow-up. Patients were taught to identify early skin signs of psoriasis relapse, and early on-demand access to remote consultation was available, with on-site visits to the hospital whenever necessary.

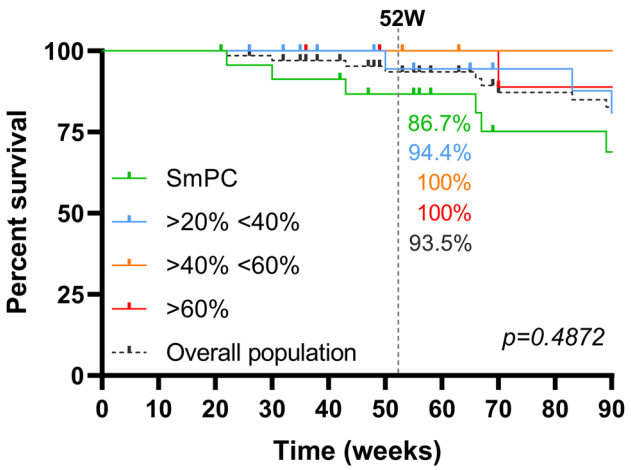

Fig. 4 Survival over 90 weeks. Cumulative probability of drug survival over 90 weeks. Each event corresponds to a patient discontinuation, caused by either an adverse event, lack of efficacy or patient death

Dose interval modification of biologics is a widespread approach in real-life practice [33–35] and is also becoming a recommended way of action in therapeutic guidelines of specialised scientific societies [34, 35]. This approach confirms that dose-interval extension is applied to patients with good response, while dose-escalation is offered to patients with more severe disease [30, 36]. However, available data from these studies are limited, as they only collect data on tumour necrosis factor-alpha (TNFα), IL-12/23, and IL-17 inhibitors, without including the newer IL-23 inhibitors, such as guselkumab.

To fill this gap, the authors distributed their 69-patient population into four groups, depending on the real use of guselkumab. Interestingly, no dose-escalation regimen was needed in any case, and no differences were observed in relation to age, sex, BMI, duration of psoriasis, severity at the start of treatment, or comorbidities between the dose-interval groups. Contrarily, the dose-interval efficacy seems to be related to treatment history, especially the number and duration of biologic therapy.

The data obtained from this study are comparable those observed in the GUIDE study [37], which showed how guselkumab in SR patients sustained disease control with a dose-interval every 16 weeks (q16w) versus the current q8w specified in the SmPC, thus needing 50% fewer administrations [38]. In the GUIDE study, a higher probability of being a SR was associated with a short disease duration and bio-naïve status. A similar trend occurs in this study, with good control despite a more prolonged dose interval in patients with less exposure to biologics and SR to guselkumab [37–40].

Dosage modification of other biologic families does not seem to be as the IL-23 inhibitors. In the OPTIMISE study [41], secukinumab was unable to extend its dosing regimens (300 mg) from every q4w to q6w without detrimental efficacy and persistence. These clinical results seem to confirm the differential impact of pathogenetic mechanisms on clinical long-term control [42].

Based on our data, using different dosing intervals across the four pre-defined patient groups did not result in loss of disease control in terms of efficacy and persistence during the 90-week follow-up. Similarly, a previous study by Ruiz Villaverde et al, which analysed the switch from ustekinumab to guselkumab, found no differences after 52 weeks between patients who maintained q12w and those who started with q8w dosing [43]. Drug survival analysis of biologic agents in psoriasis is crucial as it helps evaluate clinical results such as effectiveness, safety, and factors associated with adherence to treatment. Currently, guselkumab has demonstrated the best long-term results in large population survival studies [20, 44, 45]. Series assessing the efficacy of guselkumab in real clinical practice are limited [15, 16, 18, 46] especially in terms of using different dosing intervals. Nonetheless, existing data on persistence and efficacy are comparable to our findings. The multicentre PERSIST study [15], for example, had a persistence rate of 92.4% at Week 52, which is slightly lower than the 93.5% we observed. The study also had efficacy results of 58.4% and 78.8% for absolute PASI $\leq$ 1 and PASI $\leq$ 3 score at 52 weeks, respectively, in the same way as our findings.

Although biologic survival rate tends to be higher in bio-naïve patients, statistically significant differences between them and bio-experienced patients for any of the approved biologics are challenging to find. There are few real-world evidence series that evaluate differences between these subpopulations [46, 47], but persistence and effectiveness tend to be superior in naïve patients. In our study, no significant differences in terms of efficacy or survival rates between the two subpopulations was observed, but more than 60% of bio-naïve patients achieved better sustained clearance rates (PASI $\leq$ 1) compared to bio-experienced patients who did not exceed 50%.

Due to the lack of the absence of biological biomarkers to guide drug selection in clinical practice, finding clinical clues towards better efficacy and safety is mandatory. Super responder definition and patient profiling are gaining interest in this context [48–52]. Super-responder refers to a subgroup of moderate to severe psoriasis patients who exhibit faster and higher rates of response to biological treatment than the general population. Reich et al identified SRs in the guselkumab VOYAGE 1&2 EECCs as those who achieved complete clearance at Weeks 20 and 28 from the beginning of treatment, with 40.8% of the patients achieving this characterisation [49]. The study found that these SRs had a lower BMI, less use of previous biological treatments, lower PASI and body surface area (BSA) at baseline, and achieved PASI 100 in less time. In our cohort, SR patients are predominantly male, younger, with lower BMI, shorter duration of psoriasis, fewer total comorbidities, especially psoriatic arthritis, and are mostly bio-naïve. We observed significant differences in terms of efficacy and survival rates between SR and nSR, which is consistent with previous findings. We also found that persistence to treatment after 52 weeks could be a variable that allows better identification of this subtype of patients.

Contrary to what could be expected, the use of different dosing intervals did not result in loss of disease control in our study. Drug survival analysis is crucial in evaluating the effectiveness and safety of biologic agents in psoriasis treatment. Guselkumab has shown the best long-term results in large population survival studies [20, 44, 45]. In the absence of biological biomarkers to guide drug selection, identifying SR and patient profiling can provide clinical clues towards better efficacy and safety. Our study found significant differences.

5 Conclusion

The previous paper and the data presented in this cohort offer valuable insights into identifying the best candidates for an on-demand approach, as proposed in our study. The clinical characteristics that have been identified provide a clear framework for assessing the appropriateness of this approach. However, it is essential to exercise caution when making individual decisions to "jump over" the SmPC dosage. A careful evaluation of various clinical factors such as baseline characteristics, line of treatment, complete and stable response, among others, is necessary.

In addition to clinical factors, it is essential to consider organisational issues such as limited accessibility to dermatology services, patient preferences, commitment, and ability for early loss of response and flare identification. These factors should be considered before making any decisions that may affect the patient's treatment outcome. The strategy here described could be helpful in overcoming barriers to achieve effective treatment and to improve patient outcomes.

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Declarations

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Conflict of Interest Pedro Herranz-Pinto has received honoraria for acting as a consultant and/or speaker and/or investigator for AbbVie, Almirall, Amgen, Biogen, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Janssen, LEO Pharma, Eli Lilly, Novartis, Pfizer, Sanofi and UCB Pharma. Rosa Feltes-Ochoa has received honoraria for acting as a consultant and/or speaker and/or investigator for AbbVie, Almirall, Amgen, Celgene, Janssen, LEO Pharma, Sanofi and Novartis. Ander Mayor-Ibarguren has received honoraria for acting as a consultant and/or speaker and/or investigator for AbbVie, Almirall, Amgen, Janssen, LEO Pharma, Eli Lilly and Novartis. Maria Luisa Alonso-Pacheco has received honoraria for acting as a consultant and/or speaker and/or investigator for AbbVie, Almirall, Amgen, Biogen, Celgene, Janssen, LEO Pharma, Eli Lilly, and Novartis. Guillermo Servera-Negre, Jose Manuel Busto-Leis, Maria Angeles Gonzalez-Fernández and Alicia Herrero-Ambrosio declare no conflict of interest.

Availability of Data and Materials Not applicable

Ethics The present study was conducted in accordance with the Declaration of Helsinki (initially published in 1964) on Ethical Principles for Medical Research Involving Human Subjects and after approval by the local ethical committees.

Consent to Participate Informed consent was waived due to the study's retrospective design. Data were properly anonymised before the analysis.

Consent for Publication Not applicable.

Code Availability Not applicable.

Author Contributions All authors participated in data collection and interpretation of the data, provided critical feedback on the manuscript, approved the final manuscript for submission, and were accountable for the accuracy and integrity of the article.

References

1. Parisi R, Iskandar IYK, Kontopantelis E, Augustin M, Griffiths CEM, Ashcroft DM, Global Psoriasis Atlas. National, regional, and worldwide epidemiology of psoriasis: systematic analysis and modelling study. BMJ. 2020;369:m1590. https://doi.org/10.1136/bmj.m1590.
2. Feldman SR. Psoriasis causes as much disability as other major medical diseases. J Am Acad Dermatol. 2020;82(1):256–7. https://doi.org/10.1016/j.jaad.2019.09.071.
3. Bellinato F, Gisondi P, Girolomoni G. Latest advances for the treatment of chronic plaque psoriasis with biologics and oral small molecules. Biologics. 2021;15:247–53. https://doi.org/10.2147/BTT.S267428.
4. Markham A. Guselkumab: first global approval. Drugs. 2017;77(13):1487–92. https://doi.org/10.1007/s40265-017-0805-4.
5. Blauvelt A, Papp KA, Griffiths CEM, Randazzo B, Wasfi Y, Shen YK, Li S, Kimball AB. 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):405–17. https://doi.org/10.1016/j.jaad.2016.11.041.
6. Reich K, Armstrong AW, Foley P, Song M, Wasfi Y, Randazzo B, Li S, Shen YK, Gordon KB. 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):418–31. https://doi.org/10.1016/j.jaad.2016.11.042.
7. Deodhar A, Helliwell PS, Boehncke WH, Kollmeier AP, Hsia EC, Subramanian RA, Xu XL, Sheng S, Agarwal P, Zhou B, Zhuang Y, Ritchlin CT, DISCOVER-1 Study Group. 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(10230):1115–25. https://doi.org/10.1016/S0140-6736(20)30265-8.
8. Mease PJ, Rahman P, Gottlieb AB, Kollmeier AP, Hsia EC, Xu XL, Sheng S, Agarwal P, Zhou B, Zhuang Y, van der Heijde D, McInnes IB, DISCOVER-2 Study Group. Guselkumab in biologic-naive patients with active psoriatic arthritis (DISCOVER-2): a double-blind, randomised, placebo-controlled phase 3 trial. Lancet. 2020;395(10230):1126–36. https://doi.org/10.1016/S0140-6736(20)30265-8.
9. tremfya-epar-product-information_en.pdf [Internet]. [cited November 30, 2022]. Accessed date 2 nov 2022 https://www.ema.europa.eu/en/documents/product-information/tremfya-epar-product-information_en.pdf.
10. Augustin M, Jazra M, Öztürk B. Long-term drug survival over 5 years of continuous guselkumab treatment in patients with moderate-to-severe psoriasis: a post hoc analysis of the vOYAGE 1. In: Poster at 6th World Psoriasis & Psoriatic Arthritis Conference. 2021.
11. Reich K, Griffiths CEM, Gordon KB, Papp KA, Song M, Randazzo B, Li S, Shen YK, Han C, Kimball AB, Armstrong AW, Foley P, Blauvelt A. Maintenance of clinical response and consistent safety profile with up to 3 years of continuous treatment with guselkumab: Results from the VOYAGE 1 and VOYAGE 2 trials. J Am Acad Dermatol. 2020;82(4):936–45. https://doi.org/10.1016/j.jaad.2019.10.018.
12. Reich K, Papp KA, Armstrong AW, Wasfi Y, Li S, Shen YK, Randazzo B, Song M, Kimball AB. Safety of guselkumab in patients with moderate-to-severe psoriasis treated through 100 weeks: a pooled analysis from the randomized VOYAGE 1 and VOYAGE 2 studies. Br J Dermatol. 2019;180(5):1039–49. https://doi.org/10.1111/bjd.17438.
13. Reich K, Gordon KB, Strober BE, Armstrong AW, Miller M, Shen YK, You Y, Han C, Yang YW, Foley P, Griffiths CEM. Five-year maintenance of clinical response and health-related quality of life improvements in patients with moderate-to-severe psoriasis treated with guselkumab: results from VOYAGE 1 and VOYAGE 2. Br J Dermatol. 2021;185(6):1146–59. https://doi.org/10.1111/bjd.20351.
14. Reich K, Armstrong AW, Langley RG, Flavin S, Randazzo B, Li S, Hsu MC, Branigan P, Blauvelt A. Guselkumab versus secukinumab for the treatment of moderate-to-severe psoriasis (ECLIPSE): results from a phase 3, randomised controlled trial. Lancet. 2019;394(10201):831–9. https://doi.org/10.1016/S0140-6736(19)31781-2.
15. Gerdes S, Asadullah K, Hoffmann M, Korge B, Mortazawi D, Wegner S, Personke Y, Gomez M, Sticherling M. Real-world evidence from the non-interventional, prospective, German multicentre PERSIST study of patients with psoriasis after 1 year of treatment with guselkumab. J Eur Acad Dermatol Venereol. 2022;36(9):1568–77. https://doi.org/10.1111/jdv.17852.
16. Ghislain PD, Failla V, Lambert J, Soenen R, Grine L, Tannous J, Guiot F, Willaert F, Fierens H, Vandaele M, Boonen H, Saerens J, Meuleman V, Stockman A, Belpaire A, Swimberghe S, Temmerman L, Dekeyser S, Lambert JM, de Schaetzen V, de la Brassinne M, Benhadou F. Effectiveness and tolerability of guselkumab in patients with psoriasis: a longitudinal Belgian retrospective multicenter study. JAAD Int. 2021;4:15–7. https://doi.org/10.1016/j.jdin.2021.09.007.
17. Ruiz-Villaverde R, Rodriguez-Fernandez-Freire L, Armario-Hita JC, Pérez-Gil A, Galán-Gutiérrez M. Guselkumab: mid-term effectiveness, drug survival, and safety in real clinical practice. Dermatol Ther. 2021;34(2):e14798. https://doi.org/10.1111/dth.14798.
18. Del Alcázar E, López-Ferrer A, Martínez-Doménech Á, Ruiz-Villaverde R, Llamas-Velasco MDM, Rocamora V, Julià M, Notario J, Fernández-Freire LR, Sahuquillo-Torralba A, Vidal D, Rivera R, Carretero G, Mateu A, de la Cueva P, Carrascosa JM. 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. Dermatol Ther. 2022;35(2):e15231. https://doi.org/10.1111/dth.15231.
19. Dapavo P, Siliquini N, Mastorino L, Avallone G, Merli M, Agostini A, Cariti C, Viola R, Stroppiana E, Verrone A, Ortoncelli M, Quaglino P, Ribero S. Efficacy, safety, and drug survival of IL-23, IL-17, and TNF-alpha inhibitors for psoriasis treatment: a retrospective study. J Dermatolog Treat. 2022;33(4):2352–7. https://doi.org/10.1080/09546634.2021.1973847.
20. Torres T, Puig L, Vender R, Lynde C, Piaserico S, Carrascosa JM, Gisondi P, Daudén E, Conrad C, Mendes-Bastos P, Ferreira P, Leite L, Lu JD, Valerio J, Bruni M, Messina F, Nidegger A, Llamas-Velasco M, Del Alcazar E, Mufti A, White K, Caldarola G, Teixeira L, Romanelli P, Desai K, Gkalpakiotis S, Romanelli M, Yeung J, Nogueira M, Chiricozzi A. Drug survival of IL-12/23, IL-17 and IL-23 inhibitors for psoriasis treatment: a retrospective multi-country, multicentric cohort study. Am J Clin Dermatol. 2021;22(4):567–79. https://doi.org/10.1007/s40257-021-00601-1.
21. Marletta D, Murgia G, Cattaneo A, Carrera C, Marzano A. Single-centre real-life experience of guselkumab in patients with moderate-to-severe plaque psoriasis. J Drugs Dermatol JDD. 2021;21(8):864–6. https://doi.org/10.36849/JDD.6962.
22. Megna M, Tommasino N, Potestio L, Battista T, Ruggiero A, Noto M, Fabbrocini G, Genco L. Real-world practice indirect comparison between guselkumab, risankizumab, and tildrakizumab: results from an italian 28-week retrospective study. J Dermatolog Treat. 2022;33(6):2813–20. https://doi.org/10.1080/09546634.2022.2081655.
23. Ruggiero A, Fabbrocini G, Cinelli E, Megna M. Real-world practice indirect comparison between guselkumab and risankizumab: results from an Italian Retrospective Study. Dermatol Ther. 2022;35(1):e15214. https://doi.org/10.1111/dth.15214.
24. 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. https://doi.org/10.1111/dth.13964.
25. Masson Regnault M, Shourick J, Jendoubi F, Tauber M, Paul C. Time to relapse after discontinuing systemic treatment for psoriasis: a systematic review. Am J Clin Dermatol. 2022;23(4):433–47. https://doi.org/10.1007/s40257-021-00686-8.
26. Rivera R, Martorell A, López A, Salgado L, Sahuquillo A, de la Cueva P, Herranz P, Ratón JA, Ferrán M, Izu R, Ruiz-Genao D, García-Donoso C, Carrascosa JM. Maintenance of response following discontinuation of guselkumab and secukinumab in Spanish patients who participated in the ECLIPSE study. J Eur Acad Dermatol Venereol. 2021;35(1):e65–7. https://doi.org/10.1111/jdv.16870.
27. Blauvelt A, Leonardi CL, Gooderham M, Papp KA, Philipp S, Wu JJ, Igarashi A, Flack M, Geng Z, Wu T, Camez A, Williams D, Langley RG. Efficacy and safety of continuous risankizumab therapy vs treatment withdrawal in patients with moderate to severe plaque psoriasis: a phase 3 randomized clinical trial. JAMA Dermatol. 2020;156(6):649–58. https://doi.org/10.1001/jamadermatol.2020.0723.
28. Warren RB, Carrascosa JM, Fumero E, Schoenenberger A, Lebwohl MG, Szepietowski JC, Reich K. Time to relapse after tildrakizumab withdrawal in patients with moderate-to-severe psoriasis who were responders at week 28: Post hoc analysis through 64 weeks from reSURFACE 1 trial. JEADV. 2021;35(4):919–27. https://doi.org/10.1111/jdv.16964.
29. Sanz-Gil R, Pellicer A, Montesinos MC, Valcuende-Cavero F. Improved effectiveness from individualized dosing of self-administered biologics for the treatment of moderate-to-severe psoriasis: a 5-year retrospective chart review from a Spanish University

Hospital. J Dermatolog Treat. 2020;31(4):370–7. https://doi.org/10.1080/09546634.2019.1646783.
30. Gambardella A, Licata G, Sohrt A. Dose adjustment of biologic treatments for moderate-to-severe plaque psoriasis in the real world: a systematic review. Dermatol Ther (Heidelb). 2021;11(4):1141–56. https://doi.org/10.1007/s13555-021-00608-1.
31. Carrascosa JM, Garcia-Doval I, Pérez-Zafrilla B, Carretero G, Vanaclocha F, Daudén E, De la Cueva-Dobao P, Belinchón I, Alsina M, López-Estebaranz JL, Ferrán M, Torrado R, Rivera R, Carazo C, Barboza L, Ferrándiz C, BIOBADADERM Study Group. Use of off-label doses is frequent in biologic therapy for moderate to severe psoriasis: a cross-sectional study in clinical practice. J Dermatolog Treat. 2015;26(6):502–6. https://doi.org/10.3109/09546634.2014.999550.
32. Tan KJ, Noliza Encarnacion MR, Marushchak O, Anvekar R. Management of psoriasis during the coronavirus disease 2019 pandemic. J Clin Aesthet Dermatol. 2021;14(9):41–4. https://doi.org/10.1016/j.jcad.2021.07.012.
33. Gordon KB, Armstrong AW, Foley P, Song M, Shen YK, Li S, Muñoz-Elías EJ, Branigan P, Liu X, Reich K. Guselkumab efficacy after withdrawal is associated with suppression of serum IL-23-regulated IL-17 and IL-22 in psoriasis: VOYAGE 2 Study. J Invest Dermatol. 2019;139(12):2437-2446.e1. https://doi.org/10.1016/j.jid.2019.06.143.
34. Carrascosa JM, Puig L, Belinchón Romero I, Salgado-Boquete L, del Alcázar E, Andrés Lencina JJ, Moreno D, de la Cueva P. Actualización práctica de las recomendaciones del Grupo de Psoriasis de la Academia Española de Dermatología y Venereología (GPS) para el tratamiento de la psoriasis con terapia biológica. Parte 1. «Conceptos y manejo general de la psoriasis con terapia biológica». Actas Dermosifiliogr. 2022;113(3):261–77. https://doi.org/10.1016/j.ad.2022.01.001.
35. Carrascosa JM, Puig L, Romero IB, Salgado-Boquete L, del Alcázar E, Lencina JJA, Moreno D, de la Cueva P. Actualización práctica de las recomendaciones del Grupo de Psoriasis de la Academia Española de Dermatología y Venereología (GPS) para el tratamiento de la psoriasis con terapia biológica. Parte 2 «Manejo de poblaciones especiales, pacientes con comorbilidad y gestión del riesgo». Actas Dermosifiliogr. 2022;113(6):583–609. https://doi.org/10.1016/j.ad.2022.03.002.
36. Romero-Jimenez RM, Escudero-Vilaplana V, Baniandres Rodriguez O, García Martín E, Mateos Mayo A, Sanjurjo SM. Association between clinical factors and dose modification strategies in the treatment with ustekinumab for moderate-to-severe plaque psoriasis. J Dermatolog Treat. 2018;29(8):792–6. https://doi.org/10.1080/09546634.2018.1451989.
37. Eyerich K, Weisenseel P, Pinter A, Schäkel K, Asadullah K, Wegner S, Muñoz-Elias EJ, Bartz H, Taut FJH, Reich K. IL-23 blockade with guselkumab potentially modifies psoriasis pathogenesis: rationale and study protocol of a phase 3b, randomised, double-blind, multicentre study in participants with moderate-to-severe plaque-type psoriasis (GUIDE). BMJ Open. 2021;11(9):e049822. https://doi.org/10.1136/bmjopen-2021-049822.
38. Knut S, Khusru A, Andreas P. Prolonged q16w treatment interval of guselkumab is non-inferior to q8w dosing for maintaining disease control in super responders: primary results from GUIDE at Week 68 in patients with psoriasis. In: Poster Presented at the ESDR; Sep 2022.
39. Schaekel K. Early disease intervention in psoriasis leads to a faster and higher rate of complete skin clearance: week 28 results from the GUIDE study. In: Proceedings of the ISDS Conference. 2021; New York, NY, USA.
40. Schäkel K. Prognostic factors for early PASI 100 response in psoriasis patients treated with guselkumab: Results from the GUIDE study. In: Poster Presented at the AAD; March 2022.
41. Reich K, Blauvelt A, Tsai TF, Tyring S, Vanaclocha F, Kingo K, et al. Secukinumab dosing optimization in patients with moderate-to-severe plaque psoriasis: results from the randomized, open-label OPTIMISE study. Br J Dermatol. 2020;182(2):426–34. https://doi.org/10.1111/bjd.18143.
42. Mehta H, Mashiko S, Angsana J, Rubio M, Hsieh YCM, Maari C, et al. Differential changes in inflammatory mononuclear phagocyte and T-cell profiles within psoriatic skin during treatment with guselkumab vs. secukinumab. J Invest Dermatol. 2021;141(7):1707-1718.e9. https://doi.org/10.1016/j.jid.2020.12.012.
43. Ruiz-Villaverde R, Chinchay FV, Rodriguez-Fernandez-Freire L, Armario-Hita JC, Pérez-Gil A, Galán-Gutiérrez M. Guselkumab dosing interval optimization in adult patients with moderate-to-severe psoriasis switching from ustekinumab. Dermatol Ther. 2022;35(11):e15835. https://doi.org/10.1111/dth.15835.
44. Yiu ZZN, Becher G, Kirby B, Laws P, Reynolds NJ, Smith CH, Warren RB, Griffiths CEM, BADBIR Study Group. Drug survival associated with effectiveness and safety of treatment with guselkumab, ixekizumab, secukinumab, ustekinumab, and adalimumab in patients with psoriasis. JAMA Dermatol. 2022;158(10):1131–41. https://doi.org/10.1001/jamadermatol.2022.2269.
45. Egeberg A, Rosenø NAL, Aagaard D, Lørup EH, Nielsen ML, Nymand L, Kristensen LE, Thyssen JP, Thomsen SF, Cordtz RL, Loft N, Skov L, Bryld LE, Rasmussen MK, Højgaard P, Kristensen S, Dreyer L. Drug survival of biologics and novel immunomodulators for rheumatoid arthritis, axial spondyloarthritis, psoriatic arthritis, and psoriasis—a nationwide cohort study from the DANBIO and DERMBIO registries. Semin Arthritis Rheum. 2022;53:151979. https://doi.org/10.1016/j.semarthrit.2022.03.018.
46. Mälkönen T, Nuutinen P, Hallinen T, Soini E, Nissinen R, Wennerström C, Rantanen T, Hagman JH, Harvima R, Höök-Nikanne J, Ilves T, Lintu P, Malanin K, Soramäki I, Tasanen K, Teho A, Vähävihu K, Itälinna S, Leinonen P, Sarajärvi P, Huilaja L, Pasternack R. Guselkumab treatment outcomes and persistence in a nationwide real-world cohort of patients with plaque psoriasis. Acta Derm Venereol. 2022;102:adv00631. https://doi.org/10.2340/actadv.v101.910.
47. Daudén E, de Lima GPG, Armesto S, Herrera-Acosta E, Vidal D, Villarasa E, Rivera R, de la Cueva P, Martorell A, Ballesca F, Belinchón I, Carretero G, Rodríguez L, Romero-Maté A, Pujol-Montcusí J, Salgado L, Sahuquillo-Torralba A, Coto-Segura P, Baniandrés O, Feltes R, Alsina M, Llamas-Velasco M. Multicenter retrospective study of secukinumab drug survival in psoriasis patients in a daily practice setting: a long-term experience in Spain. Dermatol Ther (Heidelb). 2021;11(6):2207–15. https://doi.org/10.1007/s13555-021-00618-w.
48. Talamonti M, D'Adamio S, Galluccio T, Andreani M, Pastorino R, Egan CG, Bianchi L, Galluzzo M. High-resolution HLA typing identifies a new «super responder» subgroup of HLA-C06:02-positive psoriatic patients: HLA-C06:02/HLA-C*04, in response to ustekinumab. J Eur Acad Dermatol Venereol. 2019;33(10):e364–7. https://doi.org/10.1111/jdv.15862.
49. Reich K, Strober B, Langley R, Song M, Shen YK, You Y, Foley P, Blauvelt A. Characterization of super responders to guselkumab treatment in moderate to severe psoriasis: results from the VOYAGE 1 and 2 clinical trials. J Am Acad Dermatol. 2020;83(6):AB1145. https://doi.org/10.1016/j.jaad.2020.09.1179.
50. Ruiz-Villaverde R, Rodriguez-Fernandez-Freire L, Armario-Hita JC, Pérez-Gil A, Galán-Gutiérrez M. Super responders to guselkumab treatment in moderate-to-severe psoriasis: a real clinical practice pilot series. Int J Dermatol. 2022;61(8):1029–33. https://doi.org/10.1111/ijd.15819.

51. Ruiz-Villaverde R, Vasquez-Chinchay F, Rodriguez-Fernandez-Freire L, Armario-Hita JC, Pérez-Gil A, Galán-Gutiérrez M. Super-responders in moderate-severe psoriasis under guselkumab treatment: myths, realities and future perspectives. Life (Basel). 2022;12(9):1412. https://doi.org/10.3390/life12090141.

52. Loft N, Egeberg A, Rasmussen MK, Bryld LE, Nissen CV, Dam TN, Ajgeiy KK, Iversen L, Skov L. Prevalence and characterization of treatment-refractory psoriasis and super-responders to biologic treatment: a nationwide study. J Eur Acad Dermatol Venereol. 2022;36(8):1284–91. https://doi.org/10.1111/jdv.17913.