Dermatol Ther (Heidelb) (2023) 13:787–801
https://doi.org/10.1007/s13555-023-00893-4

ORIGINAL RESEARCH

Long-Term Efficacy, Safety, and Drug Survival of Guselkumab in Patients with Psoriasis: Real-World Data from the Czech Republic BIOREP Registry

Jan Hugo · Martina Kojanova · Barbora Turkova · Spyridon Gkalpakiotis on behalf of the BIOREP Study Group

Received: December 18, 2022 / Accepted: January 18, 2023 / Published online: February 1, 2023

ABSTRACT

Background: Real-world data on the long-term use of guselkumab for treatment of psoriasis are still limited.
Objective: We aimed to evaluate long-term efficacy, safety, and drug survival of guselkumab in a real-world setting.
Methods: This is a retrospective study analyzing Czech Republic registry (BIOREP) data of patients treated with guselkumab.
Results: In total, 333 patients were included. Improvement in Psoriasis Area and Severity Index (PASI) score was significant. Mean PASI score decreased from 16 at baseline to 0.7, 0.9, and 0.8 after 12, 24, and 36 months, respectively. Absolute PASI scores of ≤ 3 and ≤ 1 were achieved in 93.9% and 77.9%, 94.2% and 71.0%, and 94.8% and 70.7% of patients after 12, 24, and 36 months, respectively. Response PASI 90 and PASI 100 were attained in 81.8% and 57.1%, 75.4% and 50.7%, and 75.9% and 55.2% of patients after 12, 24, and 36 months, respectively. The percentage of patients achieving PASI 90 and PASI 100 responses was higher throughout the study in bio-naive and in normal-weight patients, while presence of psoriatic arthritis had no influence. Improvement in Dermatology Life Quality Index (DLQI) score was also significant; mean DLQI score decreased from 14.2 at baseline to 0.9, 1.0, and 0.7 after 12, 24, and 36 months, respectively. Patients with PASI 100 had lower mean DLQI throughout the study compared with patients with PASI 90. Major reason for discontinuation was loss of effectiveness in 7.1% of patients, while only 0.6% were due to adverse events. Overall cumulative drug survival was high, with only a minimal decline over time, reaching 91.6%, 87.0%, and 85.5% after 12, 24, and 36 months, respectively. Drug survival was not affected by previous biological treatment, patient weight, or presence of psoriatic arthritis.
Conclusions: This real-world study demonstrated the long-term effectiveness, good safety profile, and high drug survival of guselkumab treatment over a period of 36 months.

Keywords: Psoriasis; Guselkumab; Real world; Biological therapy; Registries; BIOREP

Members of BIOREP Study Group are listed in the acknowledgements section.

J. Hugo (✉) · S. Gkalpakiotis
Department of Dermatovenereology, Third Faculty of Medicine, Charles University and University Hospital Kralovske Vinohrady, Prague, Czech Republic
e-mail: jan.hugo@fnkv.cz

M. Kojanova
Department of Dermatovenereology, First Faculty of Medicine and General University Hospital, Charles University, Prague, Czech Republic

B. Turkova
Value Outcomes, Prague, Czech Republic

Key Summary Points

Why carry out this study?

Patients registered in clinical trials can be quite different from those from daily clinical practice, mainly due to strict exclusion criteria, so real-world data are of high importance.

Real-world analyses of guselkumab are still limited, and most of these analyses were of up to 1 year of therapy.

What was learned from the study?

This study shows the high efficacy and good safety profile of guselkumab during long-term use.

Previous exposure to biologic therapy, being overweight, and presence of psoriatic arthritis did not show to be negative factors for drug survival.

INTRODUCTION

Psoriasis is a chronic immune-mediated skin disease, with an estimated prevalence of 2–4% in Western countries [1], having a significant impact on patients' quality of life [2]. In the past decade, psoriasis has been proven to be associated with a number of cardiometabolic comorbidities, such as obesity, arterial hypertension, type 2 diabetes mellitus, dyslipidemia, or non-alcoholic fatty liver disease [3]. The recognition of the link between psoriasis and these diseases is related to a shift in the conception of psoriasis, from the earlier view of a simply cutaneous disorder to the current view as a systemic inflammatory disease [4]. At the molecular level, psoriasis was identified as a T-cell-mediated disease, previously with a major role attributed to Th1 cells, but later findings highlighted the central role of Th17 cells, with cytokine interleukin (IL)-23 as the "master regulator" [5]. On the basis of these advances in the understanding of the pathophysiology of psoriasis, a new class of selective IL-23 inhibitors has been invented [6]. The first member of this drug group is guselkumab, a fully human immunoglobulin G1 λ (IgG1λ) monoclonal antibody, specifically binding to the p19 subunit of IL-23 [7]. A number of clinical trials with guselkumab have been conducted (VOYAGE 1, VOYAGE 2, NAVIGATE, ECLIPSE, ORION, IXORA-R, POLARIS), all demonstrating good efficacy with high achievement percentages not only for Psoriasis Area and Severity Index (PASI) 75 but also for PASI 90 and 100 [8]. Patients who participate in clinical trials are quite different from those seen in daily clinical practice for many reasons (e.g., strict exclusion criteria, age distribution). Therefore, real-world evidence (RWE) provides important information about specific attributes of different biologics in different patients. Due to the novelty of the drug, there is a strong need for long-term, real-world data.

The objective of our study was to assess the efficacy, drug survival, safety, and impact on quality of life in patients with moderate-to-severe psoriasis in real-life settings treated with guselkumab in the Czech Republic.

METHODS

This was a multicentric (specialized dermatology centers in the Czech Republic compiled in the BIOREP registry) retrospective study, utilizing data analysis from adult patients with moderate-to-severe psoriasis treated with guselkumab. BIOREP is a web-based database of patients with non-oncological dermatological diseases who are treated with biological or targeted therapy in the Czech Republic. For patients with psoriasis, the BIOREP database contains their demographic data, comorbidities, PASI scores, Dermatology Life Quality Index (DLQI) scores, and the efficacy and safety of the drugs used. The registry was launched in May 2005 and is under supervision by Czech Dermatovenereology Society. In the Czech Republic, biologic therapy is administered at 38 specialized centers, 36 of which are included in the BIOREP registry. At the time of analysis of

this study, guselkumab was being administered in 26 centers. We included every patient who received at least one dose of guselkumab 100 mg administered subcutaneously. The cut-off date for our analysis was 31 October 2022. Patients included in the analysis were both biologic (bio)-naive (guselkumab administered as first-line biologic drug) and bio-experienced (previous exposure to one or more biologic drugs). The study was conducted in accordance with the Declaration of Helsinki of 1964 and all subsequent amendments, and all patients provided written informed consent. Institutional review board approval was not required for this study, and patient-level data used for analysis were de-identified. Permission to access/use data from BIOREP registry was obtained. At the baseline visit, demographic data [age, sex, weight, height, body mass index (BMI)] and data on course of psoriasis, comorbidities, personal medical history, family health history, smoking status, and previous systemic and biologic therapy were collected. In addition, the age at onset of psoriasis and age at onset of guselkumab therapy were recorded. Data on PASI and DLQI scores and adverse events were collected during patient visits at months 3, 6, 12, 18, 24, 30, and 36. We specifically focused on the PASI 90 and PASI 100, and categorized our patients according to previous exposure to biologic drugs, presence of psoriatic arthritis (PsA), and BMI (< 25 and ≥ 25 kg/m^2). We also compared the change in the DLQI score of patients who achieved PASI 90 and PASI 100 responses. In addition, we performed a drug survival analysis.

Statistical Analysis

Epidemiological data (demographic and psoriasis characteristics and personal medical history), disease severity (PASI and DLQI), BMI, comorbidities, and previous treatments were summarized using descriptive statistics for the purposes of study analysis.

Descriptive statistics were used to evaluate the dataset on the basis of the number of patients and their percentage proportion in groups relative to categorical variables; the mean and standard deviation (SD) were used for continuous variables. Time to discontinuation of guselkumab treatment was estimated using Kaplan–Meier survival curves and compared with the log-rank test. The P-value < 0.05 was considered to be statistically significant. The statistical analyses were performed using R software (R Core Team 2019).

RESULTS

Patient Characteristics and Previous Treatments

A total number of 333 patients with plaque psoriasis (336 treatment series) were enrolled in this study, with a predominance of male patients (66.7%; $n = 222$). The mean ($\pm$ SD) age at the initiation of guselkumab therapy was 48.6 ± 13.3 years and the mean duration of disease was 22.1 ± 13.2 years. A positive family history of psoriasis was found in 135 patients (40.5%). According to BMI, 31.5% of patients were overweight (BMI 25–29.99 kg/m^2) and 48.0% of patients were obese (BMI ≥ 30 kg/m^2). At the baseline, the mean BMI of the patients was 30.3 ± 6.6 kg/m^2. A total of 70 patients (21.0% of all patients) had concomitant PsA at the start of guselkumab treatment; of these patients, 22.9% had asymmetric oligoarticular arthritis, 11.4% symmetric polyarthritis, 11.4% distal interphalangeal arthropathy, and 7.1% spondylitis, and in 47.1% the form of PsA was not specified. Almost three-quarters of the patients (72.4%) had at least one other comorbidity, with cardiovascular (39.3%) and metabolic/endocrine (37.5%) being the most frequent. Sixteen patients had a history of previous malignancy; in most cases, the malignancies were diagnosed less than 5 years before the initiation of therapy. Of the 333 patients, 122 (36.6%) were active smokers and 48 (14.4%) were ex-smokers.

Mean PASI score at baseline was 16.0 ± 7.7, with the highest score being 47.4. Impairment in quality of life was assessed by DLQI at baseline with a mean score of 14.2 ± 6.5. Most of the patients have been previously treated by phototherapy (80.5%) and with methotrexate

(78.4%), 62.8% had used acitretin and 42% cyclosporine. A total of 48.6% patients were bio-naive (6.0% were treated with apremilast), and 51.4% had been treated with at least one biologic drug [16.8% had been treated in the past with tumor necrosis factor (TNF) inhibitor, 12.6% with IL-12/23 inhibitor, 19.8% with IL-17 inhibitors, 0.3% with IL-23 inhibitor risankizumab] (Table 1).

Guselkumab Treatment

In the study population, all patients received at least one dose of guselkumab. By the time of the analysis 313, 231, 138, and 58 patients had completed 3, 12, 24, and 36 months of the treatment, respectively.

The mean (± SD) PASI score decreased from 16.0 ± 7.7 at baseline to 2.0 ± 3.5 after 3 months of therapy, to 0.7 ± 1.4 after 12 months, to 0.9 ± 1.6 after 24 months, and to 0.8 ± 1.2 after 36 months (Fig. 1).

Absolute PASI scores of ≤ 3 and ≤ 1 were achieved in 81.8% ($n = 256$) and 54.0% ($n = 169$) of patients after 3 months of therapy, in 93.9% ($n = 217$) and 77.9% ($n = 180$) of patients after 12 months, in 94.2% ($n = 130$) and 71.0% ($n = 98$) of patients after 24 months, and in 94.8% ($n = 55$) and 70.7% ($n = 41$) of patients after 36 months, respectively (Fig. 2).

PASI 90 and PASI 100 responses were observed in 61.7% ($n = 193$) and 32.9% ($n = 103$) of patients after 3 months of therapy, in 81.8% ($n = 189$) and 57.1% ($n = 132$) of patients after 12 months, in 75.4% ($n = 104$) and 50.7% ($n = 70$) of patients after 24 months, and in 75.9% ($n = 44$) and 55.2% ($n = 32$) of patients after 36 months, respectively (Fig. 3). The percentage of patients achieving PASI 90 and PASI 100 responses was higher at all timepoints of the study in bio-naive patients compared with bio-experienced patients (Fig. 4a). PASI 90 and PASI 100 responses were higher at all timepoints of the study in normal weight patients (BMI < 25 kg/m^2) compared with overweight patients (BMI ≥ 25 kg/m^2) (Fig. 4b). The percentage of patients achieving PASI 90 and PASI 100 responses varied at different time

Table 1 Demographic characteristics of patients at baseline, comorbidities, and previous systemic therapy

Number of patients	333
Men	222 (66.7%)
Age (years)	50.3 (± 13.3)
Age at the time of diagnosis (years)	26.5 (± 14.2)
Age at the time of initiation of guselkumab (years)	48.6 (± 13.3)
Duration of psoriasis (years)	23.8 (± 13.2)
Duration from diagnosis to the initiation of guselkumab (years)	22.1 (± 13.2)
Family history of psoriasis	135 (40.5%)
BMI (kg/m^2)	30.3 (± 6.6)
BMI category	
Underweight (< 18.5 kg/m^2)	4 (1.2%)
Normal (18.5–24.99 kg/m^2)	64 (19.2%)
Overweight (25–29.99 kg/m^2)	105 (31.5%)
Obese (≥ 30 kg/m^2)	160 (48.0%)
Types of psoriasis	
Plaque	333 (100%)
Exanthematic	19 (5.7%)
Erythrodermic	14 (4.2%)
Palmoplantar	7 (2.1%)
Palmoplantar pustulosis	7 (2.1%)
Inverse	19 (5.7%)
Nail	72 (21.6%)
Psoriatic arthritis	70 (21.0%)

Table 1 continued

At least one comorbidity	241 (72.4%)
Cardiovascular diseases	131 (39.3%)
Metabolic/endocrine disorders	125 (37.5%)
Gastrointestinal and hepatic disease	37 (11.1%)
Psychiatric disorders	31 (9.3%)
Pulmonary diseases	29 (8.7%)
Neurological diseases	20 (6.0%)
Urological/renal diseases	17 (5.1%)
Malignancy	16 (4.8%)
Musculoskeletal disorders	14 (4.2%)
Dermatological diseases	13 (3.9%)
Ocular diseases	7 (2.1%)
Hematologic diseases	7 (2.1%)
Chronic infectious diseases	4 (1.2%)
Other	77 (23.1%)
Smokers	122 (36.6%)
Ex-smokers	48 (14.4%)
Previous systemic therapy	
Phototherapy	268 (80.5%)
Methotrexate	261 (78.4%)
Retinoid	209 (62.8%)
Cyclosporine	140 (42.0%)
Other	28 (8.4%)
Previous therapy (yes)	171 (51.4%)
Anti-TNF	56 (16.8%)
IL-12/23	42 (12.6%)
IL-17	66 (19.8%)
IL-23	1 (0.3%)
Other	26 (7.8%)
PASI	16.0 (± 7.7)
DLQI	14.2 (± 6.5)

Values are *n* (%) of patients or mean (± SD)
PASI Psoriasis Area and Severity Index, *DLQI* Dermatology Life Quality Index, *BMI* body mass index

points of the study between patients with PsA and those without (Fig. 4c).

The mean (± SD) DLQI score decreased from 14.2 ± 6.5 at the baseline to 2.0 ± 3.2 after 3 months of therapy, to 0.9 ± 2.1 after 12 months, to 1.0 ± 2.7 after 24 months, and to 0.7 ± 1.4 after 36 months (Fig. 5a). The mean DLQI score was lower at all timepoints of the study in patients with PASI 100 response compared with patients with PASI 90 response (Fig. 5b).

Overall cumulative drug survival was 91.6% after 12 months of therapy, 87.0% after 24 months, and 85.5% after 36 months. By further analyses, we found that drug survival was not affected by previous biological treatment, patient weight, or the presence of PsA (Fig. 6a–d).

A total of 26 adverse events (AEs) were reported in 23 patients (6.9% of all patients). The most common AE was coronavirus disease 2019 (COVID-19). Malignant tumors were diagnosed in three patients a few months after initiation of therapy. On the basis of consultation with the oncologists, guselkumab therapy was temporarily interrupted in two cases (endometrial carcinoma and colorectal carcinoma), while in the other patient (prostate adenocarcinoma) therapy was continued without any interruption (Table 2).

Discontinuation or switch of guselkumab therapy occurred in 41 cases (12.2% of all patients). Loss of effectiveness was the major

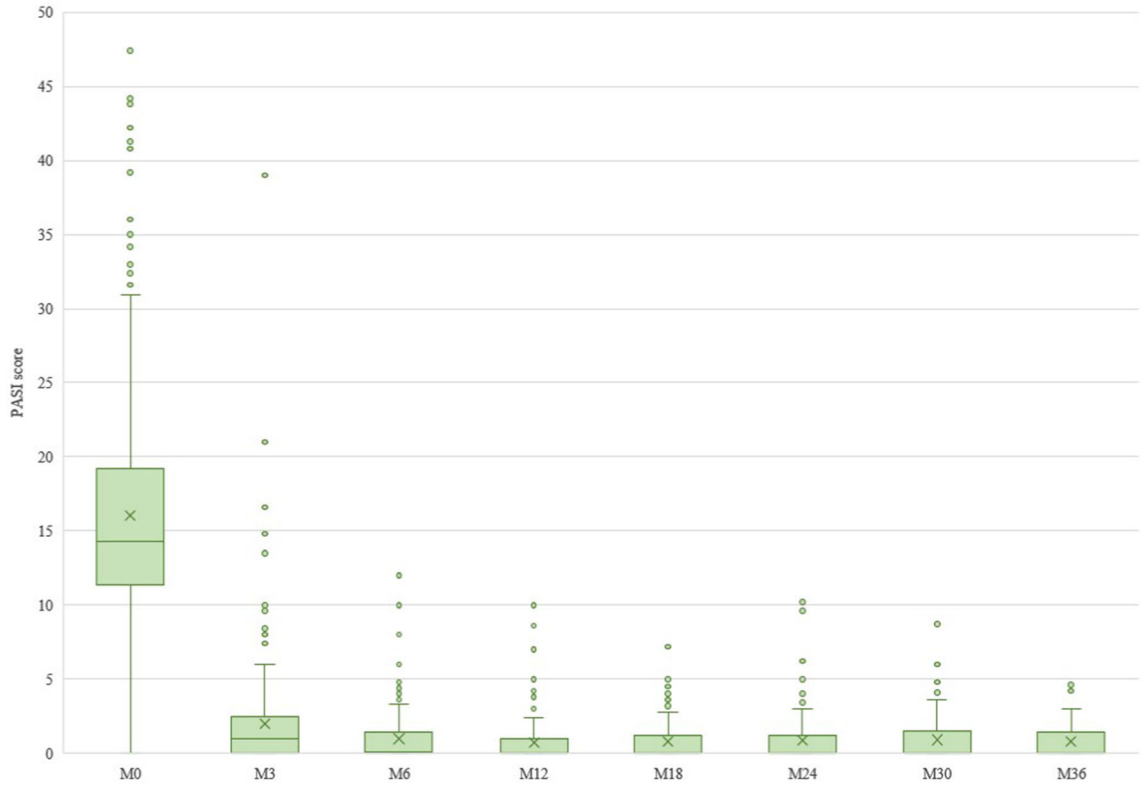

Fig. 1 Changes in mean PASI score

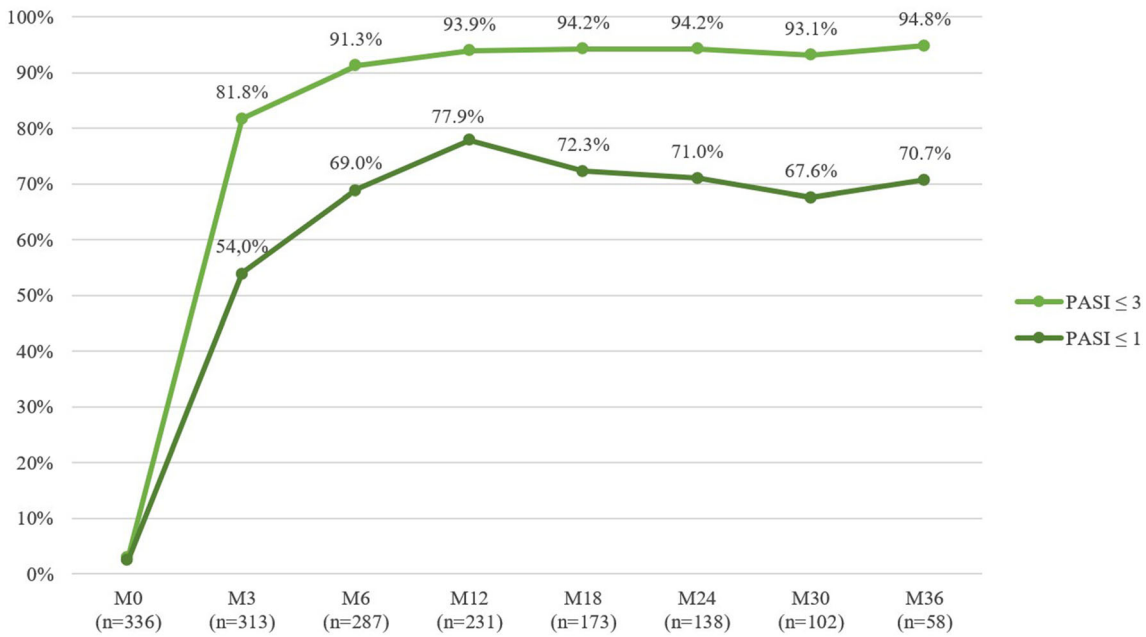

Fig. 2 Percentage of patients achieving PASI $\leq$ 3 and $\leq$ 1

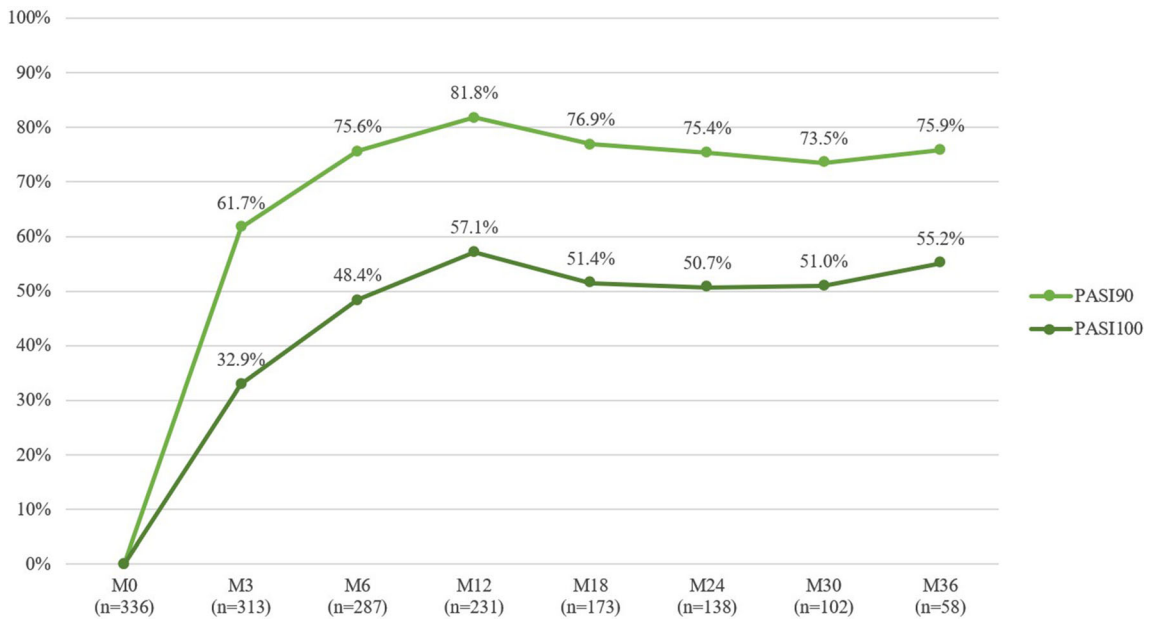

Fig. 3 Development in improvement in PASI score in category of PASI 90 and PASI 100

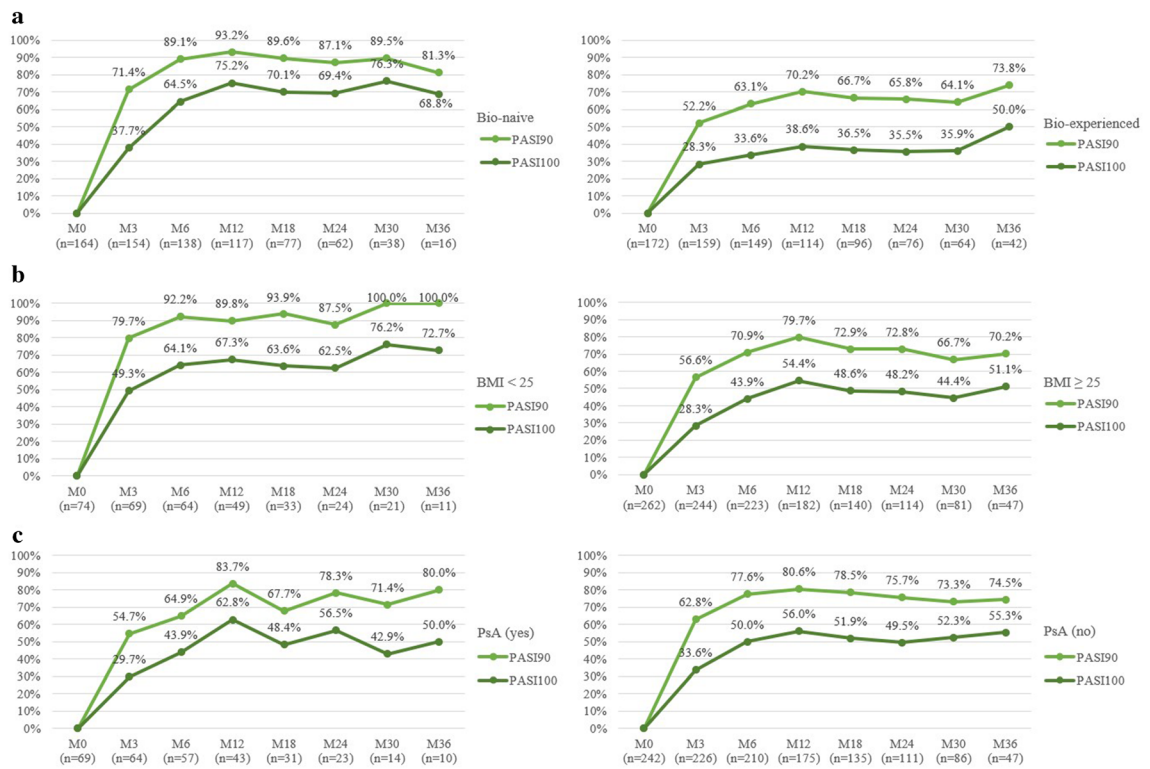

Fig. 4 Achievement of PASI 90 and PASI 100 **a** in bio-naive and bio-experienced patients; **b** in patients with BMI under 25 kg/m^2 and over 25 kg/m^2; **c** in patients with and without PsA

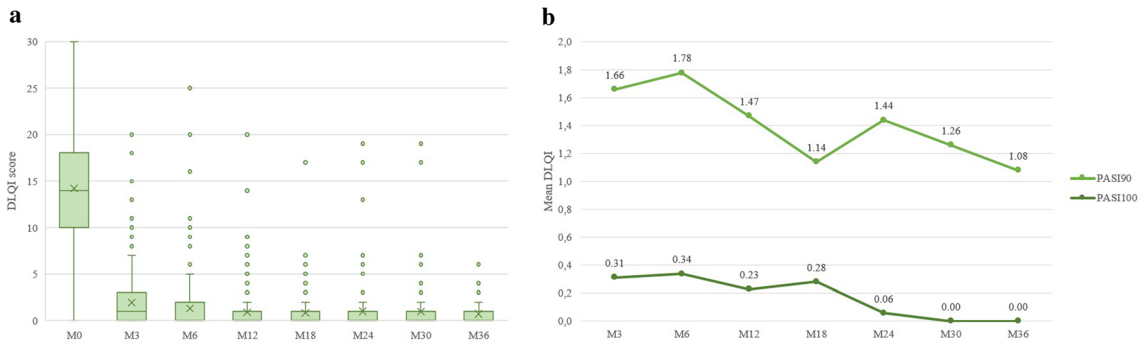

Fig. 5 Mean DLQI **a** all patients; **b** in the PASI 90 and PASI 100 category

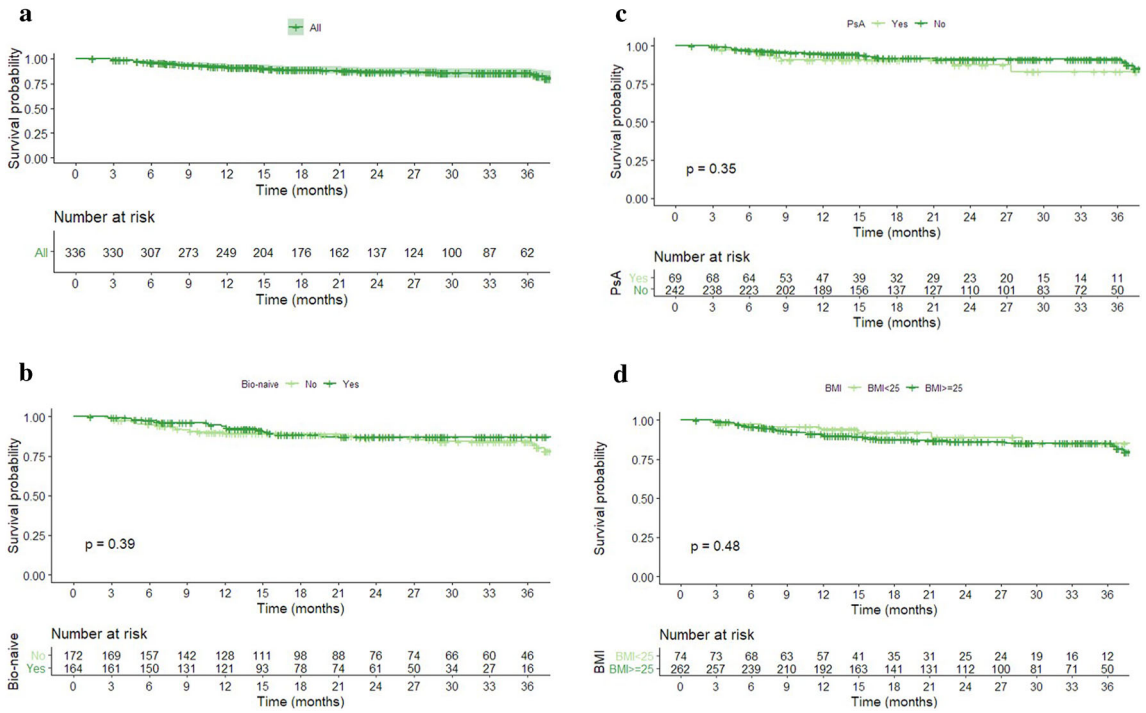

Fig. 6 Drug survival in: **a** all patients; **b** by bio-naivety; **c** by presence of psoriatic arthritis; **d** by BMI

reason for termination in 7.1% of patients. Table 3 summarizes the reasons for discontinuation of drug treatment.

DISCUSSION

This multicenter retrospective study analyzed data from the Czech Republic Registry for Biological Treatment (BIOREP), demonstrating effectiveness, drug survival, and safety profile of guselkumab in a real-world setting.

The analysis of demographic data showed a high percentage of obese patients (48.0%) and a high mean age (48.6 ± 13.3) at the initiation of therapy, which corresponds to the general psoriatic population in BIOREP [9]. Moreover, a relatively high percentage of this study population were bio-naive patients (48.6%), although guselkumab is one of the newest biologics in the psoriasis treatment. This may be explained by physicians' preference to initiate treatment with a drug that has a high chance of achieving PASI 100, since achieving complete

Table 2 Adverse events

Adverse events (AEs)	*N*
Infections	17
COVID-19	11
Other infections	6
Dermatological AEs[a]	1
Malignancy[b]	3
Other AEs[c]	5 (1[d])
Total AEs	26

[a]Worsening of atopic dermatitis
[b]Endometrial carcinoma (1), prostate adenocarcinoma (1), colorectal carcinoma (1)
[c]Exacerbation of chronic obstructive pulmonary disease (3); cause of death in one of them—respiratory failure); transient ischemic attack (1); total hip replacement after injury (1)
[d]Cause of death

Table 3 Reason for discontinuation

Reason for discontinuation	
Loss of effectiveness	24 (7.1%)
Patient non-cooperation	5 (1.5%)
Adverse events[a]	2 (0.6%)
Surgical procedure	2 (0.6%)
Pregnancy	1 (0.3%)
Other	3 (0.9%)
Death[b]	4 (1.2%)
Total	41 (12.2%)

[a]Worsening of atopic dermatitis (1), transient ischemic attack (1)
[b]Acute gastric ulcer with bleeding and perforation (1), cardiorespiratory failure (1), respiratory failure (1), heart failure (1)

skin clearance is known to positively correlate with improvement in the DLQI [10].

The effect of guselkumab therapy on skin involvement was fast. The mean (± SD) PASI score dropped from 16.0 ± 7.7 at baseline to 2.0 ± 3.5 after 3 months, which correlates with other real-world data [11–13]. A further decrease in the PASI score to 0.7 ± 1.4 was observed after 12 months. This is comparable to the results by Ruggiero et al. (mean PASI 0.8) [14] and Ruiz-Villaverde et al. (mean PASI 0.9) [15]. The achieved improvement remained entirely stable and PASI score was 0.8 ± 1.2 after 36 months. Real-world evidence for mean PASI score with a treatment duration of about 3 years is available only from Megna et al. (120 weeks) with a slightly worse result (mean PASI 1.0) [16].

An absolute PASI score ≤ 3 has been recently suggested as one of the ideal goals of therapy [17]. PASI ≤ 3 were achieved by 81.8%, 93.9%, and 94.8% of patients after 3, 12, and 36 months of therapy, respectively. PASI ≤ 1 were achieved by 54.0%, 77.9%, and 70.7% of patients after 3, 12, and 36 months of therapy, respectively. These results are considerably better than published results at similar time intervals by Gerdes et al. (PASI ≤ 3 in 65% and 79% and corresponding PASI ≤ 1 in 34.2% and 50.8% of patients after 3 and 7 months, respectively) [18], Mälköne et al. (PASI ≤ 2 in 80% of patients after 9–14 months) [19], and with modified NRI method by Del Alcázar et al. (PASI ≤ 4 in 78.4% and 80.1% and corresponding PASI ≤ 2 in 63.8% and 72.7% of patients after 4 and 6 months, respectively) [11].

PASI 90 and PASI 100 are increasingly recommended as an ideal treatment goal [20]. After 3 months of therapy with guselkumab, PASI 90 and PASI 100 were achieved in 61.7% and 32.9% of our patients. This is similar to results by Ruiz-Villaverde et al. (PASI 90 in 56.3% and PASI 100 in 38.0% after 3 months) [15] and Benhadou et al. (PASI 90 in 55.4% and PASI 100 in 32.1% after 4 months) [13] and quite better than results by Peláez Bejarano et al. (PASI 90 in 31.8% and PASI 100 in 22.7% after 3 months) [12]. After 12 months of therapy the response rate increased further; PASI 90 and PASI 100 were achieved in 81.8% and 57.1% of our patients, respectively. This is similar to results by Ruiz-Villaverde et al. (PASI 90 in 71.0% and PASI 100 in 51.6%, after 12 months) [15] and Ruggiero et al. (PASI 90 in 73.9% and PASI 100 in 43.5%, after 11 months) [14]. At the end of the follow-up period, after 36 months of

therapy, the response rate decreased only marginally, and PASI 90 and PASI 100 were achieved in 75.9% and 55.2% of our patients, respectively. This is close to the results by Megna et al. (PASI 90 in 77.4% and PASI 100 in 54.8%, after 120 weeks) [16].

A number of studies evaluating TNF-inhibitors and IL-17 inhibitors have revealed that the best therapeutic response is achieved in bio-naive patients [21–23]. In our study population with guselkumab treatment, we observed that PASI 90 and PASI 100 responses were better in bio-naive patients throughout the follow-up period. This is consistent with the findings of study by Galluzzo et al., which also reports poorer efficacy in patients treated with guselkumab who have experience with prior biologic therapy [24]. Contrary to these conclusions, other real-life analyses of guselkumab by Fougerousse et al. [25], Benhadou et al. [13], and Megna et al. [16] found no difference in efficacy between bio-naive and bio-experienced patients. More data are necessary to conclude if previous biologic therapy is a negative predictive factor for PASI 90 and PASI 100 in patients treated with guselkumab.

The TNF-α inhibitors have well-known worse outcomes in overweight patients [26, 27]; even analysis of IL-17 inhibitors tend to present better clearance rates in normal weight patients [28, 29]. In our population treated with guselkumab, the PASI 90 and PASI 100 responses were better throughout the follow-up period in normal weight patients (BMI < 25) compared with overweight patients (BMI ≥ 25). Our results are in contrast with other real-world studies [24, 31, 32] that reported no difference in PASI score improvement between obese and normal weight patients. However, the different conclusions can be explained by the fact that the studies focused on a possible difference in the overall PASI score.

Conclusions of whether the presence of PsA affects the efficacy of biological therapy are inconsistent in the literature. Some studies did not find a significant difference [32–36] and some studies have documented a negative influence on the efficacy [37–40], contrary to one in which a positive effect was reported [41]. In our population, the presence of PsA did not worsen but also did not improve the achievement of PASI 90 and PASI 100 responses. Until now, only one other real-world study has statistically evaluated the efficacy of guselkumab between patients with and without PsA, and it found no impact on treatment efficacy [18].

Psoriasis bears a substantial disease burden for patients. The improvement in quality of life was rapid; after just 3 months of therapy with guselkumab the mean (± SD) DLQI score dropped from 14.2 ± 6.5 at baseline to 2.0 ± 3.5. The decrease continued and after 12 months DLQI score was 0.9 ± 2.1. The achieved improvement remained stable until the end of the study period, not decreased to 1, where a score of 0–1 means that the disease has none or minimal impact on quality of life. Compared with other real-world studies that evaluated DLQI within 6–18 months after initiating guselkumab therapy, our results are similar and support the evidence that patients achieving PASI 100 response have a better quality of life than those having PASI 90 response [11, 15, 18, 42].

Overall cumulative drug survival (DS) was high, with only a minimal decline over time, attaining 91.6% after 12 months of therapy, 87.0% after 24 months, and 85.5% after 36 months of therapy. Our data correlate with other RWE in the assessment of one-year [43, 47], two-year drug survival on treatment [15, 22, 44–46]. Three-year survival data on treatment have not yet been published.

We further investigated the possible influence of several factors on drug survival, namely previous exposure to biological therapy, patient weight, and presence of PsA. In our population, there was no statistically significant difference between bio-naive and bio-experienced patients. This is consistent with the findings of the analysis by Dapavo et al. [43] and contrary to the analysis by Lytvyn et al. [45], where lower DS was observed in bio-experienced patients. In our population, we also did not find a statistically significant difference between patients with and without concomitant PsA. Our findings are in contrast to analyses by Iznardo et al. [44] and Van Muijen et al. [46], where a trend towards shorter DS in patients with PsA was observed. In our population, drug survival was

not affected even by patient weight. In this matter, no other studies have evaluated the possible impact of patient weight on DS specifically for guselkumab yet. We consider our findings to be of considerable importance because real-world analyses typically find a negative impact of weight on DS, with these conclusions being applicable to all previous drug classes, both TNF inhibitors [26, 27], IL-12/23 inhibitor [41, 48], and IL-17 inhibitors [22, 49].

In the study population 23 patients (6.9% of all patients) experienced an AE. Most of the reported AEs were of a non-significant transient character and did not lead to treatment discontinuation. The most common infectious AE was COVID-19, but this specific infectious disease is known to affect patients on biological therapy as often as those without biological therapy [50]. We did not see any worse course of COVID-19 in our patients. Similar results have been published in other studies evaluating patients in a real-world setting, addressing overall favorable safety profile and good tolerance with no new safety signals [11, 15, 18, 42, 44, 51, 52].

A total of 41 patients (12.2% of all patients) discontinued treatment. Most of the cases (7.1% of all patients; $n = 24$) were due to loss of efficacy. Insufficient efficacy as the main reason for discontinuing guselkumab therapy, and only a low percentage of other reasons, has also been stated in other studies published to date [15, 43–45]

The strength of our study is a longer follow-up period with a larger number of patients compared with most previously published studies evaluating guselkumab. An advantage is also a detailed analysis of high skin improvement (PASI 90 and PASI 100) and drug survival, including an assessment of possible influencing factors. The limitations of our study are typical of studies that use real-world data, the retrospective design, and the absence of a control group.

CONCLUSIONS

This study confirmed data from clinical trials and previous real-world analyses regarding the high efficacy and good safety profile of guselkumab. We were able to show that both efficacy and safety remain stable over a long time period and do not tend to deteriorate in any significant way. Drug survival is not influenced by previous biological therapy, higher BMI, or the presence of PsA. No new safety signals arise.

ACKNOWLEDGEMENTS

The authors thank the participants of the study. The authors also wish to thank all dermatologists and collaborators, who participated in creating BIOREP, for their efforts and dedication to the project. BIOREP Study Group Members: Zdenek Antal, Petr Arenberger, Jirina Bartonová, Linda Blahova, Petra Brodska, Petr Bohac, Hana Buckova, Martin Cetkovsky, Petra Cetkovska, Jana Cadova, Dominika Diamantova, Magdalena Dobiasova, Hana Duchkova, Jorga Fialova, Olga Filipovska, Jana Földesova, Petra Gkalpakioti, Martina Grycova, Jiri Horazdovsky, Eva Horka, Katerina Hrazdirova, Eduard Hrncir, Jana Chlebkova, Jaromira Janku, Lucie Jaresova, Renata Kopova, Dora Kovandova, Silvie Krchova, Lenka Kulmanova, Natalie Kunesova, Iva Lomicova, Romana Machackova, Alena Machovcova, Hana Malikova, Martina Matzenauer, Miroslav Necas, Helena Nemcova, Radka Neumannova, Michaela Novakova, Jitka Osmerova, Veronika Pallova, Lucie Petru, Blanka Pinkova, Zuzana Plzakova, Marie Policarova, Tomas Pospisil, Filip Rob, Miloslav Salavec, Marie Selerova, Veronika Slonkova, Jiri Strok, Ivana Strouhalova, David Stuchlik, Alena Stumpfova, Jaroslav Sevcik, Jan Sternbersky, Katerina Svarcova, Katerina Tepla, Martin Tichy, Hana Tomkova, Yvetta Vantuchova, Ivana Vejrova, Iva Zampachova.

Funding. No funding or sponsorship was received for this study or publication of this article.

Authorship. All named authors meet the International Committee of Medical Journal Editors (ICMJE) criteria for authorship for this article, take responsibility for the integrity of the work as a whole, and have given their approval for this version to be published.

Author Contribution. Hugo J. made substantial contributions to conception and design, acquisition of data, analysis and interpretation of data, drafted the article, and reviewed it critically for important intellectual content, approved the final version to be published, and agreed to be accountable for all aspects of the work related to its accuracy or integrity; Kojanova M. made substantial contributions to the conception and design, acquisition and interpretation of data, drafted the article, and reviewed it critically for important intellectual content, approved the final version to be published, and agreed to be accountable for all aspects of the work related to its accuracy or integrity; Turkova B. analyzed and interpreted the data, reviewed the article critically for important intellectual content, approved the final version to be published, and agreed to be accountable for all aspects of the work related to its accuracy or integrity; Gkalpakiotis S. made substantial contributions to conception and design, reviewed the article critically for important intellectual content, gave final approval for the version to be published, and agreed to be accountable for all aspects of the work related to its accuracy or integrity.

Disclosures. Jan Hugo has served as a speaker for Abbvie, Amgen, Eli-Lilly, Eucerin, Janssen, Novartis and Sandoz. Martina Kojanova and Spyridon Gkalpakiotis served as consultants, speakers, or investigators for Abbvie, Amgen, Eli-Lilly, Janssen, Leo Pharma, Novartis, Pfizer, Sanofi, and UCB. Barbora Turkova declares that she has nothing to disclose.

Compliance with Ethics Guidelines. The study was conducted in accordance with the Helsinki Declaration of 1964 and all subsequent amendments, and all patients provided written informed consent. Patient-level data used for this analysis were de-identified, and Institutional Review Board approval was not required for this study. Permission to access/use data from BIOREP registry was obtained.

Data Availability. The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

REFERENCES

1. Di Meglio P, Villanova F, Nestle FO. Psoriasis. Cold Spring Harb Perspect Med. 2014;4(8): a015354.
2. Rapp SR, Feldman SR, Exum ML, Fleischer AB Jr, Reboussin DM. Psoriasis causes as much disability as other major medical diseases. J Am Acad Dermatol. 1999;41(3 Pt 1):401–7.
3. Woo YR, Park CJ, Kang H, Kim JE. The risk of systemic diseases in those with psoriasis and psoriatic arthritis: from mechanisms to clinic. Int J Mol Sci. 2020;21(19):7041.
4. Srivastava AK, Chand Yadav T, Khera HK, et al. Insights into interplay of immunopathophysiological events and molecular mechanistic cascades in psoriasis and its associated comorbidities. J Autoimmun. 2021;118: 102614.

5. Pastor-Fernández G, Mariblanca IR, Navarro MN. Decoding IL-23 signaling cascade for new therapeutic opportunities. Cells. 2020;9(9):2044.

6. Gooderham MJ, Papp KA, Lynde CW. Shifting the focus—the primary role of IL-23 in psoriasis and other inflammatory disorders. J Eur Acad Dermatol Venereol. 2018;32(7):1111–9.

7. Nogueira M, Torres T. Guselkumab for the treatment of psoriasis—evidence to date. Drugs Context. 2019;9(8): 212594.

8. Light JG, Su JJ, Feldman SR. Clinical utility of guselkumab in the treatment of moderate-to-severe plaque psoriasis. Clin Cosmet Investig Dermatol. 2021;15(14):55–63.

9. Kojanova M, Fialova J, Cetkovska P, et al. Characteristics and risk profile of psoriasis patients included in the Czech national registry BIOREP and a comparison with other registries. Int J Dermatol. 2017;56(4):428–34.

10. Korman NJ, Malatestinic W, Goldblum OM, et al. Assessment of the benefit of achieving complete versus almost complete skin clearance in psoriasis: a patient's perspective. J Dermatol Treat. 2022;33(2): 733–9.

11. 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. Dermatol Ther. 2022;35(2): e15231.

12. Peláez Bejarano A, Robustillo Cortés MA, Villar SP. Guselkumab in moderate-to-severe plaque psoriasis: effectiveness in real clinical practice. Rev Chil Dermatol. 2020;36(3):93–7.

13. 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):e837–9.

14. Ruggiero A, Fabbrocini G, Cinelli E, Megna M. Guselkumab and risankizumab for psoriasis: a 44-week indirect real-life comparison. J Am Acad Dermatol. 2021;85(4):1028–30.

15. 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.

16. Megna M, Potestio L, Fabbrocini G, Ruggiero A. Long-term efficacy and safety of guselkumab for moderate to severe psoriasis: a 3-year real-life retrospective study. Psoriasis (Auckl). 2022;14(12): 205–12.

17. Amatore F, Villani AP, Tauber M, Viguier M, Guillot B, Psoriasis Research Group of the French Society of Dermatology. French guidelines on the use of systemic treatments for moderate-to-severe psoriasis in adults. J Eur Acad Dermatol Venereol. 2019;33(3): 464–83.

18. Gerdes S, Bräu B, Hoffmann M, et al. Real-world effectiveness of guselkumab in patients with psoriasis: health-related quality of life and efficacy data from the noninterventional, prospective, German multicenter PERSIST trial. J Dermatol. 2021;48(12): 1854–62.

19. Mälkönen T, Nuutinen P, Hallinen T, et al. Guselkumab treatment outcomes and persistence in a nationwide real-world cohort of patients with plaque psoriasis. Acta Derm Venereol. 2022;102: adv00631.

20. Torres T, Puig L. Treatment goals for psoriasis: should PASI 90 become the standard of care? Actas Dermosifiliogr. 2015;106(3):155–7.

21. Wade R, Sharif-Hurst S, Dias S. Patient characteristics as effect modifiers for psoriasis biologic treatment response: an assessment using network meta-analysis subgroups. Syst Rev. 2020;9:132.

22. Torres T, Puig L, Vender R, et al. 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: 567–79.

23. Zweegers J, Otero ME, van den Reek JM, et al. Effectiveness of biologic and conventional systemic therapies in adults with chronic plaque psoriasis in daily practice: a systematic review. Acta Derm Venereol. 2016;96(4):453–8.

24. 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.

25. 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):e644–6.

26. Singh S, Facciorusso A, Singh AG, et al. Obesity and response to anti-tumor necrosis factor-α agents in patients with select immune-mediated inflammatory diseases: a systematic review and meta-analysis. PLoS One. 2018;13: e0195123.

27. Højgaard P, Glintborg B, Kristensen LE, Gudbjornsson B, Love TJ, Dreyer L. The influence of obesity on response to tumour necrosis factor-α inhibitors in psoriatic arthritis: results from the DANBIO and ICEBIO registries. Rheumatology (Oxford). 2016;55(12):2191–9.

28. Zafiriou E, Daponte AI, Siokas V, Tsigalou C, Dardiotis E, Bogdanos DP. Depression and obesity in patients with psoriasis and psoriatic arthritis: is IL-17-mediated immune dysregulation the connecting link? Front Immunol. 2021;21(12): 699848.

29. Sbidian E, Chaimani A, Garcia-Doval I, et al. Systemic pharmacological treatments for chronic plaque psoriasis: a network meta-analysis. Cochrane Database Syst Rev. 2017;12(12):CD011535.

30. Hung YT, Lin YJ, Chiu HY, Huang YH. Impact of previous biologic use and body weight on the effectiveness of guselkumab in moderate-to-severe plaque psoriasis: a real-world practice. Ther Adv Chronic Dis. 2021;29(12):20406223211046684.

31. Bardazzi F, Viviani F, Merli Y, et al. Guselkumab for the treatment of psoriasis: a 60-week real-life multicenter retrospective experience. Expert Opin Biol Ther. 2022;13:1–6.

32. Paul C, van de Kerkhof P, Puig L, Unnebrink K, Goldblum O, Thaçi D. Influence of psoriatic arthritis on the efficacy of adalimumab and on the treatment response of other markers of psoriasis burden: subanalysis of the BELIEVE study. Eur J Dermatol. 2012;22(6):762–9.

33. Oguz Topal I, Baysak S, Altunay İK, et al. Evaluation of the efficacy, safety, and side effects of secukinumab in patients with moderate-to-severe psoriasis: real-world data from a retrospective multicenter study. An Bras Dermatol. 2022;97(5): 566–74.

34. Ortiz-Salvador JM, Saneleuterio-Temporal M, Magdaleno-Tapial J, et al. A prospective multicenter study assessing effectiveness and safety of secukinumab in a real-life setting in 158 patients. J Am Acad Dermatol. 2019;81(2):427–32.

35. Kokolakis G, Vadstrup K, Hansen JB, Carrascosa JM. Brodalumab is associated with high rates of complete clearance and quality of life improvement: a subgroup analysis of patients with psoriasis and concomitant psoriatic arthritis. Dermatology. 2022;238(4):620–9.

36. Greb JE, Garber C, Gottlieb AB. Effect of psoriatic arthritis on treatment response in patients with moderate to severe psoriasis. J Drugs Dermatol. 2016;15(8):917–22.

37. Huang H, Cai ML, Hong XJ, et al. Real-world data on the use of secukinumab as treatment for moderate-to-severe psoriasis in Chinese patients. Eur J Dermatol. 2020;30(5):554–60.

38. Rompoti N, Katsimbri P, Kokkalis G, et al. Real world data from the use of secukinumab in the treatment of moderate-to-severe psoriasis, including scalp and palmoplantar psoriasis: a 104-week clinical study. Dermatol Ther. 2019;32(5): e13006.

39. Bonifati C, Capoccia R, Graceffa D, Morrone A. Effectiveness of systemic therapies in patients with obesity and psoriasis: a single-center retrospective study. Acta Dermatovenerol Croat. 2021;29(2): 88–93.

40. Mastorino L, Susca S, Megna M, et al. Risankizumab shows high efficacy and maintenance in improvement of response until week 52. Dermatol Ther. 2022;35(5): e15378.

41. Pirro F, Caldarola G, Chiricozzi A, et al. Impact of body mass index on the efficacy of biological therapies in patients with psoriasis: a real-world study. Clin Drug Investig. 2021;41(10):917–25.

42. Malara G, Trifirò C, Bartolotta A, et al. Real-world effectiveness and safety of guselkumab for the treatment of psoriasis: a 6-month prospective study in a series of psoriatic patients. Eur Rev Med Pharmacol Sci. 2021;25(1):406–12.

43. Dapavo P, Siliquini N, Mastorino L, et al. Efficacy, safety, and drug survival of IL-23, IL-17, and TNF-alpha inhibitors for psoriasis treatment: a retrospective study. J Dermatol Treat. 2022;33(4): 2352–7.

44. Iznardo H, Vilarrasa E, López-Ferrer A, Puig L. Real-world drug survival of guselkumab, ixekizumab and secukinumab for psoriasis. Br J Dermatol. 2021;185(3):660–2.

45. Lytvyn Y, Zaaroura H, Mufti A, AlAbdulrazzaq S, Yeung J. Drug survival of guselkumab in patients with plaque psoriasis: a 2 year retrospective, multicenter study. JAAD Int. 2021;8(4):49–51.

46. Van Muijen ME, Thomas SE, Vellinga D, et al. Real-world data reveal long drug survival for guselkumab in patients with plaque psoriasis. Acta Derm Venereol. 2022;102:adv00755.

47. Li Y, Lu JJ, Zhong XY, et al. Drug survival outcomes associated with the real-world use of ixekizumab, secukinumab, guselkumab, and adalimumab for the treatment of plaque psoriasis in China: a 52-week single-center retrospective study. Clin Cosmet Investig Dermatol. 2022;20(15):2245–52.

48. Zweegers J, van den Reek JM, van de Kerkhof PC, et al. Body mass index predicts discontinuation due to ineffectiveness and female sex predicts discontinuation due to side-effects in patients with psoriasis treated with adalimumab, etanercept or ustekinumab in daily practice: a prospective, comparative, long-term drug-survival study from the BioCAPTURE registry. Br J Dermatol. 2016;175(2):340–7.

49. Kojanova M, Hugo J, Velackova B, et al. Efficacy, safety, and drug survival of patients with psoriasis treated with IL-17 inhibitors—brodalumab, ixekizumab, and secukinumab: real-world data from the Czech Republic BIOREP registry. J Dermatol Treat. 2022;33(6):2827–37.

50. Gisondi P, Bellinato F, Chiricozzi A, Girolomoni G. The risk of COVID-19 pandemic in patients with moderate to severe plaque psoriasis receiving systemic treatments. Vaccines (Basel). 2020;8(4):728.

51. Ghislain PD, Failla V, Lambert J, et al. Effectiveness and tolerability of guselkumab in patients with psoriasis: a longitudinal Belgian retrospective multicenter study. JAAD Int. 2021;1(4):15–7.

52. Jung SW, Lim SH, Jeon JJ, Heo YW, Choi MS, Hong SP. Comparison of the efficacy and safety of biologics (secukinumab, ustekinumab, and guselkumab) for the treatment of moderate-to-severe psoriasis: real-world data from a single Korean center. Biomedicines. 2022;10(5):1058.