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ORIGINAL ARTICLE

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Effectiveness of guselkumab in patients with facial and/or genital psoriasis: Interim analysis results at Week 12 from the GULLIVER study

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Abstract

Background: Facial (FP) and genital psoriasis (GP) significantly affect patients' quality of life. Despite the advances in treatments, limited data on efficacy and safety are available on these difficult-to-treat areas. Guselkumab is an interleukin (IL)-23 inhibitor which has been proven effective in treating patients with moderate-to-severe plaque psoriasis.

Objectives: The aim of this interim analysis was to report the efficacy and safety of guselkumab in the treatment of patients with FP and/or GP.

Materials and Methods: GULLIVER is a 52-week Italian observational study to evaluate the effectiveness and safety of guselkumab in a real-life setting in patients with FP and/or GP. Adult patients with facial and/or genital moderate-to-severe psoriasis (sPGA score ≥ 3) were included. The primary endpoint of this analysis was the percentage of patients achieving a facial or genital sPGA score of 0 (clear) or 1 (almost clear), at Week 12. The change in the score of the facial or genital sPGA components in patients with a score ≥3 for each sPGA component was assessed. PASI score in patients with a baseline PASI above or below 10 was evaluated.

Results: Overall, 351 patients were included in the study; 83.3% of FP and 76.5% of GP patients achieved the primary endpoint. Similar response rates were observed for the facial or genital sPGA components in patients with a baseline facial or genital sPGA score ≥3 in each component. Among patients with a baseline PASI score >10, mean PASI score improved from 19.0 (SD 8.3) to 2.2 (SD 4.8). Forty-four AEs were observed in 32 patients; two mild and transient AEs (fatigue and nausea) were considered treatment related. No SAEs were observed.

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[Correction added on 9th July 2024 after first online publication: An author's name has been corrected to M. R. Bongiorno.]

Conclusions: Guselkumab, showing to be effective and safe in treating FP and GP, may be a valid therapeutic option for patients with psoriasis localized in these difficult-to-treat areas.

INTRODUCTION

Psoriasis is a chronic, inflammatory skin disorder that significantly impacts quality of life (QoL), social functioning and personal relationships.[1] It is associated with various comorbidities, including psoriatic arthritis, cardiometabolic diseases and mood disorders.[2] Adequate treatment of facial (FP) and genital (GP) psoriasis represents an unmet medical need due to challenges associated with treatments and their negative impact on patients' QoL.

FP affects 17%–46% of psoriasis patients[3] and is often indicative of more severe psoriasis. Patients with FP may exhibit higher Psoriasis Area Severity Index (PASI) scores compared to those without facial involvement.[4] FP is associated with earlier onset and longer disease duration, and often requires more extensive treatment.[5] Facial lesions often cause irritation and can display photosensitivity in 5%–20% of patients.[3]

Approximately 30%–63% of psoriasis patients experience psoriatic lesions in the genital area (GP) during their disease course.[1,6,7] GP is more common in men. GP plaques are typically thinner and less scaly due to pronounced friction in this region[8]; lesions are prone to maceration, fissuring and irritation due to mechanical stresses.[9] GP may have a major negative impact on patients' psychological well-being, sexual health and QoL.[1,6]

Treatment of FP and GP remains a significant unmet medical need; there are limited effective therapeutic options available. Despite the considerable morbidity and psychosocial impact associated with FP and GP, there is a lack of data on the efficacy of treatments for these conditions.[10] Topical therapies, such as corticosteroids alone or combined with vitamin D derivatives,[11,12] are commonly used; however, non-adherence due to the difficulties in applying these and maintaining treatment schedules may complicate their use.[13] Other conventional therapies may not be suitable as facial and genital regions often do not respond to such treatments.[9,14] Promising data for biologic therapy for FP and GP have emerged;[15–17] however, evidence is still limited overall.[18,19]

Guselkumab is a fully human monoclonal antibody that targets the p19 subunit of interleukin (IL)-23.[20] Large, randomized, multinational phase III trials (VOYAGE 1, VOYAGE 2, NAVIGATE and ECLIPSE) have demonstrated the clinical efficacy and safety of guselkumab in the treatment of moderate-to-severe plaque psoriasis in adults, and its positive impact on patients' QoL.[21–25] A large, pooled psoriasis data set from the VOYAGER 1 and 2 studies showed that guselkumab was effective in treating regional psoriasis of the scalp, palms and/or soles, and fingernails.[26] Real-life studies for guselkumab have also emerged more recently.[27–29] To date, however, no data on the effectiveness of guselkumab in treating FP and GP are available, creating a knowledge gap regarding the use of guselkumab for these conditions.

The GULLIVER study is a large 52-week observational, noninterventional study that aims to evaluate the effectiveness and safety of guselkumab in daily clinical practice on patients with FP and/or GP. Herein, we present the results of the interim analysis of data from the overall GULLIVER study population of 351 patients at 12 weeks after initiating guselkumab treatment.

MATERIALS AND METHODS

Overview of study design

GULLIVER is an ongoing prospective, single country (Italy), multicentre, noninterventional study to evaluate the effectiveness, impact on QoL, safety and treatment satisfaction with guselkumab in psoriasis patients with significant involvement of the genital and/or facial areas in real-world clinical practice. Study design is displayed in Figure S1. Guselkumab treatment is not determined or assigned by study procedures but is based on normal clinical practice following the summary of product characteristics (SmPC). Guselkumab 100 mg is administered by subcutaneous injection at Weeks 0 and 4, and then every 8 weeks through Week 52. A patient could be enrolled at any time after the first injection of guselkumab (Week 0) and before completion of the next visit (Week 4 or 12) according to clinical practice. For all patients, data derived from Week 0 (V week 0) are collected retrospectively while data derived from the visits at Week 12 (V week 12), Week 28 (V week 28) and Week 52 (V week 52) are collected prospectively.

Baseline data collection included patients' clinical characteristics, measures of clinical response and patient-reported outcomes (see Table S1).

GULLIVER is performed in 38 dermatological centres in Italy. The study is conducted by the investigators according to the ethical principles of the Declaration of Helsinki. The study protocol was approved on 21 January 2020 by the Ethics Committee (EC) of the coordinating centre and acknowledged by the other participating sites. All patients provided written informed consent prior to undergoing study procedures. GULLIVER is registered on ClinicalTrials.gov (NCT04439526).

Participants

Patients affected by FP and/or GP with a static Physician Global Assessment (sPGA) score ≥3 for either or both body

sites were enrolled in the study. Patients meeting severity criteria for both body sites were assigned to one of the two groups (facial or genital), based on the regional localization with the higher degree of severity. Eligible patients were male or female outpatients ≥18 years of age, with a confirmed diagnosis of psoriasis requiring systemic treatment and a significant involvement, defined as a sPGA score ≥3, of the genitals and/or facial area, who started treatment with guselkumab for psoriasis according to the SmPC. PASI score >10 was not considered among the inclusion criteria, since according to the Italian Medicines Agency[30] (AIFA) biologic drugs for psoriasis can be reimbursed, after therapeutic failure of a prior synthetic conventional disease-modifying antirheumatic drug (DMARD), in patients with either PASI >10 or body surface area (BSA) >10% (moderate-to-severe psoriasis) or PASI <10 or BSA <10%, if patients have lesions in special localizations such as face, genitalia, palms, soles or nails. sPGA is widely used for assessment of FP and GP severity and response to treatment.[17,31,32] Exclusion criteria included contraindication to use of guselkumab, treatment with an investigational drug (including investigational vaccines) or use of an invasive investigational medical device within 30 days before the start of guselkumab treatment, and inability to read, write or understand and sign the inform consent form.

TABLE 1 Demographic and disease characteristics at baseline of the patient population under study.

	Facial psoriasis (*N* = 147)	Genital psoriasis (*N* = 204)	Total (*N* = 351)
Age (years)			
Mean (SD)	41.9 (14.9)	47.4 (15.7)	45.1 (15.5)
Median (range)	39.0 (18–81)	47.0 (19–86)	44.0 (18–86)
Gender			
Male, *n* (%)	83 (56.5%)	121 (59.3%)	204 (58.1%)
Female, *n* (%)	64 (43.5%)	83 (40.7%)	147 (41.9%)
Ethnicity			
White, *n* (%)	145 (98.6%)	197 (96.6%)	342 (97.4%)
Other, *n* (%)	2 (1.4%)	7 (3.4%)	9 (2.6%)
Weight (kg)			
Mean (SD)	79.8 (21.6)	79.3 (18.2)	79.5 (19.6)
BMI group			
BMI < 25 kg/m^2, *n* (%)	48 (32.7%)	75 (36.8%)	123 (35.0%)
BMI > =25 and <30 kg/m^2, *n* (%)	37 (25.2%)	66 (32.4%)	103 (29.3%)
BMI > =30 kg/m^2, *n* (%)	39 (26.5%)	38 (18.6%)	77 (21.9%)
Missing, *n* (%)	23 (15.6%)	25 (12.3%)	48 (13.7%)
Duration of psoriasis			
<20 years, *n* (%)	99 (67.3%)	151 (74.0%)	250 (71.2%)
>20 years, *n* (%)	48 (32.7%)	53 (26.0%)	101 (28.8%)
No of patients with at least one previous therapy for psoriasis, *n* (%)	138 (93.9%)	188 (92.2%)	326 (92.9%)
Treatment category			
Topic	65 (44.2%)	99 (48.5%)	164 (46.7%)
Systemic	103 (70.1%)	143 (70.1%)	246 (70.1%)
Biologic	55 (37.4%)	83 (40.7%)	138 (39.3%)
sPGA Score			
Moderate	76 (51.7%)	118 (57.8%)	194 (55.3%)
Moderate to severe	57 (38.8%)	62 (30.4%)	119 (33.9%)
Severe	14 (9.5%)	24 (11.8%)	38 (10.8%)

Assessments

In this interim analysis, treatment efficacy was assessed through Week 12. Regional psoriasis was evaluated using the sPGA for genital area (genital sPGA) and the sPGA for facial area (facial sPGA), in which the erythema, thickness and scaling of the lesions were assessed based on 6-point rating scale: 0 (clear), 1 (almost clear), 2 (mild), 3 (moderate), 4 (moderate to severe) and 5 (severe).[33] In patients with a PASI score above or below 10 at baseline, the improvement in PASI score at Week 12 was evaluated using PASI 75, 90 and 100.[34] The assessment of patients' QoL (see Table S1) collected in the study was not considered in this interim analysis.

Endpoints

The primary efficacy endpoint of this interim analysis was the percentage of participants achieving a facial or genital sPGA score of 0 (clear) or 1 (almost clear) at Week 12. Furthermore, as secondary endpoint for both FP and GP groups, the change in the score of the individual facial or genital sPGA components (erythema, thickness and scaling), in patients with a score ≥3 for each sPGA component, was analysed through Week 12. The percentage of participants achieving PASI 75, PASI 90 and PASI 100 responses among participants with a PASI score above or below 10 at baseline was evaluated at Week 12, as well. Being this an interim analysis, the impact of variables age, disease duration and previous biologic treatment on the clinical response will

TABLE 2 Proportion of patients achieving facial or genital sPGA score 0 or 1 at Week 12.

	Statistics	Facial psoriasis (*N* = 144)	Genital psoriasis (*N* = 200)	Total (*N* = 344)
Achieving sPGA score 0 or 1				
No	*n* (%)	24 (16.7%)	47 (23.5%)	71 (20.6%)
Yes	*n* (%)	120 (83.3%)	153 (76.5%)	273 (79.4%)
	95% CI	76.4–88.5	70.2–81.8	74.8–83.3

be discussed in the paper with the final results. A summary of adverse events (AEs) that occurred during the 12-week timeframe of this interim analysis is provided.

Statistical methods

Sample size considerations of the GULLIVER study were based on estimation precision for the percentage of participants achieving a facial or genital sPGA score of 0 or 1 at Week 52 after initiating treatment. A sample size of 400 evaluable patients (200 with FP and 200 with GP) would allow estimation of the two-sided 95% CI with a width equal to 7.8% (confidence limits from 75.8% to 83.6%) for the percentage of participants achieving this endpoint when the expected percentage is equal to 80% based on phase III clinical trial data.

This interim analysis was conducted using data for 351 patients (147 with FP and 204 with GP). Median, mean and standard deviation (SD) were calculated for quantitative variables and absolute values and percentages for categorial variables. All categorical endpoint results are presented with 95% confidence interval (CI), as no formal statistical hypothesis has been formulated. The 95% CI is also calculated according to Wilson's method.[35] The lower number of patients included in the interim analysis compared to the planned population does not impact the precision of the study (see Method S1).

RESULTS

Demographic and clinical baseline characteristics

The GULLIVER study enrolled 351 patients between July 2020 and November 2022. The list of 36 enrolling centres is shown in Table S2.

This interim analysis, conducted in the entire population enrolled in the study, assessed efficacy and safety data after 12 weeks of treatment with guselkumab.

Baseline characteristics for the FP and GP groups and the overall study population are presented in Table 1. Patients were generally middle-aged [FP = 41.9 (14.9); GP = 47.4 (15.7) years], mostly male (FP = 56.5%; GP = 59.3%) and had a body mass index consistent with being overweight [FP = 27.5 (6.8) kg/m^2; GP = 26.8 (5.2) kg/m^2]. A substantial proportion of patients in both groups had a high degree of disease severity [facial or genital sPGA score of 4 or 5; (FP = 48.3%; GP = 42.2%)]. At baseline, a total of 145 patients (FP = 54; GP = 91) had a PASI score less than or equal to 10 while 180 patients (FP = 83; GP = 97) a PASI score greater than 10. Additionally, 32.7% of FP patients and 26% of GP patients had a duration of disease exceeding 20 years. Prior to entering the study, more than 90% of patients reported receiving previous treatments for psoriasis (topical, systemic or biologic); 189 patients (53.8%) were naïve to treatment with biologics.

Clinical response

High response rates, as assessed by facial or genital sPGA, were observed at 12 weeks for both the FP and GP groups. Detailed results are provided in Table 2.

In the FP group, 83.3% of patients achieved a sPGA score of 0/1, indicating clear or almost clear skin (Figure 1). Similarly, a score of 0 or 1 for erythema, thickness and scaling was achieved in 85.7%, 88.9% and 93.0% of patients with a score ≥3 in each sPGA analysed component, respectively (Figure S2).

In the GP group, 76.5% of patients achieved a sPGA score of 0/1 at Week 12 (Figure 1). Among patients with a score ≥3 for the single components of the genital sPGA at baseline, a score of 0 or 1 for erythema, thickness and scaling was achieved by 77.7%, 84.9% and 86.4% of patients, respectively (Figure S2).

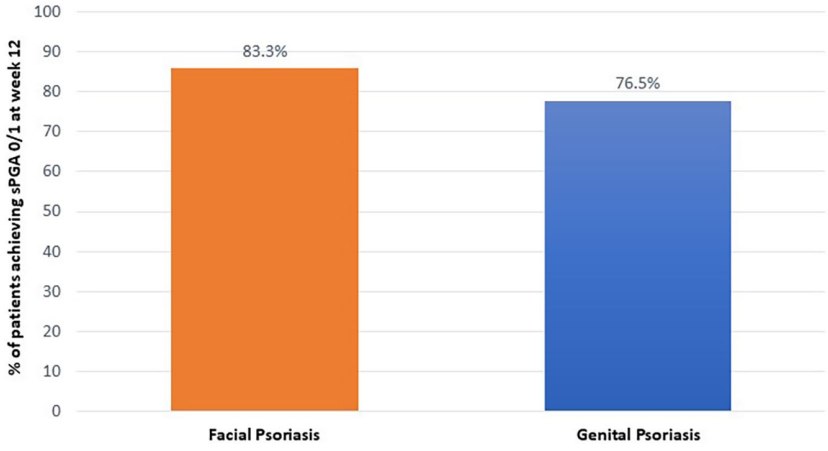

FIGURE 1 Percentage of patients achieving a facial or genital sPGA score of 0/1 at Week 12.

TABLE 3 PASI score at baseline and at Week 12 in patient population with a PASI score ≤10 and in patient population with a PASI score >10 at baseline.

PASI baseline	Actual value								Change from baseline							
	n	Mean	SD	Min	Q1	Median	Q3	Max	Mean	SD	Min	Q1	Median	Q3	Max	95% CI
≤10																
Baseline	145	6.1	2.3	1.2	4.4	6.3	7.8	10.0								
Week 12	142	1.1	1.6	0.0	0.0	0.4	1.7	9.0	−5.0	2.5	−10.0	−6.9	−4.9	−3.3	1.8	−5.4, −4.5
>10																
Baseline	180	19.0	8.3	10.1	12.8	17.0	21.8	53.6								
Week 12	176	2.2	4.8	0.0	0.0	0.3	2.9	44.0	−17.0	8.2	−49.3	−20.2	−15.4	−11.8	10.2	−18.2, −15.8

Among patients with PASI >10 at baseline, significant improvement in PASI score was observed. Mean PASI score decreased from 19.0 (8.3) at baseline to 2.2 (4.8) at Week 12. In patients with PASI ≤10 at baseline, the mean PASI score decreased from 6.1 (2.3) to 1.1 (1.6) (Table 3). Data on PASI score 75, 90 and 100 for both groups are displayed in Table S3.

Forty-four AEs were observed in 32 patients, two mild and transient treatment-related AEs (fatigue and nausea) were reported, and both occurred in one GP patient. No serious AEs (SAEs) were reported, and no AEs led to discontinuation of the study.

DISCUSSION

FP and GP pose a significant burden of disease for patients with psoriasis, affecting their relationships, psychosocial and sexual well-being.[9,36,37]

Efficacy and safety data on biologics in the treatment of facial and genital psoriasis, deriving from both RCT and real-world studies, remain limited.[16,17,19,32,38,39] To our knowledge, GULLIVER, with 351 evaluable patients, is the largest real-life observational study in which the effectiveness of a biologic agent was assessed specifically on the treatment on FP and GP.

In this interim analysis, we found that guselkumab was highly effective in treating patients with genital and facial psoriasis, with complete or almost complete clearance (sPGA score of 0/1) at Week 12 achieved in 83.3% of patients with FP and 76.5% of patients with GP. The results of this Week 12 interim analysis showed that guselkumab is effective and safe in the treatment of FP and GP. These results are particularly significant considering the therapeutic challenges and the substantial impact of FP and GP on patients' QoL associated with FP and GP, and this addressing an unmet medical need.

Recent publications present efficacy and safety data on biologics.[16,17,19,32,38,39] Ixekizumab, administered to 149 patients (74 placebo and 75 treatment) at 160 and 80 mg over 12 weeks, achieved complete or nearly complete resolution of GP in 73.3% of treated patients.[38] The observational Psoriasis Study in Health Outcomes on six different biologics reported clearance rates between 72.6% and 84.3% in face/neck psoriasis and between 61.3% and 86.3% in GP at Week 12.[40] GULLIVER's results align with the most recent data on treatments for FP and GP.

Furthermore, guselkumab induced a marked reduction of PASI score at Week 12 in patients with baseline PASI >10. The proportions of patients achieving PASI 75/90/100 responses in the GULLIVER study were consistent with results reported in randomized clinical trials for guselkumab efficacy[21–25] or real-world evidence.[29,41–55] Similarly, safety outcomes are consistent with the overall favourable safety and tolerability profile of guselkumab established in clinical trials and real-world use.

The added value of this analysis is that GULLIVER is the largest real-life study of a single biologic treatment

(guselkumab) focused on patients with FP and/or GP and provides robust real-world data supporting the effectiveness and safety of guselkumab in the treatment of FP and GP. The results of this interim analysis are particularly significant considering the therapeutic challenges and the substantial impact of FP and GP on patients' QoL and the unmet medical need. Moreover, the study contributes to underscore the value of real-world data in observational clinical trials on different patient groups that are typically excluded from randomized clinical trials.

The main limitation of this paper is that this is an interim analysis of the first 12 weeks of treatment with guselkumab; the complete analysis through Week 52 will provide a more robust dataset that will better inform the durability of the observed responses.

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CONFLICT OF INTEREST STATEMENT

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DATA AVAILABILITY STATEMENT

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

ETHICS STATEMENT

The study is conducted by the investigators according to the ethical principles of the Declaration of Helsinki.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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