



ORIGINAL ARTICLE

Real-world evidence from the non-interventional, prospective, German multicentre PERSIST study of patients with psoriasis after 1 year of treatment with guselkumab

S. Gerdes,^{1,*}  K. Asadullah,^{2,3} M. Hoffmann,⁴ B. Korge,⁵ D. Mortazawi,⁶ S. Wegner,⁷ Y. Personke,⁷ 
M. Gomez,⁷ M. Sticherling⁸

¹Psoriasis Center Kiel, Department of Dermatology, University Medical Center Schleswig-Holstein, Campus Kiel, Kiel, Germany

²Department of Dermatology, Venereology and Allergology, Charité – Universitätsmedizin Berlin, Berlin, Germany

³Prof. Dr. med. Asadullah, Hautarztpraxis, Potsdam, Germany

⁴Dermatology Practice Dr. Matthias Hoffmann, Witten, Germany

⁵Dermatology Practice Dr. Bernhard Korge, Düren, Germany

⁶Dermatology Practice Dr. Dariusch Mortazawi, Remscheid, Germany

⁷Janssen-Cilag GmbH, MAF, Neuss, Germany

⁸Department of Dermatology, University Hospital of Erlangen, Deutsches Zentrum für Immuntherapie, Erlangen, Germany

*Correspondence: S. Gerdes. E-mail: sgerdes@dermatology.uni-kiel.de

Abstract

Background PERSIST was a prospective, non-interventional, long-term, German multicentre study of patients with moderate-to-severe psoriasis receiving guselkumab, an approved monoclonal antibody that binds to the p19 subunit of interleukin (IL)-23, in a real-world setting.

Objectives Evaluation of the efficacy and safety of guselkumab, and its effect on health-related quality of life (HRQoL), in patients with moderate-to-severe psoriasis who have received 52 weeks of treatment.

Methods Patients (≥18 years old) were prescribed guselkumab as per routine clinical practice. End points assessed include Psoriasis Area and Severity Index (PASI), Physician's Global Assessment (PGA), target Nail Psoriasis Severity Index (NAPSI), and the Dermatology Life Quality Index (DLQI).

Results Overall, 303 patients were enrolled and treated with guselkumab. Mean disease duration was 21.0 years, and 77.2% and 51.2% of patients had received ≥1 prior conventional systemic or ≥1 prior biologic therapy, respectively. Mean PASI score decreased from 16.4 at baseline to 3.0 by Week (W) 28, and further decreased to 2.4 by W52, while the proportion of patients achieving an absolute PASI score of ≤1 increased from 1.3% at baseline, to 50.8% at W28 and to 58.4% by W52. PASI90 and PASI100 responses also showed marked improvements between W28 and W52, regardless of biologic treatment history. Clearance of psoriatic skin was observed in difficult-to-treat areas, with the percentage of patients achieving a PGA score ≤1 increasing between W28 and W52. Guselkumab improved HRQoL; mean DLQI score decreased from 13.7 at baseline to 2.8 by W28, and further decreased to 2.4 by W52. At W52, 64.6% of patients achieved a DLQI score ≤1. The cumulative probability of drug survival was 92.4% at W52.

Conclusions Guselkumab is efficacious and well tolerated regardless of previous biologic therapies, comorbidities or psoriasis manifestation in difficult-to-treat areas. No new safety signals were observed.

Received: 1 December 2021; Accepted: 21 April 2022

Conflicts of interest

SG was an advisor and/or received speakers' honoraria and/or received grants and/or participated in clinical trials of the following companies: AbbVie, Affibody AB, Akari Therapeutics Plc, Almirall-Hermal, Amgen, Anaptys Bio, Argene BV, AstraZeneca AB, Biogen Idec, Bioskin, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Dermira, Eli Lilly, Foamix, Forward Pharma, Galderma, Hexal AG, Incyte Inc., Janssen-Cilag, Johnson & Johnson, Klinge Pharma, Kymab, LEO Pharma, Medac, MSD, Neubourg Skin Care GmbH, Novartis, Pfizer, Principia Biopharma, Regeneron Pharmaceutical, Sandoz Biopharmaceuticals, Sanofi-Aventis, Trevi Therapeutics and UCB Pharma; KA was an advisor and/or received speakers' honoraria and/or received grants and/or participated in clinical trials of the following companies: AbbVie, Akribes, Almirall, Antabio, Arctoris, Bayer, DEKA Biosciences, Emeritipharma, Galderma, Janssen, LEO Pharma, L'Oréal,

Study code: CNT01275PSO4051.

Novartis, Nuvisan, Pierre Fabre, Sanofi Genzyme and UCB Pharma; MH was an advisor and/or received speakers' honoraria and/or received grants and/or participated in clinical trials of the following companies: AbbVie, Amgen, Boehringer Ingelheim, Eli Lilly, Galderma, GSK, Janssen, LEO Pharma, Medac, MSD, Novartis, Pfizer and UCB Pharma; BK was an advisor and/or received speakers' honoraria and/or received grants and/or participated in clinical trials of the following companies: AbbVie, Amgen, Astella, Beiersdorf, Biogen, Celgene, Dr. Pfleger, Eli Lilly, Galderma, Janssen, LEO Pharma, Medac, Novartis, Sanofi and UCB Pharma; DM was an advisor and/or received speakers' honoraria and/or received grants and/or participated in clinical trials of the following companies: AbbVie, Amgen, Celgene, Eli Lilly, Janssen-Cilag, LEO Pharma, Moberg Pharma, Novartis, Sandoz, Sanofi Genzyme and UCB Pharma; SW, YP and MG are employees of Janssen-Cilag GmbH; MS was an advisor and/or received speakers' honoraria and/or received grants and/or participated in clinical trials of the following companies: AbbVie, Actelion, Amgen, Celgene, Eli Lilly, Galderma, GSK, Janssen-Cilag, LEO Pharma, MSD, Mundipharma, Novartis, Pfizer, Regeneron, Sanofi and UCB Pharma.

Funding sources

This study was sponsored by Janssen-Cilag GmbH (Germany).

Introduction

Psoriasis is a chronic systemic inflammatory disorder that affects the skin of 2–4% of the general population in Europe,¹ with many patients requiring lifelong treatment to manage the disease and its associated comorbidities.¹ As such, psoriasis has a significant impact on health-related quality of life (HRQoL).^{2–5} The evidence supporting the use of biologic therapies in patients with psoriasis is primarily based on randomized controlled trials (RCTs). However, in the real-world setting, patients with psoriasis often have a greater burden of disease despite a lower absolute Psoriasis Area and Severity Index (PASI) than patients in RCTs; patients in the real-world setting have typically received more conventional systemic and biologic therapies and have more comorbidities. As these are factors that can influence the effectiveness and tolerability of treatments,^{6,7} real-world evidence (RWE) is critical to understand the efficacy and safety of therapies in specific patient populations that are usually excluded from RCTs.^{8–10}

Guselkumab is a fully human monoclonal antibody that binds to the p19 subunit of interleukin (IL)-23.¹¹ Long-term efficacy and safety of guselkumab treatment have been demonstrated in the phase III double-blind VOYAGE 1 and VOYAGE 2 studies vs. placebo and adalimumab,^{12–16} as well as in the phase III double-blind, head-to-head ECLIPSE study vs. secukinumab.¹⁷ Although long-term RWE is limited for IL-23 inhibitors in psoriasis, several studies have now demonstrated the efficacy and safety of guselkumab in the real-world setting.^{7,18–25} PERSIST was a non-interventional study investigating the effect of guselkumab and ustekinumab treatment on long-term efficacy, safety and HRQoL in patients with moderate-to-severe psoriasis, in routine clinical practice.²⁵ Published PERSIST data demonstrated that guselkumab is safe and effective over 28 weeks in the real-world setting.²⁵ This current publication focuses on patients treated with guselkumab, at Week (W) 52.

Methods

Study design

PERSIST was a prospective, non-interventional, multicentre study. First initiated in 2016 with ustekinumab-treated patients, a study amendment was approved in January 2018 to also evaluate guselkumab-treated patients. The 2-year observational period for guselkumab was conducted at 55 German sites, in accordance with the International Conference on Harmonisation Good Clinical Practice (ICH-GCP) guidelines and with approval from the respective Research Ethics Committees. All patients provided written informed consent.

Patients

Documented patients were ≥ 18 years old and had a diagnosis of moderate-to-severe plaque psoriasis for ≥ 2 years. All patients in this analysis were prescribed guselkumab based on the treating physician's decision as per routine clinical practice. Patients discontinued from the study if another biologic therapy was initiated, or until consent withdrawal. Concomitant medications for psoriasis (excluding biologic therapy) were permitted as part of routine clinical care. Patient baseline demographic data were reported based on the point in time in which they were enrolled (see [Appendix S1](#) for details).

End points and assessments

The primary end point was the proportion of patients with a Dermatology Life Quality Index (DLQI) score ≤ 1 at W28; this result has been reported previously.²⁵ Secondary end points included HRQoL at W52, measured by DLQI, and the effectiveness of guselkumab at W52, measured by PASI, area-specific Physician's Global Assessment (PGA) and target Nail Psoriasis Severity Index (NAPSI) scores (described in greater detail in the [Appendix S1](#)). Results from these assessments after 28 weeks of

guselkumab treatment have been reported previously.²⁵ Patient numbers at each time point are approximate values, as visits were adapted to routine clinical practice. Safety was assessed at data cut-off (14 August 2020) by evaluating adverse events (AEs) using terms as defined by Medical Dictionary for Regulatory Activities (MedDRA version 20.0).

Statistical analysis

Enrolment of approximately 300 patients was planned, with as observed analyses conducted for all end points. Mean scores are presented with the standard deviation (SD). Statistical analyses are described in greater detail in the [Appendix S1](#).

Results

Patients

Overall, 303 patients were enrolled into PERSIST after routine prescription of guselkumab; data were available for 293 patients at W4, 283 patients at W16, 269 patients at W28 and 247 patients at W52. There were 38 (12.5%) patient withdrawals before W52; 9 (3.0%) because of AEs.

Baseline characteristics have been reported previously²⁵ and are shown in Tables 1 and 2, and Table S1. In total, 234 (77.2%) patients had received ≥ 1 prior conventional systemic therapy, and 155 patients (51.2%) had received ≥ 1 prior biologic therapy. Of note, the proportion of patients who received prior conventional systemic or biologic therapy decreased over time (Table 1), and the largest reductions over time in prescribed biologic therapies were adalimumab, ustekinumab and etanercept (Table S2). The most common reasons for switching from a previous therapy to guselkumab were insufficient efficacy (78.9%) and intolerance (15.5%; Table S2); the proportion of patients switching from specific biologic therapies to guselkumab because of insufficient efficacy is shown in Table S3. Overall, 56.4% of patients were receiving concomitant medications for psoriasis or other comorbidities at baseline (Table S1).

Efficacy outcomes

Mean PASI score decreased from 16.4 at baseline to 3.0 (SD ± 5.6) by W28, and further decreased to 2.4 (± 4.7) by W52. The proportion of patients with an absolute PASI score ≤ 5 increased over time, from 8.6% at baseline to 83.1% by W28, and to 84.5% by W52 (Fig. 1a), while the percentage of patients achieving an absolute PASI score of ≤ 2 or ≤ 1 increased from 68.4% and 50.8% at W28, respectively, to 71.8% and 58.4% by W52 (Fig. 1a). The proportion of patients with a PASI score ≤ 1 increased from W28 to W52 across all body mass index (BMI) categories, although it was achieved by a greater proportion of patients with a BMI < 25 than with a BMI of 25–30 or > 30 (Fig. 2).

PASI90 and PASI100 responses showed marked improvements from W28 to W52 in the overall patient population

(including those who were biologic naïve and those who were previously treated with biologic therapies; Fig. 1c,d). By W52, 78.4% ($n = 192$), 62.9% ($n = 154$) and 40.4% ($n = 99$) of patients achieved a PASI75, PASI90 and PASI100 response respectively (Fig. 1b,c,d). A higher proportion of biologic-naïve patients ($n = 127$) achieved PASI75 (86.6% vs. 69.5%), PASI90 (78.0% vs. 46.6%) and PASI100 responses (50.4% vs. 29.7%) at W52, compared with patients previously treated with biologic therapy ($n = 118$, Fig. 1b,c,d). A greater proportion of biologic pretreated patients who had not received any IL-17 inhibitors ($n = 54$) achieved a PASI75 (72.2% vs. 67.2%), PASI90 (51.9% vs. 42.2%) and PASI100 response (37.0% vs. 23.4%) at W52, than those who had received previous IL-17 inhibitors ($n = 64$, Fig. S1).

Among patients with an area-specific baseline PGA score ≥ 2 , severe involvement of the scalp, palmoplantar or anogenital regions was observed in 23.5% ($n = 47$), 18.5% ($n = 15$) and 9.3% ($n = 11$) respectively (Fig. 3). By W52, the proportions of patients with severe scalp, palmoplantar or anogenital psoriasis had decreased to 0.6% ($n = 1$), 1.5% ($n = 1$) and 0% respectively. Complete or almost complete clearance (PGA ≤ 1) was achieved at W52 by 91.4% ($n = 148$), 86.4% ($n = 57$) and 86.6% ($n = 84$) of patients with scalp, palmoplantar and anogenital psoriasis, respectively, among those with a baseline PGA score ≥ 2 ; these percentages are greater than observed at W28 for each location. The mean target NAPSI score decreased from 4.2 (± 2.2) at baseline to 1.2 (± 2.0) at W52, a relative mean change of -71.4% (± 46.1 ; Fig. 4). In line with this improvement, the mean number of affected nails was 6.8 (± 3.6) at baseline, which decreased to 3.3 (± 3.6) at W28 and to 2.3 (± 3.5) at W52.

Patient-reported outcomes

At W52, 64.6% ($n = 157$) of patients receiving guselkumab achieved a DLQI score ≤ 1 , indicating no effect of psoriasis on quality of life, while 86.4% ($n = 210$) of patients had no or only a small effect of psoriasis on quality of life (DLQI score 0–5; Fig. 5a). In sub-analyses by biologic therapy history, a DLQI score ≤ 1 was achieved at W52 by 52.1% of patients who had received prior biologic therapy, and by 76.2% of patients who had not received any prior biologic therapy. A greater proportion of biologically pretreated patients who had not received any IL-17 inhibitors achieved a DLQI score ≤ 1 at W52, compared with patients who had received previous IL-17 inhibitors (57.4% vs. 47.6%).

Mean DLQI score decreased from 13.7 at baseline to 2.8 (± 4.1) by W28, and further decreased to 2.4 (± 4.1) by W52 (Fig. 5b). In sub-analyses by biologic therapy history, mean DLQI score decreased from 12.4 (± 7.6) at baseline to 3.6 (± 4.5) by W28, and to 3.3 (± 4.7) by W52, in the population of patients who had received prior biologic therapy. For patients who had not received any prior biologic therapy, the baseline DLQI score

Table 1 Baseline characteristics of patients

Characteristic	Patients (N = 303*)	Patients 1–101 (n = 101)	Patients 102–202 (n = 101)	Patients 203–303 (n = 101)
Mean age, years (SD)	49.7 (13.8)	49.4 (13.6)	51.6 (13.5)	48.1 (14.3)
Gender, n (%)				
Male	193 (63.7)	62 (61.4)	61 (60.4)	70 (69.3)
Female	110 (36.3)	39 (38.6)	40 (39.6)	31 (30.7)
Mean age at first diagnosis, years (SD)	28.7 (14.6)	27.0 (13.6)	29.9 (14.1)	29.1 (16.0)
Mean duration of psoriasis, years (SD)	21.0 (14.0)	22.4 (13.7)	21.7 (14.0)	19.0 (14.1)
Mean BMI, kg/m ² (SD), n = 252	29.7 (6.3)	30.5 (6.2)	29.5 (6.4)	29.1 (6.3)
Mean PASI (SD)	16.4 (10.8)	15.7 (9.5)	16.7 (11.5)	16.9 (11.4)
Mean BSA, % (SD), n = 302	27.5 (20.1)	23.3 (16.4)	29.6 (20.8)	29.5 (22.1)
Mean DLQI (SD), n = 299	13.7 (7.5)	14.5 (7.5)	11.7 (7.0)	14.8 (7.6)
PSSD, mean (SD), n = 294				
Symptom	51.9 (25.9)	52.8 (25.5)	46.6 (25.4)	56.4 (26.0)
Sign	60.8 (22.4)	60.1 (21.9)	57.8 (23.1)	64.5 (21.8)
Psoriatic arthritis, n (%)	84 (27.7)	31 (30.7)	30 (29.7)	23 (22.8)
Scalp PGA ≥ 1 , n (%), n = 302	239 (79.1)	76 (76.0)	81 (80.2)	82 (81.2)
Palmoplantar PGA ≥ 1 , n (%), n = 302	104 (34.4)	27 (26.7)	40 (39.6)	37 (37.0)
Anogenital PGA ≥ 1 , n (%), n = 300	153 (51.0)	50 (49.5)	51 (51.5)	52 (52.0)
Target NAPS ≥ 1 , n (%), n = 297	136 (45.8)	43 (43.9)	46 (46.5)	47 (47.0)
Prior psoriasis therapy, n (%)				
Conventional systemic	234 (77.2)	83 (82.2)	80 (79.2)	71 (70.3)
Biologic	155 (51.2)	55 (54.5)	59 (58.4)	41 (40.6)
Of those who received ≥ 1 biologic				
1 biologic	80 (51.6)	31 (56.4)	26 (44.1)	23 (56.1)
2 biologics	43 (27.7)	14 (25.5)	17 (28.8)	12 (29.3)
≥ 3 biologics	32 (20.6)	10 (18.2)	16 (27.1)	6 (14.6)

*N = 303 unless stated otherwise in left-hand column.

Patients 1–101 were enrolled between January and June 2018, followed by patients 102–202 who were enrolled between June and November 2018 and then patients 203–303 who were enrolled between November 2018 and May 2019.

BMI, body mass index; BSA, body surface area; DLQI, Dermatology Life Quality Index; NAPS, Nail Psoriasis Severity Index; PASI, Psoriasis Area and Severity Index; PGA, Physician's Global Assessment; PSSD, Psoriasis Symptoms and Signs Diary; SD, standard deviation.

Table 2 Comorbidities at baseline

Comorbidities	Total
Patients with at least 1 comorbidity, n (%)	161 (53.1)
Arterial hypertension	69 (22.8)
Type 2 diabetes mellitus	31 (10.2)
Depression	22 (7.3)
Obesity*	16 (5.3)
Hypothyroidism	12 (4.0)
Chronic obstructive pulmonary disease	9 (3.0)
Hypercholesterolaemia	8 (2.6)
Asthma	8 (2.6)
Hyperuricaemia	7 (2.3)
Coronary artery disease	7 (2.3)

*Obesity was defined as 'reported obesity' and did not require a specific BMI value. 44.0% of patients had a BMI >30 kg/m².

Comorbidities included in the table were present in $\geq 2\%$ of patients.

BMI, body mass index.

was 15.0 (± 7.3), and this decreased to 1.9 (± 3.5) by W28 and to 1.5 (± 3.3) by W52. In analyses of patients who had baseline PGA scores ≥ 2 for area-specific psoriasis, a DLQI score ≤ 1 was

achieved by 67.3% ($n = 107$) of patients with scalp psoriasis, 57.6% ($n = 38$) with palmoplantar psoriasis, 57.9% ($n = 55$) with anogenital psoriasis and 65.4% ($n = 70$) with nail psoriasis at W52.

Safety and drug survival

By W52, the cumulative probability of drug survival was 92.4% (Fig. 6). Overall, 44 patients (14.5%) experienced 74 treatment-related AEs; most AEs were mild ($n = 28$) or moderate ($n = 37$; Table 3). The most common treatment-related AEs were viral upper respiratory tract infection (2.6%), diarrhoea (1.7%) and pruritus (1.3%). AEs leading to treatment discontinuation were reported for nine patients (3.0%; Table S4). Treatment-related serious AEs occurred in four patients (1.3%) and included one case (0.3%) each of bronchitis, Epstein–Barr virus infection, malignant neoplasm and pemphigoid.

Discussion

PERSIST provides critical information on the efficacy and safety of guselkumab in a patient population that includes those who

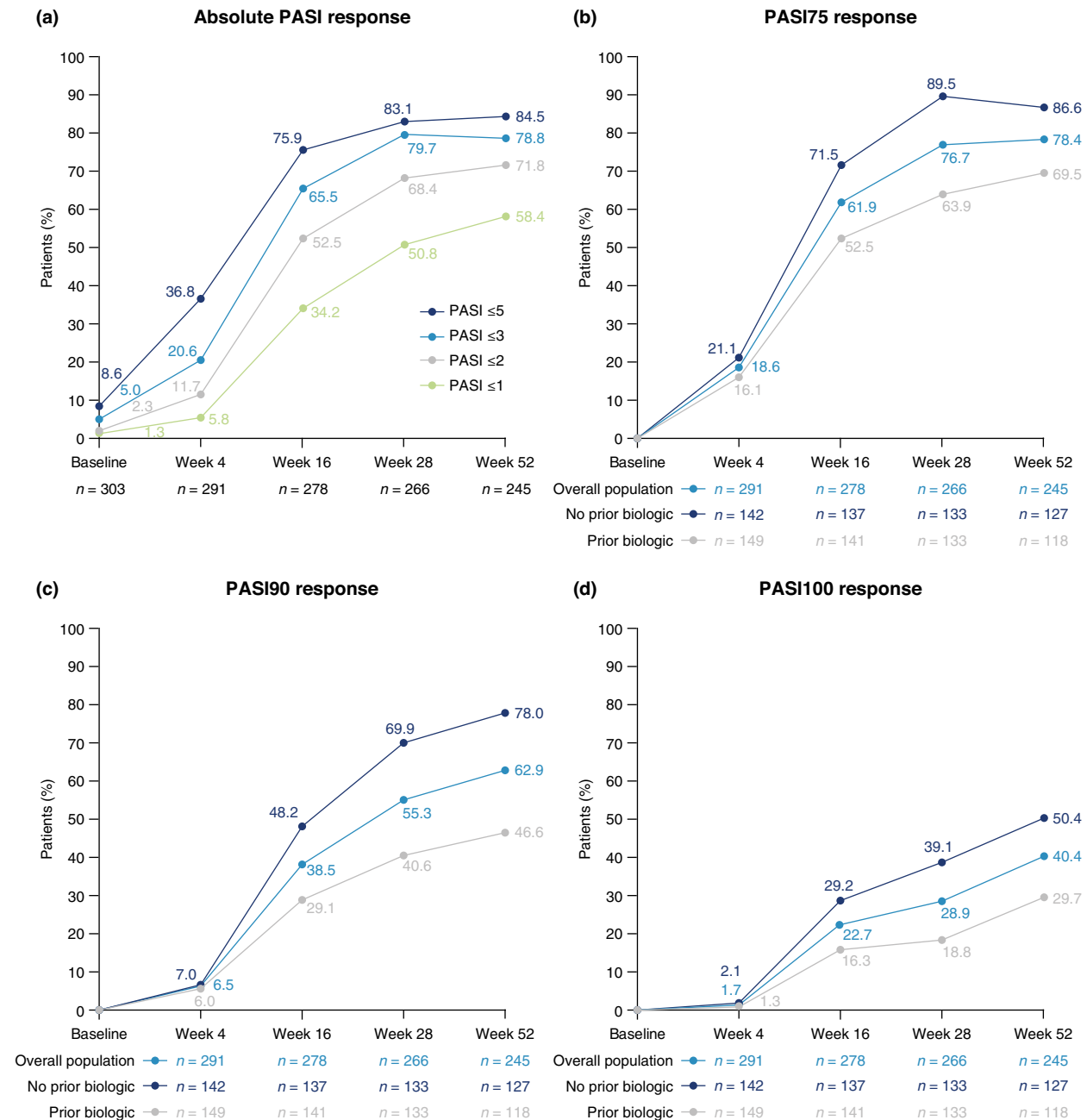


Figure 1 Proportion of patients achieving absolute PASI scores (a) and PASI75 (b), PASI90 (c) and PASI100 (d) response (by biologic treatment history) over time. PASI, Psoriasis Area and Severity Index.

are typically excluded from RCTs. The PERSIST patient population is representative of the psoriasis population receiving systemic treatment in Germany based on the similarities in patient baseline characteristics between PERSIST and the German psoriasis registry PsoBest.²⁶ Numerous baseline characteristics were

also similar to other large registries of patients receiving biologic therapies, such as BADBIR (British Association of Dermatologists Biologic and Immunomodulators Register)²⁷ and the observational study PSO-BIO-REAL (plaque psoriasis treated with biologics in a real-world setting),⁶ although these studies

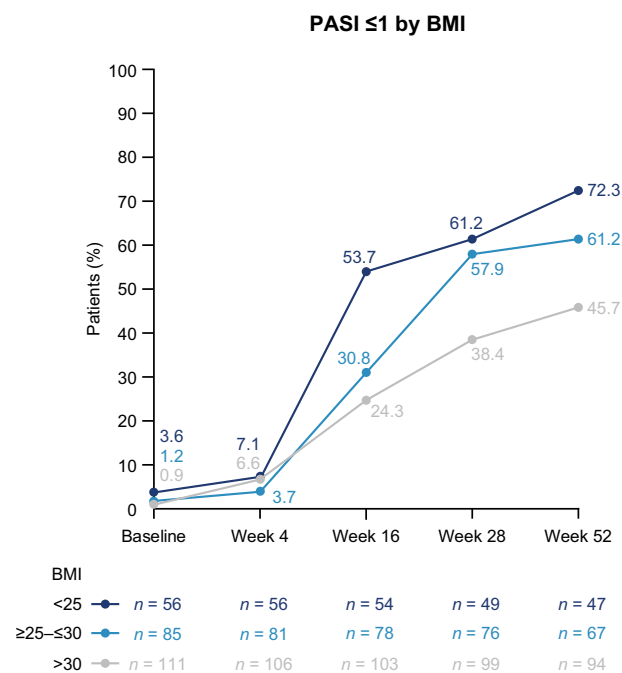


Figure 2 Proportion of patients achieving PASI ≤1 over time by BMI subgroup. BMI, body mass index; PASI, Psoriasis Area and Severity Index. [Correction added on 5 July 2022, after first online publication: In Figure 2, the blue colours in the figure key were switched and corrected in this version.]

included a greater proportion of patients with ≥1 comorbidities compared with PERSIST.

As expected with a RWE study and in line with the studies discussed above, there are some notable differences in baseline characteristics between patients in PERSIST and those in RCTs such as VOYAGE 1 and 2 and ECLIPSE.^{12,13,17} In particular, and as reported previously, a greater proportion of patients had received conventional systemic and biologic therapies in PERSIST than in VOYAGE 1 and 2 and ECLIPSE.^{12,13,17,25} This may account for the lower baseline PASI score in PERSIST than in the RCTs (16.4 vs. 20.0–22.1, respectively), despite the patients in PERSIST having a greater burden of disease.^{12,13,17} Of note, the VOYAGE studies excluded patients previously treated with adalimumab or guselkumab,^{12,13} and ECLIPSE excluded patients who had received secukinumab or guselkumab.¹⁷ In PERSIST, the most common prior biologic therapies were secukinumab (21.8% of patients) and adalimumab (21.5% of patients). As a result, many patients in PERSIST received guselkumab as a later treatment line for psoriasis than in the RCTs, and were enrolled into PERSIST following guselkumab approval in Europe in November 2017. Interestingly, the PERSIST baseline characteristics data indicate a change in clinician prescribing habits over time since the launch of guselkumab. The first 202 patients were recruited into PERSIST during the first year immediately after

guselkumab launch, while patients 203 to 303 were enrolled during the second year after launch. Prior conventional systemic therapies were received by 82.2% of the first 101 patients recruited, and this decreased to 70.3% for the final 101 patients enrolled. Similarly, there was a reduction over time in the proportion of patients enrolled who had received prior biologic therapies (54.5% of the first 101 patients, and 40.6% of the final 101 patients). The decrease in the proportion of patients receiving these classes of therapies over time could suggest that clinicians have gained more experience with guselkumab and feel more confident to use it in an earlier treatment line. Accordingly, insufficient efficacy/loss of efficacy as a reason to switch to guselkumab decreased over time, while intolerance to the last prior therapy increased over time (Table S2). The use of guselkumab in patients enrolled into PERSIST could be at the expense of adalimumab, ustekinumab and etanercept, which showed the greatest declines in use over time.

A greater proportion of patients with ≥1 comorbidities were enrolled into PERSIST than into the RCTs. This is reflective of the fact that a patient with any comorbidity was eligible for PERSIST, whereas the VOYAGE 1 and 2 and ECLIPSE exclusion criteria consisted of a history or current signs or symptoms of severe, progressive or uncontrolled renal, hepatic, cardiac, vascular, pulmonary, gastrointestinal, endocrine, neurological, haematological, rheumatological, psychiatric or metabolic disturbances.^{12,13,17} Overall, baseline characteristics data from PERSIST highlight that the patient population has not been selected, and is representative of the general psoriasis population.

Despite most patients in PERSIST having received prior biologic therapies or suffering from comorbidities, the effectiveness of guselkumab continued to increase over 52 weeks; by W52, 62.9% and 40.4% of patients achieved a PASI90 and PASI100 response, respectively. Although slightly lower than the relative PASI response rates of VOYAGE 1 and 2 and ECLIPSE at W48,^{12,13,17} this is to be expected given the differences in the patient populations assessed. While PASI responses were greater in biologic-naïve patients than in those who received prior biologic treatment, guselkumab was efficacious even in patients who had received previous IL-17 inhibitors. Relative PASI response rates were similar or greater in several other RWE studies of guselkumab at W52.^{7,21,23} In a study by Ruiz-Villaverde *et al* (N = 87), 71.0% and 51.6% of patients achieved a PASI90 and PASI100 response, respectively,²³ while the responses were even greater in Galluzzo *et al* (N = 52; 78.9% and 63.2% achieved PASI90 and PASI100, respectively).⁷ The variation in PASI response rates between these studies and PERSIST could be attributable to differences in patient baseline characteristics. Nonetheless, the percentage of patients in PERSIST achieving a PASI score ≤3 at W52 was similar to that observed by Galluzzo *et al* (78.8% vs. 84.2%).⁷ By W52, an absolute PASI score of ≤2 or ≤1 was achieved by 71.8% and 58.4% of patients in PERSIST,

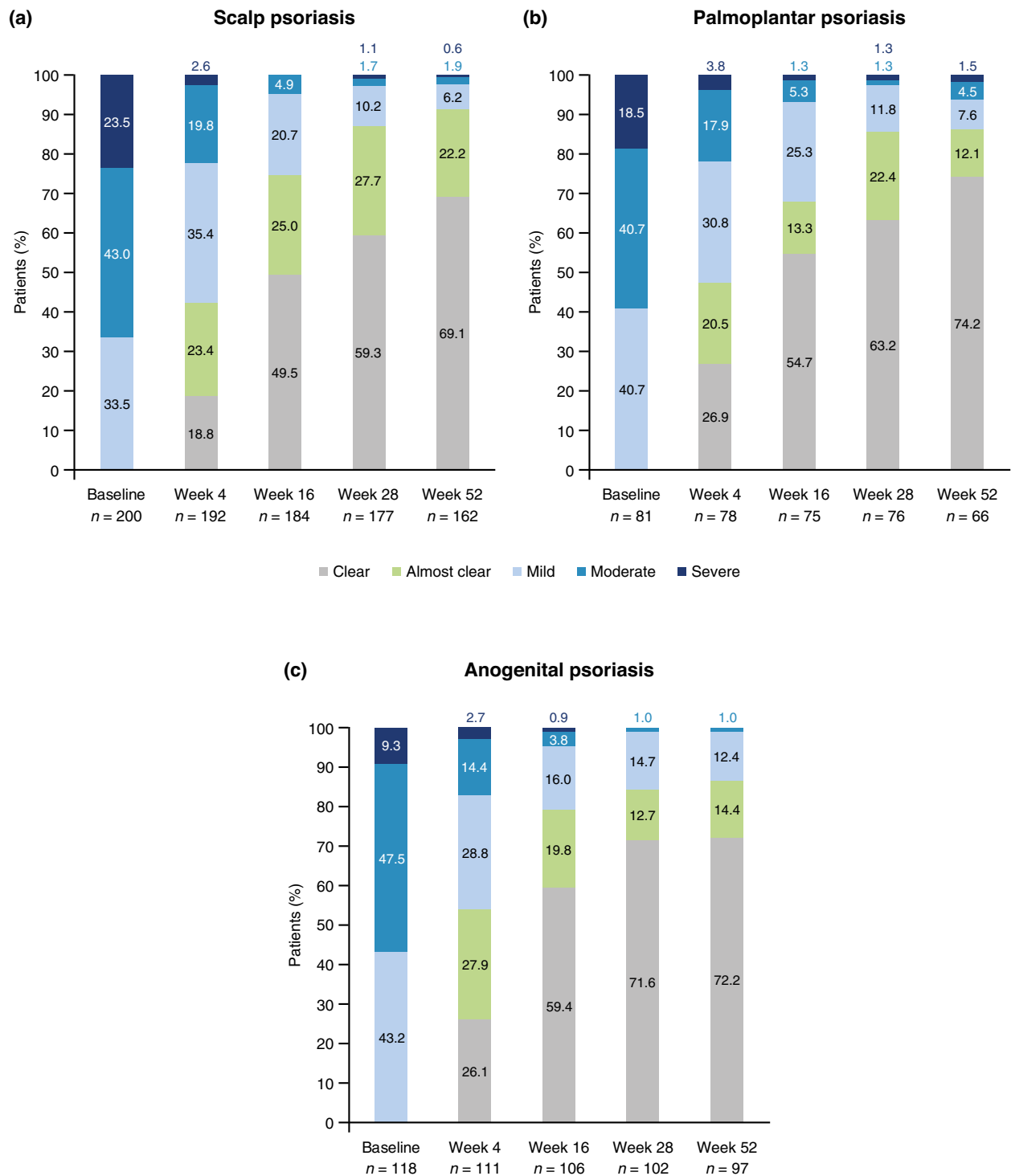


Figure 3 Proportion of PGA scores achieved over time in patients with scalp (a), palmoplantar (b) and anogenital (c) psoriasis. PGA grades the patient's psoriasis as clear (0), almost clear (1), mild (2), moderate (3) or severe (4). Patients with scalp, palmoplantar or anogenital psoriasis included in this analysis had a baseline PGA score ≥ 2 . PGA, Physician's Global Assessment.

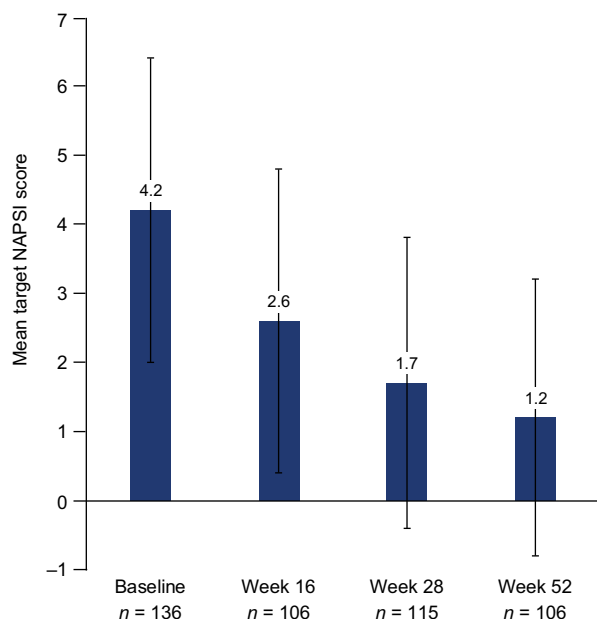


Figure 4 Mean target NAPSI (SD) score over time. Patients included in this analysis had ≥ 1 nail affected at baseline. NAPSI, Nail Psoriasis Severity Index; SD, standard deviation.

respectively. Although the proportion of patients achieving PASI ≤ 1 was smaller in patients with a higher BMI, an increased proportion of PASI ≤ 1 responders was observed across all BMI categories between W28 and W52. This is an important finding given that obesity is a common comorbidity in psoriasis (111 patients had a BMI >30 at baseline in PERSIST), and that a high BMI can have a significant negative impact on response to systemic treatments.²⁷

High levels of improvement in PGA score were observed in difficult-to-treat anatomical regions over time, including between W28 and W52. Although not directly comparable because of the different assessments used, improvement in scalp and palmoplantar psoriasis appeared greater in PERSIST than in VOYAGE 1.¹² The mean improvement in NAPSI score in PERSIST at W52 was similar to that observed in VOYAGE 1 at W48 (71.4% vs. 68.1%).¹² However, this comparison is confounded by the fact that in VOYAGE 1, NAPSI score was obtained from both fingernails and toenails, whereas in PERSIST only fingernails were assessed.

As previously reported, a clinically meaningful improvement in DLQI score was observed in PERSIST at W28, following treatment with guselkumab.²⁵ By W52, mean DLQI further

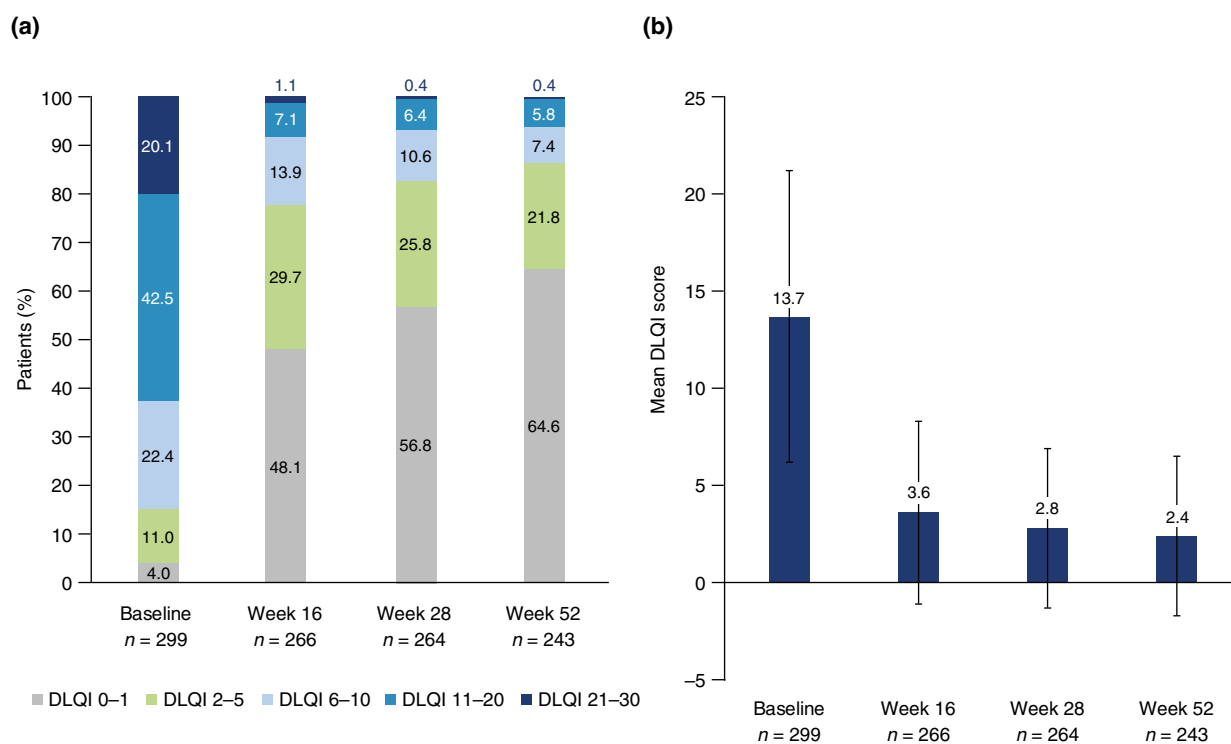


Figure 5 Proportion of patients achieving given thresholds of mean DLQI scores (a) and mean DLQI score (SD; b) over time. A DLQI score of 0–1 represents no effect of psoriasis on quality of life; 2–5, small effect; 6–10, moderate effect; 11–20, very large effect; and 21–30, extremely large effect. DLQI, Dermatology Life Quality Index; SD, standard deviation.

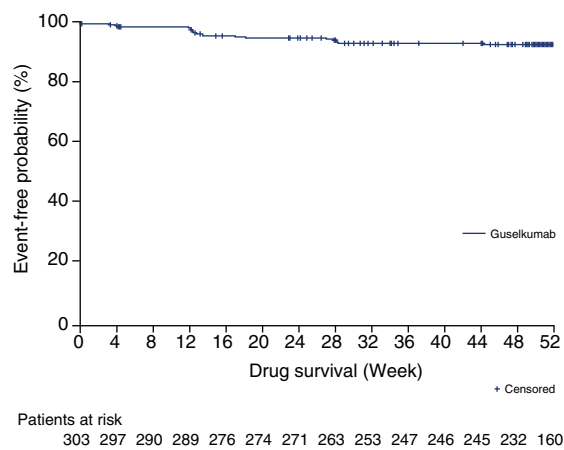


Figure 6 Kaplan–Meier curve of drug survival over 52 weeks. Cumulative probability of drug survival over 52 weeks. Each event corresponds to a patient discontinuation caused by either an adverse event, lack of efficacy or patient death (no patients died during the study). The low number of patients at risk at W52 is a methodological artefact and not related to medical reasons; most patients censored at W52 had a study visit slightly earlier than W52.

Table 3 Most common treatment-related adverse events ($\geq 1\%$) by severity ($n = 303$)

Adverse event, n (%)	Mild	Moderate	Severe	Total
Patients with at least one adverse event	23 (7.6)	22 (7.3)	8 (2.6)	44 (14.5)*
Total number of events	28	37	9	74
Viral upper respiratory tract infection	7 (2.3)	–	1 (0.3)	8 (2.6)
Diarrhoea	3 (1.0)	2 (0.7)	–	5 (1.7)
Pruritus	1 (0.3)	3 (1.0)	–	4 (1.3)
Influenza	–	3 (1.0)	–	3 (1.0)
Headache	2 (0.7)	1 (0.3)	–	3 (1.0)

*If a patient had an AE in ≥ 1 severity category, it was counted in each of the categories.

improved, and 64.6% of patients achieved a DLQI score of 0–1. The improvement in the mean DLQI score aligns with findings from other RWE studies of guselkumab.^{22,23,28} A similar proportion of patients in PERSIST achieved a DLQI score of 0–1 at W52 as in VOYAGE 1 (62.5%) at W48.¹² Overall, guselkumab-treated patients reported improvements in HRQoL, demonstrating its effectiveness even in a population that has received previous biologic therapies. Although not the focus of this manuscript, improvements in DLQI score were also observed over time in patients with psoriasis in difficult-to-treat areas. This is an important finding given that psoriasis patients with involvement of difficult-to-treat regions can have a profoundly

impacted HRQoL and significantly greater treatment needs than psoriasis patients without involvement of these regions.^{29–31}

Kaplan–Meier analyses demonstrated that the cumulative probability of drug survival was 92.4%, aligning closely with the value of 91.1% obtained with guselkumab treatment in a RWE study by Torres *et al.*³² Consistent with findings at W28 in PERSIST, guselkumab was well tolerated and had a favourable safety profile; the most common treatment-related AEs were as expected, and no new safety signals were detected. Most of the treatment-related AEs were mild or moderate in severity, were consistent with those observed in RCTs of guselkumab and occurred at a similar or lower rate.^{14,15,17,33}

A limitation of PERSIST, common to most long-term registries, is that the data reported are ‘as observed’ values. Therefore, the effectiveness of guselkumab may be slightly overestimated in some analyses, as patients who discontinued the study were not included from the point of withdrawal. However, the number of patient discontinuations was low.

In conclusion, PERSIST was a large, real-world study that provides important insights on the efficacy and safety of guselkumab outside of the RCT setting. Guselkumab is efficacious and well tolerated, even for patients who have received several previous biologic therapies or have comorbidities or psoriasis in difficult-to-treat areas, evidenced through its positive impact on both physician-assessed and patient-reported outcomes.

Acknowledgements

This study was sponsored by Janssen-Cilag GmbH (Germany). Medical writing support, funded by Janssen-Cilag GmbH (Germany), was provided by Joe Pickering PhD from Mudskipper Business Limited. Open Access funding enabled and organized by Projekt DEAL.

Data availability statement

Research data are not shared.

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Supporting information

Additional Supporting Information may be found in the online version of this article:

Appendix S1 Efficacy, quality of life, and safety assessments.