



## ORIGINAL ARTICLE

# Effectiveness, safety and quality-of-life effects of guselkumab and ustekinumab in patients with psoriasis: Week 104 results from the non-interventional, prospective, German multicentre PERSIST study

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**Abstract**

**Background:** PERSIST was a prospective, non-interventional, real-world study of guselkumab and ustekinumab in adult patients with moderate-to-severe plaque psoriasis in Germany.

**Objectives:** To examine effectiveness, safety and quality-of-life (QoL) outcomes to Week (W) 104 of treatment with guselkumab and ustekinumab in patients with moderate-to-severe plaque psoriasis.

**Methods:** Patients (≥18 years of age) received guselkumab or ustekinumab as per routine clinical practice. Outcomes to W104 were examined separately in guselkumab and ustekinumab recipients. An ad hoc exploratory analysis of outcomes with guselkumab versus ustekinumab was also performed following propensity score matching.

**Results:** Overall, 302 and 313 patients received guselkumab and ustekinumab, respectively. Patients in both cohorts experienced improvements in disease activity and QoL that were maintained to W104, with 64.7% and 63.6% of guselkumab- and 54.6% and 64.4% of ustekinumab-treated patients achieving a Psoriasis Area and Severity Index (PASI) 90 response and a Dermatology Life Quality Index (DLQI) 0/1 score, respectively. Propensity score matching yielded well-balanced baseline characteristics except for prior biologic use, which was higher in guselkumab versus ustekinumab recipients (51.7% vs. 32.0%). Achievement of PASI ≤1 at W104 was more common in guselkumab versus ustekinumab recipients (58.7% vs. 49.7%). The W104 PASI90 response rate was 65.6% with guselkumab and 56.0% with ustekinumab; corresponding rates for PASI100 were 44.3% and 28.5%. In guselkumab recipients, response rates were higher in biologic-naïve versus biologic-experienced patients (PASI90, 77.1% vs. 53.4%; PASI100, 55.0% vs. 33.0%). A high level of response for QoL outcomes was observed for both treatments.

**Conclusions:** Ustekinumab and guselkumab led to improvements in physician-assessed and patient-reported outcomes that were sustained for up to 2 years, with no new safety signals identified. Following propensity score matching, greater improvements in PASI outcomes were observed with guselkumab versus ustekinumab.

Study code: CNTO1275PSO4051.

The study is registered at the German Paul-Ehrlich-Institut (PEI) <https://www.pei.de/DE/regulation/klinische-pruefung/anwendungsbeobachtungen/awb-node.html>

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Improvements with guselkumab were highest in biologic-naïve patients, highlighting the value of early treatment.

## INTRODUCTION

Psoriasis is a chronic systemic inflammatory condition that affects approximately 2% of people across western and central Europe.<sup>1</sup> The most common manifestation of psoriasis is sharply demarcated erythematous lesions; these are the result of a hyperproliferative epidermis arising from hyperkeratosis and impaired epidermal cornification.<sup>2,3</sup> Psoriatic lesions can be localized on elbows, knees, nails, scalp, palmoplantar and anogenital regions,<sup>2,4</sup> or cover the entirety of the skin.<sup>2</sup> People with psoriasis often have a markedly reduced quality of life (QoL) compared with the general population.<sup>5</sup>

Research has identified the interleukin (IL)-23 pathway as a key player in the immunopathogenesis of psoriasis,<sup>6</sup> which has enabled the development of targeted biologic therapies that are used in clinical practice. Ustekinumab and guselkumab are fully human monoclonal antibodies binding IL-23 that were approved for the treatment of moderate-to-severe plaque psoriasis in Europe in 2009 and 2017, respectively. Ustekinumab targets IL-12/23p40, while guselkumab binds to the p19 subunit of IL-23.

The efficacy and tolerability of ustekinumab and guselkumab in patients with psoriasis have been demonstrated in several large clinical trials,<sup>7-13</sup> but it is important how these results translate to patients in everyday clinical practice. For this reason, the non-interventional PERSIST study was established to evaluate the effectiveness, safety and QoL effects of guselkumab and ustekinumab in patients with moderate-to-severe psoriasis in routine clinical care. Previous PERSIST publications have demonstrated the effectiveness and favourable safety profile of guselkumab after 28 and 52 weeks of treatment.<sup>14,15</sup> Notably, patients experienced a continuous reduction in disease activity from baseline to Week (W) 52 of treatment, as measured using the Psoriasis Area and Severity Index (PASI) and Physician's Global Assessment (PGA) instruments. Guselkumab use was also associated with an improvement in patient QoL, assessed using the Dermatology Life Quality Index (DLQI), with no new safety signals identified.

The current publication reports effectiveness, safety and QoL outcomes at W104 in patients treated with either ustekinumab or guselkumab in the PERSIST study, with propensity score-based matching used to compare outcomes between the two treatments.

## METHODS

### Study design

Details of the PERSIST study have been described previously<sup>14,15</sup> and are presented in the Appendix S1. In short, PERSIST was a prospective, non-interventional study

conducted at 55 sites across Germany in accordance with the International Conference on Harmonisation Good Clinical Practice (ICH-GCP) guidelines and with approval from the respective Research Ethics Committees.<sup>14,15</sup> Treatment with ustekinumab or guselkumab was per the treating physician's decision, in line with routine clinical care and consistent with the approved label.

### Patients

Patients were aged  $\geq 18$  years and had been diagnosed with moderate-to-severe plaque psoriasis for a period of  $\geq 2$  years.<sup>14,15</sup> All patients provided written informed consent.

### Endpoints and assessments

The primary endpoint of the study was the proportion of patients with a DLQI score of  $\leq 1$  after 28 weeks of treatment. These data have been previously reported for the guselkumab cohort, along with various other endpoints at W28 and 52.<sup>14,15</sup>

In the current analysis, efficacy and QoL outcomes were examined separately over time to W104 in the ustekinumab and guselkumab cohorts. These included, the proportion of patients who achieved an absolute PASI score of  $\leq 5$ ,  $\leq 3$  and/or  $\leq 1$ ; the proportion of patients who achieved a  $\geq 75\%$  (PASI75),  $\geq 90\%$  (PASI90), or 100% (PASI100) improvement of PASI score compared with baseline; the proportion of patients achieving a PGA score of 0 or 1 for scalp, palmoplantar or anogenital psoriasis (restricted to patients with PGA values  $\geq 2$  in these respective body regions at baseline); mean improvement in target Nail Psoriasis Severity Index (NAPSI); the proportion of patients achieving a DLQI score  $\leq 1$ ; and mean improvement in Psoriasis Symptoms and Signs Diary (PSSD).<sup>16</sup>

Safety data were assessed at a cut-off date of 23 September 2021 for both cohorts. In the current analysis, treatment-related adverse events (AEs [defined per version 20.0 of the Medical Dictionary for Regulatory Activities]) up to W104 were separately examined in the ustekinumab and guselkumab cohorts.

### Statistical analysis

#### Sample size and data handling

Enrolment of approximately 300 patients into each of the ustekinumab and guselkumab cohorts was planned with as-observed analyses conducted for all endpoints. Mean scores are presented with the standard deviation. Statistical analyses are described in greater detail in the Appendix S1.

## Propensity analysis

An ad hoc exploratory analysis of outcomes with ustekinumab versus guselkumab was performed using a propensity score-based method to match patients in both cohorts based on their baseline characteristics; the aim of this matching procedure was to reduce the potential bias in estimated effects obtained from observational studies. A propensity score was calculated using logistic regression; treatment (i.e. ustekinumab or guselkumab) was the dependent variable, while sex, age, weight, disease duration and baseline PASI, DLQI and psoriatic arthritis (PsA) were used as matching covariates. Patients were then matched based on the propensity score (1:1 matching without replacement) using the nearest neighbour method, with the guselkumab treatment group used as the basis to which ustekinumab recipients were matched to.

## RESULTS

### Ustekinumab cohort

Overall, 313 patients were included in the ustekinumab cohort; baseline demographics, disease characteristics and comorbid conditions are shown in [Table S1](#).

### Efficacy and quality of life

Key efficacy and QoL outcomes to W104 of ustekinumab treatment are detailed in [Table 1](#). Mean PASI score decreased over time to W104, while the proportions of patients with an absolute PASI score of  $\leq 5$ ,  $\leq 3$  and  $\leq 1$  increased over time. Regarding the primary endpoint, at W28, 52.0% of patients treated with ustekinumab achieved a DLQI score  $\leq 1$  (no effect of psoriasis on QoL), consistent with a previous analysis.<sup>17</sup> A continued increase in the proportion of patients achieving a DLQI score  $\leq 1$  was observed to W104.

### Safety

The cumulative probability of ustekinumab drug survival at W104 was 77.7% ([Figure 1](#)). Overall, 20.8% of patients experienced  $\geq 1$  treatment-related AE, with the most common being clinically diagnosed viral upper respiratory tract infection and oral candidiasis ([Table 2](#)). Most treatment-related AEs were mild or moderate in severity. Selected treatment-related AEs are shown in [Table 2](#). There were no cases of malignant or benign neoplasms, non-melanoma skin cancer (NMSC), lymphoma, inflammatory bowel disease (IBD), active tuberculosis (TB) or major adverse cardiovascular events (MACE). The rate of non-IBD gastrointestinal disorders was low, as was the rate of cardiac disorders. All-cause AEs that led to treatment discontinuation occurred in 29 patients (9.3%). Five patients (1.6%) reported six serious AEs (SAEs) that were considered treatment related (anal abscess,  $n=2$ ;

ophthalmic herpes zoster,  $n=1$ ; tongue discomfort,  $n=1$ ; pyrexia,  $n=1$ ; psoriasis,  $n=1$ ). There was one death reported in the cohort (intestinal ischaemia; 0.3%); this was considered non-treatment related.

### Guselkumab cohort

Data were available for 302 patients in the guselkumab cohort. Baseline demographics, disease characteristics and comorbid conditions are shown in [Table S2](#).

### Efficacy and quality of life

Key efficacy and QoL outcomes to W104 of treatment with guselkumab are detailed in [Table 3](#). Mean PASI score decreased over time to W104, while the proportion of patients with an absolute PASI score of  $\leq 5$ ,  $\leq 3$  and  $\leq 1$  increased over time, with W104 rates of 86.8%, 81.7% and 57.5%, respectively. The proportions of patients achieving PASI90, and PASI100 responses increased to W104 in the overall patient population (64.7% and 43.6% of patients, respectively) and in the subsets of patients who were biologic naïve and biologic experienced. Response rates over time were consistently higher in biologic-naïve versus biologic-experienced patients. In biologic-experienced patients, PASI responses at W104 were greater in those who had received a biologic other than an IL-17 inhibitor versus those who had received an IL-17 inhibitor.

In patients with a baseline PGA score  $\geq 2$  for scalp, palmoplantar or anogenital psoriasis, the proportion with complete or almost complete clearance increased over time, with W104 rates of 90.3% for scalp psoriasis, 93.2% for palmoplantar psoriasis and 93.1% for anogenital psoriasis (vs. 0% at baseline for all three regions). Among patients with  $\geq 1$  affected nail at baseline, mean target NAPSI score decreased over time, from 4.2 at baseline to 1.0 at W104.

Mean DLQI score improved over time to W104, with 63.6% of patients achieving a DLQI score  $\leq 1$  at W104 (vs. 4.1% at baseline). The proportion achieving a DLQI score  $\leq 1$  at W104 was higher in those who were biologic naïve versus biologic experienced. In biologic-experienced patients, the W104 DLQI score  $\leq 1$  response rate was higher in those who had not received an IL-17 inhibitor, compared with those who had received an IL-17 inhibitor. Mean PSSD scores decreased over time.

### Safety

The cumulative probability of guselkumab drug survival at W104 was 90.0% ([Figure 1](#)). Overall, 17.9% of patients experienced  $\geq 1$  treatment-related AE, with the most common being viral upper respiratory tract infection (3.0%) and diarrhoea (1.7%) ([Table 4](#)). Most treatment-related AEs were mild or moderate in severity. Treatment-related adverse events of special interest are shown in [Table 4](#). There were no cases of *Candida* infection, NMSC, lymphoma, IBD, active TB or

**TABLE 1** Key efficacy and quality-of-life outcomes to Week 104 in patients treated with ustekinumab ( $N=313$ ).

Assessment	Baseline	Week 16	Week 28	Week 52	Week 104
Mean PASI score (SD)	15.8 (9.4) [ $n=312$ ]	3.9 (4.4) [ $n=292$ ]	3.3 (4.3) [ $n=273$ ]	2.5 (2.9) [ $n=248$ ]	2.0 (3.3) [ $n=205$ ]
Absolute PASI score, $n/N$ (%)					
≤5	26/312 (8.3)	220/292 (75.3)	222/273 (81.3)	205/248 (82.7)	186/205 (90.7)
≤3	10/312 (3.2)	166/292 (56.8)	176/273 (64.5)	171/248 (69.0)	166/205 (81.0)
≤1	0/312 (0)	69/292 (23.6)	94/273 (34.4)	102/248 (41.1)	101/205 (49.3)
PASI90 response, $n/N$ (%)					
Overall	–	85/292 (29.1)	108/273 (39.6)	116/248 (46.8)	112/205 (54.6)
Biologic naïve	–	57/201 (28.4)	77/188 (41.0)	83/173 (48.0)	81/144 (56.3)
Biologic experienced	–	28/91 (30.8)	31/85 (36.5)	33/75 (44.0)	31/61 (50.8)
PASI100 response, $n/N$ (%)					
Overall	–	27/292 (9.2)	47/273 (17.2)	61/248 (24.6)	58/205 (28.3)
Biologic naïve	–	16/201 (8.0)	34/188 (18.1)	44/173 (25.4)	47/144 (32.6)
Biologic experienced	–	11/91 (12.1)	13/85 (15.3)	17/75 (22.7)	11/61 (18.0)
PGA score of clear or almost clear (in patients with PGA ≥2 at baseline), $n/N$ (%)					
Scalp psoriasis	0/237 (0)	155/221 (70.1)	157/207 (75.8)	152/192 (79.2)	133/160 (83.1)
Palmoplantar psoriasis	0/58 (0)	38/53 (71.7)	38/49 (77.6)	33/40 (82.5)	30/32 (93.8)
Anogenital psoriasis	0/121 (0)	93/112 (83.0)	94/106 (88.7)	87/97 (89.7)	81/83 (97.6)
Mean NAPSI score (SD) (in patients with ≥1 affected nail at baseline)	3.9 (2.2) [ $n=152$ ]	2.3 (2.1) [ $n=142$ ]	1.8 (1.9) [ $n=129$ ]	1.4 (1.9) [ $n=108$ ]	0.9 (1.5) [ $n=90$ ]
Mean DLQI score (SD)	12.9 (7.1) [ $n=310$ ]	3.8 (4.8) [ $n=289$ ]	3.1 (4.4) [ $n=269$ ]	2.7 (4.0) [ $n=247$ ]	2.0 (3.5) [ $n=202$ ]
DLQI score 0/1, $n/N$ (%)					
Overall	10/310 (3.2)	122/289 (42.2)	140/269 (52.0)	138/247 (55.9)	130/202 (64.4)
Biologic naïve	5/212 (2.4)	83/200 (41.5)	98/187 (52.4)	100/171 (58.5)	95/143 (66.4)
Biologic experienced	5/98 (5.1)	39/89 (43.8)	42/82 (51.2)	38/76 (50.0)	35/59 (59.3)
Mean PSSD score (SD)					
Symptoms	48.0 (26.2) [ $n=307$ ]	NR	13.6 (18.3) [ $n=262$ ]	11.3 (16.5) [ $n=240$ ]	9.0 (15.1) [ $n=193$ ]
Signs	58.0 (22.2) [ $n=307$ ]	NR	18.9 (20.1) [ $n=262$ ]	15.8 (18.0) [ $n=240$ ]	12.0 (15.5) [ $n=193$ ]

Note: The observed decrease in the number of evaluable patients over time in both cohorts reflects patient loss to follow-up, withdrawal of consent or missed single visits (the time window for each study visit was  $\pm 8$  weeks; if a planned visit did not occur within this window, it was not documented or it became the next documented visit, where relevant).

Abbreviations: DLQI, Dermatology Life Quality Index; NAPSI, Nail Psoriasis Severity Index; NR, not recorded; PASI, Psoriasis Area and Severity Index; PGA, Physician's Global Assessment; PSSD, Psoriasis Symptoms and Signs Diary; SD, standard deviation.

MACE. Reports of non-IBD gastrointestinal events and cardiac events were rare, and three patients had malignant or benign neoplasms. All-cause AEs that led to treatment discontinuation occurred in 12 patients (4.0%). Overall, three patients (1.0%) reported four treatment-related SAEs (bronchitis,  $n=1$ ; Epstein–Barr virus infection,  $n=1$ ; anal cancer,  $n=1$ ; prostate cancer,  $n=1$ ), and there were no deaths.

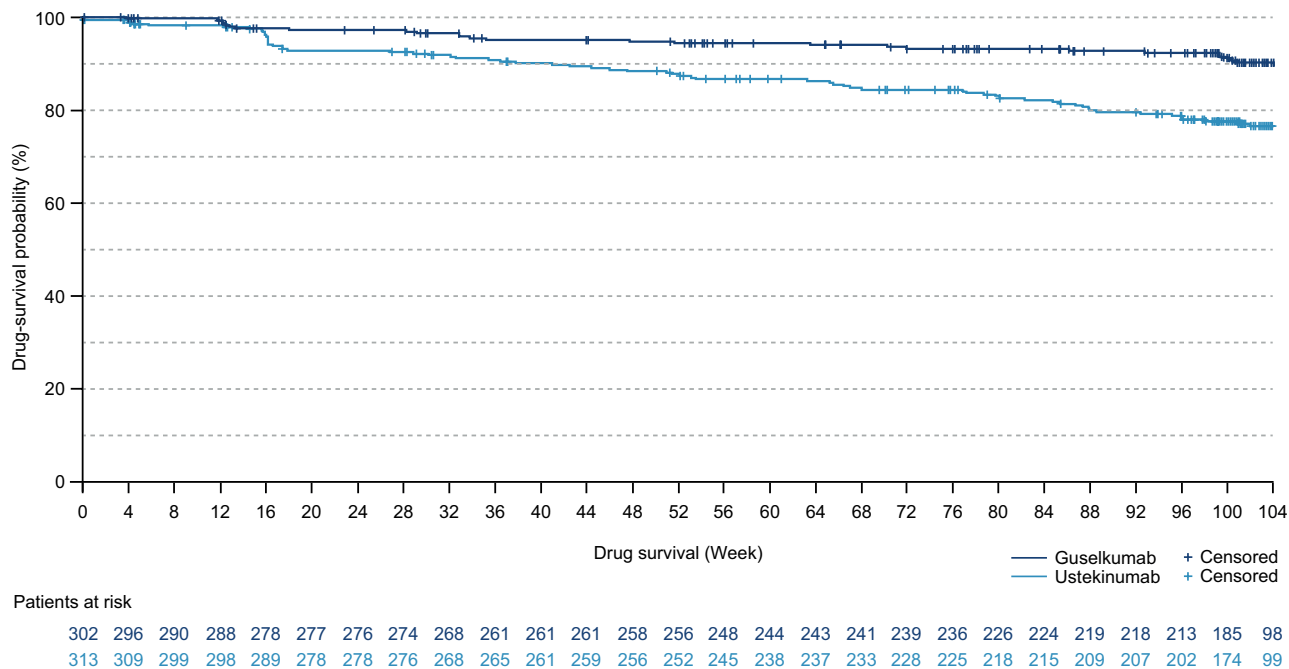
### Propensity-matching analysis

Using propensity score matching, 294 patients from the ustekinumab and guselkumab cohorts were matched and included into the analysis; 19 and 8 patients were excluded, respectively, as they were unable to be matched to another patient. Baseline characteristics were well balanced between

the two matched groups, with the exception of prior psoriasis therapy, particularly biologics. Guselkumab-treated patients were more likely to have received biologics (51.7% vs. 32.0%,  $p<0.001$ ) and to have received a biologic immediately before enrolment (45.2% vs. 24.1%,  $p<0.001$ ), than ustekinumab-treated patients (Table S3). Of the biologic-experienced patients, receipt of only one biologic was more frequent in the ustekinumab cohort versus the guselkumab cohort (68.1% vs. 51.3%,  $p=0.007$ ); conversely, receipt of  $\geq 3$  agents was more frequent in the guselkumab cohort (21.1% vs. 7.4%,  $p=0.007$ ).

### Efficacy and quality of life

The proportions of patients with an absolute PASI score of  $\leq 5$ ,  $\leq 3$ ,  $\leq 1$  and 0 increased over time with ustekinumab



**FIGURE 1** Kaplan–Meier curve showing cumulative probability of guselkumab and ustekinumab drug survival over 104 weeks. Each event corresponds to a patient discontinuation, resulting from an AE, lack of efficacy or patient death (one patient in the ustekinumab cohort and no patients in the guselkumab cohort died over the course of follow-up). The low number of patients at risk at W104 is a methodological artefact (i.e. most patients censored at W104 had a study visit slightly earlier than W104) and is not due to medical reasons. There were two events each for guselkumab and ustekinumab between W100 and W104. AE, adverse event; W, Week.

and guselkumab (Figure S1); however, achievement of PASI score  $\leq 1$  at W104 was more common in those who received guselkumab versus ustekinumab ( $n/N = 125/213$  [58.7%] and  $n/N = 96/193$  [49.7%], respectively). The same was true for achievement of an absolute PASI score of 0 at W104 ( $n/N = 94/212$  [44.3%] and  $n/N = 55/193$  [28.5%], respectively). Achievement of relative PASI responses, overall and according to history of biologic use, also increased to W104 in both cohorts (Figure 2). However, in the overall population, responses were higher in guselkumab- than ustekinumab-treated patients at most time points. Additionally, there was greater separation of response rates between biologic-naïve and biologic-experienced patients who were receiving guselkumab versus ustekinumab, with greater response rates observed in those who were biologic naïve.

The proportion of patients with area-specific complete/almost complete clearance of scalp, palmoplantar or anogenital psoriasis increased over time, regardless of treatment (Figure S2). For scalp psoriasis, guselkumab-treated patients appeared to have better results than ustekinumab-treated patients. The decrease in mean target NAPSI score at W104 was similar in patients treated with ustekinumab (baseline, 3.8; W104, 0.9 [relative change, -74.1]) and guselkumab (baseline, 4.1; W104, 0.8 [relative change, -75.4]).

Achievement of a DLQI score  $\leq 1$  increased to W104 in both cohorts, with almost identical results at W104 (ustekinumab,  $n/N = 123/191$  [64.4%]; guselkumab,  $n/N = 135/209$

[64.6%]) (Figure 3). However, among biologic-naïve patients, a greater proportion of guselkumab ( $n/N = 82/107$  [76.6%]) than ustekinumab ( $n/N = 89/135$  [65.9%])-treated patients achieved a DLQI score  $\leq 1$  at W104. PSSD outcomes are reported in the Appendix S1.

## Safety

The proportions of ustekinumab- and guselkumab-treated patients who experienced  $\geq 1$  treatment-related AE and who experienced selected treatment-related AEs are shown in Table S4. In total, 20.7% and 18.0% of ustekinumab- and guselkumab-treated patients, respectively, experienced  $\geq 1$  treatment-related AE. Ustekinumab recipients more often experienced viral upper respiratory tract infections (7.1% vs. 3.1%) and a lack of efficacy (3.7% vs. 0.3%), compared with guselkumab recipients; otherwise, rates of treatment-related AEs with the two treatments were generally low. For both treatments, most treatment-related AEs were mild or moderate in severity. Rates of selected treatment-related AEs were low in both cohorts, with no cases of IBD, NMSC, active TB or MACE. The overall rate of treatment-related AEs was 20.2%–23.0% in ustekinumab recipients who were biologic naïve or biologic experienced, and in biologic-experienced guselkumab recipients. However, guselkumab recipients who were biologic naïve had a lower rate of treatment-related AEs (12.7%) (Table S5).

**TABLE 2** Treatment-related adverse events (reported in  $\geq 1\%$  of patients) and selected treatment-related adverse events in patients treated with ustekinumab ( $N = 313$ ).

AEs, $n$ (%)	Mild	Moderate	Severe	Total <sup>a</sup>
Treatment-related AEs				
Patients with $\geq 1$ event	40 (12.8)	33 (10.5)	5 (1.6)	65 (20.8)
Total number of events	62	40	8	110
Viral upper respiratory tract infection	19 (6.1)	9 (2.9)	1 (0.3)	24 (7.7)
Oral candidiasis	–	3 (1.0)	–	3 (1.0)
Selected treatment-related AEs				
<i>Candida</i> infection	–	3 (1.0)	–	3 (1.0)
COVID-19	–	–	–	–
Malignant and benign neoplasms	–	–	–	–
NMSC	–	–	–	–
Lymphoma	–	–	–	–
Gastrointestinal disorders (excluding IBD) <sup>b</sup>	3 (1.0)	3 (1.0)	–	6 (1.9)
IBD	–	–	–	–
Active TB during study <sup>c</sup>	–	–	–	–
Cardiac disorders (primary SOC) <sup>d</sup>	–	1 (0.3)	–	1 (0.3)
MACE	–	–	–	–

Note: MACE was defined as any of the following: non-fatal MI, non-fatal stroke and cardiovascular death.

Abbreviations: AE, adverse event; COVID-19, coronavirus disease 2019; IBD, inflammatory bowel disease; MACE; major adverse cardiovascular event; MI, myocardial infarction; NMSC; non-melanoma skin cancer; SOC, system organ class; TB, tuberculosis.

<sup>a</sup>If a patient had an adverse event in  $\geq 1$  severity category, it was counted in each of the categories.

<sup>b</sup>Gastrointestinal disorders included: nausea,  $n = 3$ ; upper abdominal pain,  $n = 2$ ; diarrhoea,  $n = 2$ ; tongue discomfort,  $n = 1$ .

<sup>c</sup>At screening, latent TB was reported in one patient (0.3%), but no active cases of TB were identified. One patient (0.3%) received concomitant isoniazid.

<sup>d</sup>Cardiac disorders included: atrial fibrillation,  $n = 1$ .

## DISCUSSION

Outcomes with ustekinumab and guselkumab in patients with plaque psoriasis have been studied extensively in phase III clinical studies,<sup>7-13</sup> with results demonstrating a high degree of efficacy and improvements in QoL over a 5-year period.<sup>18-20</sup> PERSIST was a non-interventional prospective study designed to obtain data on the real-world effectiveness of ustekinumab and guselkumab in patients with moderate-to-severe psoriasis across Germany, over 2 years. PERSIST data demonstrated that both ustekinumab and guselkumab showed high levels of effectiveness and improved QoL to W104 in patients in routine clinical care, including those who would have been ineligible to participate in clinical trials. Importantly, the effectiveness of both treatments at W104 extended to difficult-to-treat regional psoriasis manifestations. Drug survival rates were high for ustekinumab and particularly for guselkumab, indicating the treatment benefits obtained in routine clinical care. Although PASI outcomes at W104 in PERSIST tended to be numerically lower than those at similar timepoints in the phase III trials,<sup>21,22</sup> this can be explained, at least in part, by differences in baseline characteristics. For example, a higher proportion of guselkumab-treated patients in PERSIST had received prior conventional systemic and biologic therapies or had comorbidities, for example, PsA, than in the randomized-controlled VOYAGE studies.<sup>7,12</sup>

PERSIST provided the opportunity to compare real-world outcomes in ustekinumab and guselkumab-treated patients. Post hoc propensity matching was undertaken to match patients treated with ustekinumab or guselkumab according to their baseline characteristics. Following propensity matching, an analysis of baseline characteristics showed that more guselkumab- than ustekinumab-treated patients were biologic experienced. Of the biologic-experienced patients, those treated with guselkumab versus ustekinumab had more often received multiple biologic therapies. In addition to highlighting the heavier biologic load in guselkumab recipients, PERSIST data also showed that patients most often received ustekinumab as a first-line biologic treatment, whereas guselkumab was used as a later-in-line biologic treatment (i.e. after failure of several other biologics, including ustekinumab). This is noteworthy because studies have demonstrated higher efficacy with guselkumab in patients who are biologic naïve.<sup>23,24</sup> Nonetheless, following propensity matching, patients treated with guselkumab versus ustekinumab demonstrated greater improvements in PASI outcomes. In particular, guselkumab recipients more often achieved higher PASI90 and PASI100 response rates as well as absolute PASI scores of  $\leq 3$  or  $\leq 1$  at W104. These findings align with results from the COMPASS analysis, which assessed the relative efficacy of guselkumab (100 mg) and ustekinumab (45 or 90 mg) as maintenance therapies for

**TABLE 3** Key efficacy and quality-of-life outcomes to Week 104 in patients treated with guselkumab (N=302).

Characteristic	Baseline	Week 16	Week 28	Week 52	Week 104
Mean PASI score (SD)	15.7 (9.8) [n=302]	3.9 (5.14) [n=281]	2.9 (5.2) [n=267]	2.5 (4.9) [n=245]	2.4 (4.7) [n=219]
Absolute PASI score, n/N (%)					
≤5	26/302 (8.6)	212/281 (75.4)	222/267 (83.1)	206/245 (84.1)	190/219 (86.8)
≤3	15/302 (5.0)	183/281 (65.1)	211/267 (79.0)	191/245 (78.0)	179/219 (81.7)
≤1	4/302 (1.3)	93/281 (33.1)	135/267 (50.6)	143/245 (58.4)	126/219 (57.5)
PASI90 response, n/N(%)					
Overall	–	106/281 (37.7)	145/267 (54.3)	153/245 (62.4)	141/218 (64.7)
Biologic naïve	–	65/138 (47.1)	92/132 (69.7)	98/126 (77.8)	85/112 (75.9)
Biologic experienced	–	41/143 (28.7)	53/135 (39.3)	55/119 (46.2)	56/106 (52.8)
No prior IL-17 inhibitor	–	24/68 (35.3)	31/63 (49.2)	28/54 (51.9)	30/51 (58.8)
Prior IL-17 inhibitor	–	17/75 (22.7)	22/72 (30.6)	27/65 (41.5)	26/55 (47.3)
PASI100 response, n/N (%)					
Overall	–	62/281 (22.1)	77/267 (28.8)	98/245 (40.0)	95/218 (43.6)
Biologic naïve	–	39/138 (28.3)	52/132 (39.4)	64/126 (50.8)	61/112 (54.5)
Biologic experienced	–	23/143 (16.1)	25/135 (18.5)	34/119 (28.6)	34/106 (32.1)
No prior IL-17 inhibitor	–	14/68 (20.6)	16/63 (25.4)	19/54 (35.2)	20/51 (39.2)
Prior IL-17 inhibitor	–	9/75 (12.0)	9/72 (12.5)	15/65 (23.1)	14/55 (25.5)
PGA score of clear or almost clear (in patients with PGA ≥2 at baseline), n/N (%)					
Scalp psoriasis	0/199 (0)	138/185 (74.6)	151/175 (86.3)	146/160 (91.3)	131/145 (90.3)
Palmoplantar psoriasis	0/82 (0)	53/76 (69.7)	65/77 (84.4)	57/66 (86.4)	55/59 (93.2)
Anogenital psoriasis	0/118 (0)	85/107 (79.4)	86/102 (84.3)	83/96 (86.5)	81/87 (93.1)
Mean NAPSI score (SD) (in patients with ≥1 affected nail at baseline)	4.2 (2.2) [n=136]	2.6 (2.4) [n=108]	1.7 (2.1) [n=117]	1.2 (2.0) [n=108]	1.0 (1.5) [n=93]
Mean DLQI score (SD)	13.6 (7.5) [n=296]	3.6 (4.7) [n=268]	2.7 (4.0) [n=262]	2.5 (4.2) [n=241]	2.0 (3.5) [n=214]
DLQI score 0/1, n/N (%)					
Overall	12/296 (4.1)	129/268 (48.1)	148/262 (56.5)	150/241 (62.2)	136/214 (63.6)
Biologic naïve	4/144 (2.8)	73/130 (56.2)	89/130 (68.5)	92/123 (74.8)	83/110 (75.5)
Biologic experienced	8/152 (5.3)	56/138 (40.6)	59/132 (44.7)	58/118 (49.2)	53/104 (51.0)
No prior IL-17 inhibitor	5/70 (7.1)	29/66 (43.9)	32/63 (50.8)	29/54 (53.7)	29/52 (55.8)
Prior IL-17 inhibitor	3/82 (3.7)	27/72 (37.5)	27/69 (39.1)	29/64 (45.3)	24/52 (46.2)
Mean PSSD score (SD)					
Symptoms	51.6 (25.8) [n=292]	NR	12.5 (17.8) [n=252]	11.3 (18.3) [n=233]	10.5 (18.5) [n=204]
Signs	60.8 (22.4) [n=292]	NR	16.0 (19.4) [n=252]	13.9 (19.5) [n=233]	13.2 (19.6) [n=204]

Note: There was one less patient in this cohort, compared with previous reports<sup>14,15</sup>; this followed the exclusion of one patient after it was discovered they did not have plaque psoriasis (i.e. they were ineligible for the study). The observed decrease in the number of evaluable patients over time reflects patient loss to follow-up, withdrawal of consent, or missed single visits (the time window for each study visit was ±8 weeks; if a planned visit did not occur within this window, it was not documented or it became the next documented visit, where relevant).

Abbreviations: DLQI, Dermatology Life Quality Index; IL, interleukin; NAPSI, Nail Psoriasis Severity Index; NR, not recorded; PASI, Psoriasis Area and Severity Index; PGA, Physician's Global Assessment; PSSD, Psoriasis Symptoms and Signs Diary; SD, standard deviation.

moderate-to-severe plaque psoriasis, using individual patient data from the VOYAGE 1 and 2 and NAVIGATE randomized controlled trials.<sup>25</sup> Multivariable logistic regression analyses adjusted for a range of clinically relevant baseline characteristics, and demonstrated that guselkumab was associated with significantly greater achievement of PASI75, 90 and 100 responses compared with ustekinumab, through 40 weeks.<sup>25</sup>

Additionally, relative PASI response rates at W104 in PERSIST were greater in biologic-naïve versus biologic-experienced patients for both treatments, and there was greater separation between the groups for those who were receiving guselkumab versus ustekinumab. This could be a result of the biologic-experienced patients in the guselkumab cohort having received more treatment lines than patients in the ustekinumab cohort.

**TABLE 4** Treatment-related adverse events (reported in  $\geq 1\%$  of patients) and selected treatment-related adverse events in patients treated with guselkumab ( $N=302$ ).

AE, n (%)	Mild	Moderate	Severe	Total <sup>a</sup>
Treatment-related AEs				
Patients with $\geq 1$ event	34 (11.3)	23 (7.6)	8 (2.6)	54 (17.9)
Total number of events	50	46	13	109
Viral upper respiratory tract infection	7 (2.3)	1 (0.3)	1 (0.3)	9 (3.0)
Diarrhoea	3 (1.0)	2 (0.7)	–	5 (1.7)
Headache	3 (1.0)	2 (0.7)	–	4 (1.3)
Pruritis	1 (0.3)	3 (1.0)	–	4 (1.3)
Influenza	–	3 (1.0)	–	3 (1.0)
Psoriasis	–	3 (1.0)	–	3 (1.0)
Weight increased	2 (0.7)	1 (0.3)	–	3 (1.0)
Selected treatment-related AEs				
<i>Candida</i> infection	–	–	–	–
COVID-19	–	–	–	–
Malignant and benign neoplasms <sup>b</sup>	1 (0.3)	1 (0.3)	1 (0.3)	3 (1.0)
NMSC	–	–	–	–
Lymphoma	–	–	–	–
Gastrointestinal disorders (excluding IBD) <sup>c</sup>	6 (2.0)	4 (1.3)	1 (0.3)	10 (3.3)
IBD	–	–	–	–
Active TB during study <sup>d</sup>	–	–	–	–
Cardiac disorders (primary SOC) <sup>e</sup>	–	1 (0.3)	–	1 (0.3)
MACE	–	–	–	–

Note: MACE was defined as any of the following: non-fatal MI, non-fatal stroke and cardiovascular death.

Abbreviations: AE, adverse event; COVID-19, coronavirus disease 2019; IBD, inflammatory bowel disease; MACE; major adverse cardiovascular event; NMSC; non-melanoma skin cancer; SOC, system organ class; TB, tuberculosis.

<sup>a</sup>If a patient had an adverse event in  $\geq 1$  severity category, it was counted in each of the categories.

<sup>b</sup>Comprised two cases of benign adenoma and one case each of anal and prostate cancer.

<sup>c</sup>Gastrointestinal disorder included: diarrhoea,  $n=5$ ; nausea,  $n=2$ ; stomatitis,  $n=2$ ; flatulence,  $n=1$ ; and gastritis,  $n=1$ .

<sup>d</sup>At screening, latent TB was reported in one patient (0.3%) and a positive *Mycobacterium tuberculosis* complex test was reported in another patient ( $n=1$ , 0.3%), however, no active cases of TB were identified. These two patients continued in the study, and the former received concomitant rifampicin.

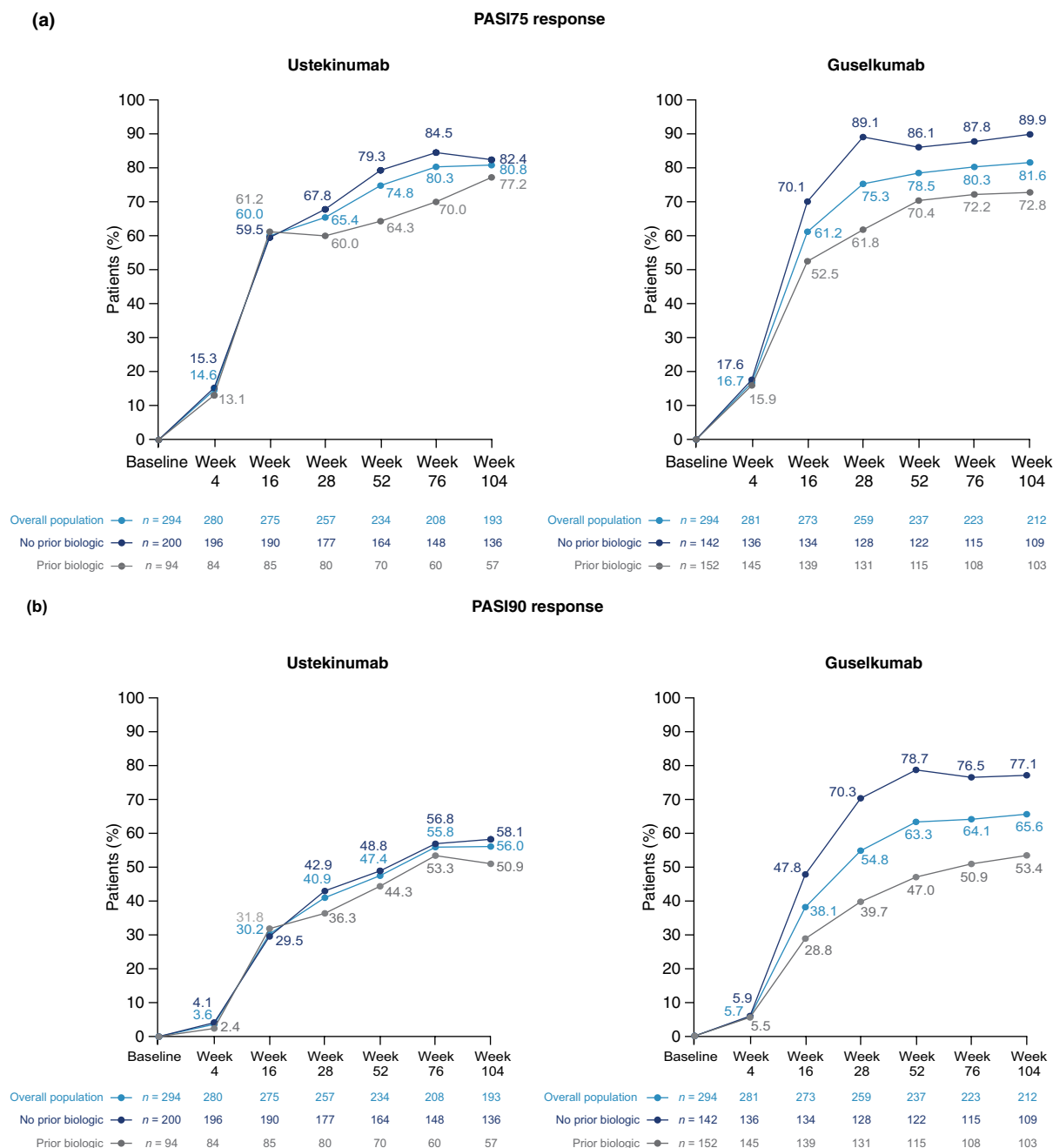
<sup>e</sup>Cardiac disorders included: cardiovascular disorder,  $n=1$ .

Propensity-matched data demonstrated similar QoL outcomes between cohorts at W104. The between-treatment similarity in QoL could be because guselkumab patients were assessed at a later point in time than ustekinumab recipients, and in a later biologic treatment line. As such, guselkumab recipients may have been more familiar with biologic therapies, accustomed to QoL improvements obtained in previous lines of therapy, and so may have had greater treatment expectations. Additionally, ustekinumab-treated patients not responding/not experiencing QoL improvements may have discontinued the study, thereby leaving a population with an overall higher QoL. Similar to achievement of a PASI response, the proportion achieving a DLQI  $\leq 1$  response at W104 was greater in biologic-naïve than biologic-experienced patients for both cohorts. Among biologic-naïve patients, a greater proportion of guselkumab- than ustekinumab-treated patients achieved a DLQI score  $\leq 1$  at W104. These data, in addition to the high rate of drug survival, highlight the benefit of administering guselkumab earlier in the treatment pathway. Indeed, the clinical

benefits of early intervention with guselkumab in patients with psoriasis have been reported from the ongoing GUIDE study.<sup>26,27</sup>

Safety findings were consistent with the well-known data for ustekinumab and guselkumab, including previous PERSIST publications.<sup>14,15</sup> No new safety signals were detected, and there were few treatment-related AEs over 2 years, including no cases of IBD or MACE. There were fewer treatment-related AEs than in clinical trials of guselkumab,<sup>7,12,13,28</sup> though patients may have reported AEs less frequently in PERSIST. Following propensity matching, rates of treatment-related AEs with ustekinumab and guselkumab were generally similar, although viral upper respiratory tract infection and lack of efficacy were reported more often in ustekinumab recipients.

The limitations of PERSIST have been described previously.<sup>14,15</sup> A possible limitation of the propensity-matching analysis is that it does not consider that patients received ustekinumab or guselkumab at different time periods. Additionally, while propensity score matching is useful to



**FIGURE 2** Proportion of patients treated with ustekinumab or guselkumab who achieved (a) Psoriasis Area and Severity Index (PASI) 75 (b), PASI90 and (c) PASI100 responses (overall and by biologic treatment history) over time to Week 104 (propensity-matching analysis). The observed decrease in the number of evaluable patients over time in both cohorts reflects patients lost to follow-up, withdrawal of consent or missed single visits (the time window for each study visit was  $\pm 8$  weeks. If a planned visit did not occur within this window, it was not documented or it was counted towards the next visit window, where relevant).

control for confounding variables, differences in patient and/or disease characteristics may remain. These limitations, however, should not detract from the strengths of the study, including the length of the follow-up period: while numerous other studies have reported on the effectiveness and safety of guselkumab in real-world datasets,<sup>23,24,29-41</sup> PERSIST is one of the largest studies to report outcomes over 2 years.<sup>42</sup>

In conclusion, data from the real-world PERSIST study demonstrate improvements in physician-assessed and patient-reported outcomes with ustekinumab and guselkumab in patients with psoriasis that are sustained for up to 2 years, with no new safety signals identified. An ad hoc exploratory analysis of outcomes with ustekinumab versus guselkumab using propensity matching demonstrated greater improvements in PASI outcomes in guselkumab recipients. Improvements

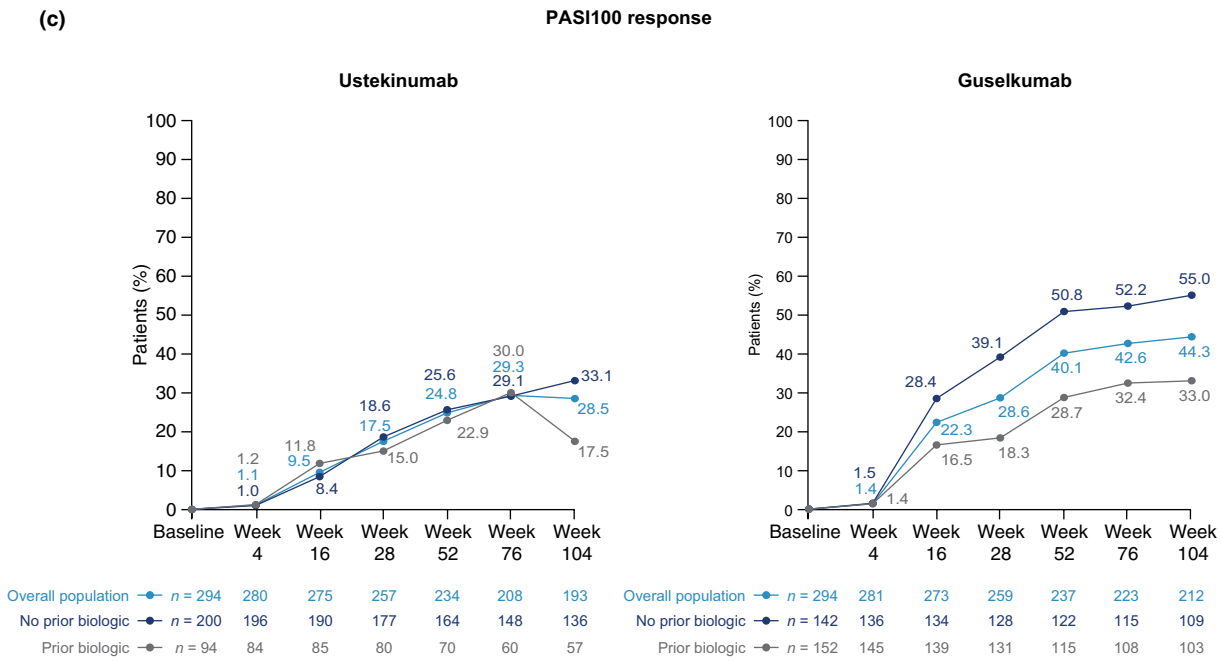


FIGURE 2 (Continued)

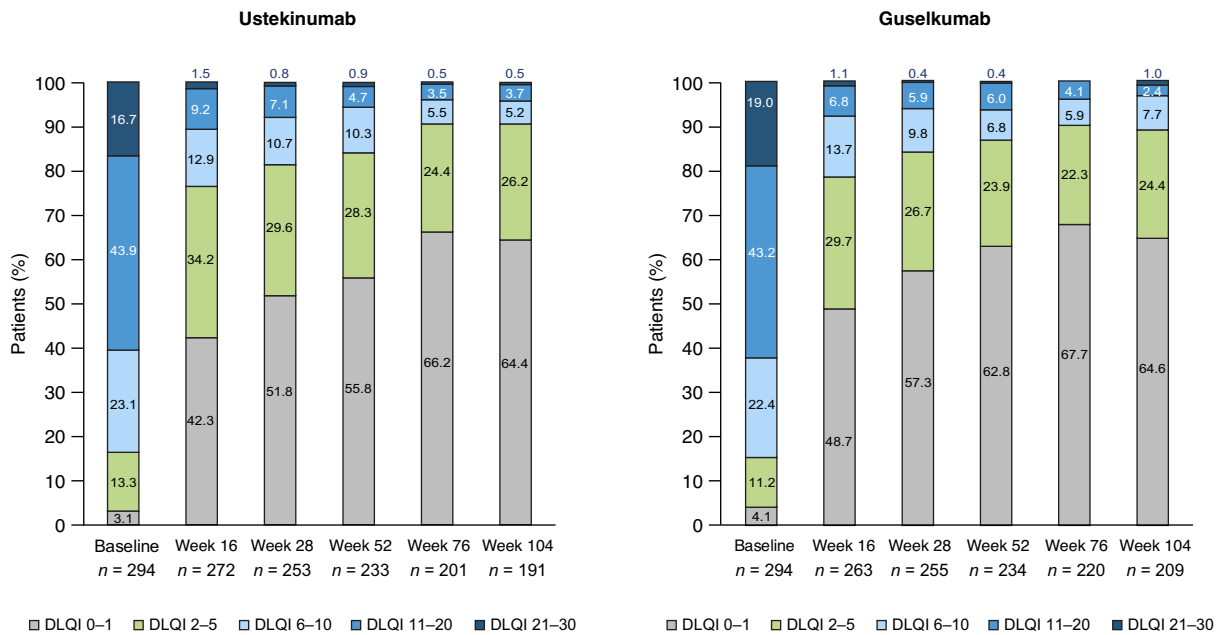


FIGURE 3 Proportion of patients treated with ustekinumab and guselkumab who achieved given thresholds of mean Dermatology Life Quality Index (DLQI) scores over time to Week 104 (propensity-matching analysis). The observed decrease in the number of evaluable patients over time in both cohorts reflects patient loss to follow-up, withdrawal of consent, or missed single visits (the time window for each study visit was  $\pm 8$  weeks. If a planned visit did not occur within this window, it was not documented or it became the next documented visit, where relevant). DLQI score: 0/1, no effect of psoriasis on quality of life; 2–5, small effect; 6–10, moderate effect; 11–20, very large effect; 21–30, extremely large effect.

were greatest in those who were biologic naïve versus biologic experienced, and this was more pronounced in guselkumab than ustekinumab recipients, thereby highlighting the value of early intervention with guselkumab.

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## CONFLICT OF INTEREST STATEMENT

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, AnaptysBio, Argenx 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 GmbH, 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; MH was an advisor and/or received speakers' honoraria and/or received grants and/or participated in clinical trials of the following companies: AbbVie, Almirall, Amgen, Boehringer Ingelheim, Eli Lilly, Galderma, GSK, Janssen-Cilag GmbH, LEO Pharma, Medac, MSD, Novartis, Pfizer 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, Emeriti Pharma, Galderma, Janssen-Cilag GmbH, LEO Pharma, L'Oréal, Novartis, Nuvisan, Pierre Fabre, Sanofi Genzyme 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, Almirall, Amgen, Astellas, Beiersdorf, Biogen, Celgene, Dr. Pflieger, Eli Lilly, Galderma, Janssen-Cilag GmbH, 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, Almirall, Amgen, Celgene, Eli Lilly, Janssen-Cilag GmbH, LEO Pharma, Moberg Pharma, Novartis, Sandoz, Sanofi Genzyme and UCB Pharma; NK, YP, ST, SW and FK are employees of Janssen-Cilag GmbH; MG is an employee of Janssen Global Services LLC; FT owns Taut Science And Service GmbH, a consultancy specialising in clinical development and Medical Affairs, and is receiving consultancy fees from 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, Almirall, Amgen, Boehringer Ingelheim, Celgene, Eli Lilly, Galderma, GSK, Janssen-Cilag GmbH, LEO Pharma, MSD, Novartis, Pfizer, Regeneron, Sanofi and UCB Pharma.

## DATA AVAILABILITY STATEMENT

Research data are not shared.

## ETHICS STATEMENT

PERSIST was conducted in accordance with the International Conference on Harmonisation Good Clinical Practice

(ICH-GCP) guidelines and with the Helsinki Declaration of 1975, as revised in 1983.

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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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