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Five-year maintenance of clinical response and health-related quality of life improvements in patients with moderate-to-severe psoriasis treated with guselkumab: results from VOYAGE 1 and VOYAGE 2*

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Summary

Background Psoriasis is a chronic disease requiring long-term therapy.
Objectives Physician- and patient-reported outcomes were evaluated through week 252 in VOYAGE 1 and VOYAGE 2.
Methods In total, 1829 patients were randomized at baseline to receive guselkumab 100 mg every 8 weeks, placebo or adalimumab. Patients receiving placebo crossed over to guselkumab at week 16. Patients receiving adalimumab crossed over to guselkumab at week 52 in VOYAGE 1, and randomized withdrawal and retreatment occurred at weeks 28–76 in VOYAGE 2; all patients then received open-label guselkumab through week 252. Efficacy and health-related quality of life (HRQoL) endpoints were analysed through week 252. Safety was monitored through week 264.
Results The proportions of patients in the guselkumab group who achieved clinical responses at week 252 in VOYAGE 1 and VOYAGE 2, respectively, were 84·1% and 82·0% [≥ 90% improvement in Psoriasis Area and Severity Index (PASI)]; 82·4% and 85·0% [Investigator's Global Assessment (IGA) 0 or 1]; 52·7% and 53·0% (100% improvement in PASI) and 54·7% and 55·5% (IGA 0). HRQoL endpoints were achieved as follows: 72·7% and 71·1% of patients (Dermatology Life Quality Index 0 or 1: no effect on patient's life); 42·4% and 42·0% [Psoriasis Symptoms and Signs Diary (PSSD) symptom score = 0] and 33·0% and 31·0% (PSSD sign score = 0). As measured in VOYAGE 2 only, approximately 45% of patients achieved ≥ 5-point reduction in Short Form-36 physical and mental component scores, and 80% reported no anxiety or depression (Hospital Anxiety and Depression Scale scores < 8). Similar findings were reported for adalimumab crossovers. These effects were maintained from week 52 in VOYAGE 1 and week 100 in VOYAGE 2. No new safety signals were identified.

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Conflicts of interest
Statements can be found in Appendix 1.

Data availability
The data sharing policy of Janssen Pharmaceutical Companies of Johnson & Johnson is available at https://www.janssen.com/clinical-trials/transparency. As noted on this site, requests for access to the study data can be submitted through the Yale Open Data Access (YODA) Project site at http://yoda.yale.edu. Datasets related to this article will be available by request or at https://www.clinicaltrials.gov (NCT02207231 and NCT02207244) when the study concludes.

*Plain language summary available online

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Conclusions Guselkumab maintains high levels of clinical response and improvement in patient-reported outcomes through 5 years in patients with moderate-to-severe psoriasis.

What is already known about this topic?

- Psoriasis is a chronic disease requiring long-term treatment.
- Guselkumab has been shown to be effective in improving clinical response and health-related quality of life (HRQoL) in more than 1800 patients through 4 years in the VOYAGE 1 and VOYAGE 2 trials.

What does this study add?

- Guselkumab maintained improvements in clinical response as well as positive effects on HRQoL and general health through 5 years in patients with moderate-to-severe psoriasis.

Long-term therapy is required for the successful management of the symptoms and signs of psoriasis, and therapeutic longevity is critical to maintenance of disease control.[1] In addition to the physical cutaneous manifestations, psoriasis affects health-related quality of life (HRQoL) and general wellbeing, including the ability to work,[2–4] and increases the risk of anxiety and depression.[5,6] Given the chronicity of the disease, some patients may experience 'cumulative life course impairment', wherein the physical, psychological and social burdens of psoriasis may result in the inability to make decisions needed to achieve long-term success in relationships, career and other aspects of daily life.[7] Data collected over long periods of time from both physicians and patients are required to confirm the durable efficacy of the currently available treatments for psoriasis.

Guselkumab, a human monoclonal antibody that inhibits interleukin-23 by targeting the p19 subunit, has been shown to be superior to placebo at week 16 and adalimumab at week 24 in two pivotal studies of patients with moderate-to-severe plaque psoriasis (VOYAGE 1 and VOYAGE 2).[8,9] The results of the individual studies through 4 years indicated sustained efficacy and a favourable benefit–risk profile both for patients receiving continuous guselkumab treatment and for those who crossed over from adalimumab to guselkumab.[10,11] VOYAGE 1 and VOYAGE 2 are now complete, and this report summarizes the therapeutic longevity of guselkumab in patients with psoriasis through 5 years.

Patients and methods

Patients and study design

VOYAGE 1 and VOYAGE 2 (clinicaltrials.gov: NCT02207231 and NCT02207244) were phase III, randomized, double-blind, placebo- and adalimumab comparator-controlled trials of guselkumab in moderate-to-severe psoriasis. While both studies evaluated the efficacy and safety of guselkumab through week 252, VOYAGE 1 included crossover to adalimumab at week 52 and VOYAGE 2 included a randomized withdrawal and retreatment period at weeks 28–76 (Figure 1).

Details of the inclusion and exclusion criteria have been reported previously.[8,9] To meet the eligibility criteria, adult patients (age ≥ 18 years) had to have a diagnosis of plaque-type psoriasis for ≥ 6 months [Psoriasis Area and Severity Index (PASI) score ≥ 12, Investigator's Global Assessment (IGA) score ≥ 3, and body surface area involved with psoriasis ≥ 10%] and be a candidate for systemic therapy or phototherapy.

One of many institutional review boards or ethics committees approved the study protocol at each site, and all patients provided written informed consent. Both studies were conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with Good Clinical Practice.

Outcome assessments

Disease severity was evaluated based on standard psoriasis measures, including PASI[12] and IGA, at regular visits through week 252. Skin-related HRQoL was self-reported by patients using dermatology-specific assessments, including the Dermatology Life Quality Index (DLQI; range 0–30: no effect to extremely large effect)[13] and the Psoriasis Symptoms and Signs Diary (PSSD; range 0–100: severity increases with score).[14–16] General HRQoL was assessed using the 36-Item Short Form Health Survey (SF-36) based on physical and mental component scores (PCS and MCS; range 0–100 each, with higher scores indicating better HRQoL).[17]

The Hospital Anxiety and Depression Scale (HADS) has seven items related to depression (HADS-D) and seven items related to anxiety (HADS-A); the total score range for each is 0–21 and a score ≥ 8 indicates anxiety or depression.[18] The Work Limitations Questionnaire (WLQ) was used to measure the effect of chronic conditions on work performance based on four domain scales (range for each is 0–100: least to most

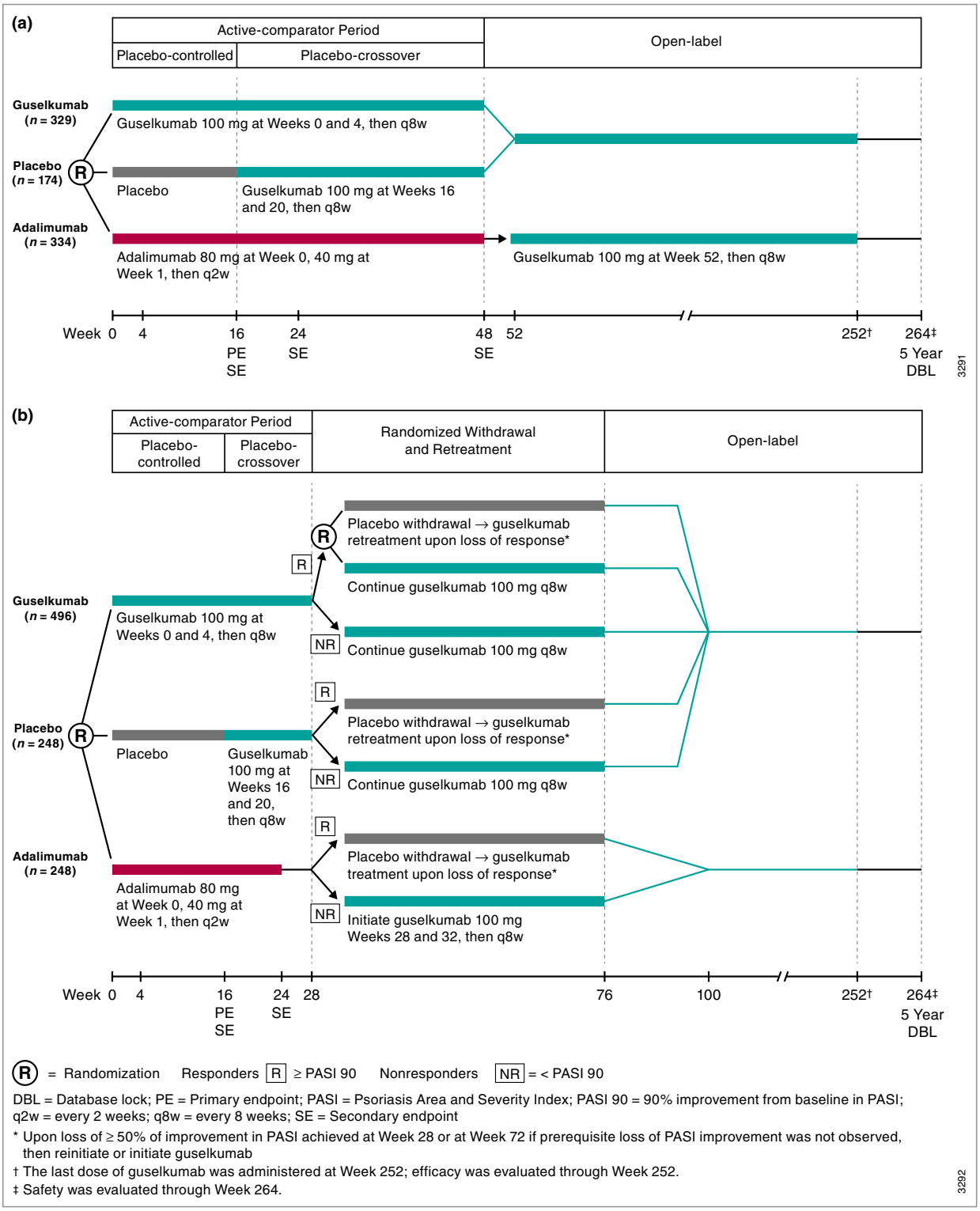

Figure 1 Study designs of (a) VOYAGE 1 and (b) VOYAGE 2 through 5 years.

limited).[19] After week 100, patient-reported outcomes (PROs) were collected approximately every 6 months.

Safety was monitored by collecting adverse event (AE) reports, and blood samples were collected to measure antibodies to guselkumab through week 264.

Statistical analyses

Efficacy endpoints included the proportions of patients in the guselkumab group achieving at least 90% or 100% improvement from baseline in PASI (PASI 90 and PASI 100,

respectively) and an IGA score of clear/minimal and clear (IGA 0/1 and IGA 0, respectively) through week 252. Absolute PASI thresholds based on scores of 0–5 were summarized; a score of 0 indicates complete clearance. HRQoL endpoints included the proportion of patients with a DLQI score indicating no effect of psoriasis (DLQI 0/1) among patients with a baseline score > 1 and the proportion of patients with PSSD scores indicating symptom-free and sign-free status (summary scores = 0) among patients with a baseline symptom or sign score > 0. The proportions of patients with clinically meaningful improvement (CMI; ≥ 5-point reductions) in SF-36 PCS and MCS scores,[20] the proportions of patients with HADS-A and HADS-D scores < 8 (indicating no anxiety or depression), and the mean change from baseline in WLQ scores were also summarized over time.

The long-term analyses were focused primarily on the efficacy and safety among patients in the guselkumab group, which included patients randomized to guselkumab at baseline as well as those randomized to placebo who crossed over to guselkumab at week 16 in VOYAGE 1 and VOYAGE 2. In addition, data are presented here for the adalimumab→guselkumab crossover group (i.e. patients randomized to adalimumab at baseline who crossed over to receive guselkumab at week 52 in VOYAGE 1 or on/after week 28 in VOYAGE 2). To evaluate continuous treatment with guselkumab, data are presented for the entire study in VOYAGE 1 (week 0–252). Assessment of long-term results is more complex in VOYAGE 2 due to inclusion of the randomized withdrawal and retreatment period (weeks 28–76) as described previously.[9,21] As some patients were retreated with guselkumab beginning at week 76, efficacy with respect to baseline was evaluated starting at week 100 to allow adequate response time in VOYAGE 2. HRQoL endpoints over time are presented from week 100 through week 252 in both studies.

In the prespecified analyses of PASI and IGA in both studies, efficacy was analysed for all guselkumab-treated patients using treatment failure rules (TFRs). These were applied for patients who discontinued the study agent for specific reasons (i.e. lack of efficacy or an AE of worsening of psoriasis) or who started a protocol-prohibited medication or therapy that could improve psoriasis. Such patients were considered nonresponders in subsequent analyses. In VOYAGE 1, sensitivity analyses were conducted to compare PASI and IGA results using other methodologies: nonresponder imputation (NRI), in which patients were considered nonresponders if data were missing after TFRs were applied, and as observed data (OBS), wherein observed data were used. Absolute PASI data were analysed using only the prespecified TFR method.

Safety data were pooled across the VOYAGE 1 and VOYAGE 2 studies for all patients who received at least one dose of study agent and were analysed according to the actual treatment received. The numbers of AEs and serious AEs per 100 patient-years (PY) of follow-up are presented by treatment group over time through week 264.

Results

Baseline patient characteristics

Of the 1829 patients randomized across the VOYAGE 1 and VOYAGE 2 studies, 1826 received treatment starting at baseline in the placebo (n = 422), guselkumab (n = 823) and adalimumab (n = 581) groups. In both studies, the demographics and disease characteristics in each group were indicative of moderate-to-severe psoriasis, and the PROs suggested that participants had significant impairment of HRQoL, with mean DLQI score > 10, mean PSSD summary scores > 50, and mean SF-36 summary scores < 50 (Tables 1 and 2).

Patient disposition

Overall, 19·6% of patients (152 of 774) in VOYAGE 1 and 23·4% (222 of 949) in VOYAGE 2 discontinued the study agent from baseline (for those originally randomized to guselkumab) and from the time of crossover to guselkumab (for those originally randomized to placebo or adalimumab) through week 252. Rates of discontinuation due to lack of efficacy were low in both guselkumab treatment groups in VOYAGE 1 (1·4% and 0·7% in the guselkumab and adalimumab→guselkumab groups, respectively) and VOYAGE 2 (1·0% and 1·8%, respectively). An AE of worsening of psoriasis was the reason for discontinuation in 0·4% and 0·5% in the guselkumab and adalimumab→guselkumab groups, respectively, in VOYAGE 2.

Efficacy

Long-term clinical response in VOYAGE 1 and VOYAGE 2

The efficacy of guselkumab was maintained in the open-label extension periods through week 252 in VOYAGE 1 and VOYAGE 2. Specifically, 84·1% of patients in VOYAGE 1 and 82·0% of those in VOYAGE 2 achieved PASI 90 at week 252 in the guselkumab group (Figure 2a, b). Similarly, 82·4% in VOYAGE 1 and 85·0% in VOYAGE 2 achieved IGA 0/1 at week 252 (Figure 3a, b). Furthermore, 52·7% of patients in VOYAGE 1 and 53·0% of those in VOYAGE 2 achieved PASI 100 (Figure 2c, d), and 54·7% in VOYAGE 1 and 55·5% in VOYAGE 2 achieved IGA 0 at week 252 (Figure 3c, d). Clinical response was maintained from week 52 in VOYAGE 1 and from week 100 in VOYAGE 2 through week 252. Rates in the adalimumab→guselkumab group were comparable with those in the guselkumab group in both studies (Figures 2 and 3).

Clinical response by analysis method in VOYAGE 1

In VOYAGE 1, clinical response was consistent and well maintained through week 252, regardless of the imputation method used to handle missing data. The PASI response rates for the TFR (primary analysis) and OBS methods and the most

Table 1 Demographic and disease characteristics at baseline: randomized patients in VOYAGE 1 and VOYAGE 2

	Placebo	Guselkumab	Adalimumab	Total
Patients, n	422	825	582	1829
Age (years), mean (SD)	43·9 (12·6)	43·8 (12·4)	43·0 (12·3)	43·6 (12·4)
Men, n (%)	292 (69·2)	589 (71·4)	419 (72·0)	1300 (71·1)
White race, n (%)	351 (83·2)	670 (81·2)	477 (82·0)	1498 (81·9)
BMI (kg m^{-2}), mean (SD)	29·3 (6·7)	29·7 (6·4)	29·7 (6·5)	29·6 (6·5)
Bodyweight (kg), mean (SD)	88·4 (21·9)	89·3 (20·5)	89·2 (21·5)	89·1 (21·2)
Duration of psoriasis (years), mean (SD)	17·8 (12·1)	17·9 (12·1)	17·3 (11·4)	17·7 (11·9)
Body surface area (%), mean (SD)	27·1 (16·3)	28·4 (16·7)	28·8 (16·7)	28·2 (16·6)
IGA score (0–4), n (%)				
Moderate (3)	322 (76·3)	632 (76·6)	436 (74·9)	1390 (76·0)
Severe (4)	100 (23·7)	192 (23·3)	143 (24·6)	435 (23·8)
PASI (0–72), mean (SD)	21·1 (8·3)	22·0 (9·1)	22·1 (9·0)	21·8 (8·9)
Psoriatic arthritis, n (%)	76 (18·0)	153 (18·5)	106 (18·2)	335 (18·3)
Prior treatments, n (%)				
Phototherapy[a]	223 (52·8)	481 (58·4)	315 (54·2)	1019 (55·8)
Systemic agents (≥ 1)[b]	241 (57·1)	541 (65·6)	374 (64·3)	1156 (63·2)
Biologic agents[c]	88 (20·9)	172 (20·8)	119 (20·4)	379 (20·7)

BMI, body mass index; IGA, Investigator's Global Assessment; PASI, Psoriasis Area and Severity Index. [a]Phototherapy includes ultraviolet B and psoralen with ultraviolet A (PUVA); data were missing for one patient in each treatment group. [b]Systemic agents include PUVA, methotrexate, ciclosporin, acitretin, apremilast and tofacitinib. [c]Biologic agents include etanercept, infliximab, alefacept, efalizumab, ustekinumab, briakinumab, secukinumab, ixekizumab and brodalumab.

Table 2 Patient-reported outcomes at baseline: randomized patients in VOYAGE 1 and VOYAGE 2

	Placebo	Guselkumab	Adalimumab	Total
DLQI (0–30), n	418	817	575	1810
	14·3 (7·2)	14·4 (7·2)	14·6 (7·1)	14·5 (7·2)
PSSD (0–100), n	327	660	475	1462
Symptom score	54·5 (24·1)	54·2 (25·6)	53·8 (25·9)	54·2 (25·3)
Sign score	58·1 (20·5)	56·5 (22·1)	57·8 (21·6)	57·3 (21·6)
SF-36 (0–100), n[a]	248	494	246	988
PCS score	47·3 (9·5)	47·5 (9·2)	48·9 (8·5)	47·8 (9·1)
MCS score	45·0 (11·3)	44·3 (11·5)	43·9 (11·5)	44·4 (11·5)
HADS (0–21), n[a]	248	495	246	989
HADS-A	6·5 (4·1)	6·9 (4·1)	6·9 (4·5)	6·8 (4·2)
Score ≥ 8, n (%)	86 (34·7)	192 (38·8)	104 (42·3)	382 (38·6)
HADS-D	5·1 (4·3)	5·3 (4·2)	5·3 (4·3)	5·3 (4·2)
Score ≥ 8, n (%)	66 (26·6)	134 (27·1)	74 (30·1)	274 (27·7)
WLQ domains (0–100)[a]				
Physical demands, n	180	352	172	704
	17·9 (21·2)	17·9 (21·7)	15·8 (19·8)	17·4 (21·1)
Time management, n	168	336	163	667
	20·5 (23·6)	18·3 (22·4)	20·5 (24·1)	19·4 (23·1)
Mental-interpersonal, n	176	346	168	690
	15·5 (19·8)	15·1 (18·5)	14·9 (18·1)	15·1 (18·7)
Output demands, n	178	346	170	694
	16·8 (22·1)	15·5 (21·6)	14·2 (19·3)	15·5 (21·2)

The data are presented as the mean (SD) unless stated otherwise. DLQI, Dermatology Life Quality Index; HADS, Hospital Anxiety and Depression Scale (A, anxiety; D, depression); MCS, mental component score; PSSD, Psoriasis Symptoms and Signs Diary; SF-36, 36-Item Short Form Health Survey; PCS, physical component score; WLQ, Work Limitations Questionnaire. [a]Collected in VOYAGE 2 only.

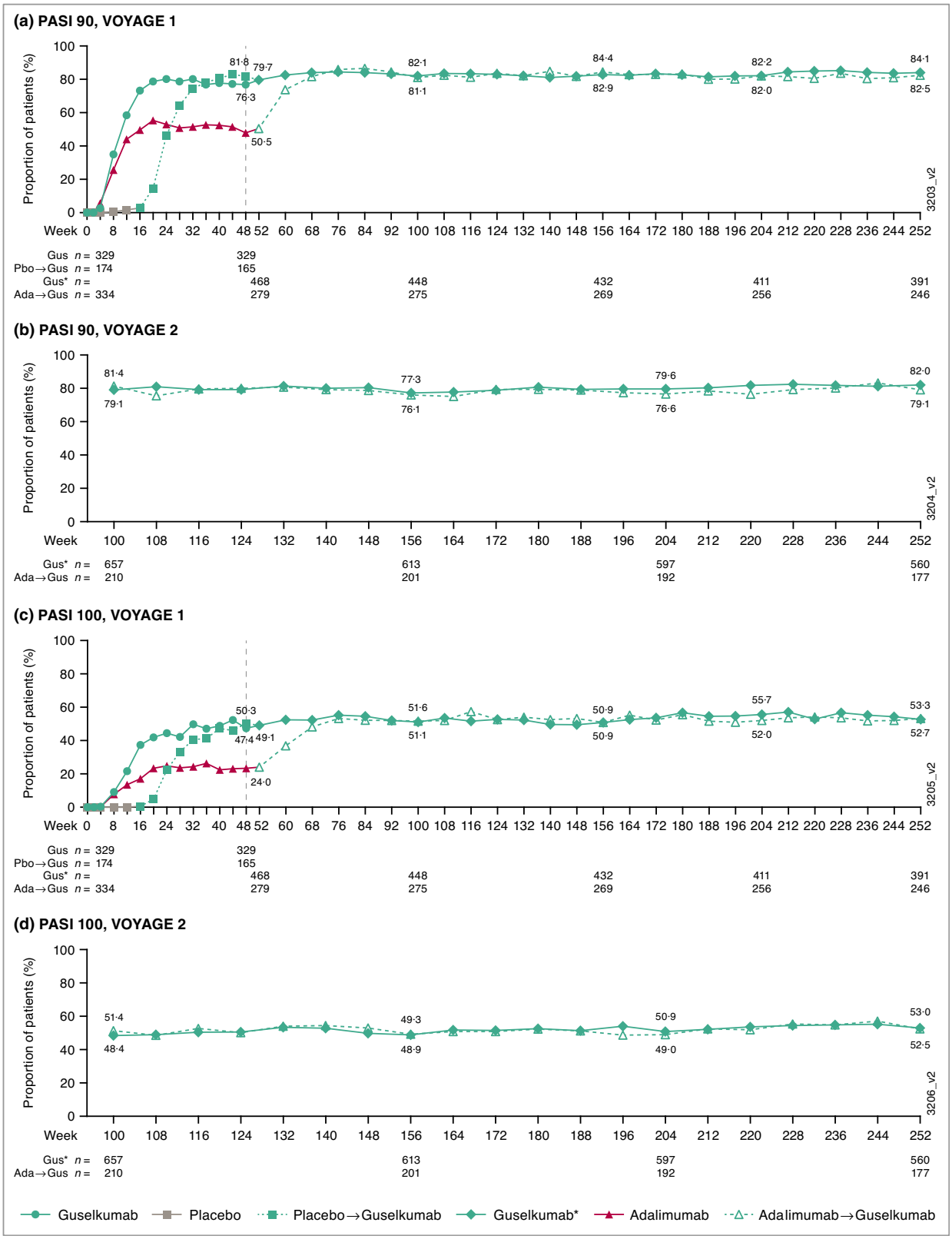

Figure 2 Psoriasis Area and Severity Index (PASI) response by treatment group through week 252: (a) PASI 90 in VOYAGE 1; (b) PASI 90 in VOYAGE 2; (c) PASI 100 in VOYAGE 1; (d) PASI 100 in VOYAGE 2. *Includes patients randomized to guselkumab at baseline and those randomized to placebo at baseline who crossed over to receive guselkumab at week 16. Ada→Gus, adalimumab crossover to guselkumab group; Pbo→Gus, placebo crossover to guselkumab group; Gus, guselkumab group; PASI 90, ≥ 90% improvement from baseline in PASI; PASI 100, 100% improvement from baseline in PASI (clear).

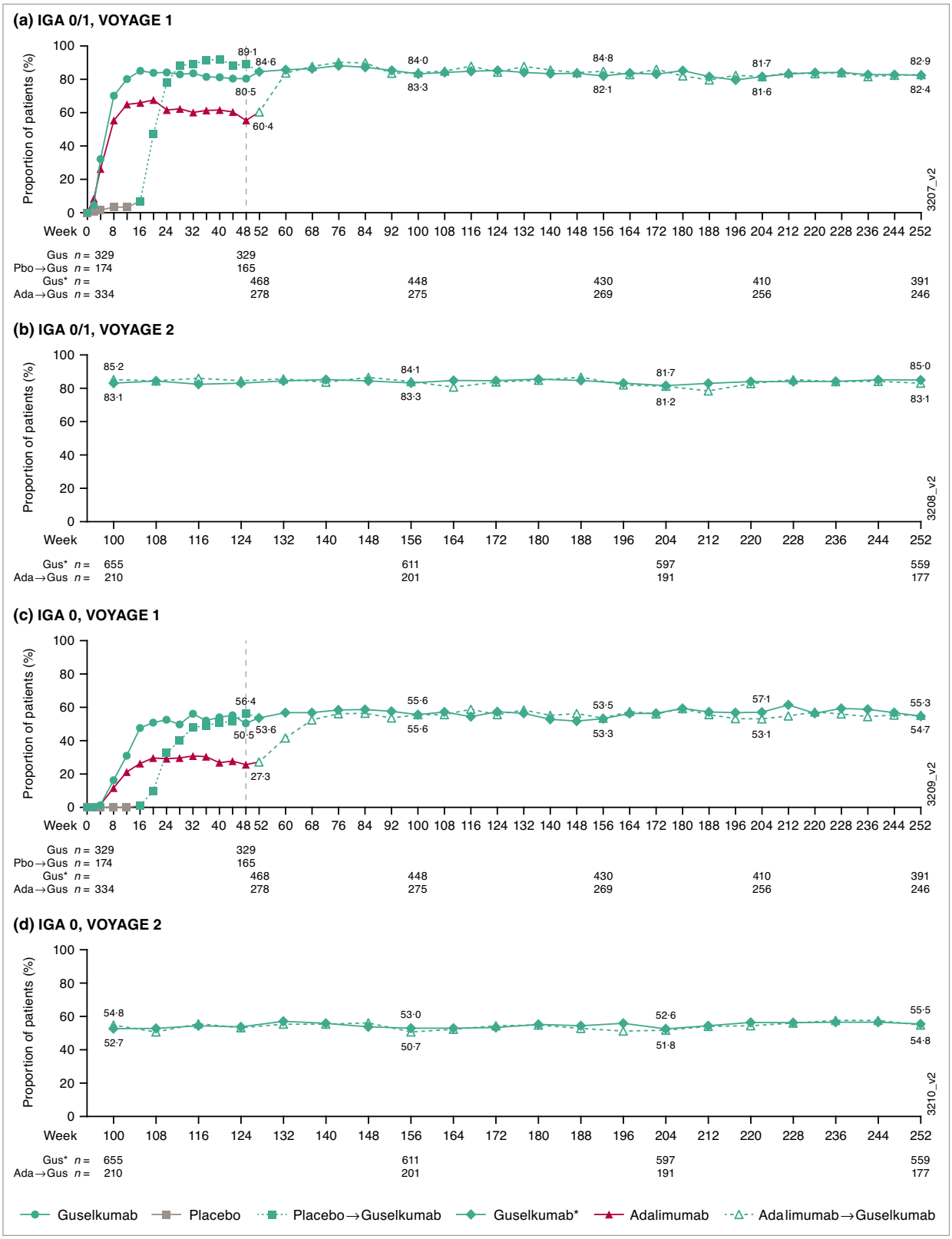

Figure 3 Investigator's Global Assessment (IGA) response by treatment group through week 252: (a) IGA 0/1 in VOYAGE 1; (b) IGA 0/1 in VOYAGE 2; (c) IGA 0 in VOYAGE 1; (d) IGA 0 in VOYAGE 2. *Includes patients randomized to guselkumab at baseline and those randomized to placebo at baseline who crossed over to receive guselkumab at week 16. Ada→Gus, adalimumab crossover to guselkumab group; Pbo→Gus, placebo crossover to guselkumab group; Gus, guselkumab group; IGA 0/1, IGA score of cleared or minimal psoriasis; IGA 0, IGA score of cleared psoriasis.

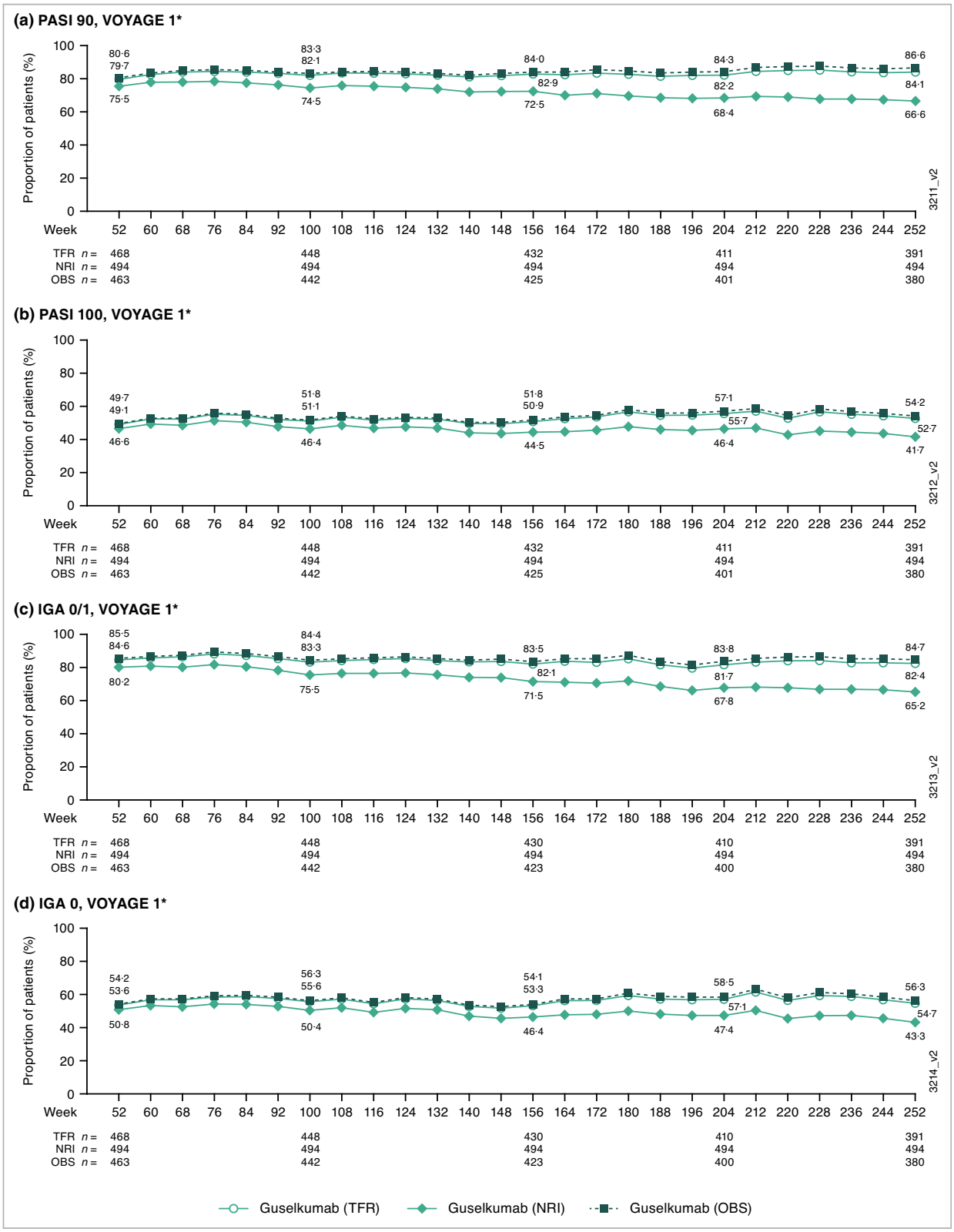

Figure 4 Clinical response by analytical method through week 252 in VOYAGE 1: (a) PASI 90; (b) PASI 100; (c) IGA 0/1; (d) IGA 0. *Includes patients randomized to guselkumab at baseline and those randomized to placebo at baseline who crossed over to receive guselkumab at week 16. IGA 0/1, Investigator's Global Assessment score of cleared or minimal psoriasis; IGA 0, IGA score of cleared psoriasis; NRI, nonresponder imputation method; OBS, as observed method; PASI 90, ≥ 90% improvement from baseline in Psoriasis Area and Severity Index; PASI 100, 100% improvement from baseline in PASI; TFR, treatment failure rules method.

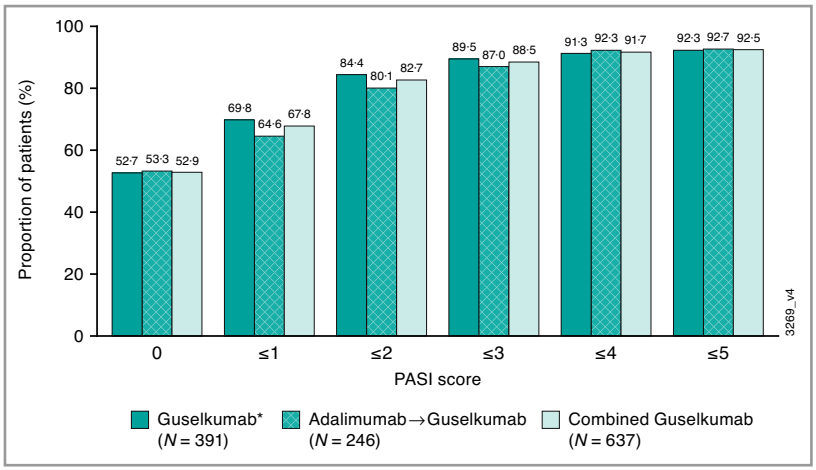

Figure 5 Proportion of patients achieving absolute Psoriasis Area and Severity Index (PASI) thresholds at week 252 in VOYAGE 1. *Includes patients randomized to guselkumab at baseline and those randomized to placebo at baseline who crossed over to receive guselkumab at week 16.

conservative NRI method, respectively, in the guselkumab group were 84·1%, 86·6% and 66·6% for PASI 90 and 52·7%, 54·2% and 41·7% for PASI 100 (Figure 4a, b). Similarly, 82·4%, 84·7% and 65·2% achieved IGA 0/1 and 54·7%, 56·3% and 43·3% achieved IGA 0 based on the TFR, OBS and NRI analyses, respectively (Figure 4c, d). Rates in the adalimumab→guselkumab group were similar to those in the guselkumab group, and rates in both groups were maintained over time starting at week 52.

Absolute Psoriasis Area and Severity Index thresholds in VOYAGE 1

To further assess the effect of continuous treatment, absolute PASI response data were analysed using the TFR method over time in VOYAGE 1 (Figure 5). At the end of the study (week 252), 52·7% of patients achieved an absolute PASI score of 0 (clear), 69·8% achieved PASI ≤ 1, 89·5% achieved PASI ≤ 3, and 92·3% achieved PASI ≤ 5 in the guselkumab group. Following crossover to guselkumab, absolute PASI responses in the adalimumab→guselkumab group were similar to those in the guselkumab group at week 252. Furthermore, these rates had been maintained over time.[10]

Long-term health-related quality of life in VOYAGE 1 and VOYAGE 2

Among patients in the guselkumab group with baseline DLQI score > 1, the proportions of patients achieving DLQI 0/1 (no effect of psoriasis on patient's life) were maintained from week 100 through week 252 in both VOYAGE 1 (75·2% and 72·7%, respectively) and VOYAGE 2 (70·2% and 71·1%,

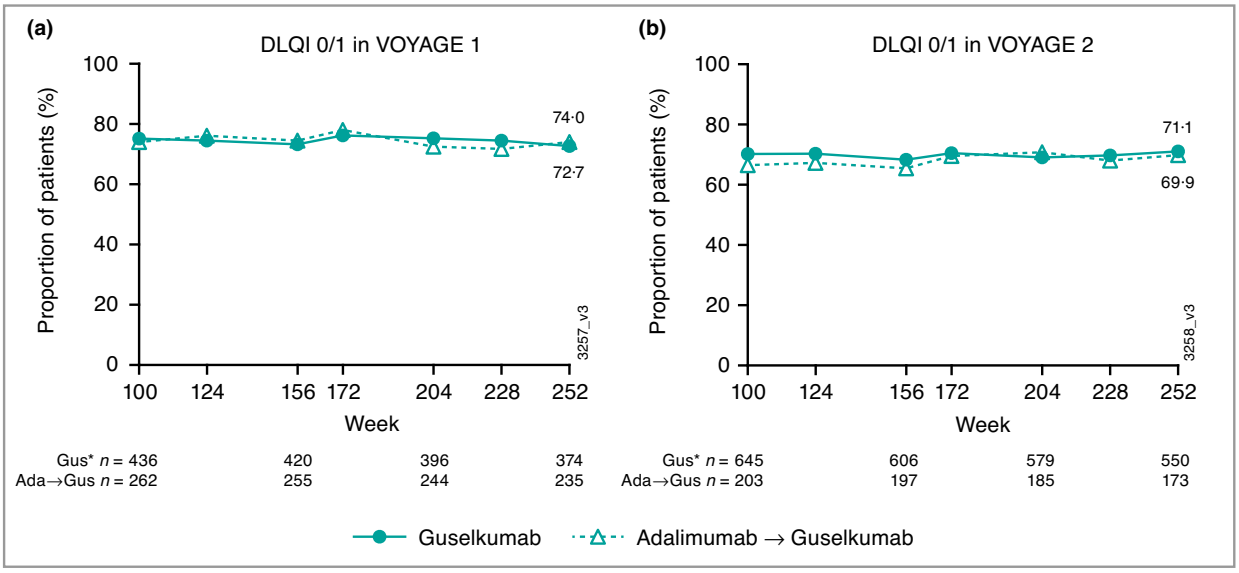

Figure 6 Proportion of patients with Dermatology Life Quality Index (DLQI) scores of 0 or 1 (indicating no effect on patient's life) from week 100 through week 252: (a) VOYAGE 1; (b) VOYAGE 2. *Includes patients randomized to guselkumab at baseline and those randomized to placebo at baseline who crossed over to receive guselkumab at week 16. Ada→Gus, adalimumab crossover to guselkumab group; Gus, guselkumab group.

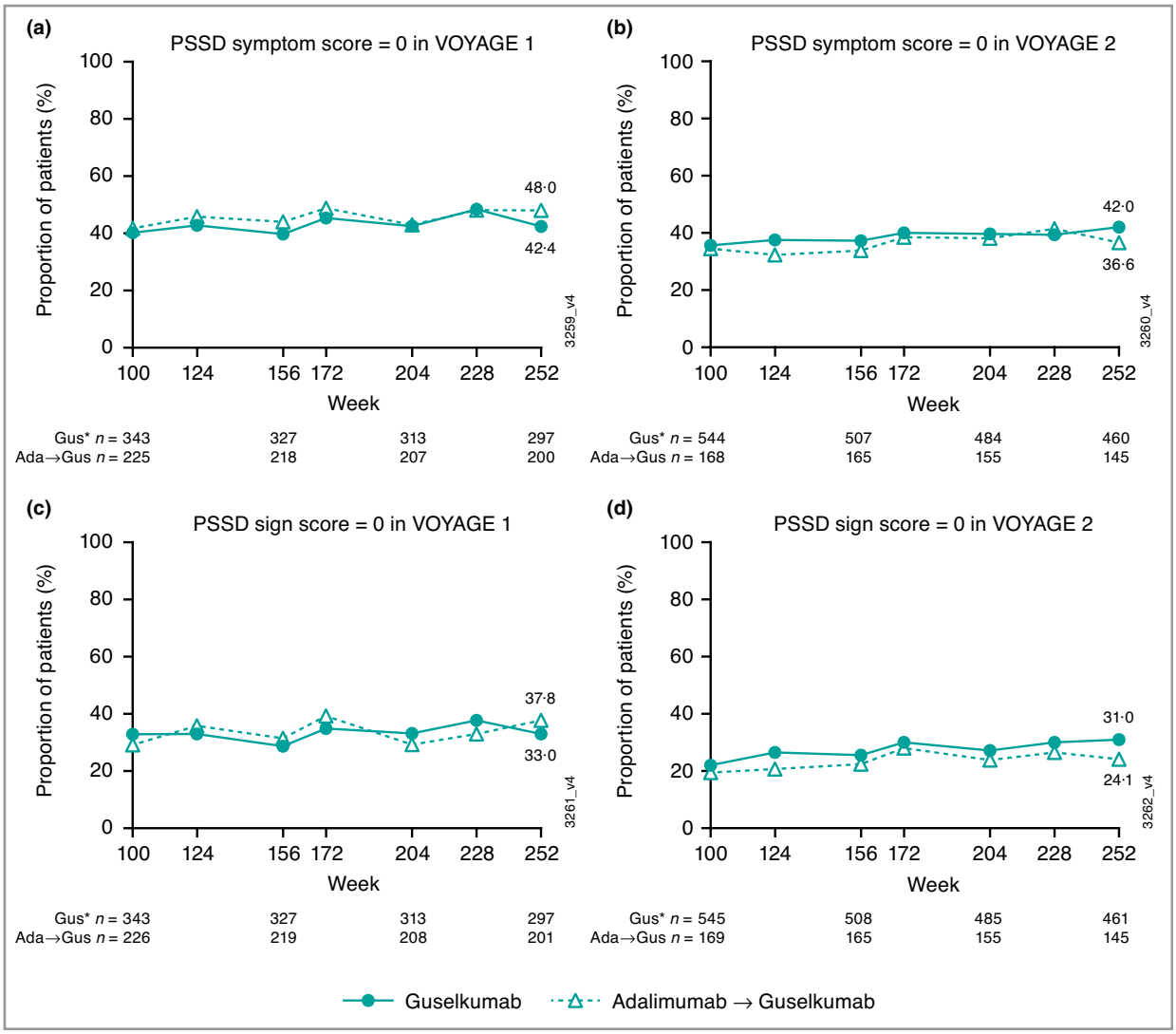

Figure 7 Proportion of patients with Psoriasis Symptoms and Signs Diary (PSSD) summary scores of 0 (indicating symptom- and sign-free status) from week 100 through week 252: (a) symptom score = 1 in VOYAGE 1; (b) symptom score = 1 in VOYAGE 2; (c) sign score = 1 in VOYAGE 1; (d) sign score = 1 in VOYAGE 2. *Includes patients randomized to guselkumab at baseline and those randomized to placebo at baseline who crossed over to receive guselkumab at week 16. Ada→Gus, adalimumab crossover to guselkumab group; Gus, guselkumab group.

respectively) (Figure 6). The results were similar over time in the adalimumab→guselkumab group in both studies.

The proportions of patients in the guselkumab group achieving PSSD summary score = 0 (symptom-free status) at week 100 and week 252, respectively, were 40·2% and 42·4% in VOYAGE 1 and 35·7% and 42·0% in VOYAGE 2 (Figure 7). Similarly, PSSD sign summary score = 0 was achieved by 32·9% (week 100) and 33·0% (week 252) in VOYAGE 1 and 22·0% (week 100) and 31·0% (week 252) in VOYAGE 2. Comparable responses were observed for all HRQoL measures in the adalimumab→guselkumab group across both studies.

Long-term health-related quality of life in VOYAGE 2

The proportions of patients with CMI (≥ 5-point improvement) from baseline in SF-36 MCS and PCS were maintained from week 100 through week 252 in the guselkumab group (Figure 8). Specifically, at week 100 and week 252, respectively, 48·8% and 45·9% achieved CMI in the PCS and 45·1% and 46·1% achieved CMI in the MCS at these timepoints. Similar results were observed in the adalimumab→guselkumab group.

The proportions of patients reporting HADS-A < 8 (no anxiety) were maintained from week 100 (77·1%) through week 252 (79·8%) in the guselkumab group (Figure 9). Likewise 83·4% and 80·5% reported HADS-D < 8 (no depression) at week 100 and week 252, respectively. Rates over time in the adalimumab→guselkumab group were similar to those in the guselkumab group.

Mean changes (improvements) from baseline at week 252 in WLQ component scores were −6·7 for physical demands, −5·5 for mental-interpersonal, −6·3 for output demands and −7·2 for time management in the guselkumab group; changes

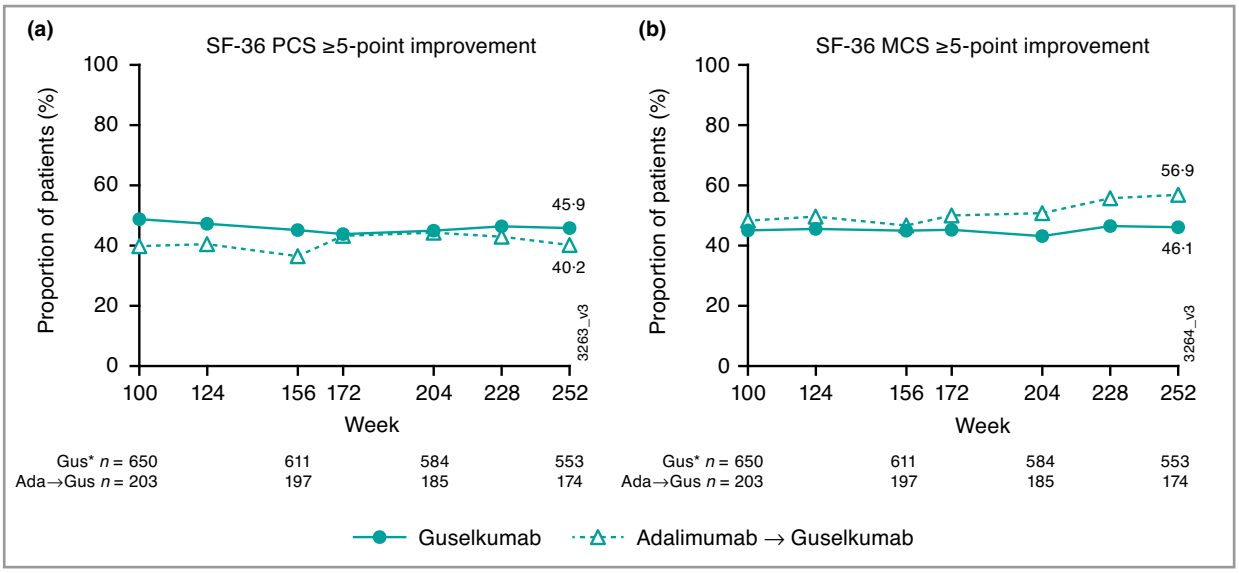

Figure 8 Proportion of patients achieving ≥5-point improvement in 36-Item Short Form Health Survey (SF-36) score from week 100 through week 252 in VOYAGE 2: (a) physical component summary (PCS); (b) mental component summary (MCS). *Includes patients randomized to guselkumab at baseline and those randomized to placebo at baseline who crossed over to receive guselkumab at week 16 (SF-36 scores not collected in VOYAGE 1). Ada→Gus, adalimumab crossover to guselkumab group; Gus, guselkumab group.

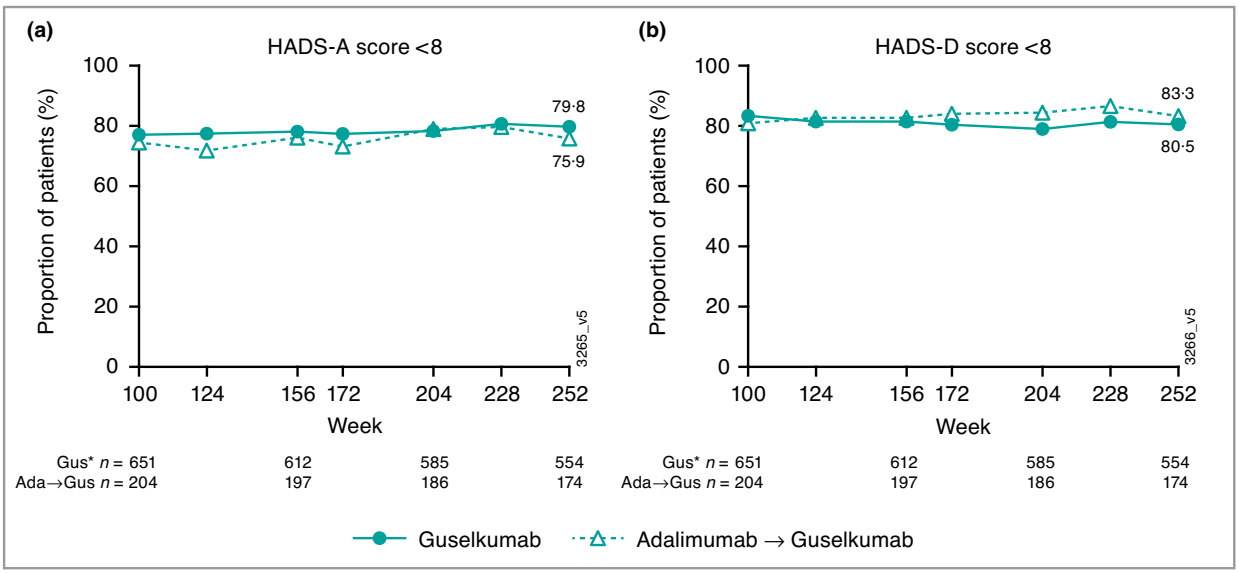

Figure 9 Proportion of patients with Hospital Anxiety and Depression Scale (HADS) score <8 from week 100 through week 252 in VOYAGE 2: (a) HADS-A < 8 (no anxiety); (b) HADS-D <8 (no depression). *Includes patients randomized to guselkumab at baseline and those randomized to placebo at baseline who crossed over to receive guselkumab at week 16 (HADS scores not collected in VOYAGE 1). Ada→Gus, adalimumab crossover to guselkumab group; Gus, guselkumab group.

in the adalimumab→guselkumab group were comparable (−7·4, −6·6, −5·1 and −8·4, respectively) (Figure 10).

Pooled safety

AEs were summarized for 1721 patients receiving continuous treatment with guselkumab, including 1221 in the guselkumab group and 500 in the adalimumab→guselkumab group through week 264. This represents a total of 7166 PY for guselkumab-treated patients (5254 PY in the guselkumab group and 1912 PY in the adalimumab→guselkumab group). Overall, 149 AEs per 100 PY (155 per 100 PY and 133 per 100 PY in the guselkumab and adalimumab→guselkumab groups, respectively) were reported through week 264. The most commonly reported AEs (> 10%) were nasopharyngitis, upper respiratory tract infection, hypertension and arthralgia.

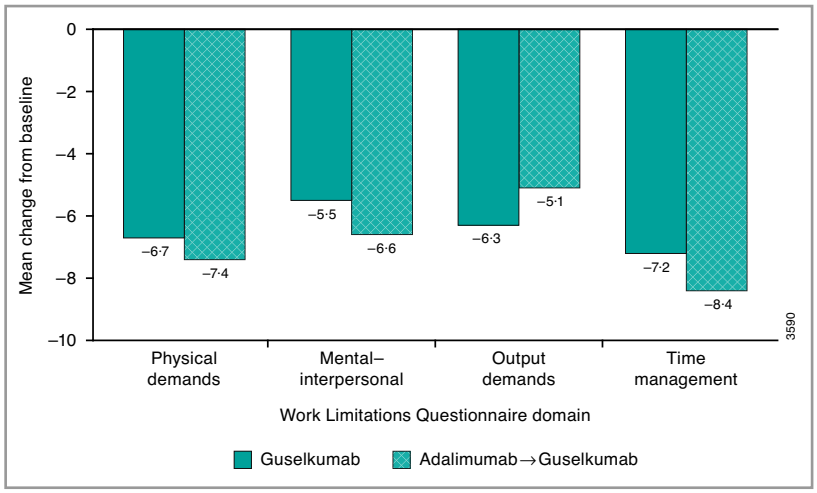

Figure 10 Mean change from baseline in component scores of the Work Limitations Questionnaire at week 252 in VOYAGE 2.

The rate per 100 PY of discontinuations due to AEs was 1·45 in the guselkumab group and 1·46 in the adalimumab→guselkumab group. The cumulative number of serious AEs was 5·01 per 100 PY in the combined guselkumab group (5·18 per 100 PY in the guselkumab group and 4·55 per 100 PY in the adalimumab→guselkumab group). Detailed safety data through 5 years are published elsewhere.[22]

Immunogenicity

Antibodies to guselkumab were detected in 14·4% (111 of 770) and 15·5% (146 of 943) of all treated patients in VOYAGE 1 and VOYAGE 2, respectively. Of those with anti-guselkumab antibodies, 4·5% (five of 111) in VOYAGE 1 and 5·5% (eight of 146) in VOYAGE 2 had neutralizing antibodies. The detection of antibodies to guselkumab was not associated with a reduction in the clinical efficacy of guselkumab (data not shown).

Discussion

Our findings based on over 1800 patients with moderate-to-severe psoriasis enrolled in two large phase III studies represent the largest cohort of patients evaluated for 5 years following treatment with an interleukin-23 inhibitor. These comprehensive results confirm that guselkumab, administered as a 100-mg subcutaneous injection at weeks 0 and 4 followed by dosing every 8 weeks, maintains long-term efficacy for at least 252 weeks in the majority of patients. After conservative TFRs were applied, over 50% achieved completely clear skin (PASI 100 and IGA 0), while over 80% maintained almost clear skin (PASI 90 and IGA 0/1) for the entire 5-year treatment period in both studies. Furthermore, over 80% of patients who received at least one dose of guselkumab continued treatment through 5 years.

Positive effects of guselkumab on HRQoL and general health were maintained through 5 years of consecutive guselkumab treatment. The benefits of guselkumab treatment, measured by physician-reported outcomes and PROs, were similar between studies, and responses for patients switched from adalimumab to guselkumab were comparable with those in the guselkumab group. This may have implications for treating patients in clinical practice, where switching from one biologic to another is sometimes needed to achieve optimal efficacy. Overall, the safety profile of guselkumab was generally consistent with previous reports, and no new concerns were noted based on the overall patterns and rates of AEs.

In VOYAGE 1, clinical response rates in the guselkumab group were maintained through week 252 regardless of the method of analysis used. This finding shows the robustness of the long-term efficacy of guselkumab in a large study population. Results based on the prespecified TFR and OBS methods, respectively, were similar: 84·1% and 86·6% achieved PASI 90, and 82·4% and 84·7% achieved IGA 0/1 among all guselkumab-treated patients at week 252. Not surprisingly, rates based on the most conservative NRI method in our study (where nonresponders were defined as patients with missing data for any reason) were lower than those based on the primary TFR and the secondary OBS analyses (e.g. 66·6% achieved PASI 90 and 65·2% achieved IGA 0/1). A similar trend in the maintenance of robust efficacy over time was observed for measures of complete skin clearance (PASI 100 and IGA 0) based on all analyses. It is notable that the NRI method used here is likely more conservative than the modified NRI methods reported in long-term extension studies of other biologics that had less stringent definitions of nonresponse.[23,24]

The PROs captured in VOYAGE 1 and/or VOYAGE 2 followed a pattern similar to that observed with clinical measures, namely improvement rates that were maintained with guselkumab treatment over time through week 252. About three-quarters of patients in the guselkumab group reported no impact of psoriasis on their lives as measured by DLQI 0/1 at week 252, which was similar to prior reports at weeks

100, 156 and 204 in both studies. The proportions of patients reporting PSSD summary scores of 0 (about 40% for symptom-free status and about 30% for sign-free status) were maintained from week 100 to week 252. Nearly half of all patients in VOYAGE 2 reported CMIs in general health status based on SF-36 PCS and MCS scores over that time period. The proportions of patients reporting no anxiety or depression at baseline (61·2% and 72·9%, respectively) increased by up to 15% by week 100 and were maintained through week 252 (79·8% and 80·5%, respectively). Finally, mean changes in WLQ component scores in guselkumab-treated patients indicated improvements in the ability to work that were sustained over time (i.e. decrease of 5–7 points across the four domains at week 252).

These analyses may have some limitations. For example, no comparator was evaluated in the long-term extension, and open-label treatment may introduce reporting bias for patients. Also, the follow-up period on guselkumab was slightly shorter (≤ 4 years for VOYAGE 1 and variable for VOYAGE 2) for patients who first received adalimumab before crossover to guselkumab. Patient retention is always a concern in long-term trials. As mentioned, < 20% of guselkumab-treated patients discontinued the study agent from baseline through 5 years across both trials; this high drug survival rate is driven mainly by the durability of efficacy and maintenance of long-term safety for guselkumab. Notably, these are actual drug survival rates (i.e. indicating the proportion of patients who continued treatment through the end of the study), unlike the probability of drug survival based on statistical modelling often reported in real-world registries.[25,26]

Our findings, which represent the culmination of the pivotal VOYAGE 1 and VOYAGE 2 trials conducted for 5 years, confirm the long-term control of psoriasis and consistent safety profile of guselkumab.[26] Therapeutic longevity via interleukin-23 inhibition was demonstrated by the maintenance of improvements in both clinical response and PROs over time. Therefore, guselkumab 100 mg every 8 weeks is an appropriate treatment choice for long-term use among the many available treatments for moderate-to-severe psoriasis.

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Appendix 1

Conflicts of interest

K.R. has served as an advisor and/or paid speaker for and/or participated in clinical trials sponsored by AbbVie, Almirall, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Eli Lilly, Forward Pharma, Galderma, Gilead, Janssen-Cilag, Kyowa Kirin, Leo, Medac, Novartis, Ocean Pharma, Pfizer, Sanofi, UCB Pharma; K.R. is co-founder of Moonlake Immunotherapeutics. K.B.G. has received research or grant support from AbbVie, Amgen, Boehringer Ingelheim, Celgene, Eli Lilly, Janssen, Novartis and UCB Pharma; and honoraria for consultation from AbbVie, Amgen, Boehringer Ingelheim, Celgene, Dermira, Eli Lilly, Janssen, Novartis and UCB Pharma. B.E.S. has received honoraria or research grants as a consultant for AbbVie, Almirall, Amgen, Arcutis, Arena, Aristea, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Dermavant, Dermira, Eli Lilly, Equillium, Janssen, LEO, Meiji Seika Pharma, Mindera, Novartis, Pfizer, GlaxoSmithKline, UCB Pharma, Sun Pharma, Ortho Dermatologics, Regeneron and Sanofi Genzyme; as a speaker for AbbVie, Amgen, Eli Lilly, Janssen and Ortho Dermatologics; as scientific director for the Corrona Psoriasis Registry; as an investigator for Dermavant, AbbVie, Corrona Psoriasis Registry, Dermira, Cara and Novartis; and as Editor-in-Chief at the *Journal of Psoriasis and Psoriatic Arthritis*. A.W.A. has served as a research investigator and/or scientific advisor to AbbVie, Boehringer Ingelheim, BMS, EPI Health, Incyte, LEO, UCB, Janssen, Lilly, Novartis, Ortho Dermatologics, Sun, Dermavant, Dermira, Sanofi, Regeneron, Pfizer and Modmed. M.M., Y.K.S., Y.Y., C.H. and Y.W.Y. are employees of Janssen and own stock in Johnson & Johnson, of which Janssen is a subsidiary. P.F. has received grant support from AbbVie, Amgen, Celgene, Janssen, LEO Pharma, Lilly, Merck, Novartis, Pfizer, Sanofi and Sun Pharma; has served as an investigator for AbbVie, Amgen, Arcutis, Aslan, AstraZeneca, BMS, Boehringer Ingelheim, Botanix, Celgene, Celtaxsys, CSL, Cutanea, Dermira, Galderma, Genentech, GSK, Hexima, Janssen, LEO Pharma, Lilly, Merck, Novartis, Pfizer, Regeneron Pharmaceuticals Inc., Reistone, Roche, Sanofi, Sun Pharma, UCB Pharma and Valeant; has served on advisory boards for AbbVie, Amgen, BMS, Celgene, Galderma, GSK, Janssen, LEO Pharma, Lilly, Merck, Novartis, Pfizer, Sanofi, Sun Pharma, UCB Pharma and Valeant; has served as a consultant for BMS, Galderma, Janssen, LEO Pharma, Lilly, Novartis, Pfizer, Roche and UCB Pharma; has received travel grants from AbbVie, Galderma, Janssen, LEO Pharma, Lilly, Merck, Novartis, Pfizer, Roche, Sun Pharma and Sanofi; and has served as a speaker for or received honoraria from AbbVie, Celgene, Galderma, GSK, Janssen, LEO Pharma, Lilly, Merck, Novartis, Pfizer, Roche and Valeant. C.E.M.G. has received honoraria as an advisory board member and/or speaker from AbbVie, Almirall, Bristol Myers Squibb, Eli Lilly, Galderma, Janssen, LEO, Novartis, Pfizer, Sun Pharma and UCB Pharma and research grants from AbbVie, Celgene, Eli Lilly, Janssen, LEO, Novartis, Pfizer and Sandoz.

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