

## ONLINE SUPPLEMENT

### Methods

This phase IIIb, randomized, double-blind study was conducted at 84 European sites (Belgium-1, Bulgaria-5, France-3, Germany-5, Hungary-6, Israel-4, Italy-3, Poland-6, Portugal-1, Russia-19, Spain-11, Ukraine-15, United Kingdom-5).

Additional secondary endpoints included American College of Rheumatology 70% improvement response, proportions of patients achieving 20% improvement in the ACR components, proportions of patients with resolution of enthesitis (Leeds Enthesitis Index score=0) or dactylitis (Dactylitis Severity Score=0) among participants with respective scores  $\geq 1$  at baseline, Investigator's Global Assessment of psoriasis (IGA score=0/1 and  $\geq 2$ -grade improvement from baseline), and PASI75/PASI90 responses in patients with  $\geq 3\%$  body surface area and IGA  $\geq 2$  at baseline, 36-item Short-Form Health Survey Mental Component Summary (MCS) change scores, proportion of patients with  $\geq 4$ -point increase (improvement) in Functional Assessment of Chronic Illness Therapy-Fatigue scores; change in Disease Activity in Psoriatic Arthritis (DAPSA) score; and overall disease status per Minimal Disease Activity (MDA) and Very Low Disease Activity (VLDA) composite indices. Additional post hoc analyses determined the proportions of patients with  $\geq 5$ -point improvement in SF-36 PCS and MCS scores; patients with HAQ-DI response (improvement  $\geq 0.35$  in patients with baseline HAQ-DI  $\geq 0.35$ ); and patients achieving DAPSA low disease activity (LDA;  $\leq 14$ ) and remission ( $\leq 4$ ).

Safety outcomes included adverse events (AEs), serious AEs, AEs necessitating study drug discontinuation, infections, serious infections, injection-site reactions, malignancies, and laboratory abnormalities per National Cancer Institute Common Terminology Criteria for Adverse Events. Treatment-emergent AEs, i.e., those that occurred or worsened after the first dose of study intervention, were coded using the Medical Dictionary for Regulatory Activities (version 23.0). Major adverse cardiovascular events were defined as nonfatal stroke, nonfatal myocardial infarction, or cardiac death.

Assuming week24 ACR20 response rates of 41% and 20%, respectively, in the guselkumab and placebo arms, respective sample sizes of 163 and 82 were estimated to provide 90% power to detect a treatment difference.

Treatment group comparisons utilized a Cochran-Mantel Haenszel test stratified at the study level by baseline use of csDMARDs (yes/no) and number of prior tumor necrosis factor-inhibitors (TNFi; 1 vs. 2) for binary endpoints or an MMRM model (missing-at-random assumption) for continuous data. Explanatory variables of the MMRM model included treatment group, an interaction term of visit with treatment group, an interaction term of visit with baseline use of csDMARDs (yes/no), an interaction term of visit with number of prior TNFi (1 vs. 2), and an interaction term of visit with baseline score.

**Supplemental Table 1. Summary of clinical laboratory abnormalities reported as AEs by maximum NCI-CTCAE grade<sup>a</sup> through week56 of the COSMOS study**

	Placebo <sup>b</sup>	Placebo→Guselkumab		Total	Randomized to Guselkumab <sup>e</sup>	
	(Week 0-24)	(Week 16-56) <sup>c</sup>	(Week 24-56) <sup>d</sup>		(Week 0-24)	(Week 0-56)
<b>Randomized participants by treatment received</b>	96	45	45	90	189	189
<b>Participants with ≥1 AE</b>						
Neutrophil count decreased	0	2 (4.4%)	0	2 (2.2%)	1 (0.5%)	2 (1.1%)
Neutropenia	0	0	0	0	3 (1.6%)	3 (1.6%)
White blood cell count decreased	1 (1.0%)	2 (4.4%)	0	2 (2.2%)	1 (0.5%)	2 (1.1%)
Leukopenia	0	0	0	0	1 (0.5%)	2 (1.1%)
Lymphopenia	1 (1.0%)	1 (2.2%)	0	1 (1.1%)	1 (0.5%)	1 (0.5%)
Alanine aminotransferase increased	4 (4.2%)	1 (2.2%)	3 (6.7%)	4 (4.4%)	5 (2.6%)	8 (4.2%)
Aspartate aminotransferase increased	2 (2.1%)	0	2 (4.4%)	2 (2.2%)	1 (0.5%)	4 (2.1%)
<b>Participants with ≥1 postbaseline assessment</b>	<b>95</b>	<b>45</b>	<b>45</b>	<b>90</b>	<b>188</b>	<b>189</b>
<b>Neutrophil Count Decreased</b>						
Grade 1 (<LLN–1.5 x 10 <sup>9</sup> /L)	4 (4.2%)	4 (8.9%)	2 (4.4%)	6 (6.7%)	9 (4.8%)	13 (6.9%)
Grade 2 (<1.5–1.0 x 10 <sup>9</sup> /L)	2 (2.1%)	2 (4.4%)	1 (2.2%)	3 (3.3%)	6 (3.2%)	7 (3.7%)
Grade 3 (<1.0–0.5 x 10 <sup>9</sup> /L)	0	1 (2.2%)	0	1 (1.1%)	0	0
Grade 4 (<0.5 x 10 <sup>9</sup> /L)	0	0	0	0	0	0
<b>White Blood Cell Count Decreased</b>						
Grade 1 (<LLN–3.0x 10 <sup>9</sup> /L)	3 (3.2%)	2 (4.4%)	1 (2.2%)	3 (3.3%)	10 (5.3%)	16 (8.5%)
Grade 2 (<3.0–2.0x 10 <sup>9</sup> /L)	1 (1.1%)	2 (4.4%)	0	2 (2.2%)	1 (0.5%)	3 (1.6%)
Grade 3 or 4 (<2.0x 10 <sup>9</sup> /L)	0	0	0	0	0	0
<b>Alanine Aminotransferase Increased</b>				0		
Grade 1 (>ULN–3.0x ULN)	16 (16.8%)	7 (15.6%)	14 (31.1%)	21 (23.3%)	46 (24.5%)	65 (34.4%)
Grade 2 (>3.0–5.0x ULN)	0	0	1 (2.2%)	1 (1.1%)	1 (0.5%)	1 (0.5%)
Grade 3 (>5.0–20.0x ULN)	1 (1.1%)	0	2 (4.4%)	2 (2.2%)	0	0
Grade 4 (>20.0x ULN)	1 (1.1%)	1 (2.2%)	0	1 (1.1%)	0	0
<b>Aspartate Aminotransferase Increased</b>						
Grade 1 (>ULN–3.0x ULN)	14 (14.7%)	6 (13.3%)	15 (33.3%)	21 (23.3%)	33 (17.6%)	48 (25.4%)
Grade 2 (>3.0–5.0x ULN)	0	1 (2.2%)	0	1 (1.1%)	1 (0.5%)	1 (0.5%)
Grade 3 (>5.0–20.0x ULN)	1 (1.1%)	0	2 (4.4%)	2 (2.2%)	0	0
Grade 4 (>20.0x ULN)	1 (1.1%)	1 (2.2%)	0	1 (1.1%)	0	0

**Supplemental Table 1. Summary of clinical laboratory abnormalities reported as AEs by maximum NCI-CTCAE grade<sup>a</sup> through week56 of the COSMOS study**

	Placebo <sup>b</sup>	Placebo→Guselkumab		Randomized to Guselkumab <sup>e</sup>		
	(Week 0-24)	(Week 16-56) <sup>c</sup>	(Week 24-56) <sup>d</sup>	Total	(Week 0-24)	(Week 0-56)

<sup>a</sup> Adverse events were coded using the Medical Dictionary for Regulatory Actions (MedDRA), Version 23.0. Laboratory findings were evaluated using National Cancer Institute Common Terminology Criteria for AEs (NCI-CTCAE), Version 4.03.

<sup>b</sup> AEs that occurred during placebo treatment in placebo-randomized patients.

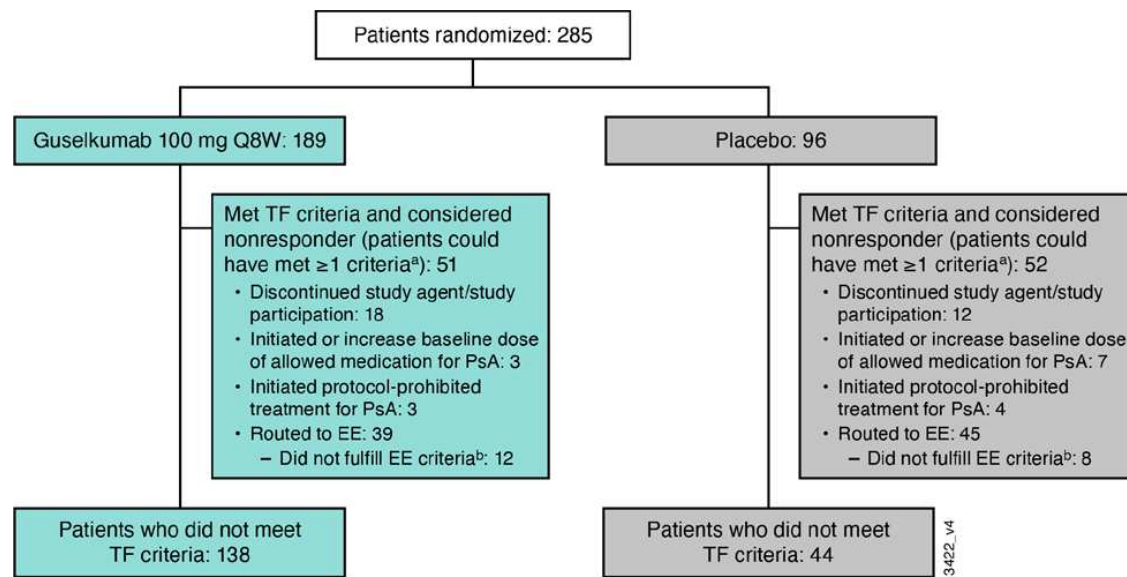
<sup>c</sup> AEs that occurred in placebo-randomized patients who entered early escape at week 16 and received  $\geq 1$  guselkumab administration.

<sup>d</sup> AEs that occurred in placebo-randomized patients who crossed over to guselkumab at week 24 received  $\geq 1$  guselkumab administration.

<sup>e</sup> Includes guselkumab-randomized patients who received  $\geq 1$  guselkumab administration and those who received an EE placebo injection at week 16.

AE, adverse event; EE, early escape, LLN, lower limit of normal, NCI-CTCAE, National Cancer Institute Common Terminology Criteria for Adverse Events, ULN, upper limit of normal

**Supplemental Figure 1. Patients included in the Primary analysis population.** Treated participants analyzed by randomized group, with those meeting treatment failure (TF) criteria considered nonresponders. csDMARDs, conventional synthetic disease-modifying antirheumatic drugs; EE, early escape; PsA, psoriatic arthritis; Q8W, every 8 weeks

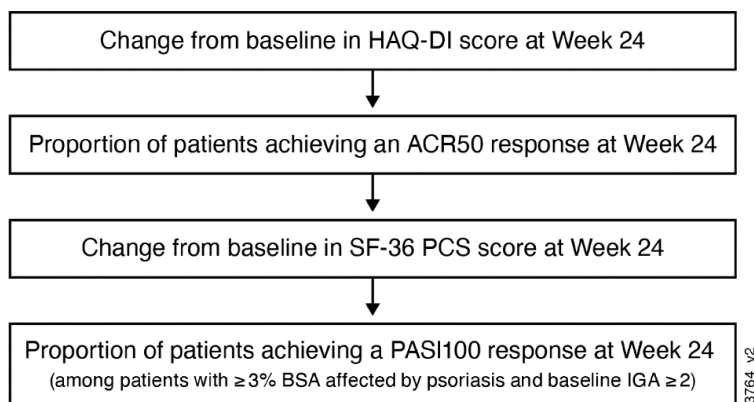


<sup>a</sup> TF criteria were: discontinuation of study agent/study participation for any reason, initiation of or increase in the dose of allowed csDMARDs or oral corticosteroids for PsA, initiation of protocol-prohibited medications/therapies for PsA, or met EE criteria.

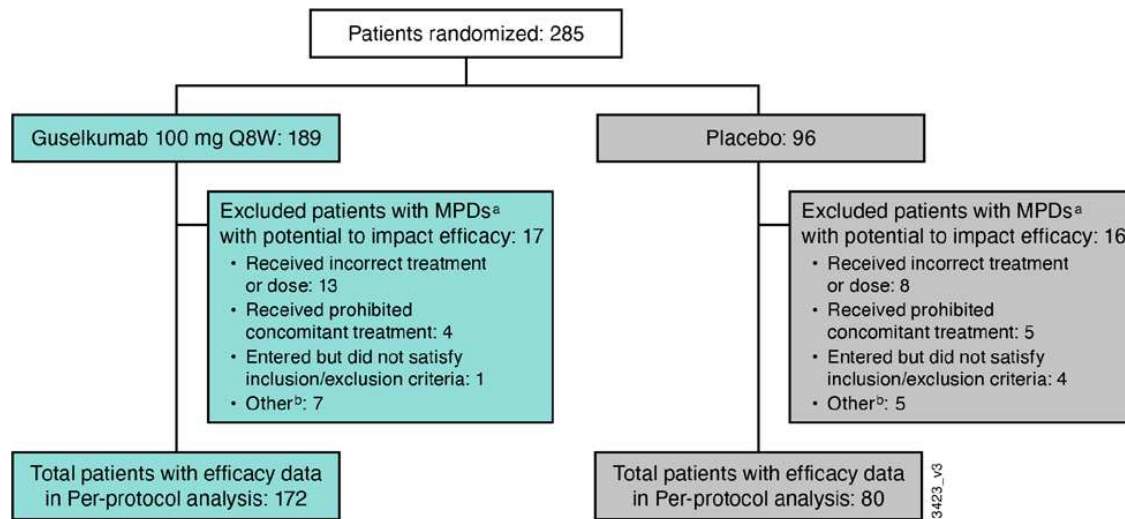
<sup>b</sup> Patients who were improperly classified as having met the EE criteria and were considered nonresponders in the primary endpoint analysis.

**Supplemental Figure 2. Hierarchical ordering of major secondary endpoints in COSMOS.**

ACR50,  $\geq 50\%$  improvement in American College of Rheumatology response criteria; BSA, body surface area; HAQ-DI, Health Assessment Questionnaire-Disability Index; IGA, Investigator's Global Assessment; PASI100, 100% improvement in Psoriasis Area and Severity Index; SF-36 PCS, 36-item Short-Form Health Survey Physical Component Summary



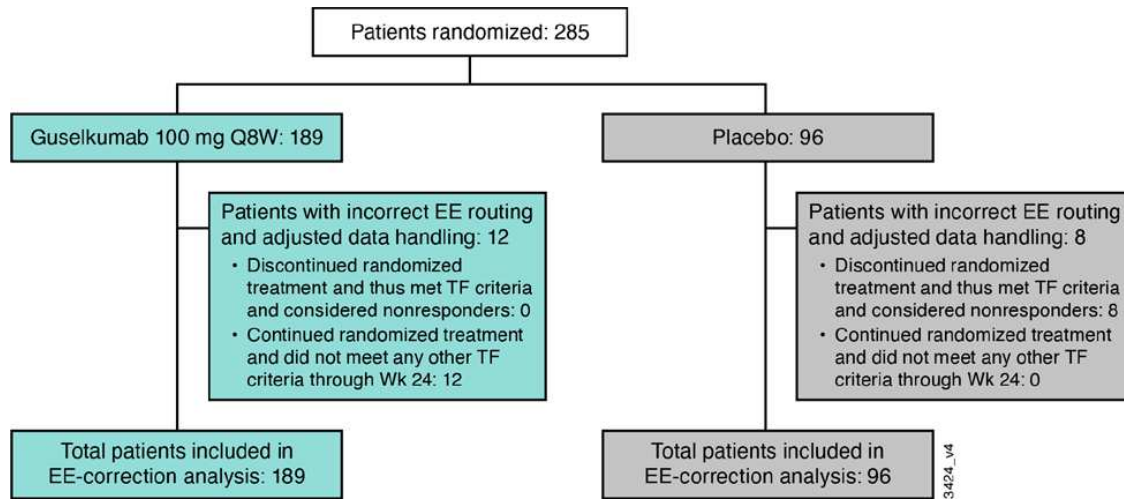
**Supplemental Figure 3. Patients included in the Per-protocol population.** Treated participants according to randomized group, excluding those with major protocol deviations (MPDs) with potential to impact efficacy. CRP, C-reactive protein; csDMARDs, conventional synthetic disease-modifying antirheumatic drugs; Q8W, every 8 weeks



<sup>a</sup> Patients could have >1 MPD that led to their exclusion from the Per-protocol analysis.

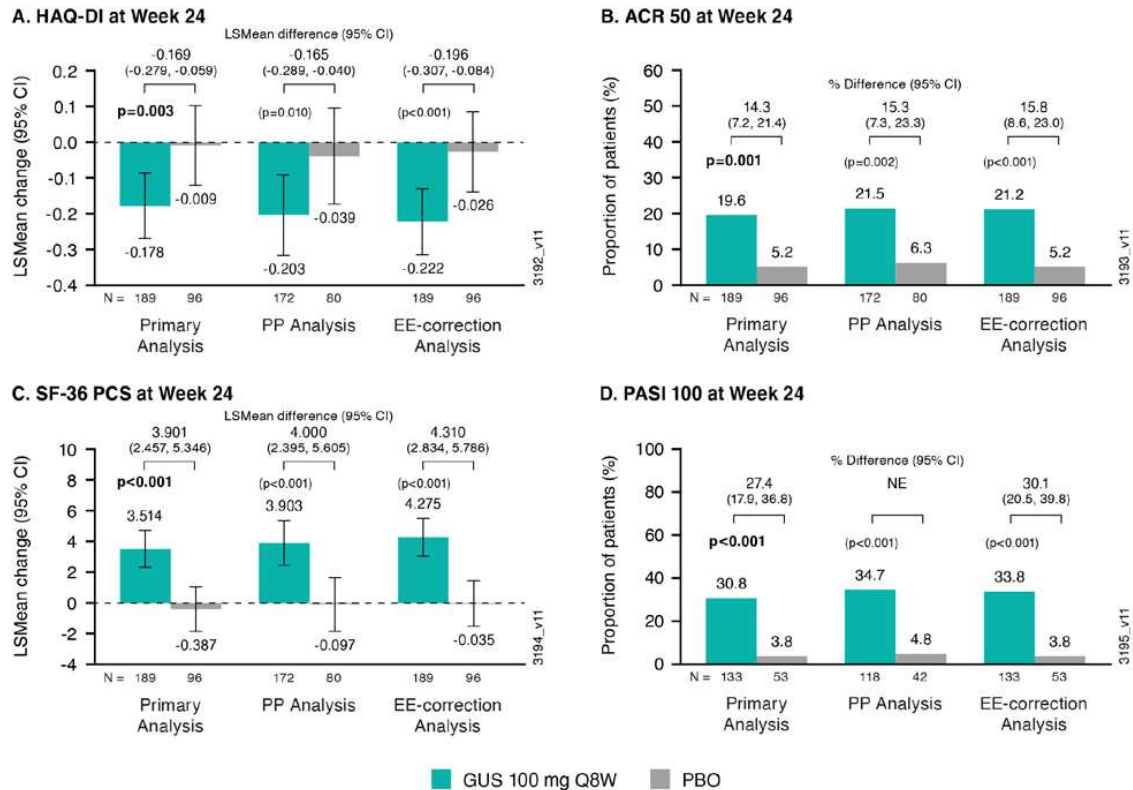
<sup>b</sup> Reasons in this category included lack of serum samples for CRP measurement (guselkumab, n=4; placebo, n=1), not receiving prior csDMARDs as indicated at screening (guselkumab, n=2; placebo, n=1), and efficacy assessments performed by someone other than the study-trained investigator (guselkumab, n=1; placebo, n=1).

**Supplemental Figure 4. Patients included in the EE-correction population.** Treated participants analyzed by randomized group, adjusted for incorrect early escape (EE) assignment. Q8W, every 8 weeks; TF, treatment failure



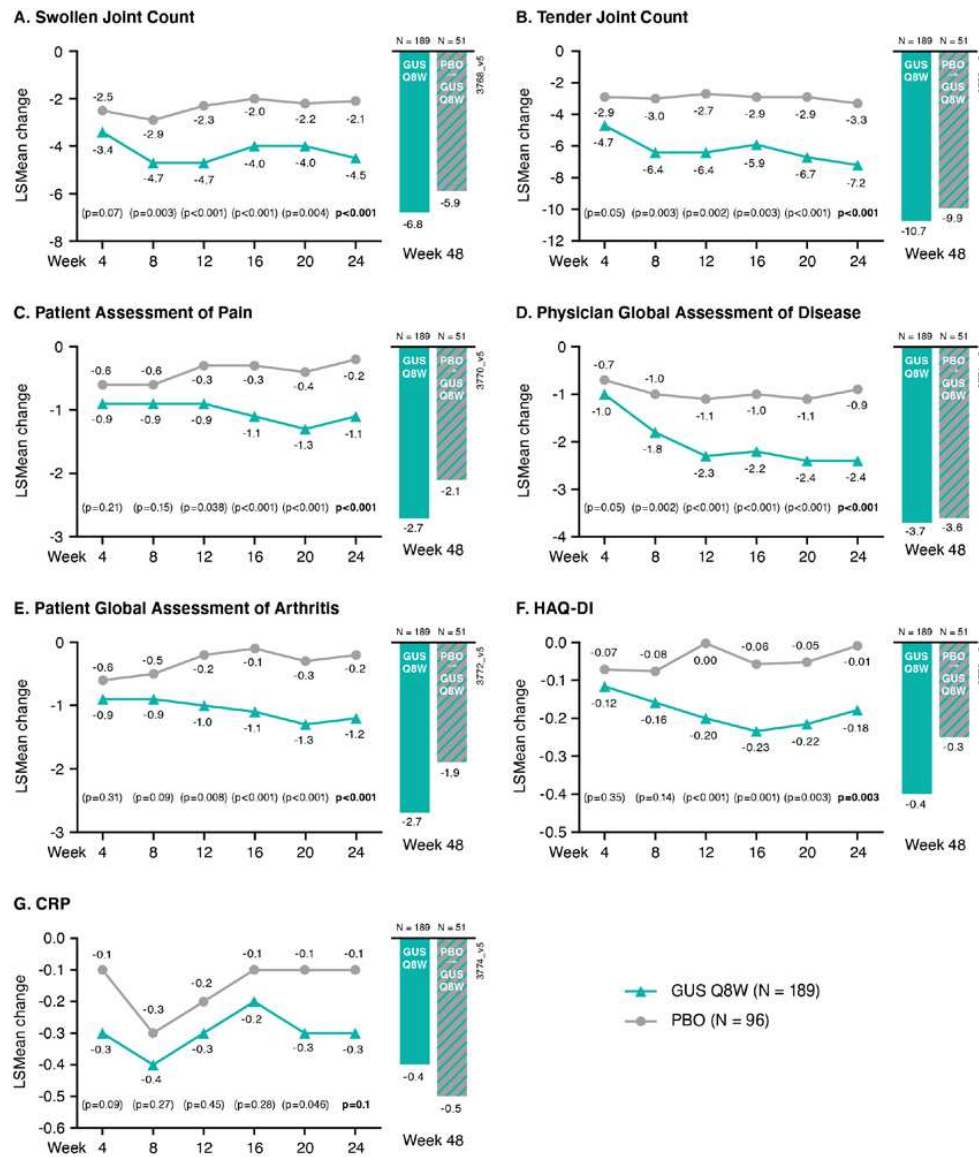


**Supplemental Figure 5. Key secondary outcomes through week 24 of COSMOS.** Results at week 24 across the Primary, PP, and EE-correction analyses for LSmean HAQ-DI change scores (A), ACR50 response (B), LSmean SF-36 PCS change scores (C), and PASI100 response (D). ACR50,  $\geq 50\%$  improvement in American College of Rheumatology criteria; CI, confidence interval; EE, early escape; GUS, guselkumab; HAQ-DI, Health Assessment Questionnaire-Disability Index; LS, least squares; PASI100, 100% improvement in Psoriasis Area and Severity Index; PBO, placebo; PP, per-protocol; Q&W, every 8 weeks; SF-36 PCS, 36-item Short-Form Health Survey Physical Component Summary



Bolded p values are adjusted for multiplicity of testing; p values shown in parentheses are not adjusted for multiplicity of testing  
NE – not estimable

**Supplemental Figure 6. Changes in ACR components through week 48 of COSMOS.** Primary analysis through week24 and post hoc NRI analysis at week48 of LSmean change and mean change in swollen joint count (A), tender joint count (B), patient assessment of pain (VAS 0-100) (C), physician global assessment of disease (VAS 0-100) (D), patient assessment of arthritis (VAS 0-100) (E), HAQ-DI score (F), and CRP (mg/dL) (G). After week 24, analyses were performed using NRI (including imputation of EE patients as nonresponders in the guselkumab group; see Patients and Methods). Results for the placebo → guselkumab group at week 48 are reported for patients who did not enter EE and crossed over to guselkumab at week24. ACR, American College of Rheumatology; CRP, C-reactive protein; EE, early escape; GUS, guselkumab; HAQ-DI, Health Assessment Questionnaire-Disability Index; LS, least squares; NRI, nonresponder imputation; PBO, placebo; Q8W, every 8 weeks; VAS, visual analog scale



Bolded p values are adjusted for multiplicity of testing; p values shown in parentheses are not adjusted for multiplicity of testing