INTRAVENOUS AND SUBCUTANEOUS GUSELKUMAB INDUCTION ARE SIMILARLY EFFICACIOUS IN PATIENTS WITH ULCERATIVE COLITIS ACROSS WEIGHT QUARTILE AND BMI SUBGROUPS: WEEK 12 RESULTS FROM THE PHASE 3 QUASAR AND ASTRO STUDIES

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Key Takeaways

- Guselkumab IV and SC induction were similarly effective in participants with moderately to severely active UC compared with placebo at Week 12 regardless of participants' baseline body weight or BMI
- Among Week 12 clinical responders, similar efficacy was observed at 1 year (Week 44 and 48 for QUASAR and ASTRO, respectively) between participants treated with either guselkumab IV or SC induction regardless of participants' baseline body weight
- Efficacy of guselkumab does not appear to be impacted by body weight or BMI, irrespective of route of induction treatment administration

Background

- Guselkumab is a dual-acting IL-23p19 subunit inhibitor that potently neutralizes IL-23 and binds to CD64, a receptor on immune cells that produce IL-23[1]
- The similar efficacy and safety of intravenous (IV) and subcutaneous (SC) induction with guselkumab in participants with moderately to severely active ulcerative colitis (UC) has been established in the phase 3 QUASAR and ASTRO studies[2,3]
- Obesity has the potential to impact the pharmacokinetic and pharmacodynamic parameters of subcutaneously administered medications[4-7]

Objective

The aim of this post-hoc analysis was to determine whether body mass and body mass index (BMI) in participants with UC differentially affect the efficacy of guselkumab SC induction compared to IV induction

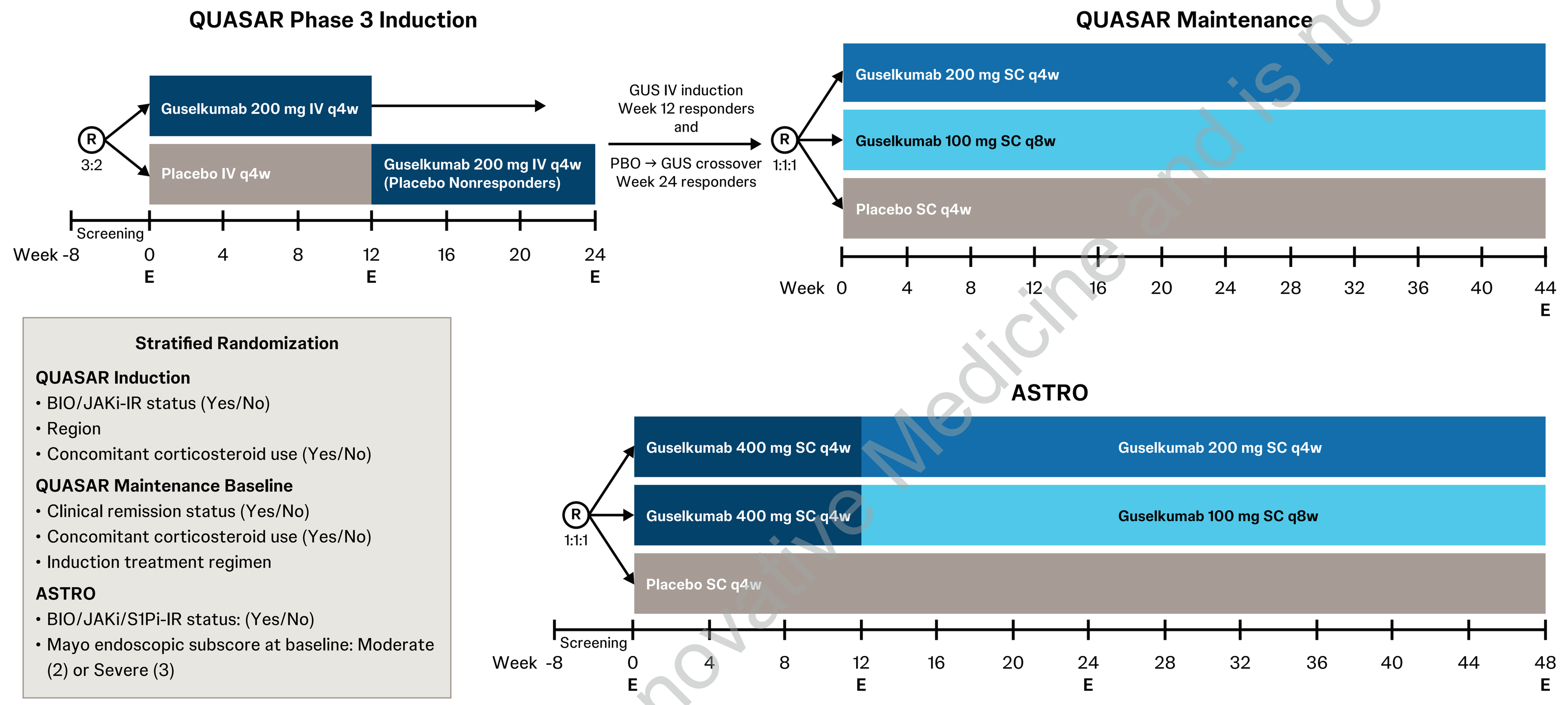
Study Designs Through Week 44/48

Key Inclusion Criteria:

- Baseline modified Mayo score of 5 to 9
- Induction baseline Mayo rectal bleeding subscore ≥1, Mayo endoscopic subscore ≥2 (centrally reviewed)
- Inadequate response/intolerance to oral corticosteroids, 6-MP/AZA, biologics,[a] JAKi, or S1Pi (ASTRO only)

Endpoints

- **Clinical response:** A decrease from baseline in the modified Mayo score by ≥ 30% and ≥ 2 points, with either a ≥ 1-point decrease from baseline in the rectal bleeding subscore or a rectal bleeding subscore of 0 or 1
- **Clinical remission:** Stool frequency subscore of 0 or 1 and not increased from baseline, a rectal bleeding subscore of 0, and an endoscopy subscore of 0, or 1 with no friability present on the endoscopy
- **Endoscopic improvement:** Endoscopy subscore of 0, or 1 with no friability present on the endoscopy
- **Endoscopic remission:** Endoscopy subscore of 0
- **Symptomatic remission:** Combination stool frequency subscore of 0 or 1 and a rectal bleeding subscore of 0, where the stool frequency subscore has not increased from induction baseline



6-MP= 6-mercaptopurine; AZA= azathioprine; BIO= biologic; E= endoscopy; GUS= guselkumab; IR= inadequate response/intolerance; JAKi= Janus kinase inhibitor; PBO= placebo; q4w=every 4 weeks; q8w=every 8 weeks; R= randomization; S1Pi= sphingosine-1-phosphate inhibitor. [a]Biologic therapies: TNF antagonists or vedolizumab. Note: QUASAR induction was comprised of two induction studies; the phase 3 induction study is shown because the Week 12 efficacy analyses presented here are focused on this population. Blinded dose adjustment was conducted in QUASAR Maintenance between Weeks 8-32 in participants meeting prespecified criteria; the corresponding data handling rules were suspended for the Week 44 analyses shown here. ASTRO included data handling rules for rescue treatment at Week 16 in participants meeting prespecified criteria; the corresponding data handling rules were suspended for the Week 48 analyses shown here. Corticosteroid tapering was required per protocol starting at Weeks 0 and 12 in QUASAR Maintenance and ASTRO, respectively. The full study designs can be found in the primary trial publications.

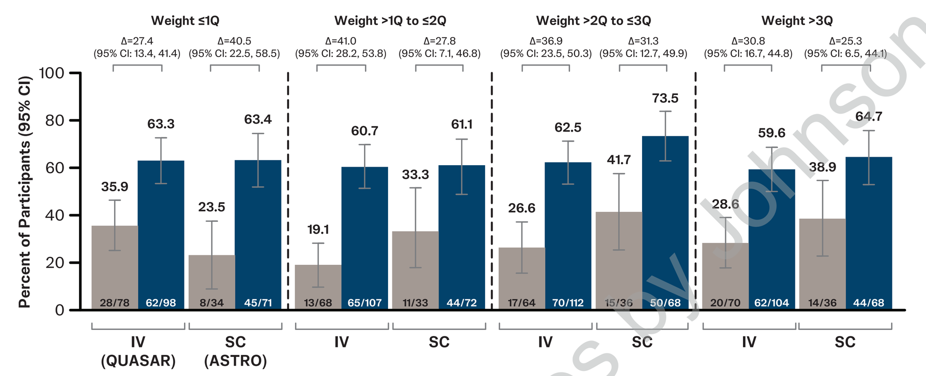
Results

Baseline Demographics and Disease Characteristics

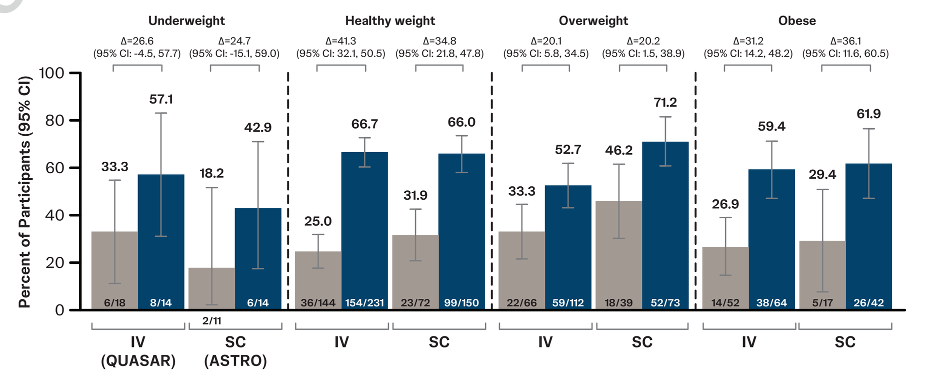
	QUASAR[a]	ASTRO
Primary analysis set	**Total N=701**	**Total N=418**
Demographics		
Weight in kg, mean (SD)	72.45 (16.84)	71.40 (16.45)
Median (Range)	70.6 (38.0; 127.1)	69.0 (37.4; 121.6)
Body mass index in kg/m^2, mean (SD)	24.92 (4.99)	24.7 (4.96)
Age in years, mean (SD)	40.5 (13.72)	41.7 (14.22)
Male, n (%)	399 (56.9%)	256 (61.2%)
Characteristics		
UC disease duration in years, mean (SD)	7.52 (7.282)	7.56 (6.674)
Modified Mayo score (0-9),[b] mean (SD)	6.9 (1.10)	6.7 (1.15)
Modified Mayo score of 7-9 (severe),[b] n (%)	452 (64.5%)	259 (62.1%)
Mayo endoscopic subscore of 3 (severe), n (%)	476 (67.9%)	234 (56.0%)
Extensive UC, n (%)	335 (47.8%)	224 (53.6%)
Biomarkers		
C-reactive protein in mg/L,[c] median (IQR)	4.2 (1.5; 10.1)	4.1 (1.4; 8.9)
Fecal calprotectin in µg/g,[d] median (IQR)	1641.0 (647.0; 3304.0)	1566.0 (641.0; 2964.0)
Concomitant UC medications at baseline, n (%)		
6-MP/AZA	138 (19.7%)	82 (19.6%)
MTX	8 (1.1%)	2 (0.5%)
Oral corticosteroids	302 (43.1%)	137 (32.8%)
BIO/JAK inhibitor therapy history, n (%)		
BIO/JAK inhibitor naïve	339 (48.4%)	243 (58.1%)
History of inadequate response/intolerance to BIO/JAK inhibitor	344 (49.1%)	168 (40.2%)

IQR= interquartile range; SD= standard deviation.
[a]Includes all participants in QUASAR induction study 2. [b]Based on N=701 for QUASAR and N=417 for ASTRO. [c]Based on N=694 for QUASAR and N=414 for ASTRO. [d]Based on N=623 for QUASAR and N=385 for ASTRO.

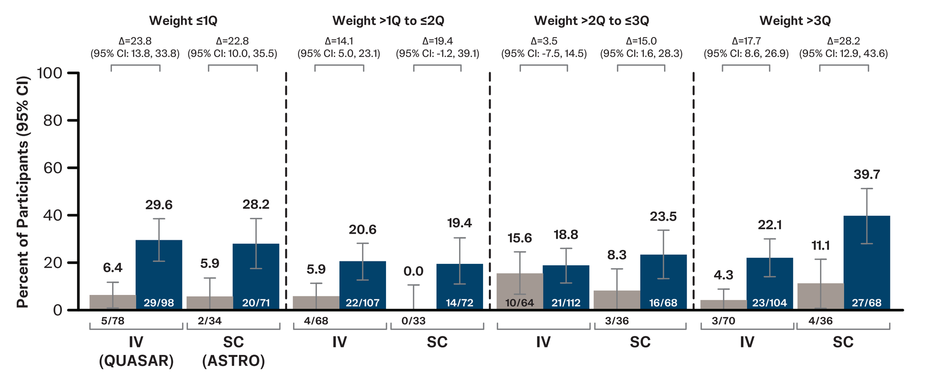
Clinical response at Week 12 by baseline weight



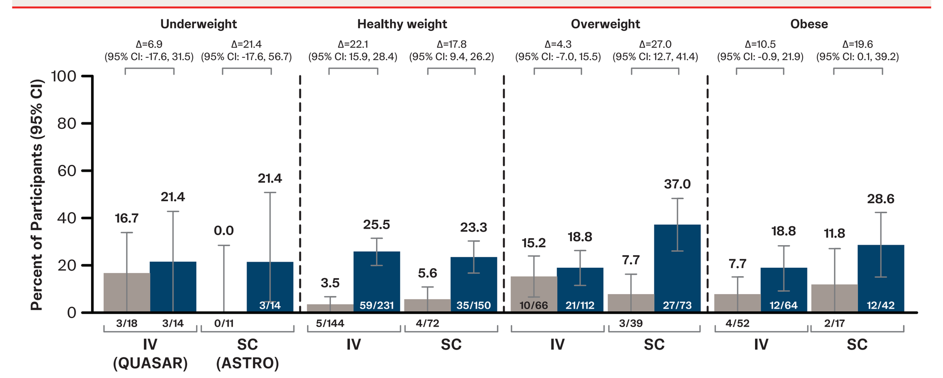
Clinical response at Week 12 by baseline BMI



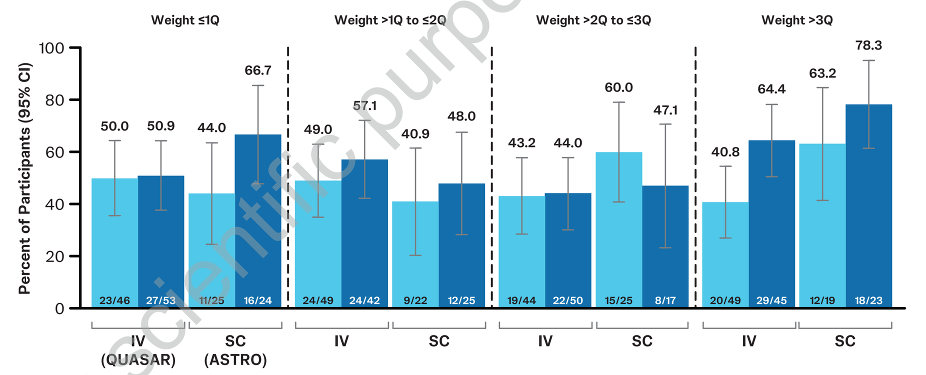
Clinical remission at Week 12 by baseline weight



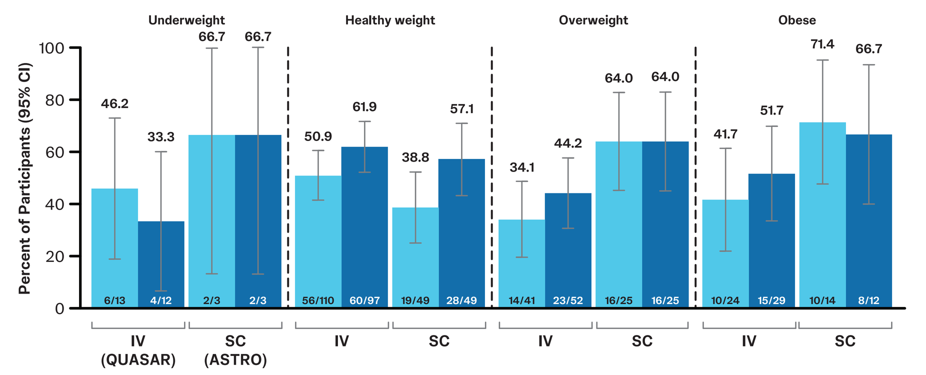
Clinical remission at Week 12 by baseline BMI



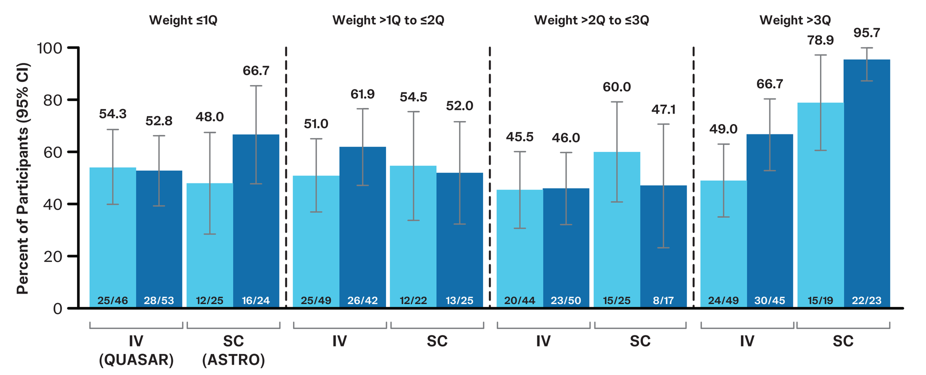
Clinical remission at Week 44/48 by baseline weight



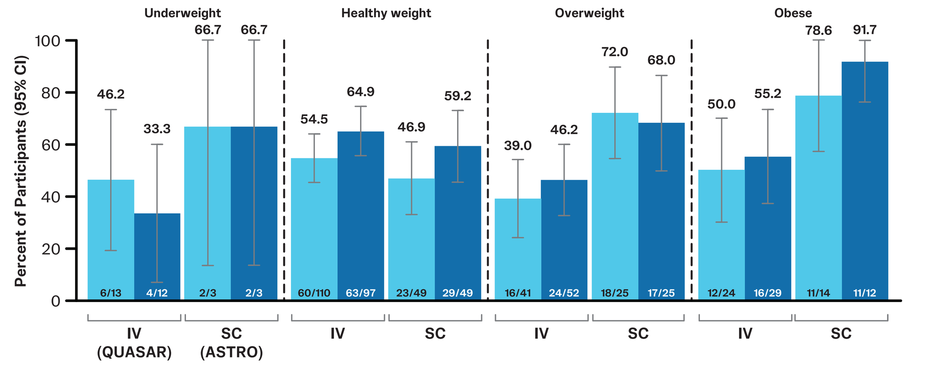
Clinical remission at Week 44/48 by baseline BMI



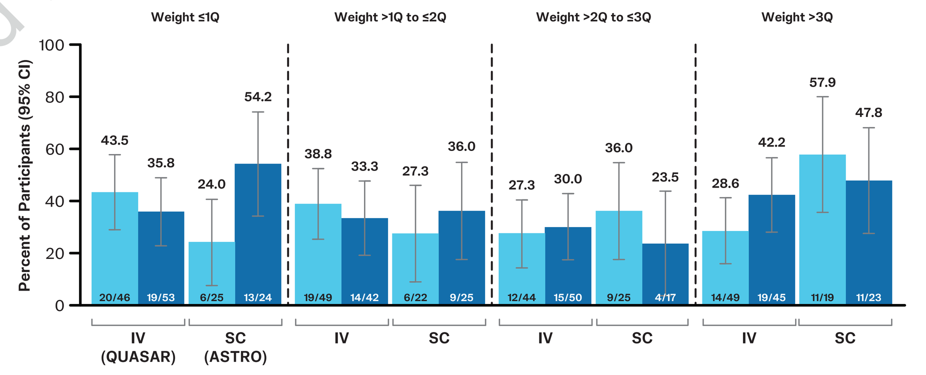
Endoscopic improvement at Week 44/48 by baseline weight



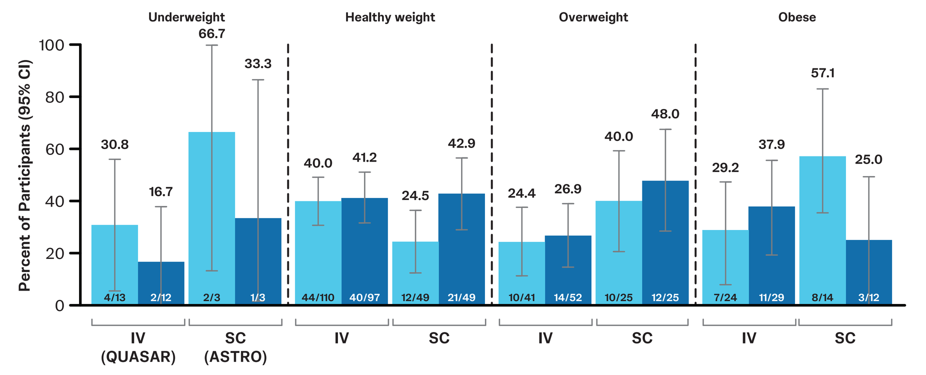
Endoscopic improvement at Week 44/48 by baseline BMI



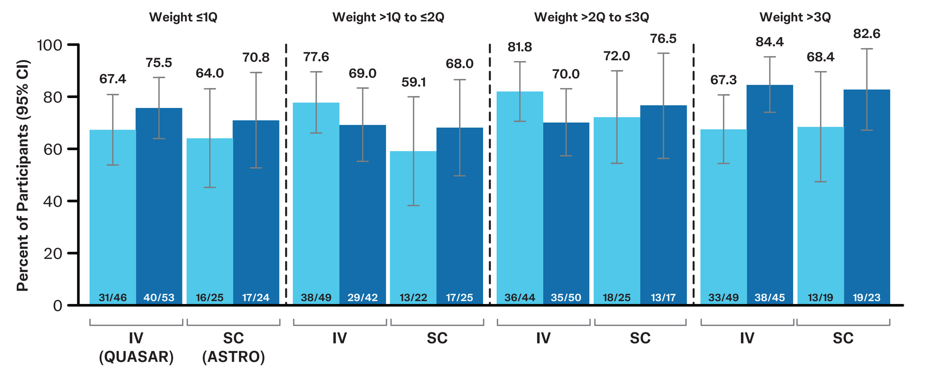
Endoscopic remission at Week 44/48 by baseline weight



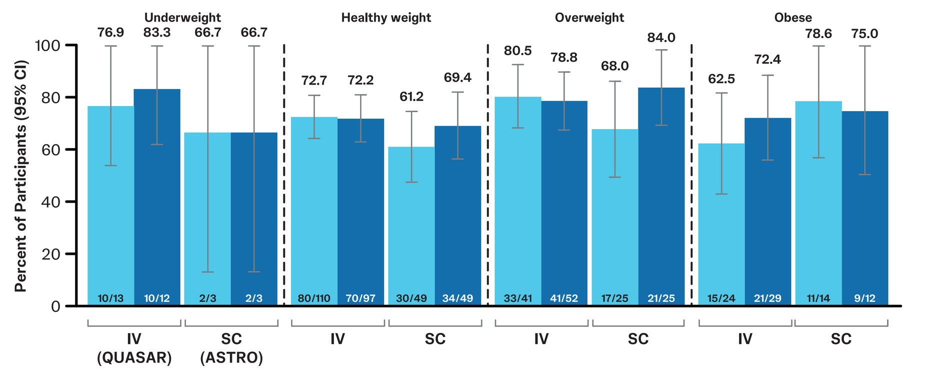
Endoscopic remission at Week 44/48 by baseline BMI



Symptomatic remission at Week 44/48 by baseline weight



Symptomatic remission at Week 44/48 by baseline BMI



Placebo (IV or SC) | GUS Induction (200 mg IV or 400 mg SC) → 100 mg SC q8w | GUS Induction (200 mg IV or 400 mg SC) → 200 mg SC q4w | GUS Induction (200 mg IV or 400 mg SC)

CI= confidence interval; Q= quartile. Note: Standard BMI subgroups were used (i.e., underweight [<18 kg/m^2], healthy weight [≥18 to <25 kg/m^2], overweight [≥25 to <30 kg/m^2], and obese [≥30 kg/m^2]). Weight quartiles were calculated for each timepoint using only the treatment arms assessed at that timepoint (i.e., placebo and guselkumab for Week 12 and only guselkumab for Week 44/48). Weight quartiles for Week 12 analyses were based on participants in the primary analysis set as follows: QUASAR—59.2 kg (Q1), 70.6 kg (Q2), 84.0 kg (Q3); and ASTRO—59.80 kg (Q1), 69.00 kg (Q2), 81.60 kg (Q3). For Week 44 endpoints in QUASAR, nonresponder imputation for participants having dose adjustment was suspended; weight quartiles for Week 44 endpoints are based on participants in the randomized full analysis set as follows: 58.0 kg (Q1), 69.0 kg (Q2), 82.1 kg (Q3). For Week 48 endpoints in ASTRO, nonresponder imputation for participants meeting rescue criteria was suspended and analysis set limited to Week 12 clinical responders; weight quartiles for Week 48 endpoints are based on participants in the Week 12 clinical responder analysis set who received maintenance guselkumab 100 mg SC q8w or guselkumab 200 mg SC q4w as follows: 61.00 kg (Q1), 70.00 kg (Q2), 82.00 kg (Q3). Participants who had an ostomy or colectomy, a prohibited change in UC medication, or discontinued study intervention for any reason (other than COVID-19 related reasons [excluding COVID-19 infection] or regional crisis) were considered not to have met the endpoint at the designated timepoint. Participants who discontinued study intervention due to COVID-19 related reasons (excluding COVID-19 infection) or regional crisis had their observed data used, if available. After accounting for these intercurrent event rules, participants who were missing data pertaining to an endpoint at a designated timepoint were considered not to have achieved the endpoint. The confidence intervals for the proportion of participants meeting the endpoint in each treatment group were based on the normal approximation confidence limits. The adjusted treatment difference(s) and confidence interval(s) were based on the Wald statistic with Cochran-Mantel-Haenszel weight. For the ">1Q to ≤2Q" subgroup in ASTRO, treatment differences were unadjusted.

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