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EFFICACY OF INTRAVENOUS AND SUBCUTANEOUS GUSELKUMAB INDUCTION BY WEIGHT AND BODY MASS INDEX IN PATIENTS WITH CROHN'S DISEASE: RESULTS FROM THE PHASE 3 GALAXI AND GRAVITI STUDIES

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Key Takeaways

- **Guselkumab IV and SC induction were similarly effective in participants with moderately to severely active CD compared with placebo at Week 12 regardless of participants' baseline body weight or BMI**
- **Similar efficacy was observed at Week 48 between participants treated with either guselkumab IV or SC induction regardless of participants' baseline body weight or BMI**
- **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]
- Similar efficacy and safety of intravenous (IV) and subcutaneous (SC) induction with guselkumab in participants with moderately to severely active Crohn's disease (CD) has been established in the phase 3 GALAXI and GRAVITI 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 evaluate whether weight and body mass index (BMI) in participants with CD differentially affect the efficacy of guselkumab SC induction compared to IV induction

GALAXI 2 & 3 and GRAVITI Study Designs Through Week 48

Key eligibility criteria

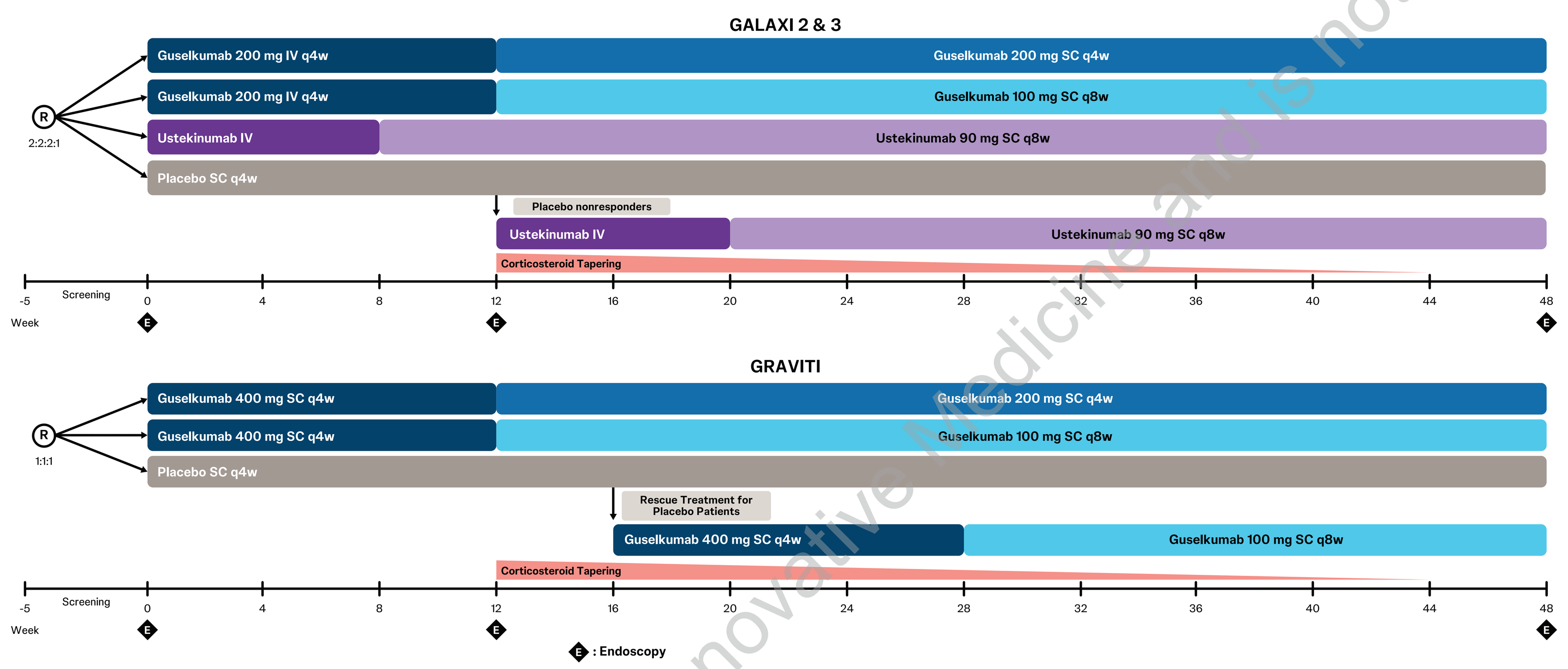
- Moderately to severely active CD (CDAI score 220–450 AND either mean daily SF OR AP above protocol thresholds[a]) and SES-CD score ≥6 (or ≥4 for isolated ileal disease)
- Inadequate response/loss of response/intolerance to oral corticosteroids, 6-MP/AZA/MTX, or biologic therapies[b]

Randomization stratified by:

- CDAI score (≤300 or >300)
- SES-CD (≤12 or >12)
- Prior BIO-failure status
- Corticosteroid use at baseline (GALAXI only)

Endpoints

- **Clinical remission:** CDAI score <150
- **Endoscopic response:** ≥50% improvement from baseline in SES-CD
- **Endoscopic remission:** SES-CD score ≤ 4 and at least a 2-point reduction from baseline and no subscore greater than 1 in any individual subcomponent
- **Deep remission:** Combination of clinical remission and endoscopic remission



AP=abdominal pain; BIO= biologic; CDAI=Crohn's disease activity index; SC=subcutaneous; SES-CD=simple endoscopic score for Crohn's disease; SF=stool frequency.
[a]GALAXI: Mean daily SF count >3 OR AP score >1; GRAVITI: Mean daily SF count ≥4 OR AP score ≥2.
[b]Biologic therapies: TNF antagonists or vedolizumab.
Note: Only the study designs through Week 48 are shown. GRAVITI included data handling rules for rescue treatment at Week 16 in participants meeting prespecified criteria; these data handling rules were suspended for the Week 48 analyses shown below. The full study designs can be found in primary trial publications (references 2 and 3 for GALAXI 2 & 3 and GRAVITI, respectively.)

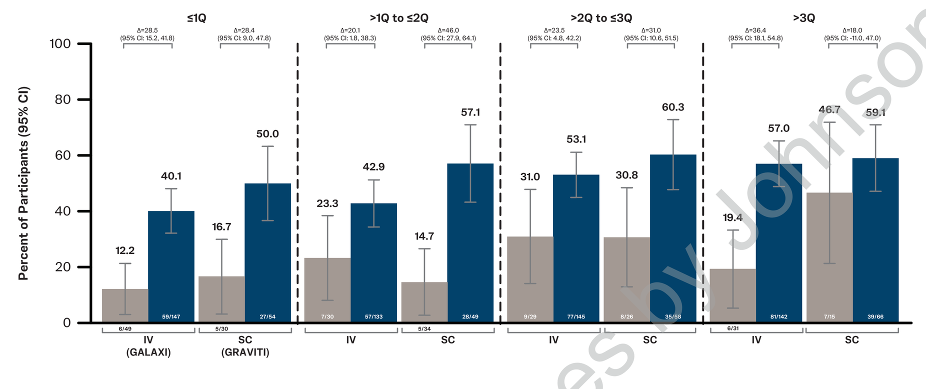
Results

Baseline Demographics and Disease Characteristics

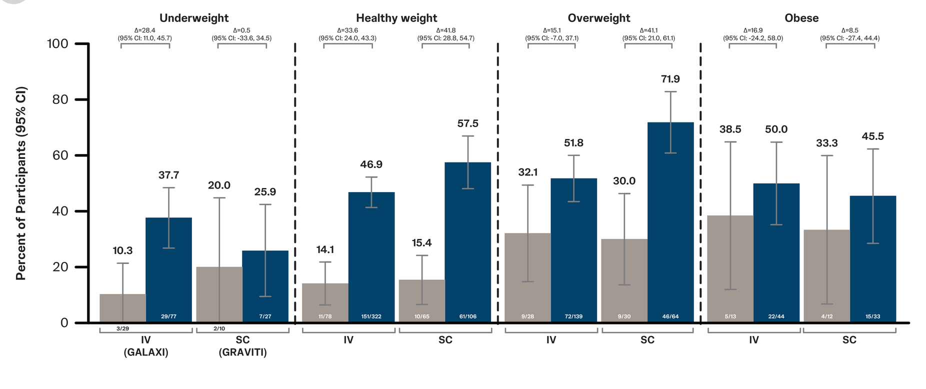
	GALAXI 2 & 3				GRAVITI			
Full analysis set	Placebo IV (N=148)	GUS 200 mg IV → 100 mg SC q8w (N=286)	GUS 200 mg IV → 200 mg SC q4w (N=296)	GUS Combined (N=582)	Placebo SC (N=117)	GUS 400 mg SC → 100 mg SC q8w (N=115)	GUS 400 mg SC → 200 mg SC q4w (N=115)	GUS Combined (N=230)
Demographics								
Weight in kg. mean (SD)	67.12 (18.14)	67.36 (16.52)	68.21 (16.36)	67.79 (16.43)	68.13 (16.20)	70.88 (19.00)	72.88 (19.28)	71.88 (19.13)
Body mass index in kg/m², mean (SD)	22.77 (5.28)	23.08 (4.60)	23.23 (4.77)	23.15 (4.68)	23.85 (4.88)	24.28 (5.62)	24.84 (6.27)	24.56 (5.95)
Age in years, mean (SD)	34.8 (12.15)	36.0 (12.24)	36.9 (13.27)	36.5 (12.77)	36.0 (12.71)	37.4 (13.32)	39.1 (12.56)	38.2 (12.95)
Male, n (%)	88 (59.5%)	154 (53.8%)	178 (60.1%)	332 (57.0%)	67 (57.3%)	66 (57.4%)	70 (60.9%)	136 (59.1%)
Characteristics								
CD duration in years, mean (SD)	7.15 (7.53)	7.12 (6.72)	7.07 (7.24)	7.09 (6.98)	6.96 (7.75)	9.17 (9.08)	7.89 (7.13)	8.53 (8.17)
CDAI score, mean (SD)	293.4 (52.72)	296.3 (54.27)	295.9 (52.74)	296.1 (53.45)	293.0 (49.09)	300.4 (54.32)	297.3 (54.69)	298.8 (54.41)
SES-CD score, mean (SD)	13.3 (7.55)	13.2 (7.43)	12.5 (7.24)	12.8 (7.34)	12.0 (6.89)	12.2 (6.85)	11.8 (7.12)	12.0 (6.97)
Endoscopic disease severity (SES-CD score), n (%)								
Moderate (7–16)	77 (52.0%)	164 (57.3%)	147 (49.7%)	311 (53.4%)	61 (52.1%)	64 (55.7%)	49 (42.6%)	113 (49.1%)
Severe (>16)	43 (29.1%)	81 (28.3%)	79 (26.7%)	160 (27.5%)	25 (21.4%)	26 (22.6%)	27 (23.5%)	53 (23.0%)
Involved disease location by central reader, n (%)								
Colon only	62 (41.9%)	113 (39.5%)	112 (37.8%)	225 (38.7%)	40 (34.2%)	41 (35.7%)	40 (34.8%)	81 (35.2%)
Ileum only	31 (20.9%)	59 (20.6%)	80 (27.0%)	139 (23.9%)	22 (18.8%)	25 (21.7%)	27 (23.5%)	52 (22.6%)
Ileum and Colon	55 (37.2%)	114 (39.9%)	104 (35.1%)	218 (37.5%)	55 (47.0%)	49 (42.6%)	48 (41.7%)	97 (42.2%)
Biomarkers								
C-reactive protein in mg/L, median (IQR)	5.1 (1.5; 15.8)	7.7 (2.6; 21.8)	6.2 (2.7; 21.3)	6.7 (2.6; 21.8)	7.9 (2.1; 14.7)	5.2 (1.7; 13.3)	5.7 (1.7; 16.1)	5.5 (1.7; 14.9)
Fecal calprotectin in μg/g,[a] median (IQR)	962.0 (255.0; 2595.0)	969.0 (404.0; 2085.0)	1045.5 (323.0; 2006.0)	1010.0 (372.0; 2054.0)	712.0 (243.0; 1724.0)	610.0 (226.0; 1554.0)	600.5 (235.0; 1650.0)	610.0 (228.0; 1608.0)
Biologic medication history, n (%)								
Bionaïve	61 (41.2%)	116 (40.6%)	128 (43.2%)	244 (41.9%)	56 (47.9%)	53 (46.1%)	52 (45.2%)	105 (45.7%)
History of inadequate response/intolerance to biologic therapy,[b] n (%)	78 (52.7%)	153 (53.5%)	147 (49.7%)	300 (51.5%)	53 (45.3%)	55 (47.8%)	53 (46.1%)	108 (47.0%)
Concomitant CD medications at baseline, n (%)								
6-MP/AZA	36 (24.3%)	85 (29.7%)	89 (30.1%)	174 (29.9%)	32 (27.4%)	28 (24.3%)	36 (31.3%)	64 (27.8%)
MTX	4 (2.7%)	2 (0.7%)	7 (2.4%)	9 (1.5%)	1 (0.9%)	1 (0.9%)	1 (0.9%)	2 (0.9%)
Oral corticosteroids	51 (34.5%)	109 (38.1%)	106 (35.8%)	215 (36.9%)	33 (28.2%)	32 (27.8%)	38 (33.0%)	70 (30.4%)

6-MP=6-mercaptopurine; AZA=azathioprine; CD=Crohn's disease; CDAI=Crohn's disease activity index; GUS=guselkumab; IQR=interquartile range; IV=intravenous; MTX=methotrexate; SC=subcutaneous; SD=standard deviation; SES-CD=simple endoscopic score for Crohn's disease. [a]Based on N=147 for placebo, N=283 for GUS 100 mg, N=294 for GUS 200 mg, and N=577 for GUS Combined in GALAXI; and N=117 for placebo, N=115 for GUS 100 mg, N=114 for GUS 200 mg and N=229 for GUS Combined in GRAVITI. [b]Primary nonresponse, secondary nonresponse, or intolerance.

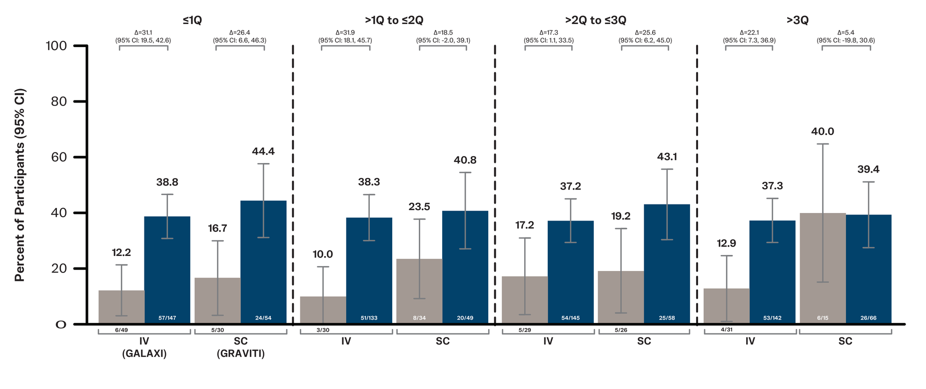
Clinical remission at Week 12 by baseline weight



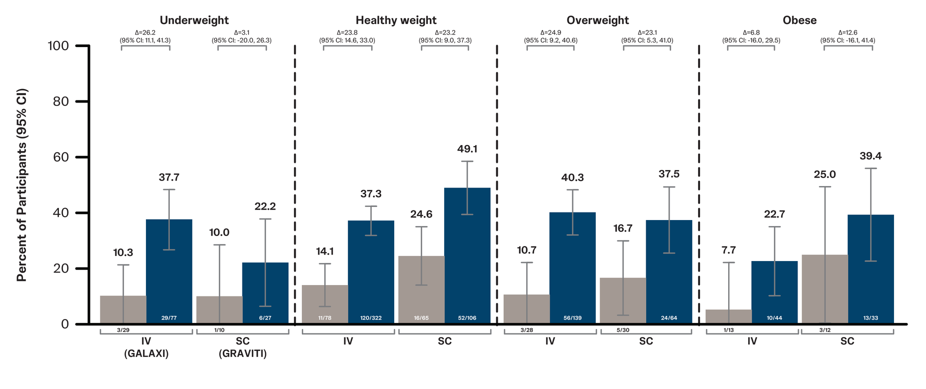
Clinical remission at Week 12 by baseline BMI



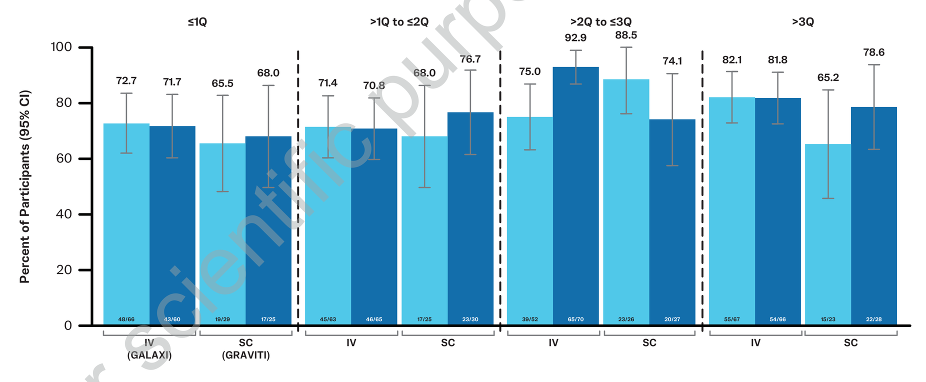
Endoscopic response at Week 12 by baseline weight



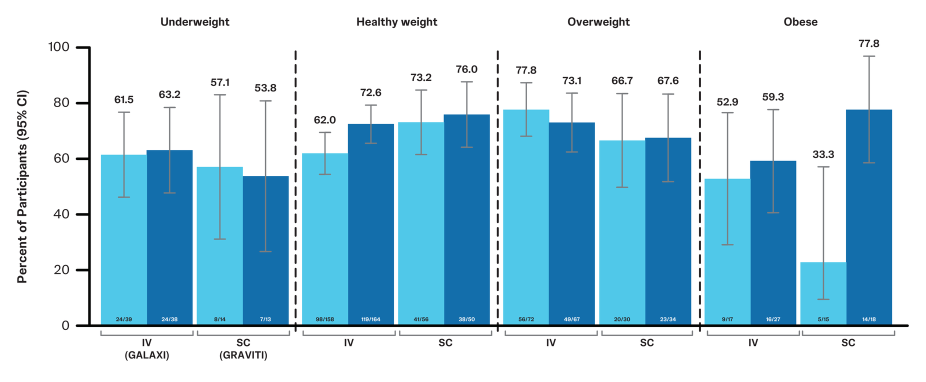
Endoscopic response at Week 12 by baseline BMI



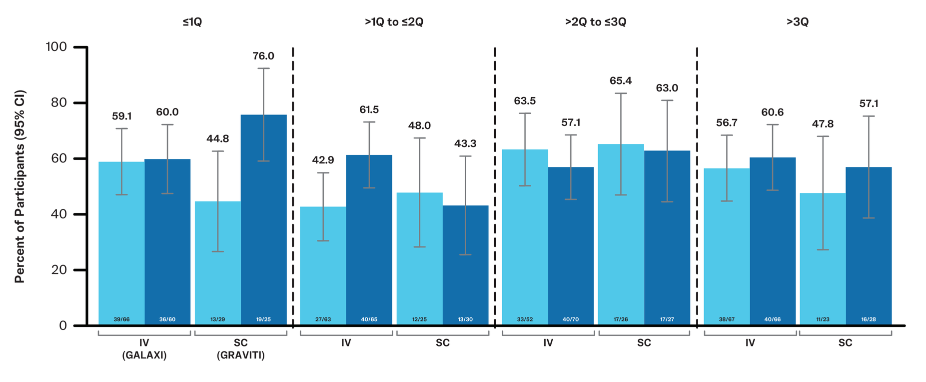
Clinical remission at Week 48 by baseline weight



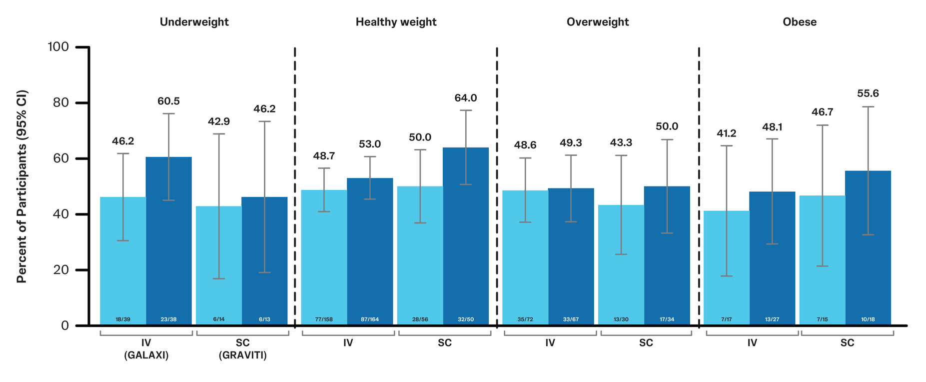
Clinical remission at Week 48 by baseline BMI



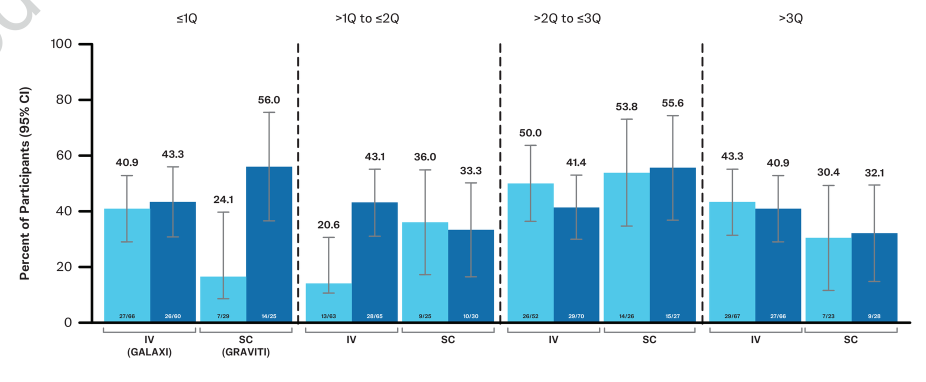
Endoscopic response at Week 48 by baseline weight



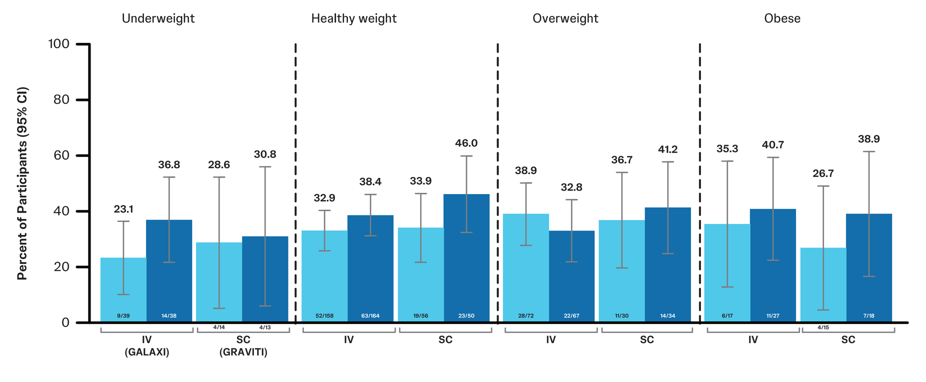
Endoscopic response at Week 48 by baseline BMI



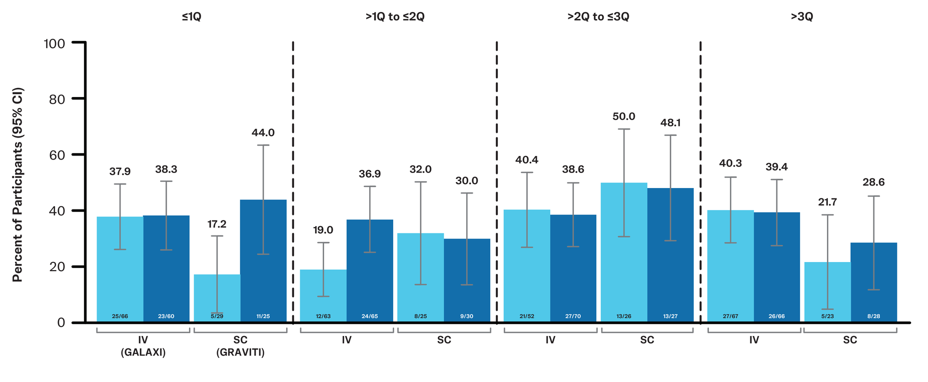
Endoscopic remission at Week 48 by baseline weight



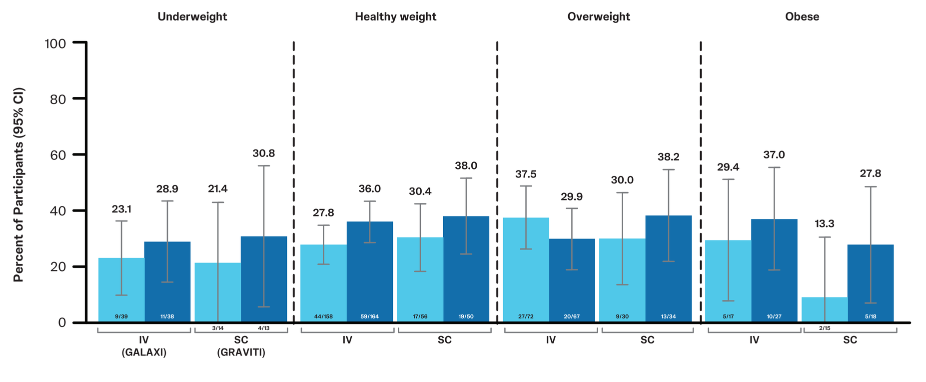
Endoscopic remission at Week 48 by baseline BMI



Deep remission at Week 48 by baseline weight



Deep remission at Week 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/m2], healthy weight [≥18 to <25 kg/m2], overweight [≥25 to <30 kg/m2], and obese [≥30 kg/m2]). 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 48). Weight quartiles for Week 12 analyses were based on participants in the primary analysis set as follows: GALAXI—57 kg (1Q), 67.1 kg (2Q), 79 kg (3Q); and GRAVITI—59 kg (1Q), 69.5 kg (2Q), 81 kg (3Q). Weight quartiles for Week 48 analyses were based on participants in the primary analysis set as follows: GALAXI—58.6 kg (1Q), 70 kg (2Q), 81 kg (3Q); and GRAVITI—62 kg (1Q), 73 kg (2Q), 85 kg (3Q). Participants who had a CD-related surgery (with the exception of minor procedures such as drainage of a superficial abscess or seton placement, etc.), a prohibited change in CD 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 the aforementioned data handling rules, participants who were missing data pertaining to an endpoint at the timepoint were considered not to have achieved the endpoint. The adjusted treatment difference(s) and confidence interval(s) were based on the common risk difference by use of Mantel-Haenszel stratum weights and the Sato variance estimator. The stratification factors are baseline CDAI score (≤300 or >300), baseline SES-CD score (≤12 or >12), BIO-failure status at baseline (yes or no), and baseline corticosteroid use (yes or no; GALAXI only).

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