Corticosteroid sparing effects of treatment with guselkumab in patients with moderately to severely active Crohn's disease: Phase 3 GRAVITI study results through week 48

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Key Takeaways

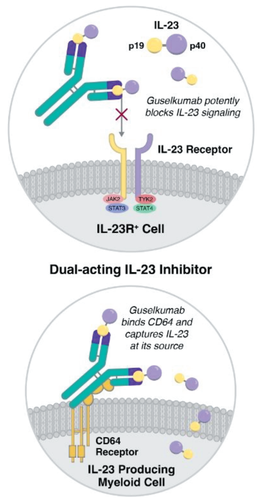
- **Among all participants receiving oral corticosteroids at baseline, greater proportions of guselkumab-treated participants were corticosteroid-free at Week 48 or for ≥90 days prior to Week 48 vs placebo**
- **In participants with moderately to severely active CD, greater proportions of guselkumab-treated participants achieved corticosteroid-free clinical and endoscopic outcomes at Week 48 vs placebo**

Background

Achieving and maintaining corticosteroid (CS)-free remission is a treatment goal for Crohn's disease (CD)

Guselkumab is a dual-acting IL-23p19 subunit inhibitor that binds to IL-23 and CD64, a receptor on cells that produce IL-23

GRAVITI is a Phase 3 double-blind, placebo-controlled, treat-through study evaluating the efficacy and safety of subcutaneous (SC) induction and maintenance treatment with guselkumab in participants with CD



Objective

To evaluate the CS-sparing effects of treatment with guselkumab vs placebo through Week 48 in the GRAVITI study

Methods

- Participants were randomized 1:1:1 to:
  - Guselkumab 400mg SC every 4 wks (q4w)→200mg SC q4w
  - Guselkumab 400mg SC q4w→100mg SC q8w
  - Placebo
- Placebo participants who met rescue criteria were eligible for rescue treatment with guselkumab at Week 16
- For participants receiving oral CS at baseline, doses were maintained through Week 12
  - Mandatory oral CS tapering began at Week 12 unless medically not feasible
- Outcomes evaluated at Week 48:

Outcome	Definition
Clinical remission*	CDAI score <150
CS-free clinical remission	CDAI score <150 and not receiving CS
90-day CS-free clinical remission	CDAI score <150 and not receiving CS for ≥90 days prior to the visit
Endoscopic response*	≥50% improvement from baseline in the SES-CD score
Endoscopic remission	SES-CD score ≤4 and at least a 2-point reduction from baseline and no subscore >1 in any individual component
90-day CS-free endoscopic response	≥50% improvement from baseline in SES-CD score and not receiving corticosteroids for ≥90 days prior to the visit
90-day CS-free endoscopic remission	SES-CD score ≤4 and a ≥2-point reduction from baseline and no subscore >1 in any individual component and not receiving corticosteroids for ≥90 days prior to the visit

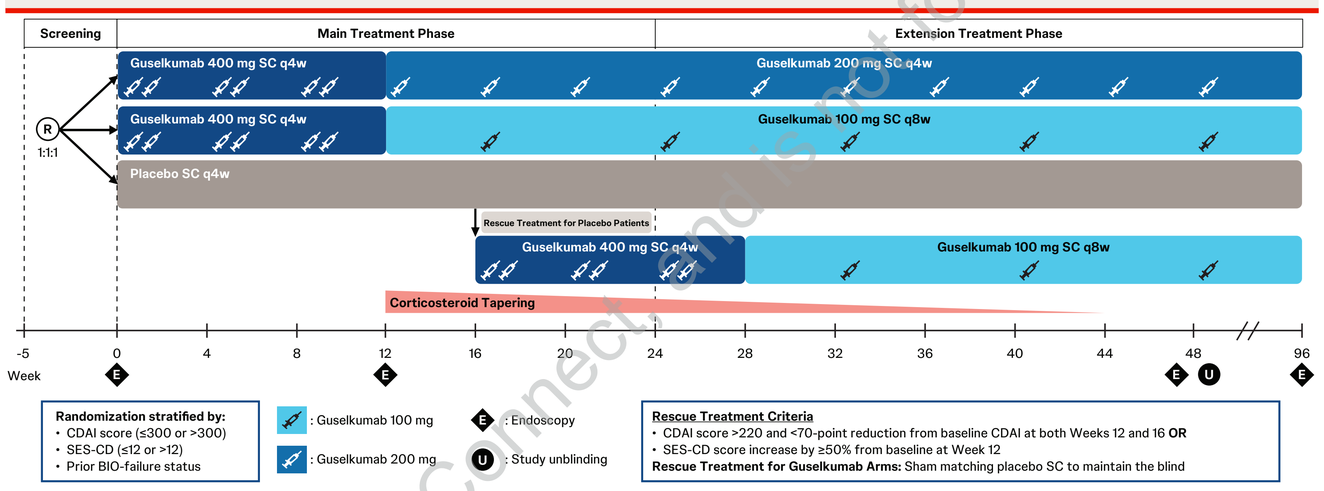
Multiplicity controlled.* ***CDAI**=Crohn's Disease Activity Index;* ***CS****=corticosteroid;* ***SES-CD****=Simple Endoscopic Score for Crohn's Disease.*

- All 90-day CS-free analyses were not multiplicity controlled

Figure 1. Phase 3, double-blind, treat-through design: GRAVITI

Key eligibility criteria

- *Moderately to severely active CD (CDAI score 220–450 AND either mean daily SF count ≥4 OR AP score ≥2) and SES-CD score ≥6 (or ≥4 for isolated ileal disease)*
- *Inadequate response/intolerance to oral corticosteroids, 6-MP/AZA/MTX, or biologic therapies[a]*



[a]Biologic therapies: TNF antagonists or vedolizumab. ***6-MP****=6-mercaptopurine;* ***AP****=abdominal pain;* ***AZA****=azathioprine;* ***BIO****=biologic;* ***CDAI****=Crohn's Disease Activity Index;* ***MTX****=methotrexate;* ***SC****=subcutaneous;* ***SES-CD****=Simple Endoscopic Score for Crohn's Disease;* ***SF****=stool frequency.*

Results

Table 1. Baseline demographics and disease characteristics

Full analysis set	Placebo SC (N=117)	Guselkumab 400 mg SC q4w → 100 mg SC q8w (N=115)	Guselkumab 400 mg SC q4w → 200 mg SC q4w (N=115)	Total (N=347)
Demographics				
Age in years, mean (SD)	36.0 (12.71)	37.4 (13.32)	39.1 (12.56)	37.5 (12.89)
Men, n (%)	67 (57.3%)	66 (57.4%)	70 (60.9%)	203 (58.5%)
Characteristics				
CD duration in years, mean (SD)	7.0 (7.75)	9.2 (9.08)	7.9 (7.13)	8.0 (8.05)
CDAI score, mean (SD)	293.0 (49.09)	300.4 (54.32)	297.3 (54.69)	296.9 (52.68)
SES-CD score, mean (SD)	12.0 (6.89)	12.2 (6.85)	11.8 (7.12)	12.0 (6.94)
Involved GI areas by central reader, n (%)				
Colon only	40 (34.2%)	41 (35.7%)	40 (34.8%)	121 (34.9%)
Ileum only	22 (18.8%)	25 (21.7%)	27 (23.5%)	74 (21.3%)
Ileum and Colon	55 (47.0%)	49 (42.6%)	48 (41.7%)	152 (43.8%)
Biomarkers				
CRP in mg/L, median (IQR)	7.9 (2.1; 14.7)	5.2 (1.7; 13.3)	5.7 (1.7; 16.1)	5.8 (1.8; 14.9)
Fecal calprotectin in µg/g,[a] median (IQR)	712.0 (243.0; 1724.0)	610.0 (226.0; 1554.0)	600.5 (235.0; 1650.0)	643.0 (235.0; 1650.0)

[a]Based on N=117 for placebo, N=115 for guselkumab 400 mg q4w → 100 mg SC q8w, N=114 for guselkumab 400 mg → 200 mg SC q4w, and N=346 for total. ***CDAI****=Crohn's Disease Activity Index;* ***CRP****=C-reactive protein;* ***GI****=gastrointestinal;* ***IQR****=interquartile range;* ***SC****=subcutaneous;* ***SD****=standard deviation.* ***SES-CD****=Simple Endoscopic Score for Crohn's Disease.*

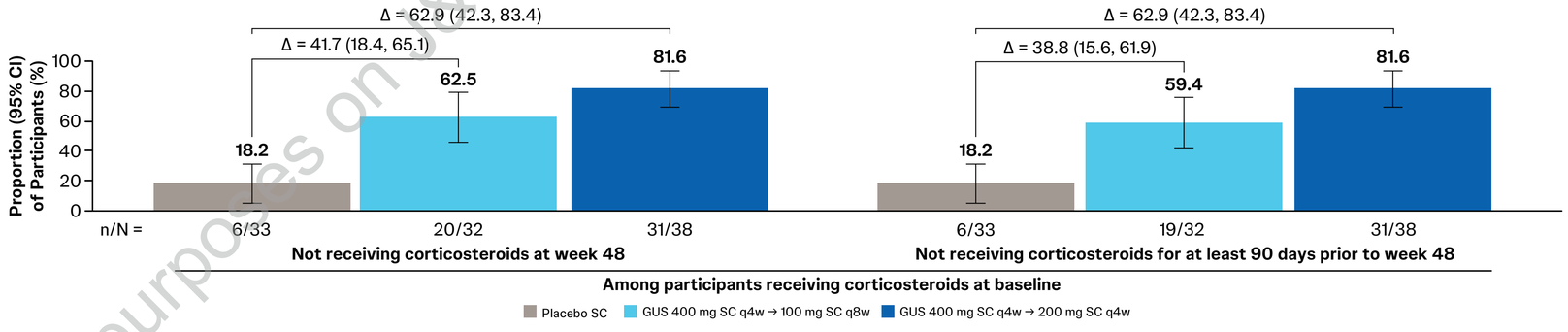
Table 2. Baseline Crohn's disease medication history and concomitant medications

Full analysis set	Placebo SC (N=117)	Guselkumab 400 mg SC q4w → 100 mg SC q8w (N=115)	Guselkumab 400 mg SC q4w → 200 mg SC q4w (N=115)	Total (N=347)
Medication history				
Biologic naïve	56 (47.9%)	53 (46.1%)	52 (45.2%)	161 (46.4)
History of previous biologic use, but no documented failure, n (%)	8 (6.8%)	7 (6.1%)	10 (8.7%)	25 (7.2%)
History of inadequate response/ intolerance[a] to biologic therapy, n (%)	53 (45.3%)	55 (47.8%)	53 (46.1%)	161 (46.4%)
At least one anti-TNF[b]	50 (94.3%)	51 (92.7%)	52 (98.1%)	153 (95.0%)
Two or more anti-TNFs[b]	11 (20.8%)	12 (21.8%)	13 (24.5%)	36 (22.4%)
Vedolizumab	8 (15.1%)	13 (23.6%)	6 (11.3%)	27 (16.8%)
Concomitant Medications				
Participants with ≥1 Crohn's disease medication at baseline, n (%)	79 (67.5%)	74 (64.3%)	84 (73.0%)	237 (68.3%)
6-MP/AZA	33 (27.4%)	28 (24.3%)	36 (31.3%)	96 (27.7%)
Methotrexate	1 (0.9%)	1 (0.9%)	1 (0.9%)	3 (0.9%)
Oral aminosalicylates	50 (42.7%)	47 (40.9%)	44 (38.3%)	141 (40.6%)
Oral corticosteroid use	33 (28.2%)	32 (27.8%)	38 (33.0%)	103 (29.7%)
Corticosteroid use (excluding budesonide)	18 (15.4%)	15 (13.0%)	28 (24.3%)	61 (17.6%)
Median (IQR) daily prednisone-equivalent dose (excluding budesonide),[c] mg	20 (10.0; 20.0)	20 (10.0; 25.0)	15.0 (10.0; 25.0)	-
Budesonide	15 (12.8%)	17 (14.8%)	10 (8.7%)	42 (12.1%)

No participants were receiving beclomethasone at baseline. [a]Primary nonresponse, secondary nonresponse, or intolerance. [b]Among participants with a history of inadequate response/intolerance to biologic therapy. [c]Medians and IQRs are based on the subset of participants receiving CS other than budesonide and beclomethasone dipropionate at baseline. ***6-MP****=6-mercaptopurine;* ***AZA****=azathioprine;* ***IQR****=interquartile range;* **SC**=subcutaneous; ***TNF****=tumor necrosis factor.*

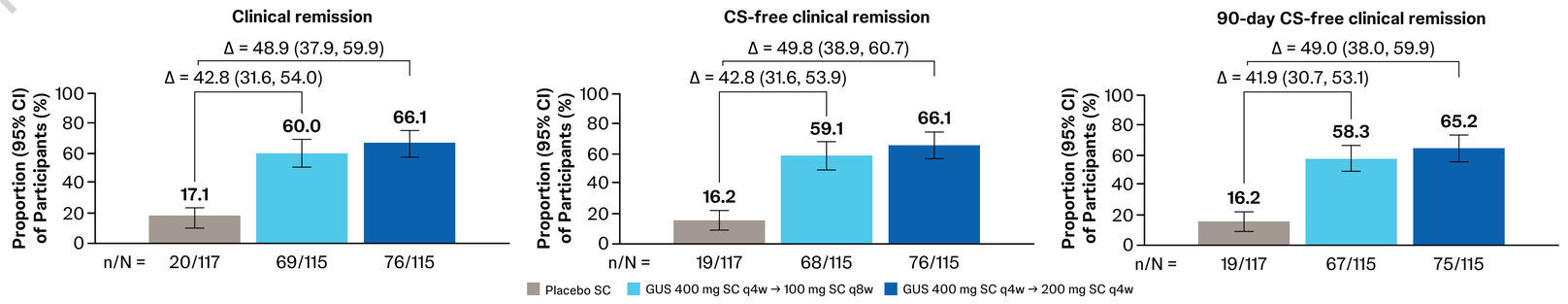
- *Among all participants receiving oral CS (prednisone or budesonide) at baseline, greater proportions of guselkumab-treated participants vs placebo were: CS-free at Week 48, CS-free for ≥90 days prior to Week 48*

Figure 2. Participants not receiving CS at Week 48 among those receiving CS at baseline



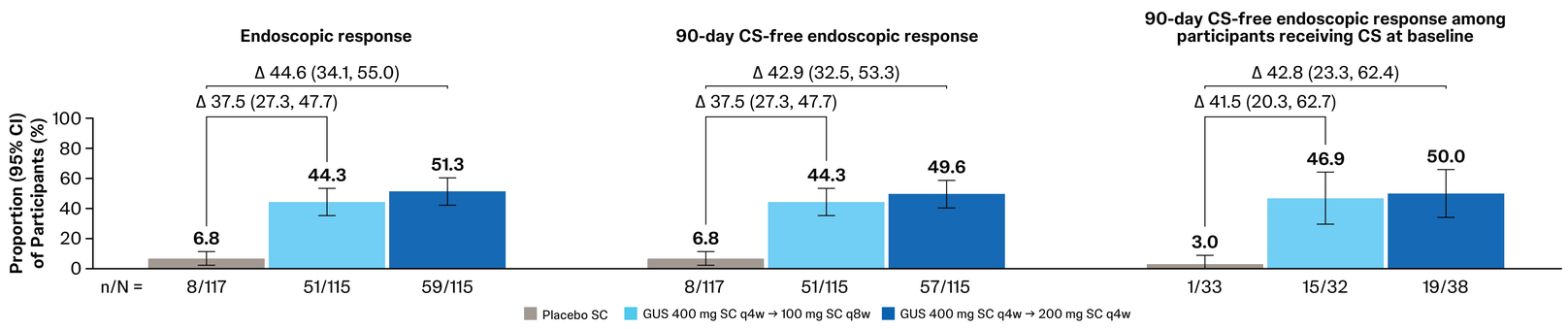
- *At Week 48, greater proportions of guselkumab-treated participants vs placebo achieved: Clinical remission, CS-free clinical remission, 90-day CS-free clinical remission*
- *99.3% (144/145) of guselkumab-treated participants in clinical remission at Week 48 were CS-free*

Figure 3. Clinical remission at Week 48



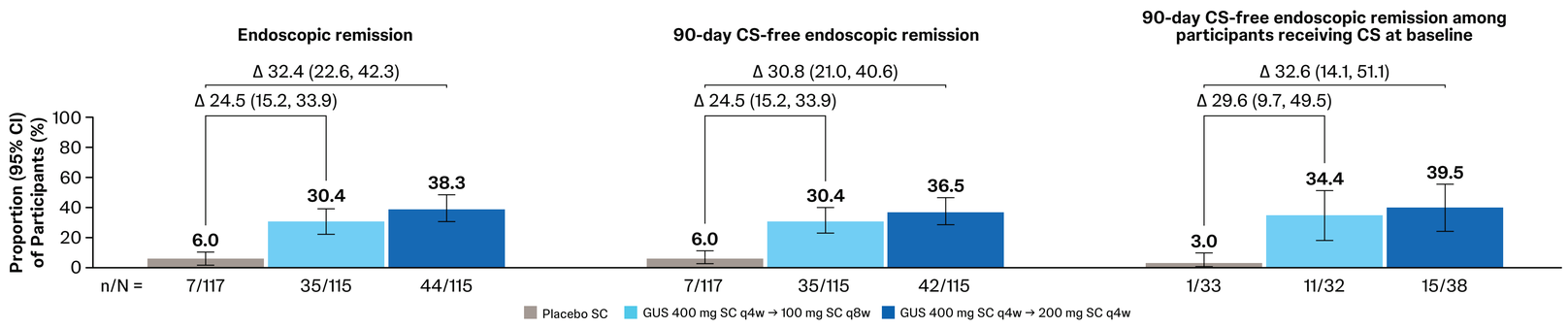
- *At Week 48, greater proportions of guselkumab-treated participants vs placebo achieved: endoscopic response, 90-day CS-free endoscopic response*
- *98.2% (108/110) of guselkumab-treated participants in endoscopic response at week 48 were CS-free for ≥90 days*

Figure 4. Endoscopic response at Week 48



- *At Week 48, greater proportions of guselkumab-treated participants vs placebo achieved: endoscopic remission, 90-day CS-free endoscopic remission*
- *97.5% (77/79) of guselkumab-treated participants in endoscopic remission at week 48 were CS-free for ≥90 days*

Figure 5. Endoscopic remission at Week 48



Δ = adjusted treatment difference. All participants in all treatment groups who met the rescue criteria were considered not to have met efficacy endpoints after Week 16. 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, met rescue criteria at Week 16 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 a designated timepoint were considered not to have achieved the endpoint. The adjusted treatment difference(s), confidence interval(s), and p-value(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), and BIO-failure status at baseline (yes or no). CS-free outcomes are not multiplicity controlled. ***CI****=confidence interval;* ***CS****=corticosteroid-free;* ***GUS****=guselkumab;* **SC**=subcutaneous.

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