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Efficacy of subcutaneous guselkumab induction therapy by baseline demographics and concomitant medications in participants with moderately to severely active Crohn's disease: Results at Week 12 from the phase 3 GRAVITI study

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Key Takeaway

In GRAVITI, guselkumab SC induction was effective in inducing clinical remission at Week 12 and endoscopic response at Week 12 across all predefined subgroups of sex, race, age, weight quartile, and concomitant CD-related medications among participants with moderately to severely active CD

Background

- Guselkumab is a dual-acting IL-23p19 subunit inhibitor that potently blocks IL-23 and binds to CD64, a receptor on immune cells that produce IL-23[1]
- The GRAVITI study established the efficacy and safety of subcutaneous (SC) induction with guselkumab in participants with moderately to severely active Crohn's disease (CD) through 48 weeks of treatment[2]

Objective

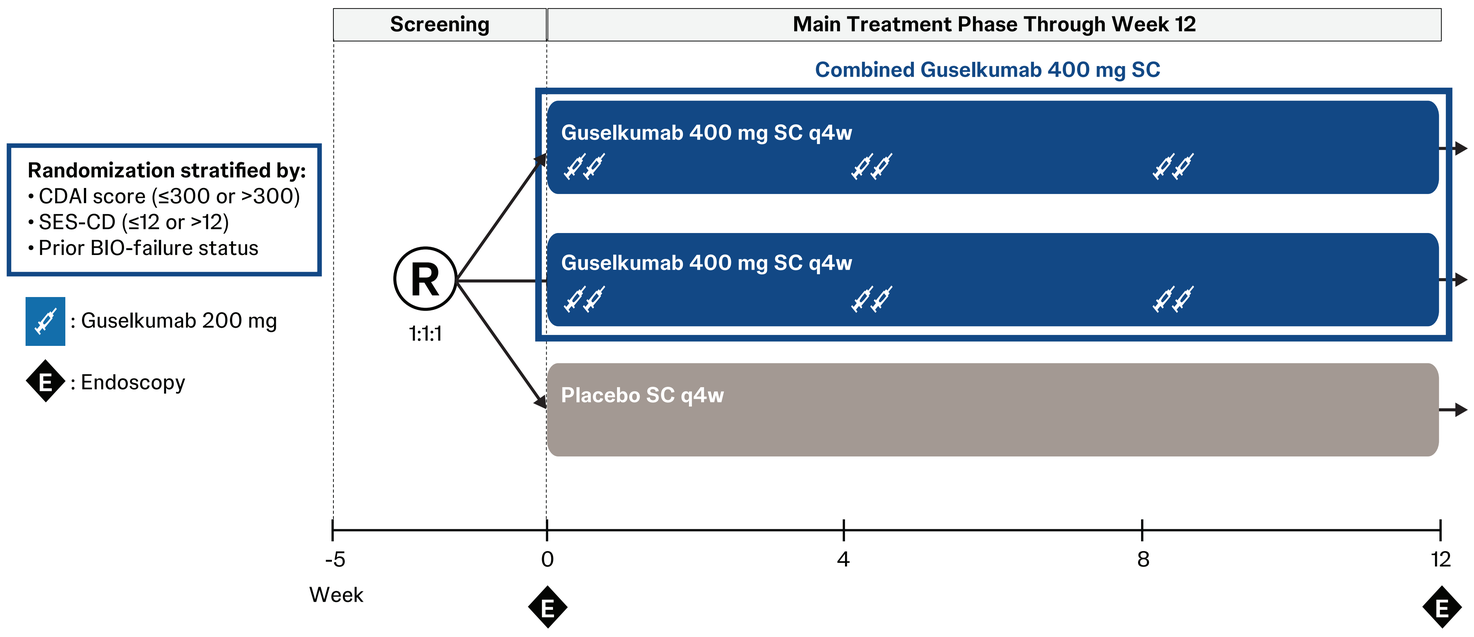
We evaluated the efficacy of guselkumab SC induction in the Week 12 co-primary endpoints of GRAVITI in subgroups based on baseline demographics and concomitant CD-related medications

Methods

GRAVITI Study Design

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.*

Endpoints

- **Clinical remission at Week 12:** CDAI score <150
- **Endoscopic response at Week 12:** ≥50% improvement from baseline in SES-CD score

Disease Characteristic Subgroups

- **Sex** (ie, Male, Female)
- **Race** (ie, White, Black or African American, Asian, Other)
- **Ethnicity** (ie, Hispanic or Latino, not Hispanic or Latino)
- **Age in years** (ie, ≤median [36], >median, <65, ≥65)
- **Weight in kg by quartile** (ie, <57.5, ≥57.5 to <68.5, ≥68.5 to <80.5, ≥80.5)
- **Crohn's disease duration in years** (ie, ≤5, >5 to ≤15, >15)
- **Concomitant CD-related medications** (ie, receiving or not receiving 5-ASA compounds, oral corticosteroids, and AZA/6-MP/MTX as discrete categories)

Results

Table 1. Baseline Demographics and Concomitant Medications

Full analysis set	Placebo (N=117)	Guselkumab 400 mg SC q4w (N=230)
Demographics		
Age in years, mean (SD)	36.0 (12.71)	38.2 (12.95)
Male, n (%)	67 (57.3%)	136 (59.1%)
Race,[a] n (%)		
White	71 (60.7%)	158 (68.7%)
Non-white	33 (28.2%)	52 (22.6%)
Black or African American	5 (4.3%)	4 (1.7%)
Asian	28 (23.9%)	48 (20.9%)
Not reported/missing	13 (11.1%)	20 (8.7%)
Ethnicity, n (%)		
Hispanic or Latino	9 (7.7%)	18 (7.8%)
Not Hispanic or Latino	93 (79.5%)	192 (83.5%)
Not reported/missing	15 (12.8%)	20 (8.7%)
Weight in kg, mean (SD)	68.1 (16.20)	71.9 (19.13)
Concomitant CD-related medications		
Participants with ≥1 CD medication at baseline, n (%)	79 (67.5%)	158 (68.7%)
Oral aminosalicylates (5-ASA compounds)	50 (42.7%)	91 (39.6%)
6-mercaptopurine/Azathioprine/Methotrexate	33 (28.2%)	66 (28.7%)
Oral corticosteroids	33 (28.2%)	70 (30.4%)

[a]*There were no participants with Native Hawaiian or Other Pacific Islander or Multiple race in the study.* ***SC****=subcutaneous;* ***SD****=standard deviation.*

Table 2. Baseline Disease Characteristics

Full analysis set	Placebo (N=117)	Guselkumab 400 mg SC q4w (N=230)
Disease characteristics		
CD duration in years, mean (SD)	7.0 (7.75)	8.5 (8.17)
CDAI score, mean (SD)	293.0 (49.09)	298.8 (54.41)
SES-CD score, mean (SD)	12.0 (6.89)	12.0 (6.97)
≤12, n (%)	72 (61.5%)	140 (60.9%)
>12, n (%)	45 (38.5%)	90 (39.1%)
Endoscopic disease severity (SES-CD score), n (%)		
Moderate (7–16)	61 (52.1%)	113 (49.1%)
Severe (>16)	25 (21.4%)	53 (23.0%)
Involved disease location by central reader, n (%)		
Colon only	40 (34.2%)	81 (35.2%)
Ileum only	22 (18.8%)	52 (22.6%)
Ileum and Colon	55 (47.0%)	97 (42.2%)
Biomarkers		
CRP in mg/L,[a] median (IQR)	7.9 (2.1; 14.7)	5.5 (1.7; 14.9)
Fecal calprotectin in µg/g,[b] median (IQR)	712.0 (243.0; 1724.0)	610.0 (228.0; 1608.0)

[a]*Normal CRP was defined as 0-5 mg/L.* [b]*Based on N=117 for placebo, N=229 for guselkumab 400 mg SC q4w, and N=346 for total.* ***CDAI****=Crohn's disease activity index;* ***CRP****=C-reactive protein;* ***IQR****=interquartile range;* ***SES-CD****=simple endoscopic score for Crohn's disease.*

Figure 1. Clinical Remission at Week 12 by Baseline Demographics and Concomitant Medications

	Clinical Remission at Week 12			
	Placebo N (%)	Guselkumab 400 mg SC N (%)	Rate Difference (95% CI)	p-value
All patients	117 (21.4)	230 (56.1)	34.9 (25.1, 44.6)	< 0.001
Sex				
Male	67 (25.4)	136 (58.1)	33.4 (20.3, 46.6)	< 0.001
Female	50 (16.0)	94 (53.2)	37.3 (22.5, 52.1)	< 0.001
Race				
White	71 (25.4)	158 (57.0)	32.3 (19.7, 44.9)	< 0.001
Non-white	33 (12.1)	52 (48.1)	38.0 (17.5, 58.4)	< 0.001
Black or African American	5 (0.0)	4 (100.0)	NE NE	NE
Asian	28 (14.3)	48 (43.8)	32.8 (10.5, 55.0)	0.004
Other	0	0	NE NE	NE
Not reported/missing	13 (23.1)	20 (70.0)	53.7 (25.3, 82.1)	< 0.001
Ethnicity				
Hispanic or Latino	9 (22.2)	18 (66.7)	NE NE	NE
Not Hispanic or Latino	93 (22.6)	192 (53.6)	30.8 (19.8, 41.8)	< 0.001
Not reported/missing	15 (13.3)	20 (70.0)	57.7 (31.5, 83.9)	< 0.001
Age (yrs)				
≤36 (median)	63 (19.0)	116 (60.3)	39.8 (26.8, 52.8)	< 0.001
>36 (median)	54 (24.1)	114 (51.8)	27.9 (13.2, 42.5)	< 0.001
<65	114 (21.9)	224 (56.3)	34.3 (24.4, 44.2)	< 0.001
≥65	3 (0.0)	6 (50.0)	NE NE	NE
Weight (kg)				
<57.5	30 (10.0)	56 (46.4)	29.5 (12.3, 46.8)	< 0.001
≥57.5 and < 68.5	36 (22.2)	51 (62.7)	42.7 (24.4, 61.0)	< 0.001
≥68.5 and < 80.5	31 (25.8)	56 (55.4)	35.0 (15.7, 54.3)	< 0.001
≥80.5	20 (30.0)	67 (59.7)	34.2 (9.4, 59.1)	0.007
Crohn's disease duration (yrs)				
≤5	67 (22.4)	103 (52.4)	31.5 (17.2, 45.9)	< 0.001
>5 to ≤15	31 (22.6)	91 (62.6)	37.9 (20.0, 55.8)	< 0.001
>15	19 (15.8)	36 (50.0)	27.2 (1.5, 52.9)	0.038
Oral 5-ASA compounds				
Receiving	50 (18.0)	91 (51.6)	33.4 (17.7, 49.1)	< 0.001
Not receiving	67 (23.9)	139 (59.0)	36.7 (24.0, 49.5)	< 0.001
Oral corticosteroids[a] *(incl. budesonide and beclomethasone dipropionate)*				
Receiving	33 (21.2)	70 (62.9)	42.7 (23.9, 61.5)	< 0.001
Not receiving	84 (21.4)	160 (53.1)	32.7 (21.2, 44.1)	< 0.001
6-MP/AZA/MTX				
Receiving	33 (30.3)	66 (59.1)	29.8 (11.7, 47.9)	0.001
Not receiving	84 (17.9)	164 (54.9)	37.3 (26.0, 48.6)	< 0.001

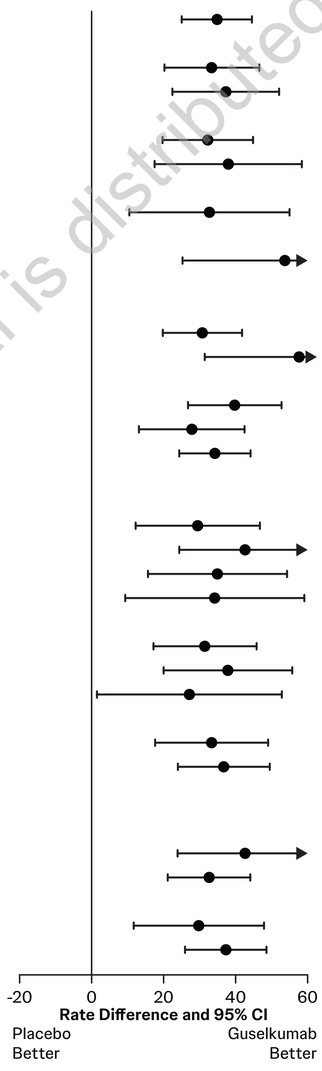
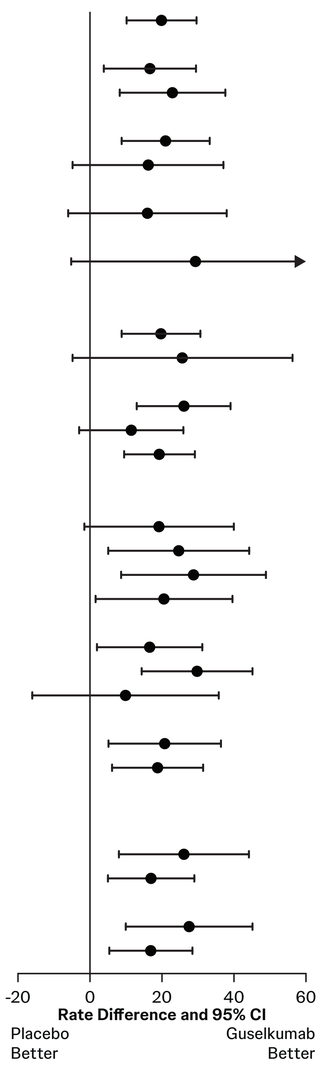


Figure 2. Endoscopic Response at Week 12 by Baseline Demographics and Concomitant Medications

	Endoscopic Response at Week 12			
	Placebo N (%)	Guselkumab 400 mg SC N (%)	Rate Difference (95% CI)	p-value
All patients	117 (21.4)	230 (41.3)	19.9 (10.2, 29.6)	< 0.001
Sex				
Male	67 (22.4)	136 (40.4)	16.7 (3.9, 29.5)	0.011
Female	50 (20.0)	94 (42.6)	22.9 (8.3, 37.6)	0.002
Race				
White	71 (21.1)	158 (39.9)	21.0 (8.8, 33.3)	< 0.001
Non-white	33 (21.2)	52 (40.4)	16.2 (-4.8, 37.1)	0.131
Black or African American	5 (20.0)	4 (50.0)	NE NE	NE
Asian	28 (21.4)	48 (39.6)	16.0 (-6.0, 38.0)	0.155
Other	0	0	NE NE	NE
Not reported/missing	13 (23.1)	20 (55.0)	29.3 (-5.2, 63.7)	0.096
Ethnicity				
Hispanic or Latino	9 (11.1)	18 (16.7)	NE NE	NE
Not Hispanic or Latino	93 (22.6)	192 (42.2)	19.7 (8.8, 30.7)	< 0.001
Not reported/missing	15 (20.0)	20 (55.0)	25.7 (-4.8, 56.3)	0.099
Age (yrs)				
≤36 (median)	63 (17.5)	116 (44.0)	26.1 (13.0, 39.1)	< 0.001
>36 (median)	54 (25.9)	114 (38.6)	11.5 (-3.0, 26.0)	0.120
<65	114 (21.9)	224 (41.1)	19.3 (9.5, 29.2)	< 0.001
≥65	3 (0.0)	6 (50.0)	NE NE	NE
Weight (kg)				
<57.5	30 (20.0)	56 (42.9)	19.2 (-1.5, 40.0)	0.069
≥57.5 and < 68.5	36 (22.2)	51 (43.1)	24.7 (5.1, 44.3)	0.014
≥68.5 and < 80.5	31 (19.4)	56 (42.9)	28.8 (8.7, 48.9)	0.005
≥80.5	20 (25.0)	67 (37.3)	20.6 (1.6, 39.6)	0.033
Crohn's disease duration (yrs)				
≤5	67 (28.4)	103 (43.7)	16.6 (2.0, 31.2)	0.026
>5 to ≤15	31 (9.7)	91 (42.9)	29.8 (14.4, 45.2)	< 0.001
>15	19 (15.8)	36 (30.6)	9.9 (-16.0, 35.8)	0.454
Oral 5-ASA compounds				
Receiving	50 (20.0)	91 (42.9)	20.8 (5.2, 36.4)	0.009
Not receiving	67 (22.4)	139 (40.3)	18.8 (6.2, 31.5)	0.004
Oral corticosteroids[a] *(incl. budesonide and beclomethasone dipropionate)*				
Receiving	33 (15.2)	70 (44.3)	26.1 (8.1, 44.2)	0.005
Not receiving	84 (23.8)	160 (40.0)	17.0 (5.0, 29.0)	0.006
6-MP/AZA/MTX				
Receiving	33 (15.2)	66 (45.5)	27.6 (10.0, 45.2)	0.002
Not receiving	84 (23.8)	164 (39.6)	16.9 (5.4, 28.5)	0.004



[a]*No participants were taking beclomethasone dipropionate at baseline. Note: 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 time-point. 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). Subgroup analyses were not evaluated (ie, rate difference, 95% CI, and p-value were not calculated) whenever there were less than 10 participants in at least 1 treatment group.* ***CI****=confidence interval.*

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