P1030

Efficacy and safety of subcutaneous guselkumab in East Asian participants with moderately to severely active Crohn's disease: Subgroup analysis of the Phase 3 GRAVITI study

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Key Takeaways

- **Efficacy of GUS as SC induction and maintenance therapy in the subgroup of East Asian participants from GRAVITI was consistent with that observed in the overall study population.**
- **The safety profile of GUS was consistent with the known safety profile in approved indications and with the overall study population.**

Background

- Guselkumab (GUS) is a dual-acting interleukin (IL)-23p19 subunit inhibitor that potently neutralises IL-23 and binds to CD64, a receptor on cells that produce IL-23[1]
- GRAVITI (NCT05197049) is a 48-week, randomized, double-blind, placebo (PBO)-controlled, treat-through trial assessing the efficacy and safety of subcutaneous (SC) GUS induction and maintenance in participants with moderately to severely active Crohn's disease (CD)[2]
- Co-primary efficacy endpoints (clinical remission at Week 12 **and** endoscopic response at Week 12) were met for GUS versus PBO in GRAVITI[2]

Objective

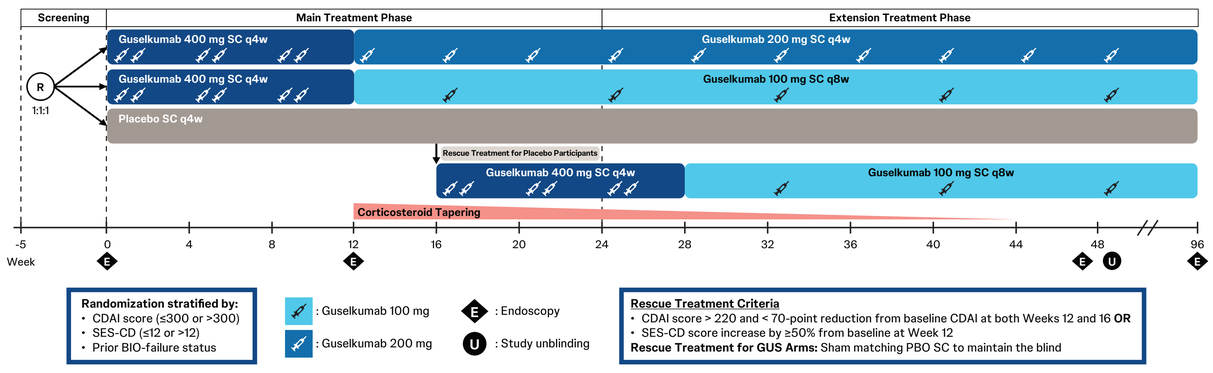
To report a subgroup analysis of GUS efficacy and safety in East Asian participants from GRAVITI

Methods

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]*



***6-MP**=6-mercaptopurine; **AP**=Abdominal pain; **AZA**=Azathioprine; **BIO**=Biologic; **CDAI**=Crohn's Disease Activity Index; **MTX**=Methotrexate; **q4w**=Every 4 weeks; **q8w**=Every 8 weeks; **SES-CD**=Simple Endoscopic Score for Crohn's Disease; **SF**=Stool frequency; **TNF**=Tumor necrosis factor. [a]Biologic therapies: TNF antagonists or vedolizumab.*

Endpoints and Statistical Considerations

Endpoints

Co-primary endpoints
- Clinical remission at Week 12
- Endoscopic response at Week 12

Additional multiplicity-controlled endpoints
- PRO-2 remission at Week 12
- Clinical response at Week 12
- Clinical remission at Week 24
- Clinical remission at Week 48
- Endoscopic response at Week 48

Other endpoints
- Endoscopic remission at Week 48
- Deep remission at Week 48

Statistical considerations
- Participants meeting prespecified treatment failure rules or had missing data were considered not to have met the endpoint
- Participants in all treatment groups (PBO or GUS) who met rescue criteria were considered not to have met endpoints after Week 16
- Endpoints assessed **through Week 12** compared the combined GUS 400 mg SC treatment arm to PBO; assessments **after Week 12** compared each GUS SC maintenance regimen to PBO[b]

***BIO**=Biologics; **CDAI**=Crohn's Disease Activity Index; **PRO-2**=Patient-Reported Outcome; **SES-CD**=Simple Endoscopic Score for Crohn's Disease. [b]In the global study population, 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), confidence interval(s), and p-value(s) were based on the common risk difference by use of the 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).*

Results

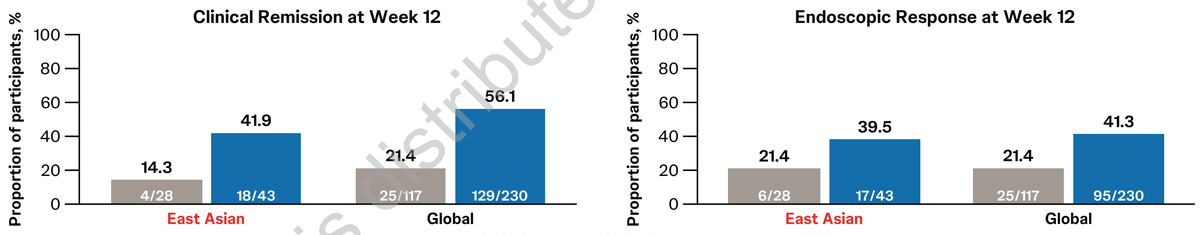
Baseline demographic and disease characteristics were generally similar between East Asian and global participants from GRAVITI

	East Asian[c] (N=71)	Global (N=347)
Demographics		
Age, yrs	34.2 (12.6)	37.5 (12.9)
Male, n (%)	47 (66.2)	203 (58.5)
Region: Asia, n (%)	71 (100)	74 (21.3)
Weight, kg	58.6 (12.9)	70.6 (18.3)
CD Disease Characteristics		
CD Disease Duration, yrs	6.0 (6.0)	8.0 (8.1)
CDAI Score	298.9 (49.7)	296.9 (52.7)
SES-CD Score	14.2 (8.7)	12.0 (6.9)
Endoscopic Disease Severity (SES-CD Score), n (%)		
7–16 (Moderate)	38 (53.5)	174 (50.1)
>16 (Severe)	19 (26.8)	78 (22.5)
Involved GI Areas by Central Reader, n (%)		
Ileum Only	8 (11.3)	74 (21.3)
Colon Only	22 (31.0)	121 (34.9)
Ileum and Colon	41 (57.7)	152 (43.8)
CRP, mg/mL, median (IQR)	9.2 (2.5; 18.0)	5.8 (1.8; 14.9)
Fecal Calprotectin, µg/g, median (IQR)	1392.0 (427.0; 2721.0)	643.0 (235.0; 1650.0)

***CDAI**=Crohn's Disease Activity Index; **CRP**=C-reactive protein; **GI**=Gastrointestinal; **IQR**=Interquartile range; **SD**=Standard deviation; **SES-CD**=Simple Endoscopic Score for Crohn's Disease. [c]Of 347 global participants in the GRAVITI primary analysis population, 71 were from study sites located in East Asia: China: n=51; Japan: n=6; South Korea: n=11; Taiwan: n=3. No statistical comparisons were made between treatment cohorts for this post hoc subgroup analysis. Data shown are mean (SD) unless otherwise noted.*

Short-term efficacy of GUS SC induction at Week 12

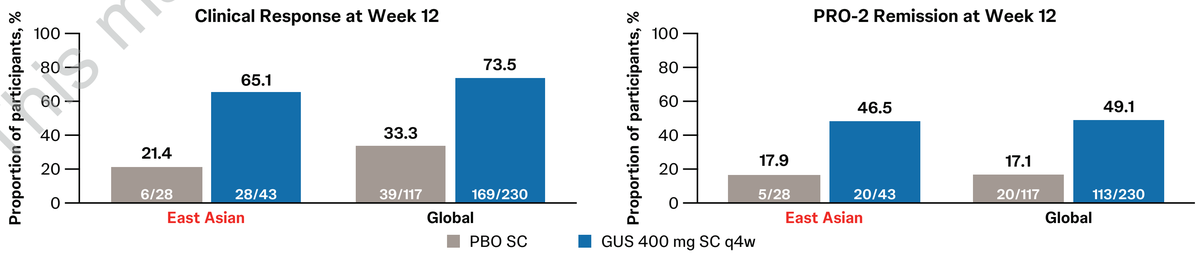
- Rates of clinical remission and endoscopic response at Week 12 were numerically higher with GUS 400 mg compared with PBO
- Clinical remission rates were numerically higher in the global study population, and endoscopic response rates were comparable



***CDAI**=Crohn's Disease Activity Index; **q4w**=every four weeks; **SES-CD**=Simple Endoscopic Score for Crohn's Disease. Primary analysis set. Clinical remission: CDAI score <150; Endoscopic response: ≥50% improvement from baseline in SES-CD score.*

Additional short-term efficacy of GUS SC induction at Week 12

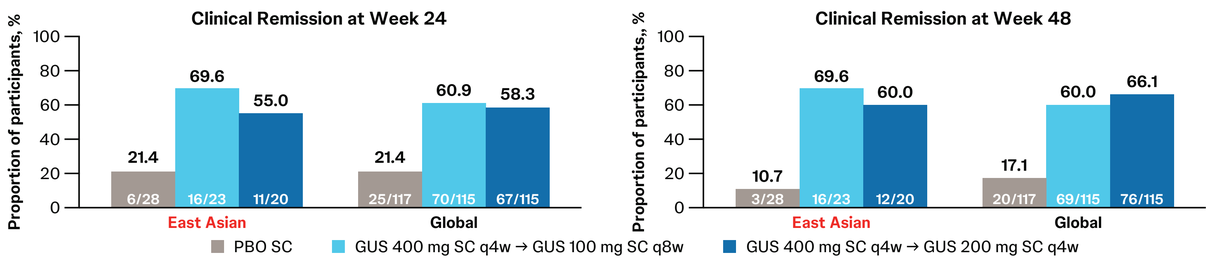
- Rates of clinical response and PRO-2 remission at Week 12 were numerically higher with GUS 400 mg SC q4w compared with PBO
- Clinical response rates were numerically higher in the global study population, and PRO-2 remission rates were comparable



***CDAI**=Crohn's Disease Activity Index; **q4w**=every four weeks; **PRO-2**=Patient-Reported Outcome. Primary analysis set. Clinical response: ≥100-point reduction from baseline in CDAI score or CDAI score <150; PRO-2 remission: Abdominal pain average daily score ≤1 and stool frequency average daily score ≤3, and no worsening of abdominal pain or stool frequency from baseline.*

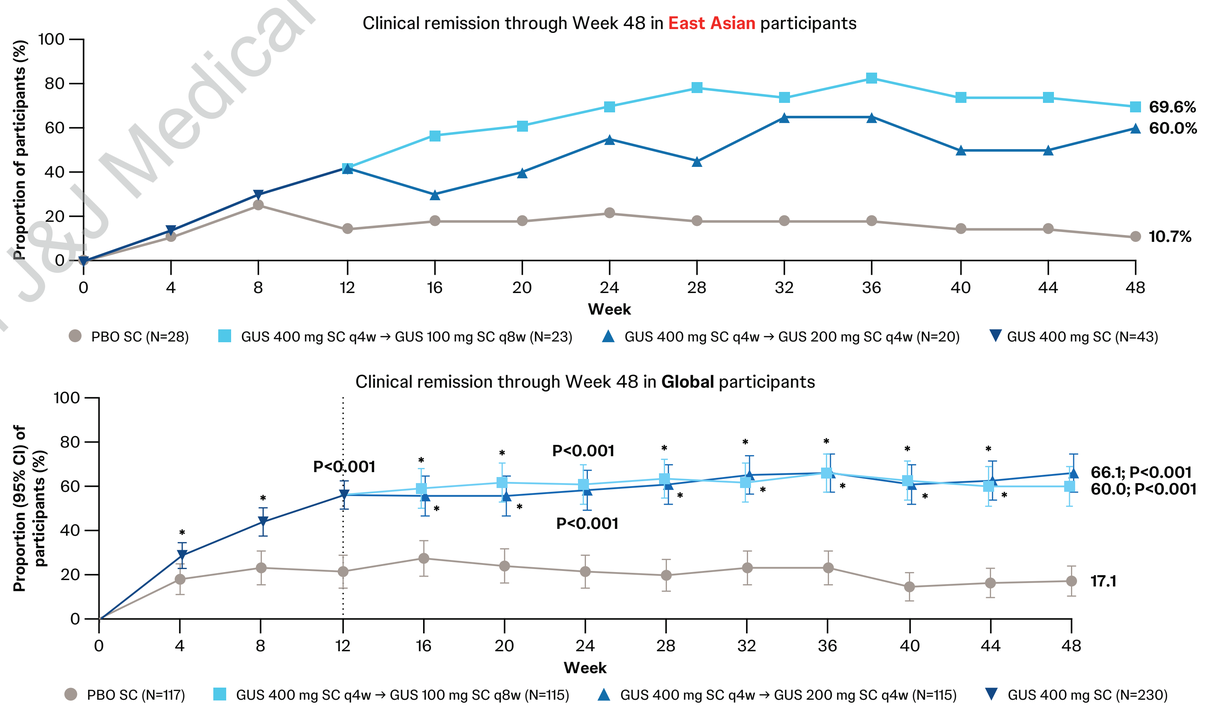
Long-term clinical outcomes of GUS SC maintenance

- Numerically higher proportions of GUS group participants achieved clinical remission at Week 24 and Week 48 relative to PBO
- Rates of achieving these endpoints were generally consistent between East Asian and global participants



***CDAI**=Crohn's Disease Activity Index; **q4w**=Every 4 weeks; **q8w**=Every 8 weeks. Primary analysis set. Clinical remission: CDAI score <150.*

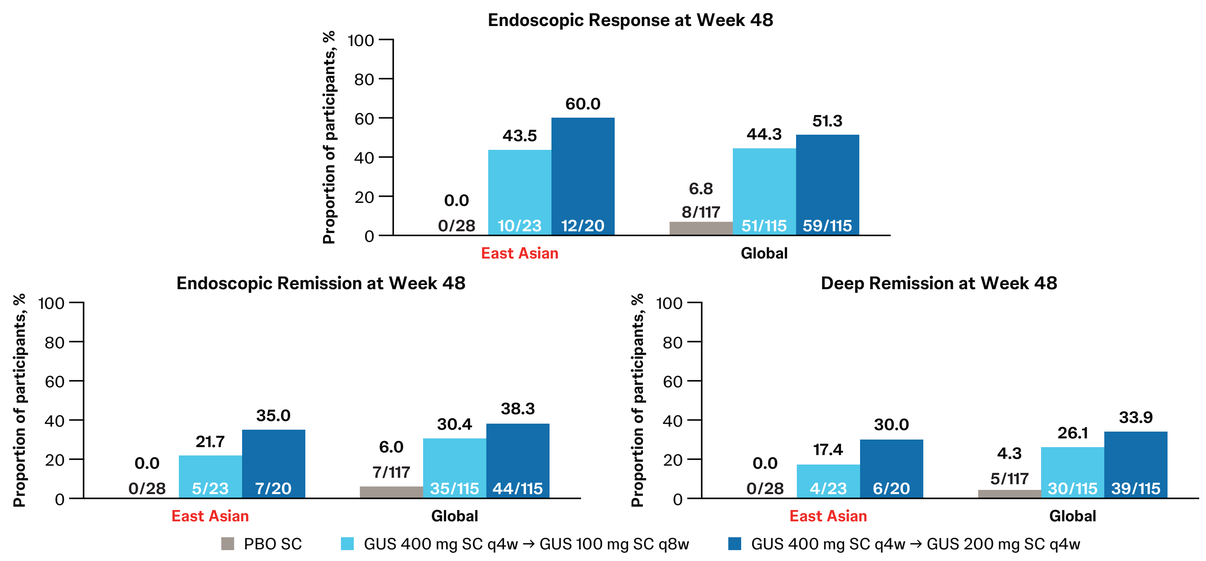
Long-term efficacy of GUS SC induction and maintenance



***CI**=confidence interval; **q4w**=Every four weeks; **q8w**=Every eight weeks. *Nominal p-value <0.05. Primary Analysis Set. Clinical remission: CDAI score <150.*

Long-term endoscopic outcomes of GUS SC maintenance

- Numerically higher proportions of GUS group participants achieved endoscopic response, endoscopic remission, and deep remission at Week 48 relative to PBO
- Rates were generally consistent between East Asian and global participants



***CDAI**=Crohn's Disease Activity Index; **q4w**=Every 4 weeks; **q8w**=Every 8 weeks; **SES-CD**=Simple Endoscopic Score for Crohn's Disease. Primary Analysis Set. Endoscopic response: ≥50% improvement from baseline in SES-CD score. Endoscopic remission: SES-CD score ≤4 and at least a 2-point reduction from baseline and no subscore greater than 1 in any individual component. Deep remission: Clinical remission (CDAI score <150) and endoscopic remission.*

Summary of safety through Week 48

- The most common TEAEs in East Asian and global participants were upper respiratory tract infections, abdominal pain, and COVID-19

	East Asian			Global		
Safety analysis set	PBO[d] (N=28)	GUS 400 mg SC q4w → 100 mg SC q8w (N=23)	GUS 400 mg SC q4w → 200 mg SC q4w (N=20)	PBO[d] (N=117)	GUS 400 mg SC q4w → 100 mg SC q8w (N=115)	GUS 400 mg SC q4w → 200 mg SC q4w (N=115)
Average duration of follow-up, weeks	25.6	47.5	48.4	30.0	47.0	48.0
Average exposure, number of administrations	6.2	6.9	12.0	7.1	6.8	11.8
Total PYs of follow-up, years	13.8	20.9	18.6	67.3	103.5	105.7
Deaths,[e] n (%)	0	0	0	0	1 (0.9%)	0
Participants with 1 or more:						
AEs, n (%)	19 (67.9)	19 (82.6)	18 (90.0)	77 (65.8%)	95 (82.6%)	92 (80.0%)
Events per 100 PYs follow-up	392.5	248.3	447.0	413.0	307.2	327.2
SAEs, n (%)	2 (7.1)	1 (4.3)	1 (5.0)	16 (13.7%)	15 (13.0%)	9 (7.8%)
Events per 100 PYs follow-up	14.5	4.8	5.4	37.1	15.5	13.2
AEs leading to discontinuation of study agent, n (%)	2 (7.1)	0	0	10 (8.5%)	4 (3.5%)	3 (2.6%)
Events per 100 PYs follow-up	14.5	0	0	14.9	6.8	2.8
Serious infections, n (%)	0	0	1 (5.0)	0	2 (1.7%)	1 (0.9%)

Three most frequent AEs in participants receiving GUS were:

- Upper respiratory tract infection (GUS 22% vs PBO 18%) (GUS 14% vs PBO 10%)
- Abdominal pain (GUS 7% vs PBO 7%) (GUS 10% vs PBO 6%)
- COVID-19 (GUS 17% vs PBO 21%) (GUS 8% vs PBO 7%)

*East Asian; Global.

***AE**=adverse event; **MedDRA**=Medical Dictionary for Regulatory Activities; **PY**=participant-years; **q4w**=Every four weeks; **q8w**=Every eight weeks; **SAE**=serious adverse event; **TEAE**=Treatment-emergent adverse event. [d]Includes all PBO participants excluding data after a participant is rescued with guselkumab. [e]Fatal gunshot wound (non-suicidal). Note: Participants are counted only once for any given event under specific column, regardless of the number of times they actually experienced the event. Adverse events are coded using MedDRA Version 26.0.*

PRESENTED BY: Q. Cao at the 20th Congress of European Crohn's and Colitis Organization (ECCO), February 19–22, 2025, Berlin, Germany. **REFERENCES: 1.** Atreya R, et al. *J Crohns Colitis.* 2024;18(suppl):S470. **2.** Panaccione R, et al. *Am J Gastro.* 2024;119(10S):p S740-S741. **ACKNOWLEDGMENTS:** Medical writing support was provided by Jackie L. Johnson, PhD of Certara under the direction of the authors in accordance with Good Publication Practice guidelines (*Ann Intern Med.* 2022;175:1298-1304). Sponsored by Janssen Research & Development, LLC, a Johnson & Johnson Company. **DISCLOSURES: WL, HG, TOK,** and **KT:** are clinical investigators for Janssen Research & Development, LLC. **TH:** has received grant support from AbbVie, Daiichi-Sankyo, EA Pharma Co, Ltd., JIMRO, Mitsubishi Tanabe Pharma Corporation, Mochida Pharmaceutical Co., Ltd., Nippon Kayaku Co., Ltd., Pfizer Inc., Takeda Pharmaceutical Co., Ltd.; consulting fees from EA Pharma Co., Ltd., Janssen Research & Development, LLC, Gilead Sciences, Eli Lilly, Bristol Myers Squibb; and lecture fees from AbbVie, EA Pharma Co, Ltd., Mitsubishi Tanabe Pharma Corporation, Takeda Pharmaceutical Co., Ltd., Mochida Pharmaceutical Co., Ltd., and Kissei Pharmaceutical Co., Ltd. **JF, MO, BW,** and **JZ:** are employees of and may own stock in Johnson & Johnson. **QC:** has served as a steering committee adviser for Bristol Myers Squibb Company and Janssen Research Development, LLC, and has received research grants from Johnson & Johnson and Takeda.