# Efficacy by baseline disease characteristics of subcutaneous guselkumab induction therapy in patients with moderately to severely active Crohn's disease: Results at Week 12 from the phase 3 GRAVITI study

G. D'Haens,[1] T. Hisamatsu,[2] F. Steinwurz,[3] A. Hart,[4] W. Liu,[5] M. Olurinde,[6] P. Ngqawa,[6] Z. Yang,[6] E. Merrall,[7] N.A. Terry,[6] B.E. Sands,[8] R. Panaccione[9] on behalf of the GRAVITI Investigators

[1]Department of Gastroenterology, Amsterdam University Medical Centers, Amsterdam, The Netherlands; [2]Kyorin University, Tokyo, Japan; [3]Hospital Israelita Albert Einstein, São Paulo, Brazil; [4]London North-West University Healthcare NHS Trust, London, UK; [5]The Second People's Hospital of Changzhou, The Third Affiliated Hospital of Nanjing Medical University, Changzhou, China; [6]Johnson & Johnson, Spring House, PA, USA; [7]Johnson & Johnson, Leiden, the Netherlands; [8]Icahn School of Medicine at Mount Sinai, New York, NY, USA; [9]University of Calgary, Calgary, AB, Canada

## 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 based on baseline disease characteristics 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

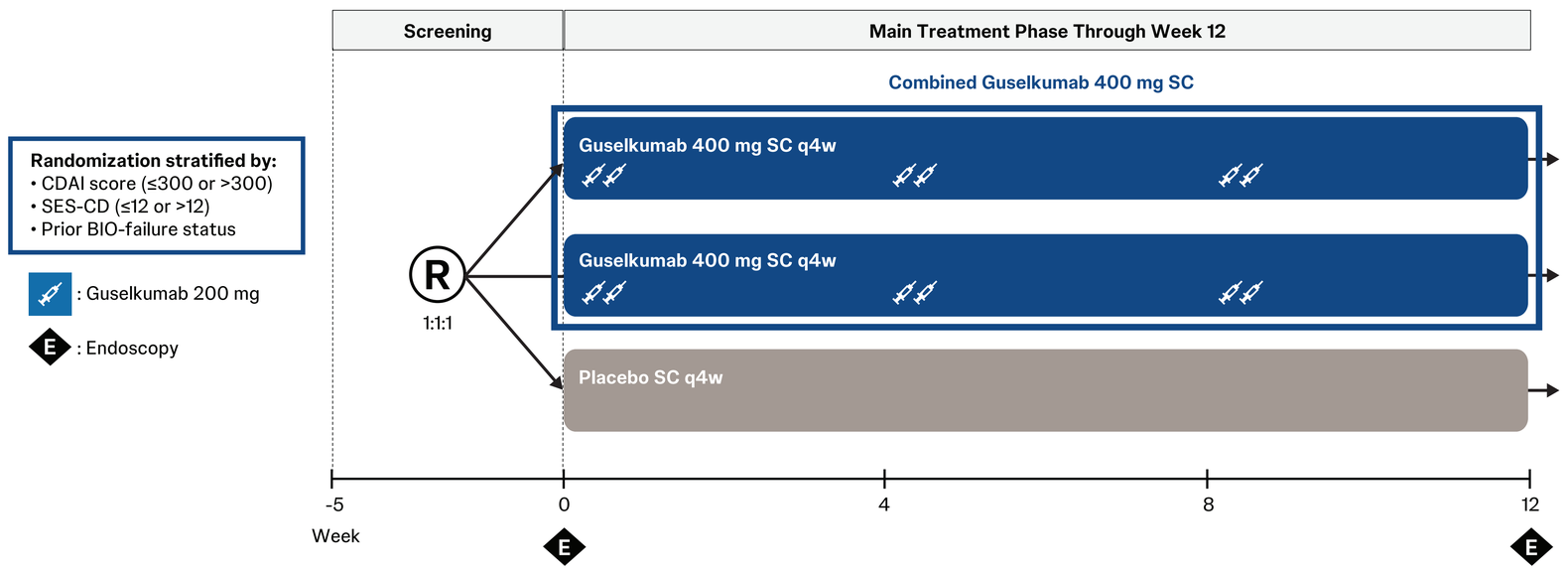
**We evaluated the efficacy of guselkumab SC induction in the Week 12 co-primary endpoints of GRAVITI in subgroups based on baseline disease characteristics**

## 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

- **Crohn's disease duration in years** (ie, ≤5, >5 to ≤15, or >15)
- **Involved disease location** (ie, ileum, colon, or both)
- **CDAI score** (ie, ≤300 or > 300)
- **SES-CD score** (ie, ≤12 or >12)
- **C-reactive protein in mg/L** (ie, ≤5 or >5; CRP)
- **Fecal calprotectin in µg/g** (ie, ≤250 or >250; FeCal)

## 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 Disease Characteristics**

| | 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 |
| **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 |
| **Involved disease location** *(based on central reader assessment)* | | | | |
| Ileum only | 22 (27.3) | 52 (55.8) | 29.2 (4.7, 53.6) | 0.020 |
| Colon only | 40 (17.5) | 81 (55.6) | 37.2 (20.9, 53.5) | <0.001 |
| Ileum and colon | 55 (21.8) | 97 (56.7) | 34.2 (19.4, 49.1) | <0.001 |
| **CDAI score** | | | | |
| ≤300 | 68 (26.5) | 137 (66.4) | 39.9 (26.9, 53.0) | <0.001 |
| >300 | 49 (14.3) | 93 (40.9) | 26.3 (12.2, 40.5) | <0.001 |
| **SES-CD** | | | | |
| ≤12 | 72 (23.6) | 140 (52.1) | 28.2 (15.2, 41.2) | <0.001 |
| >12 | 45 (17.8) | 90 (62.2) | 45.3 (31.4, 59.2) | <0.001 |
| **CRP (mg/L)** | | | | |
| ≤5 | 47 (27.7) | 110 (52.7) | 24.7 (8.5, 40.8) | 0.003 |
| >5 | 70 (17.1) | 120 (59.2) | 42.8 (30.5, 55.1) | <0.001 |
| **Fecal calprotectin (µg/g)** | | | | |
| ≤250 | 31 (25.8) | 67 (59.7) | 34.1 (13.3, 54.8) | 0.001 |
| >250 | 86 (19.8) | 162 (54.3) | 35.3 (24.1, 46.4) | <0.001 |

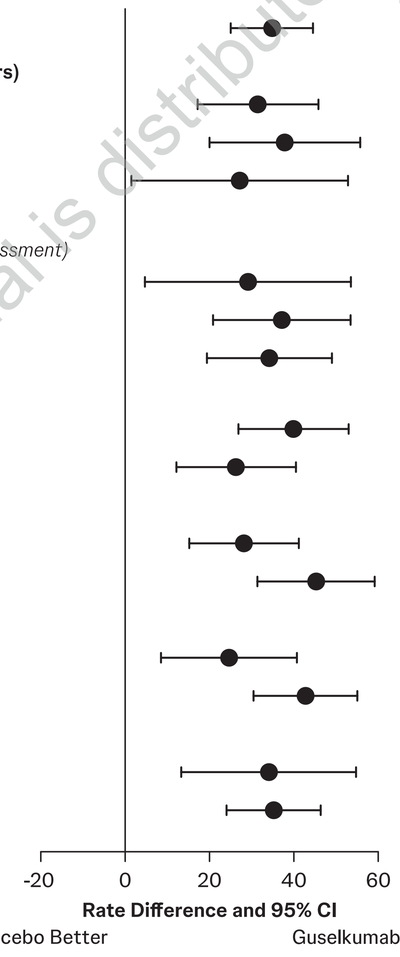
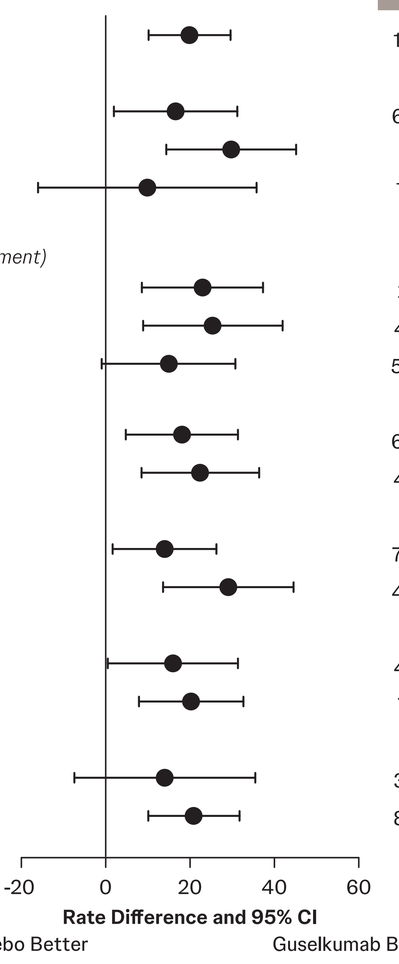



**Figure 2. Endoscopic Response at Week 12 by Baseline Disease Characteristics**

| | 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 |
| **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 |
| **Involved disease location** *(based on central reader assessment)* | | | | |
| Ileum only | 22 (4.5) | 52 (26.9) | 23.0 (8.6, 37.3) | 0.002 |
| Colon only | 40 (17.5) | 81 (43.2) | 25.4 (8.9, 42.0) | 0.003 |
| Ileum and colon | 55 (30.9) | 97 (47.4) | 15.0 (-0.9, 30.8) | 0.064 |
| **CDAI score** | | | | |
| ≤300 | 68 (26.5) | 137 (43.8) | 18.1 (4.8, 31.4) | 0.008 |
| >300 | 49 (14.3) | 93 (37.6) | 22.4 (8.5, 36.4) | 0.002 |
| **SES-CD** | | | | |
| ≤12 | 72 (20.8) | 140 (35.0) | 14.0 (1.7, 26.3) | 0.026 |
| >12 | 45 (22.2) | 90 (51.1) | 29.1 (13.6, 44.6) | <0.001 |
| **CRP (mg/L)** | | | | |
| ≤5 | 47 (27.7) | 110 (43.6) | 16.0 (0.5, 31.4) | 0.043 |
| >5 | 70 (17.1) | 120 (39.2) | 20.3 (7.9, 32.7) | 0.001 |
| **Fecal calprotectin (µg/g)** | | | | |
| ≤250 | 31 (29.0) | 67 (43.3) | 14.0 (-7.4, 35.5) | 0.200 |
| >250 | 86 (18.6) | 162 (40.1) | 20.9 (10.1, 31.8) | <0.001 |




*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 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).* ***CI****=confidence interval.*

**PRESENTED AT:** the 20th Congress of European Crohn's and Colitis Organization (ECCO), February 19–22, 2025, Berlin, Germany. **REFERENCES: 1.** Atreya R, Abreu MT, Krueger JG, et al. *J Crohns Colitis.* 2024;18(suppl):S470. **2.** Panaccione R, Hart A, Steinwurz F, et al. Efficacy and safety of subcutaneous guselkumab induction therapy in patients with moderately to severely active Crohn's disease: Results through week 48 from the phase 3 GRAVITI study. Presented at American College of Gastroenterology 2024. **ACKNOWLEDGMENTS:** The authors thank the participants, investigators, and study personnel who made the GRAVITI study possible. This work was supported by Johnson & Johnson. Under the direction of the authors and in accordance with Good Publication Practices, Rick Mearhoff of Johnson & Johnson provided writing and editorial assistance. **DISCLOSURES: GD:** reports consultancy activities for AbbVie, Agomab, Alimentiv, AstraZeneca, AMT, Bristol Myers Squibb, Boehringer Ingelheim, Celltrion, Eli Lilly, Exeliom, Galapagos, GlaxoSmithKline, Gossamerbio, Immunic, Index, Johnson & Johnson, Kaleido, Origo, Pfizer, Polpharma, Procise Diagnostics, Prometheus Laboratories, Prometheus Biosciences, Progenity, and Protagonist Therapeutics Inc.; speaker's bureau for AbbVie, Bristol Myers Squibb, Galapagos, Pfizer, and Takeda; and data monitoring board activities for AbbVie, AstraZeneca, Galapagos, and Seres Health. **TH:** received grant support from Mitsubishi Tanabe Pharma Corporation, EA pharma Co. Ltd., AbbVie GK, JIMRO Co. Ltd., Zeria Pharmaceutical Co. Ltd., Kyorin Pharmaceutical Co. Ltd., Nippon Kayaku Co. Ltd., Takeda Pharmaceutical Co. Ltd., Pfizer Inc., Mochida Pharmaceutical Co. Ltd., Boston Scientific Corporation, Kissei Pharmaceutical Co. Ltd., consulting fees from Mitsubishi Tanabe Pharma Corporation, EA pharma Co. Ltd., AbbVie GK, Janssen Pharmaceutical K.K., Pfizer Inc., Nichi-Iko Pharmaceutical Co. Ltd., Eli Lilly, Gilead Sciences, Bristol Myers Squibb, and lecture fee from Mitsubishi Tanabe Pharma Corporation, AbbVie GK, EA pharma Co. Ltd., Kyorin Pharmaceutical Co. Ltd., JIMRO Co., Janssen Pharmaceutical K.K., Mochida Pharmaceutical Co., Ltd., Takeda Pharmaceutical Co. Ltd., Pfizer Inc. Kissei Pharmaceutical Co. Ltd. **FS:** served as a clinical investigator and consultant for Janssen. **AH:** served as a clinical investigator and consultant for Janssen. **WL:** served as a clinical investigator and consultant for Janssen. **MO, PN, ZY, EM,** and **NAT:** are employees of Johnson & Johnson and own company stock/stock options. **BES:** reports consulting fees from AbbVie. Adiso Therapeutics, Agomab, Alimentiv, Amgen, AnaptysBio, Arena Pharmaceuticals, Artugen Therapeutics, Astra Zeneca, Biolojic Design, Biora Therapeutics, Boehringer Ingelheim, Boston Pharmaceuticals, Calibr, Celgene, Celltrion, ClostraBio, Equillium, Enthera, Envied Biosciences, Evommune, Ferring, Fresenius Kabi, Fiat, Galapagos, Genentech (Roche), Gilead Sciences, GlaxoSmithKline, Gossamer Bio, Imhotex, Index Pharmaceuticals, Innovation Pharmaceuticals, Inotrem, Kaleido, Kallyope, Merck, Microba, Mobius Care, Morphic Therapeutics, MRM Health, Nexus Therapeutics, Nimbus Discovery, Odyssey Therapeutics, Progenity, Prometheus Biosciences, Prometheus Laboratories, Protagonist Therapeutics, Q32 Bio, Rasayana Therapeutics, Recludix Therapeutics, Reistone Biopharma, Sanofi, Spyre Therapeutics, Sun Pharma, Surrozen, Target RWE, Teva, TLL Pharmaceutical, Tr1X, Union Therapeutics, Ventyx Biosciences; consulting and speaking fees from Abivax; consulting and speaking fees and other support from Lilly; research grants, consulting and speaking fees and other support from Bristol Myers Squibb, Janssen, Pfizer, Takeda; research grants and consulting fees from Theravance Biopharma; and stock/stock options from Ventyx Biopharma. **RP:** reports having received consulting fees from Abbivax, Abbott, AbbVie, Alimentiv (formerly Robarts), Amgen, Arena Pharmaceuticals, AstraZeneca, Biogen, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Celltrion, Cosmos Pharmaceuticals, Eisai, Elan, Eli Lilly, Ferring, Fresenius Kabi, Galapagos, Genentech, Gilead Sciences, GlaxoSmithKline, JAMP Bio, Janssen, Merck, Mylan, Novartis, Oppilan Pharma, Organon, Pandion Pharma, Pendopharm, Pfizer, Progenity, Prometheus Biosciences, Protagonist Therapeutics, Roche, Sandoz, Satisfai Health, Shire, Sublimity Therapeutics, Takeda Pharmaceuticals, Theravance Biopharma, Trellus, Viatris, Ventyx, UCB; Speaker's Fees from AbbVie, Amgen, Arena Pharmaceuticals, Bristol Myers Squibb, Celgene, Eli Lilly, Ferring, Fresenius Kabi, Gilead Sciences, Janssen, Merck, Organon, Pfizer, Roche, Sandoz, Shire, Takeda Pharmaceuticals and served on Advisory Boards for: AbbVie, Alimentiv (formerly Robarts), Amgen, Arena Pharmaceuticals, AstraZeneca, Biogen, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Eli Lilly, Ferring, Fresenius Kabi, Genentech, Gilead Sciences, GlaxoSmithKline, JAMP Bio, Janssen, Merck, Mylan, Novartis, Oppilan Pharma, Organon, Pandion Pharma, Pfizer, Progenity, Protagonist Therapeutics, Roche, Sandoz, Shire, Sublimity Therapeutics, Takeda Pharmaceuticals, and Ventyx.