OP 726

EFFICACY AND SAFETY OF GUSELKUMAB IN PARTICIPANTS WITH MODERATELY TO SEVERELY ACTIVE CROHN'S DISEASE WHO HAD MAINTENANCE DOSE ADJUSTMENT: RESULTS FROM THE PHASE 3 GALAXI 2 & 3 LONG-TERM EXTENSION

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SPEAKER DISCLOSURE

Remo Panaccione

I disclose the following financial relationships with a commercial interest:

Consulting fees from Abbivax, Abbott, AbbVie, Alimentiv (formerly Robarts), Amgen, AnaptysBio, 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, BioJAMP, Johnson & Johnson, Merck, Mylan, Novartis, Oppilan Pharma, Organon, Pandion Pharma, Pendopharm, Pfizer, Progenity, Prometheus Biosciences, Protagonist Therapeutics, Roche, Sandoz, Satisfai Health, Shire, Spyre Therapeutics, Sublimity Therapeutics, Takeda Pharmaceuticals, Theravance Biopharma, Trellus, Union Biopharma, Viatris, Ventyx Biosciences, and UCB

Speaker's fees from AbbVie, Amgen, Arena Pharmaceuticals, Bristol Myers Squibb, Celgene, Eli Lilly, Ferring, Fresenius Kabi, Gilead Sciences, Johnson & Johnson, Merck, Organon, Pfizer, Roche, Sandoz, Shire, and Takeda Pharmaceuticals

Participation in 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, BioJAMP, Johnson & Johnson, Merck, Mylan, Novartis, Oppilan Pharma, Organon, Pandion Pharma, Pfizer, Progenity, Protagonist Therapeutics, Roche, Sandoz, Shire, Sublimity Therapeutics, Takeda Pharmaceuticals, and Ventyx Biosciences.

Background & Objective

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

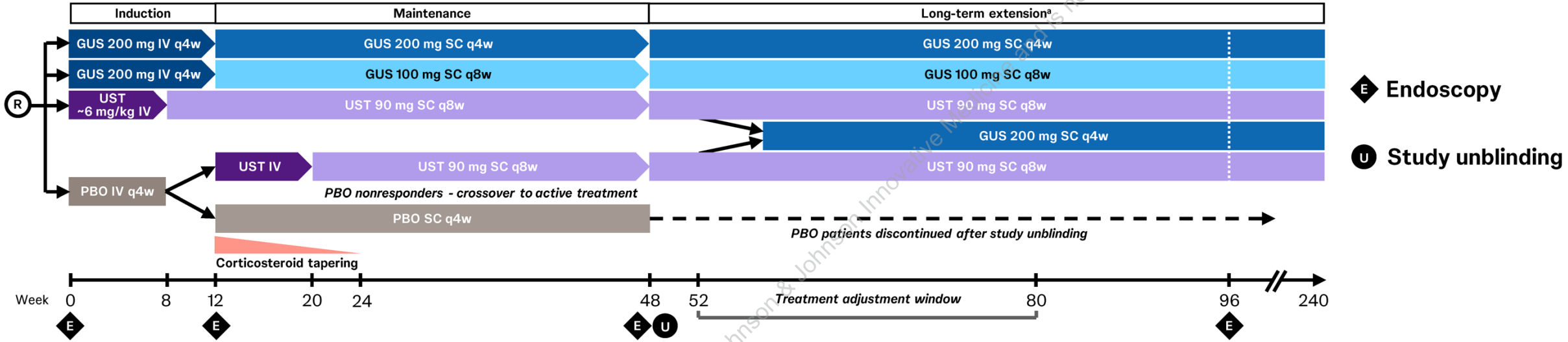
Guselkumab demonstrated efficacy and safety through Week 48 in moderately to severely active Crohn's disease in the identically designed, randomized, double-blind GALAXI 2 & 3 phase 3 trials[1]

Patients may experience flares after successful long-term maintenance therapy because of the remitting and relapsing nature of Crohn's disease

Objective: To assess the efficacy and safety of guselkumab through Week 96 in participants who dose adjusted after an inadequate response to their randomized guselkumab maintenance regimen in the long-term extension (LTE) of GALAXI 2 & 3

1. Panaccione R, Feagan BG, Afzali A, et al. Lancet. 2025;406(10501):358-375.

GALAXI 2 & 3 Design

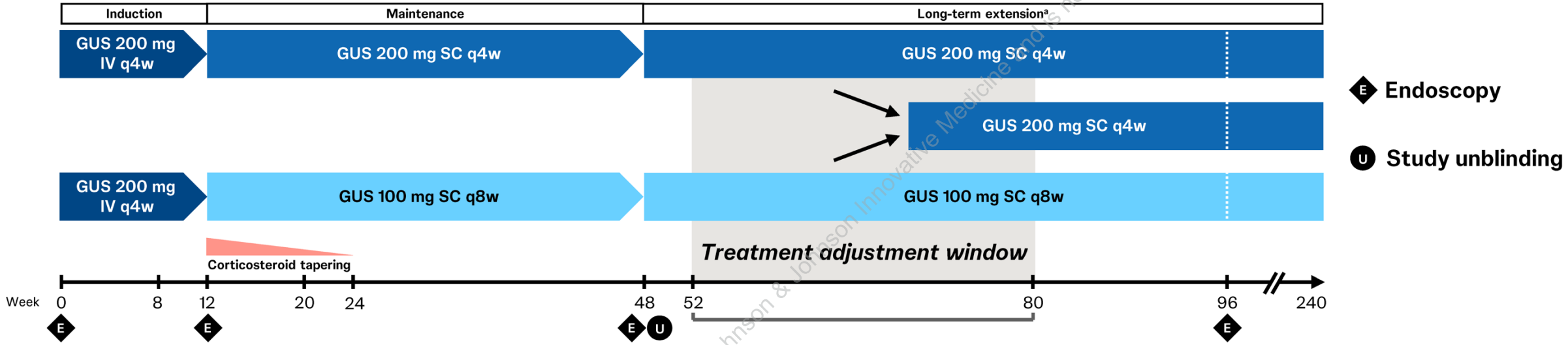


GALAXI randomization (2:2:2:1) was stratified by

- CDAI ≤300 or >300
- SES-CD ≤12 or >12
- BIO-IR (yes/no)
- Corticosteroid use at baseline (yes/no)

a. The present study includes data through 96 weeks.
BIO=biologics, CD=Crohn's disease, CDAI=Crohn's Disease Activity Index, GUS=guselkumab, IR=inadequate response or intolerance, IV=intravenous, LTE=long-term extension, PBO=placebo, q4w=every 4 weeks, q8w=every 8 weeks, SC=subcutaneous, SES-CD=Simple Endoscopic Score for Crohn's Disease, UST=ustekinumab.

GALAXI 2 & 3 Design



From Weeks 52–80 of the LTE, participants who met inadequate response criteria received a one-time dose adjustment or sham dose adjustment (if already receiving 200 mg q4w) to guselkumab 200 mg q4w

- Inadequate response criteria: not in clinical response (≥100-point reduction in CDAI from Week 0 or CDAI <150) AND CDAI ≥220

a. The present study includes data through 96 weeks.
BIO=biologics, CD=Crohn's disease, CDAI=Crohn's Disease Activity Index, GUS=guselkumab, IR=inadequate response or intolerance, IV=intravenous, LTE=long-term extension, PBO=placebo, q4w=every 4 weeks, q8w=every 8 weeks, SC=subcutaneous, SES-CD=Simple Endoscopic Score for Crohn's Disease, UST=ustekinumab.

Endpoints and Statistical Considerations

- Per the prespecified analysis plan, outcomes in participants undergoing dose adjustment in the LTE were evaluated:
  - Clinical response and clinical remission 16 weeks after dose adjustment and at Week 96
  - Endoscopic response and endoscopic remission at Weeks 48 and 96
  - Safety assessed through Week 96
- Treatment allocation in the LTE remained blinded until the Week 48 analysis was finalized
- Nonresponder imputation
  - Participants who experienced events indicative of lack of efficacy were considered nonresponders at all analysis timepoints after experiencing the event
  - Participants who were missing endpoint data at an analysis timepoint were considered not having achieved the endpoint at that timepoint

Characteristics at Baseline

	GUS 100 mg SC q8w[a]		GUS 200 mg SC q4w[a]	
	Did NOT receive dose adjustment	Received dose adjustment	Did NOT receive dose adjustment	Received sham dose adjustment
N[b]	208	29	218	24
Crohn's disease duration (y), median (IQR)	4.9 (1.8; 10.2)	8.2 (5.3; 14.5)	4.1 (1.6; 9.0)	6.3 (3.0; 14.3)
History of BIO-IR, n (%)	102 (49.0%)	17 (58.6%)	98 (45.0%)	14 (58.3%)
CDAI score, median (IQR)	280.0 (248.0; 329.0)	294.0 (263.0; 319.0)	283.5 (252.0; 334.0)	289.0 (264.0; 328.5)
SES-CD, median (IQR)	11.0 (7.0; 17.0)	13.0 (7.0; 19.0)	11.0 (7.0; 17.0)	13.0 (9.5; 18.0)
Endoscopic disease severity (per SES-CD)				
Moderate (7–16), n (%)	116 (55.8%)	14 (48.3%)	106 (48.6%)	11 (45.8%)
Severe (>16), n (%)	55 (26.4%)	12 (41.4%)	61 (28.0%)	9 (37.5%)
Involved GI areas by central reader				
Ileum only, n (%)	41 (19.7%)	6 (20.7%)	56 (25.7%)	6 (25.0%)
Colon only, n (%)	80 (38.5%)	13 (44.8%)	87 (39.9%)	6 (25.0%)
Ileum and colon, n (%)	87 (41.8%)	10 (34.5%)	75 (34.4%)	12 (50.0%)
C-reactive protein (mg/L), median (IQR)	7.2 (2.1; 19.4)	8.5 (2.9; 36.2)	6.5 (2.8; 19.8)	6.1 (2.1; 31.1)
Fecal calprotectin (µg/g), median (IQR)[c]	903.0 (390.0; 1892.0)	848.5 (403.5; 2116.5)	982.0 (319.0; 1936.5)	1354.5 (386.0; 1727.0)

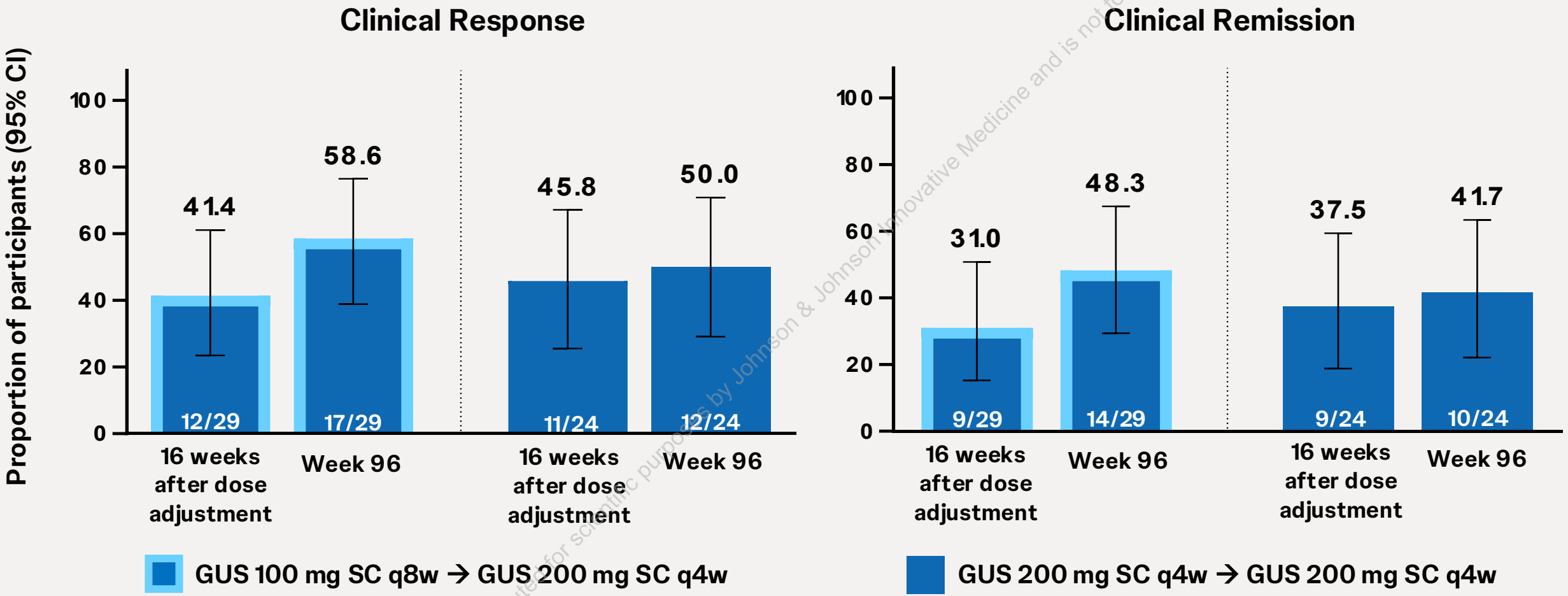
a. Treatment group at the start of the long-term extension period. Participants who had a dose adjustment between Week 52 and Week 80 received guselkumab 200 mg SC q4w. Participants who were already receiving the guselkumab 200 mg SC q4w maintenance dose and met the inadequate response criteria received a "sham" dose adjustment.
b. Participants with a Crohn's disease-related surgery (with the exception of minor procedures) prior to Week 48 or a prohibited change in Crohn's disease medications prior to Week 48 who remained on treatment and subsequently entered the LTE are excluded.
c. N=206 (GUS 100 non adjusters), 28 (GUS 100→200), 216 (GUS 200 non adjusters), and 24 (GUS 200→200) participants with evaluable samples at baseline.

Characteristics at Week 48

	GUS 100 mg SC q8w[a]		GUS 200 mg SC q4w[a]	
	Did NOT receive dose adjustment	Received dose adjustment	Did NOT receive dose adjustment	Received sham dose adjustment
N[b]	208	29	218	24
CDAI score, median (IQR)	69.5 (30.0; 128.5)	155.0 (81.0; 232.0)	68.5 (32.0; 112.0)	138.5 (72.0; 206.5)
In clinical response, n (%)	199 (95.7%)	19 (65.5%)	203 (93.1%)	18 (75.0%)
In clinical remission, n (%)	179 (86.1%)	14 (48.3%)	193 (88.5%)	13 (54.2%)
SES-CD, median (IQR)[c]	4.0 (0.0; 7.0)	7.0 (4.0; 15.0)	3.0 (1.0; 6.0)	6.0 (3.5; 10.5)
Endoscopic disease severity (per SES-CD)[c]				
Moderate (7–16), n (%)	49 (24.0%)	10 (34.5%)	36 (16.7%)	8 (33.3%)
Severe (>16), n (%)	5 (2.5%)	7 (24.1%)	6 (2.8%)	2 (8.3%)
In endoscopic response, n (%)	128 (61.5%)	9 (31.0%)	149 (68.3%)	8 (33.3%)
In endoscopic remission, n (%)	91 (43.8%)	4 (13.8%)	106 (46.2%)	5 (20.8%)
C-reactive protein (mg/L), median (IQR)[d]	1.8 (0.8; 5.8)	5.9 (0.8; 12.7)	2.2 (0.9; 4.6)	4.0 (0.6; 8.3)
Fecal calprotectin (µg/g), median (IQR)[e]	173.5 (65.0; 555.0)	591.0 (115.0; 1739.0)	121.0 (47.0; 408.0)	160.0 (49.0; 336.0)

a. Treatment group at the start of the long-term extension period. Participants who had a dose adjustment between Week 52 and Week 80 received guselkumab 200 mg SC q4w. Participants who were already receiving the guselkumab 200 mg SC q4w maintenance dose and met the inadequate response criteria received a "sham" dose adjustment.
b. Participants with a Crohn's disease-related surgery (with the exception of minor procedures) prior to Week 48 or a prohibited change in Crohn's disease medications prior to Week 48 who remained on treatment and subsequently entered the LTE are excluded.
c. N=204 (GUS 100 non adjusters), 29 (GUS 100→200), 216 (GUS 200 non adjusters), and 24 (GUS 200→200) participants with SES-CD data at Week 48.
d. N=205 (GUS 100 non adjusters), 27 (GUS 100→200), 213 (GUS 200 non adjusters), and 24 (GUS 200→200) participants with evaluable samples at Week 48.
e. N=198 (GUS 100 non adjusters), 27 (GUS 100→200), 206 (GUS 200 non adjusters), and 23 (GUS 200→200) participants with evaluable samples at Week 48.

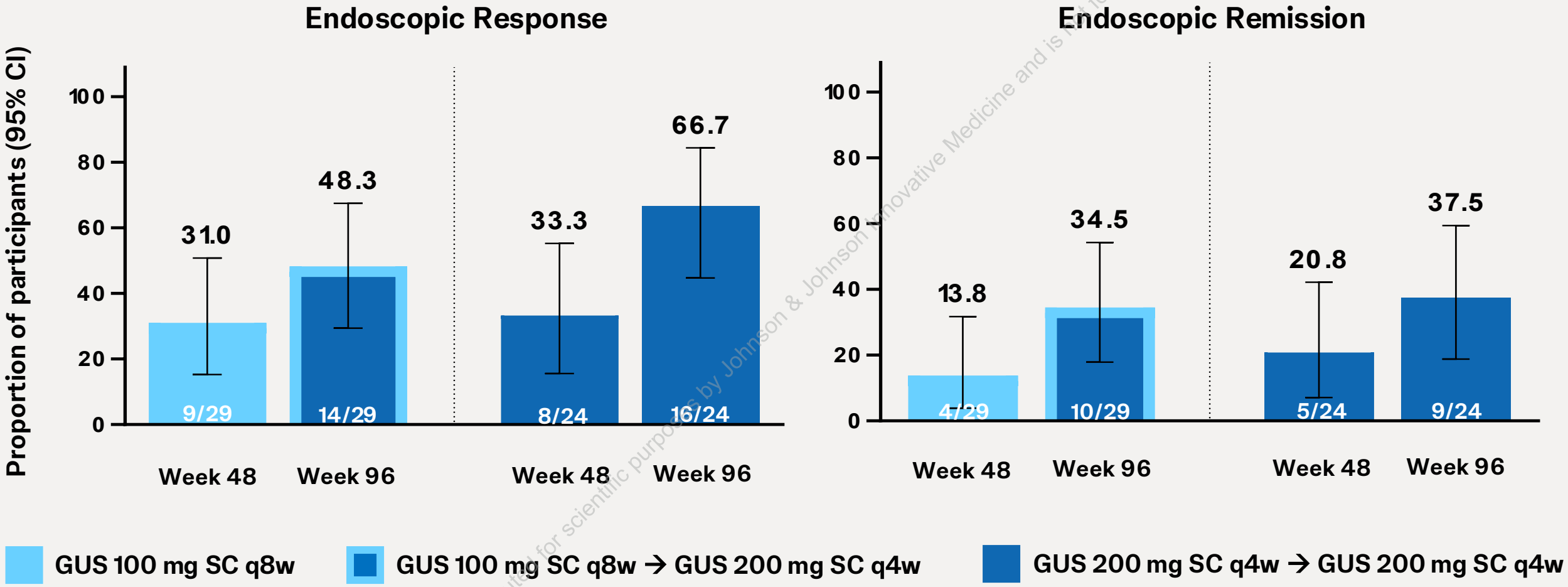
Clinical Response and Clinical Remission After Dose Adjustment



Clinical response: ≥100-point reduction in CDAI score from the time of dose adjustment or CDAI score <150
Clinical remission: CDAI score <150

Note: No participant was in clinical response or clinical remission at the time of dose adjustment per criteria for dose adjustment (not in clinical response [≥100-point reduction in CDAI from Week 0 or CDAI <150] AND CDAI ≥220).

Endoscopic Outcomes After Dose Adjustment



Endoscopic response: ≥50% improvement from Week 0 in SES-CD or SES-CD ≤2
Endoscopic remission: SES-CD ≤4 and at least a 2-point reduction from Week 0 and no subscore >1 in any individual component

Adverse Events In the LTE Before and After Dose Adjustment

	Randomized treatment and up to dose adjustment[a]	After dose adjustment[b]	Randomized treatment and up to dose adjustment[a]	After sham dose adjustment[b]
	GUS 100 mg q8w	GUS 100 mg q8w →200 mg q4w	GUS 200 mg q4w	GUS 200 mg q4w →200 mg q4w
N[c]	36	36	28	28
Average duration of follow-up, weeks	12.1	33.6	12.9	33.1
Participant–years (P–Y) of follow-up	8.3	23.2	6.9	17.7
Participants (Pts) with ≥1 AE, n (%)	19 (52.8%)	24 (66.7%)	14 (50.0%)	15 (53.6%)
Events/100 P–Y (95% CI)	360.7 (243.4, 514.9)	341.1 (270.0, 425.1)	519.1 (363.6, 718.7)	484.6 (387.6, 598.5)
Pts with ≥1 SAE, n (%)	0	3 (8.3%)	1 (3.6%)	1 (3.6%)
Events/100 P–Y (95% CI)	0.0 (0.0, 36.0)	13.0 (2.7, 37.8)	14.4 (0.4, 80.3)	5.6 (0.1, 31.4)
Pts with ≥1 AE leading to discontinuation, n (%)	0	2 (5.6%)	1 (3.6%)	0
Events/100 P–Y (95% CI)	0.0 (0.0, 36.0)	17.3 (4.7, 44.2)	14.4 (0.4, 80.3)	0.0 (0.0, 16.9)
Pts with ≥1 infection, n (%)	7 (19.4%)	12 (33.3%)	4 (14.3%)	9 (32.1%)
Events/100 P–Y (95% CI)	120.2 (57.7, 221.1)	77.7 (46.1, 122.8)	72.1 (23.4, 168.3)	84.5 (47.3, 139.4)
Pts with ≥1 serious infection, n (%)	0	1 (2.8%)	0	0
Events/100 P–Y (95% CI)	0.0 (0.0, 36.0)	4.3 (0.1, 24.1)	0.0 (0.0, 43.2)	0.0 (0.0, 16.9)
Pts who died, n (%)	0	0	0	0

a. Treatment group at the start of the long-term extension. Includes events for participants who received a dose adjustment from Week 48 up to the time point of dose adjustment, and all events from Week 48 through Week 96 for participants who never received a dose adjustment

b. Participants receiving GUS 100 mg SC q8w who met inadequate response criteria between Week 52 and Week 80 had a dose adjustment to GUS 200 mg SC q4w. Participants receiving GUS 200 mg SC q4w who met the inadequate response criteria between Week 52 and Week 80 received a "sham" dose adjustment.

c. Only events after dose adjustment (including "sham") are included in this column

Note: Participants are counted only once for any given events, regardless of the number of times they actually experienced the event. Adverse events coded using MeDRA version 27.0.

Key Takeaways

- Maintenance dose adjustment to guselkumab 200 mg q4w may benefit patients with Crohn's disease who experience inadequate response to guselkumab 100 mg q8w
- Nearly half of guselkumab 100 mg q8w participants receiving an adjustment to guselkumab 200 mg q4w achieved clinical remission or endoscopic response up to ~1 year after dose adjustment
- Efficacy outcomes in guselkumab 200 mg q4w participants who received a sham dose adjustment were generally similar to those who switched from guselkumab 100 mg q8w to 200 mg q4w
- Safety outcomes after dose adjustment were consistent with the established safety profile of guselkumab in approved indications

Interpretation is affected by small sample sizes and absence of randomization for dose adjustment

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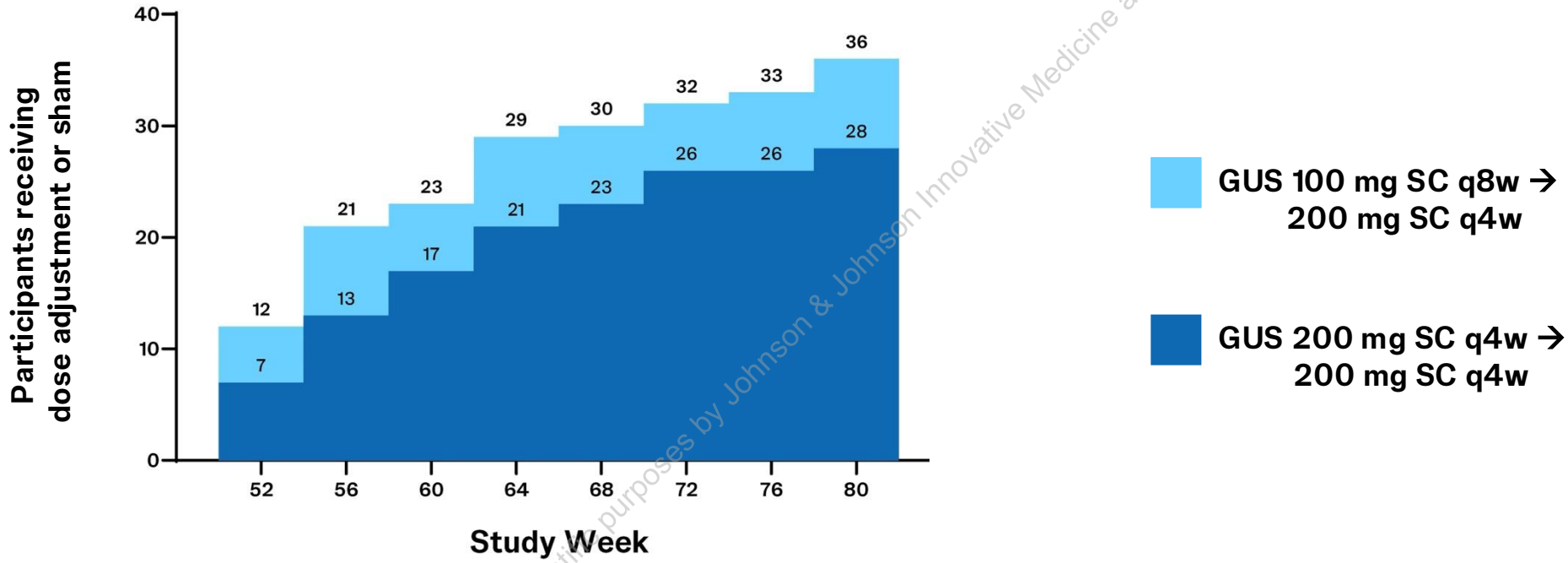
Time to Dose Adjustment by Study Week



- Among participants who underwent dose adjustment, 91.7% (GUS 100 mg SC) and 100% (GUS 200 mg SC) were blinded at the time of dose adjustment