Symptomatic Improvement With Intravenous Guselkumab Induction Therapy Is Observed Early in Patients with Moderately to Severely Active Ulcerative Colitis: Post-hoc Analysis of QUASAR

OP10

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Disclosure of Conflicts of Interest

I, Axel Dignass, declare the following potential conflicts of interest:

- Fees for participation in clinical trials, review activities such as data monitoring boards, statistical analysis, and endpoint committees from Abivax, AbbVie, Falk, Galapagos, Gilead, J&J, Pfizer, and Takeda
- Consultancy fees from AbbVie, Alfasigma, Amgen, Biogen, Boehringer, Hexal, J&J, Lilly, MSD, Pfizer, Pharmacosmos, Roche, Sandoz, Stada, Takeda, and Vifor Pharma
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Background and Objective

Symptom Relief in UC

- UC symptoms of stool frequency, rectal bleeding, and abdominal pain significantly impair HRQoL
- The STRIDE-II treat-to-target framework includes symptomatic relief as a short-term therapeutic goal in UC management[1,2]
- Early symptomatic improvement is clinically meaningful, influencing patient satisfaction, adherence, and long-term outcomes

Guselkumab (GUS)

- GUS is a dual-acting IL-23p19 subunit inhibitor that potently neutralises IL-23 and binds to CD64, a receptor on cells that produce IL-23
- Efficacy and safety of GUS IV induction → SC maintenance in UC was established in the Phase 2b/3 QUASAR program[3,4]
- In the Phase 3 ASTRO study, GUS SC induction → SC maintenance was also efficacious in UC[5]

Post-hoc Analysis of QUASAR

- **We evaluated early symptomatic improvement and remission following IV GUS induction in pts with moderately to severely active UC from the Phase 3 QUASAR induction study**

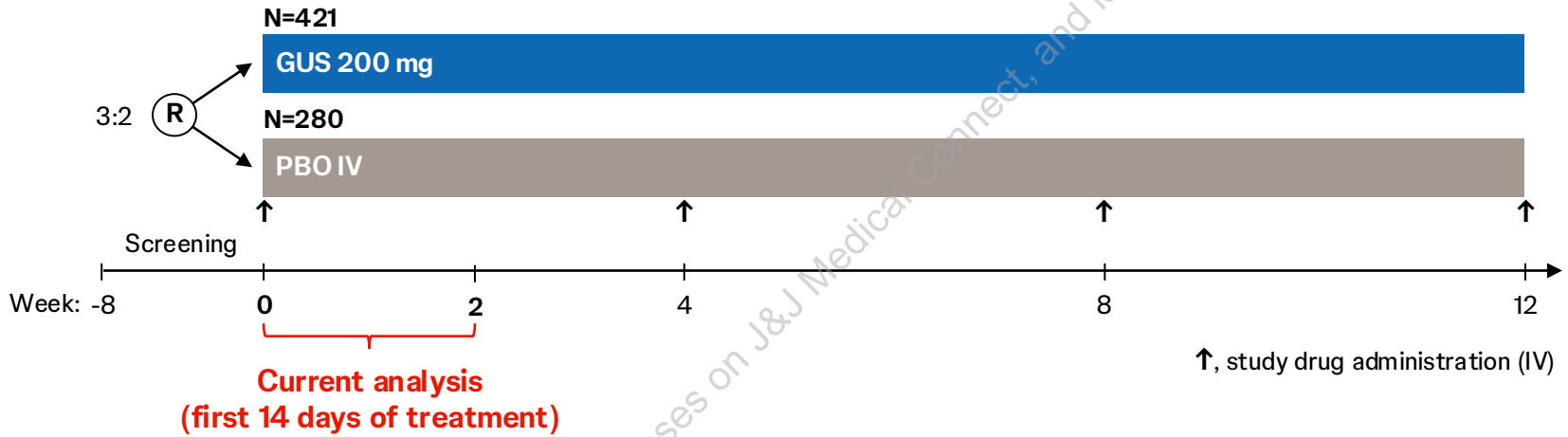
1. Turner D, et al. *Gastroenterology* 2021;160:1570-83; **2.** Dignass A, et al. *Aliment Pharmacol Ther* 2023;58:492-502; **3.** Rubin DT, et al. *Lancet* 2025;405:33-49; **4.** Peyrin-Biroulet L, et al. *Gastroenterology* 2023;165:1443-57; **5.** Long M, et al. *Lancet Gastro Hep* 2026;S2468-1253(25)00322-X. **GUS**=guselkumab, **HRQoL**=health-related quality of life, **IV**=intravenous, **pts**=participants, **SC**=subcutaneous, **UC**=ulcerative colitis.

Study Design

QUASAR Phase 3 Induction Study Design (Through Week 12)[1]

Participants
- ≥18 years of age
- Moderately to severely active UC[a]

Stable doses of oral corticosteroids (≤20 mg/day prednisone or equivalent) were permitted



Maintenance Study
GUS IV induction responders (week 12 or week 24) entered the QUASAR maintenance study

Post-hoc evaluation of symptomatic efficacy during the first 14 days of IV induction treatment in QUASAR
- LS mean changes from baseline in Mayo stool frequency and rectal bleeding subscores per daily PRO-2 data
- Symptomatic response (decrease in symptomatic Mayo score [sum of stool frequency and rectal bleeding subscores] by ≥30% and ≥1 point)
- Symptomatic remission (stool frequency subscore of 0 or 1; rectal bleeding subscore of 0)

Associations between early symptomatic efficacy and long-term outcomes in QUASAR were also explored

Rates of symptomatic response and remission at Week 2 with SC GUS 400 mg (at Weeks 0, 4, and 8) induction treatment are from the Phase 3 ASTRO study[2]

1. Rubin DT, et al. *Lancet* 2025;405:33-49; **2.** Long M, et al. *Lancet Gastro Hep* 2026;S2468-1253(25)00322-X. [a]Defined as modified Mayo score of 5-9 with a Mayo rectal bleeding subscore ≥1 and a Mayo endoscopic subscore ≥2 based on central review. **GUS**=guselkumab, **IV**=intravenous, **LS**=least squares, **PBO**=placebo, **PRO-2**, patient-reported outcome-2, **SC**=subcutaneous, **UC**=ulcerative colitis.

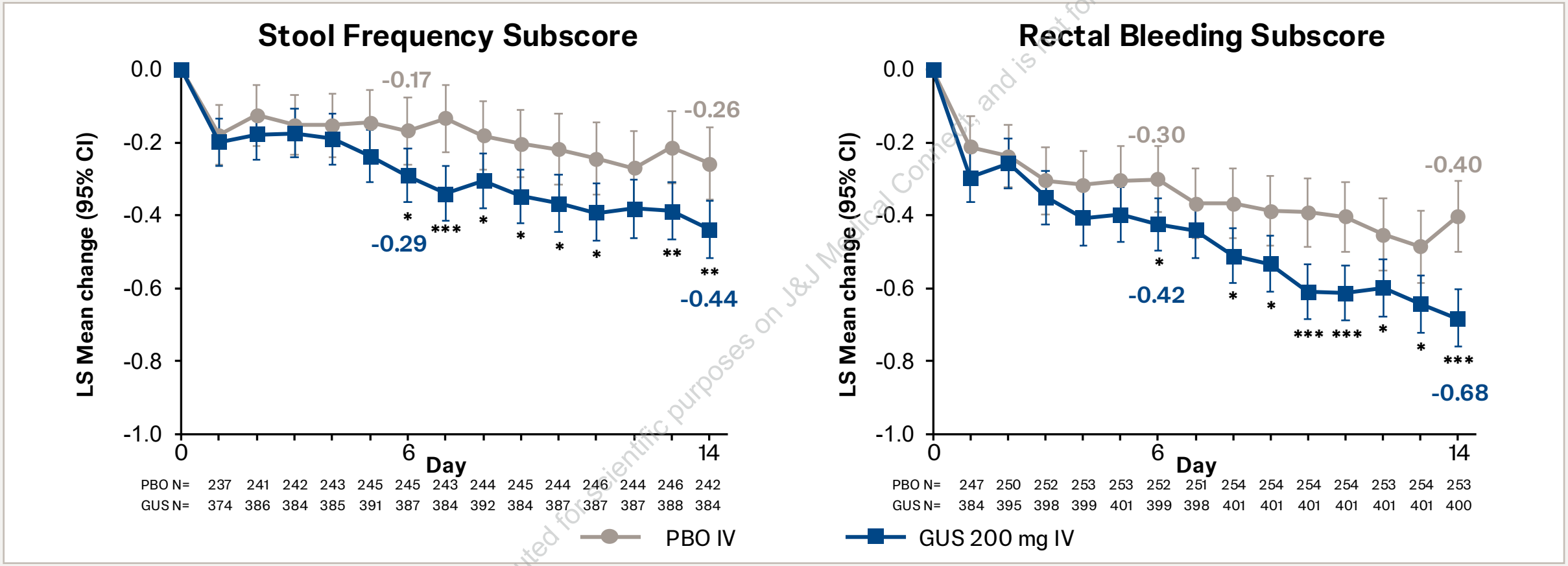
Results

QUASAR Phase 3 Induction Study: Baseline Characteristics

Baseline Characteristics		GUS 200 mg IV q4w (N = 421)	PBO IV q4w (N = 280)
Demographics			
	Age, yrs	41.0 (13.9)	39.8 (13.4)
	Male	57%	58%
	Race, Asian/Black/White	21% / 1% / 72%	22% / 1% / 73%
	Weight, kg	72.9 (16.7)	71.8 (17.0)
Disease Characteristics			
	UC disease duration, yrs	7.8 (7.7)	7.1 (6.5)
	Modified Mayo score	6.9 (1.1)	6.9 (1.1)
	Severe (7-9)	65%	64%
	Extensive UC	45%	52%
	CRP, mg/L, median (IQR)	4.3 (1.5-11.2)[a]	3.8 (1.6-9.1)[b]
	Faecal calprotectin, mg/kg, median (IQR)	1651 (647-3479)[c]	1606 (654-3077)[d]
UC Medication History			
	Oral corticosteroid use at baseline	43%	43%
	Immunosuppressant use at baseline	22%	19%
	History of BIO/JAK-IR	49%	49%
	No history of BIO/JAK-IR	51%	51%
	Biologic and JAK inhibitor-naïve[e]	95%	95%

Rubin DT, et al. *Lancet* 2025;405:33-49. Data shown are mean (SD) unless otherwise noted. [a]N=416; [b]N=278; [c]N=370; [d]N=253; [e]Denominator is participants without a history of BIO/JAK-IR.
BIO/JAK-IR=inadequate response or intolerance to biologic and/or Janus kinase inhibitor, **CRP**=C-reactive protein, **GUS**=guselkumab, **IQR**=interquartile range, **PBO**=placebo, **q4w**=every 4 weeks, **SC**=subcutaneous, **SD**=standard deviation, **UC**=ulcerative colitis.

Stool Frequency and Rectal Bleeding Subscore Changes from Baseline

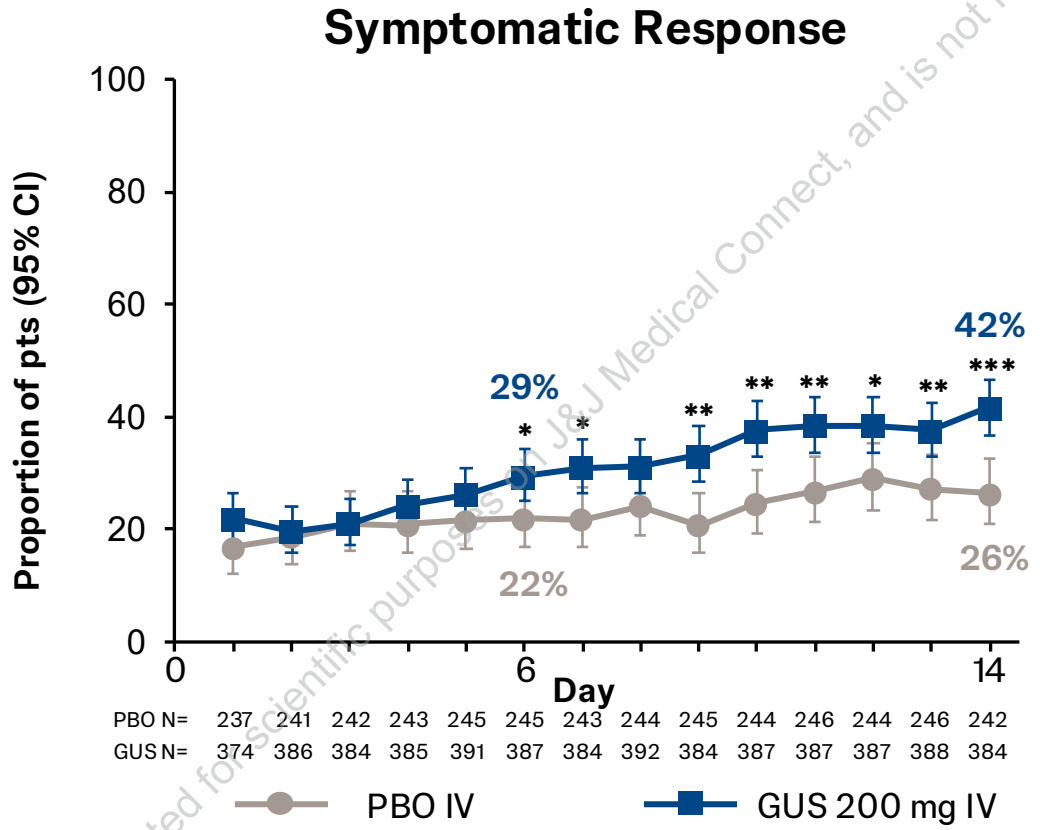


Nominal **p*<0.05, ***p*<0.01, ****p*<0.001 vs PBO, based on MMRM

By Day 6, pts receiving GUS had greater improvements in stool frequency and rectal bleeding compared with PBO

MMRM based on observed case data used to estimate changes in stool frequency and rectal bleeding subscores within the first 14 days. Explanatory variables of the MMRM include respective baseline scores, treatment groups, 2 randomisation factors (advanced therapy failure status [Yes/No] and concomitant use of corticosteroids at baseline [Yes/No]), visit (day) and an interaction term of visit with treatment group as fixed effects, and pt difference as random effect. The within-pt covariance between visit (day) was estimated via an unstructured variance-covariance matrix. **CI**=confidence interval, **GUS**=guselkumab, **IV**=intravenous, **LS**=least squares, **MMRM**=Mixed-Effect Model for Repeated Measures, **PBO**=placebo, **pts**=participants.

Symptomatic Response

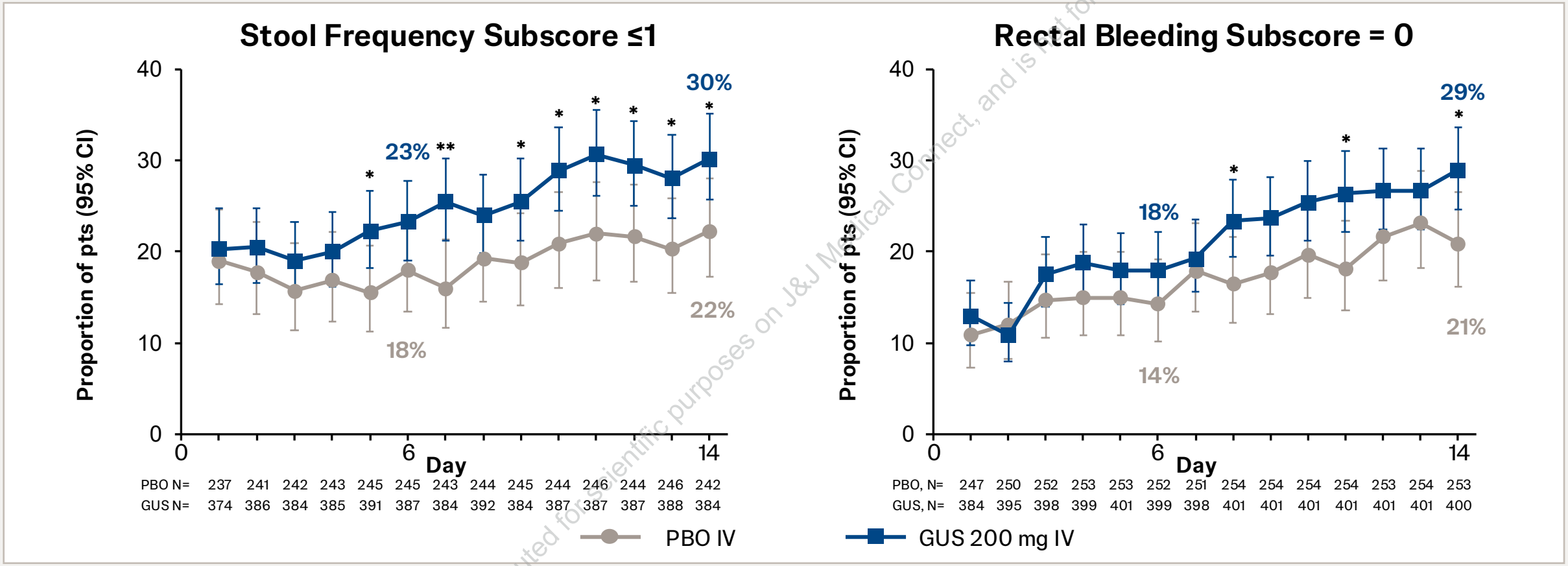


Nominal *p<0.05, **p<0.01, ***p<0.001 vs PBO, based on CMH

By Day 6, significantly greater proportions of pts receiving GUS vs PBO achieved symptomatic response

Observed case analysis. Nominal p values based on generalised CMH test adjusting for two randomisation factors (advanced therapy failure status [Yes/No] and concomitant use of corticosteroids at baseline [Yes/No]). Symptomatic response: reduction from induction baseline in symptomatic Mayo score (sum of stool frequency and rectal bleeding subscores) by ≥30% and ≥1 point. **CI**=confidence interval, **CMH**=Cochran-Mantel-Haenszel, **GUS**=guselkumab, **IV**=intravenous, **PBO**=placebo, **pts**=participants.

Stool Frequency and Rectal Bleeding Normalisation



Nominal **p*<0.05, ***p*<0.01, ****p*<0.001 vs PBO, based on CMH

Observed case analysis. Nominal p values based on generalised CMH test adjusting for two randomisation factors (advanced therapy failure status [Yes/No] and concomitant use of corticosteroids at baseline [Yes/No]). **CI**=confidence interval, **CMH**=Cochran-Mantel-Haenszel, **GUS**=guselkumab, **IV**=intravenous, **PBO**=placebo, **pts**=participants.

Early Symptomatic Improvements and Clinical Outcomes at Week 12

	PPV for Week 12 Endpoint	
	Clinical Response	Clinical Remission
Symptomatic Remission		
Within Day 1–14[a]	77%	35%
On Day 14	86%	46%
Symptomatic Response		
Within Day 1–14[a]	67%	26%
On Day 14	74%	31%

- **Day 14 symptomatic response and remission predict Week 12 clinical response with high accuracy**

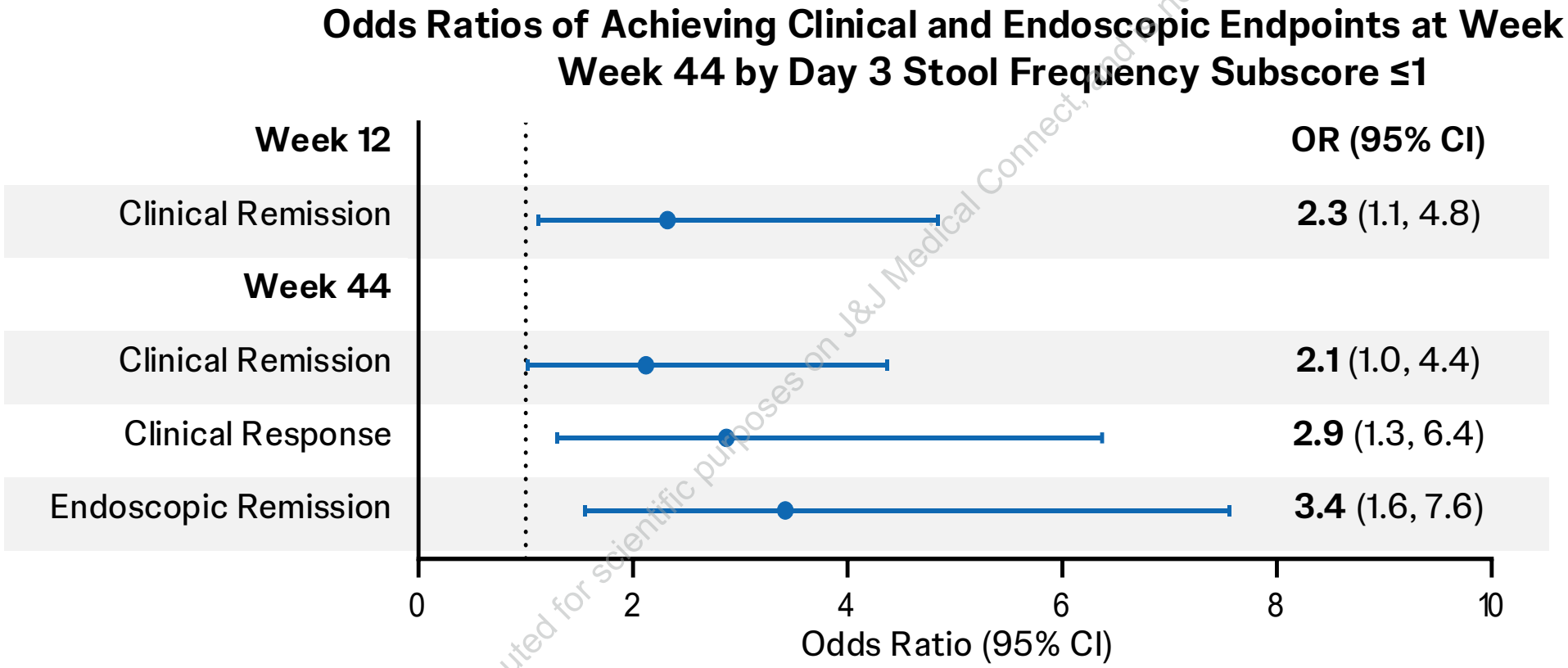
Data are reported for pts in the guselkumab group only. Symptomatic response: reduction from induction baseline in symptomatic Mayo score (sum of stool frequency and rectal bleeding subscores) by ≥30% and ≥1 point. Symptomatic remission: stool frequency subscore=0 or 1 and rectal bleeding subscore=0. PPV indicates the probability of achieving both symptom remission/response and clinical remission/response. [a]Includes pts with ≥1 symptomatic remission/response within the first 14 days. **PPV**=positive predictive value, **pts**=participants.

Early Symptomatic Improvements and Clinical, Endoscopic and QoL Outcomes at Week 44

	PPV for Week 44 Endpoint				
	Clinical Response	Clinical Remission	Endoscopic Response	Endoscopic Remission	IBDQ Remission
Symptomatic Remission					
Within Day 1–14[a]	73%	40%	41%	36%	71%
On Day 14	77%	50%	52%	40%	71%
Symptomatic Response					
Within Day 1–14[a]	72%	41%	42%	31%	62%
On Day 14	69%	42%	44%	32%	59%

Data are reported for pts in the guselkumab group only. Symptomatic response: reduction from induction baseline in symptomatic Mayo score (sum of stool frequency and rectal bleeding subscores) by ≥30% and ≥1 point. Symptomatic remission: stool frequency subscore=0 or 1 and rectal bleeding subscore=0. PPV indicates the probability of achieving both symptom remission/response and the indicated Week 44 endpoint. [a]Includes pts with ≥1 symptomatic remission/response within the first 14 days. **IBDQ**=Inflammatory Bowel Disease Questionnaire, **PPV**=positive predictive value, **pts**=participants, **QoL**=quality of life.

Exploratory Analysis of Stool Frequency Normalisation at Day 3 and Clinical and Endoscopic Outcomes at Week 12 and Week 44



Day 3 normalisation of stool frequency (stool frequency subscore ≤1) is associated with achieving long-term outcomes

Exploratory, sensitivity analysis of pts in the guselkumab treatment group. Multivariable logistic regression analysis was used to assess potential associations. Models were adjusted for baseline stool frequency/rectal bleeding subscores and randomisation factors (advanced therapy failure status [Yes/No] and concomitant use of corticosteroids at baseline [Yes/No]). For pts with non-integer number of stools in 24 hours when in remission or prior to UC the daily number of stools was rounded up to the nearest whole number. ORs were calculated using the reference group with stool frequency subscore >1. **CI**=confidence interval, **OR**=odds ratio, **pts**=participants, **UC**=ulcerative colitis.

Symptomatic Outcomes at Week 2 Following One Dose of IV or SC Guselkumab Induction

Proportion of pts at Week 2 (NRI)	IV Induction (QUASAR[1,a])		SC Induction (ASTRO[2,b])	
	GUS 200 mg IV (N = 421)	PBO IV (N = 280)	GUS 400 mg SC (N = 279)	PBO SC (N = 139)
Symptomatic Response	34%	24%	36%	26%
Symptomatic Remission	12%	9%	12%	8%

At Week 2, rates of symptomatic response and remission were similar with IV (QUASAR) and SC (ASTRO) GUS induction

1. Lichtenstein GR, et al. Presented at United European Gastroenterology Week (UEGW); October 14–17, 2023. **2.** Long M, et al. *Lancet Gastro Hep* 2026;S2468-1253(25)00322-X. NRI analysis. Symptomatic response: reduction from induction baseline in symptomatic Mayo score (sum of stool frequency and rectal bleeding subscores) by ≥30% and ≥1 point. Symptomatic remission: stool frequency subscore=0 or 1 and rectal bleeding subscore=0. [a]Week 2 symptomatic response endpoint was not multiplicity controlled. [b]Week 2 symptomatic response and remission endpoints are post hoc; values were based on the most recent 3 consecutive days within the 7 days prior. **GUS**=guselkumab, **IV**=intravenous, **NRI**=non-responder imputation, **PBO**=placebo, **pts**=participants, **SC**=subcutaneous.

Key Takeaways

- **GUS shows very early symptomatic improvement in pts with moderately to severely active UC**
- **This early improvement is associated with long-term outcomes**
- **These findings underscore the clinical relevance of early symptom control and align with STRIDE-II short-term treatment targets**
- **Proportions of pts with symptomatic improvements continued to increase after Week 2 with continued GUS induction therapy[1,2]**

1. Rubin DT, et al. *Lancet* 2025;405:33-49; **2.** Long M, et al. *Lancet Gastro Hep* 2026;S2468-1253(25)00322-X. **GUS**=guselkumab, **pts**=participants, **UC**=ulcerative colitis.

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