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

Axel Dignass,[1] Fumihito Hirai,[2] Masayuki Saruta,[3] Ayako Sasaki,[4] Shinichi Yoshigoe,[4] Jianmin Zhuo,[5] Yishen Yang,[5] Keira Herr,[6] Tadakazu Hisamatsu[7]

[1]Department of Medicine, Agaplesion Markus Hospital, Goethe University, Frankfurt, Germany; [2]Fukuoka University Faculty of Medicine, Fukuoka, Japan; [3]The Jikei University School of Medicine, Tokyo, Japan; [4]Johnson & Johnson, Tokyo, Japan; [5]Johnson & Johnson, Shanghai, China; [6]Johnson & Johnson, Singapore; [7]Kyorin University School of Medicine, Tokyo, Japan

Mo1518

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[3,5]**

Background

Symptom Relief in ulcerative colitis (UC)

- UC symptoms of stool frequency, rectal bleeding, and abdominal pain significantly impair health-related quality of life (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 neutralizes IL-23 and binds to CD64, a receptor on cells that produce IL-23
- Efficacy and safety of GUS intravenous (IV) induction → subcutaneous (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]

Objectives

This post-hoc analysis evaluated early symptomatic improvement and remission following IV GUS induction in participants (pts) with moderately to severely active UC from the Phase 3 QUASAR induction study

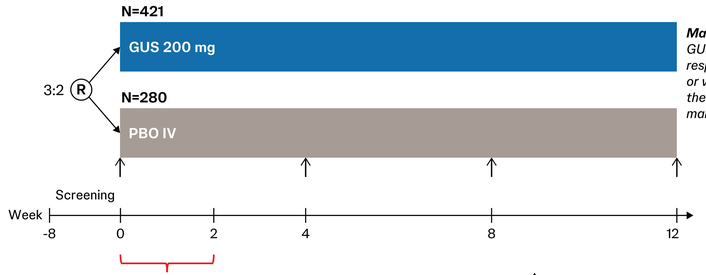
Study Design

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

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

[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,* ***PBO****=placebo,* ***R****=randomization,* ***UC****=ulcerative colitis.*

Post-Hoc Analysis

Symptomatic efficacy during the first 14 days of IV induction treatment in QUASAR was evaluated based on:

- Least-squares (LS) mean changes from baseline in Mayo stool frequency and rectal bleeding subscores per daily patient-reported outcome (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[5]

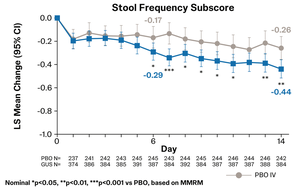
Results

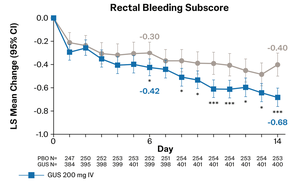
QUASAR Phase 3 Induction Study: Baseline Characteristics

		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]
	Fecal 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%

Baseline characteristics have been published previously.[3] 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,* ***SD****=standard deviation,* ***UC****=ulcerative colitis.*

Stool Frequency and Rectal Bleeding Subscore Changes from Baseline



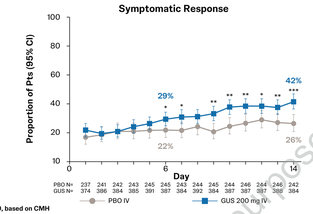


Nominal *p<0.05, **p<0.01, ***p<0.001 vs PBO, based on MMRM

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 randomization 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

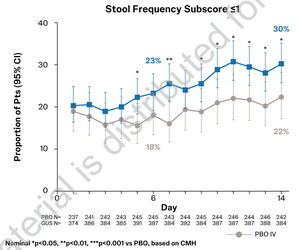


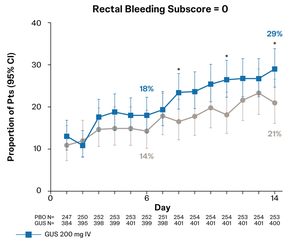
Nominal *p<0.05, **p<0.01, ***p<0.001 vs PBO, based on CMH

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

Observed case analysis. Nominal p values based on generalized CMH test adjusting for two randomization 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 Normalization





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

Observed case analysis. Nominal p values based on generalized CMH test adjusting for two randomization 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*	77%	35%
On Day 14	86%	46%
Symptomatic Response		
Within Day 1–14*	67%	26%
On Day 14	74%	31%

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

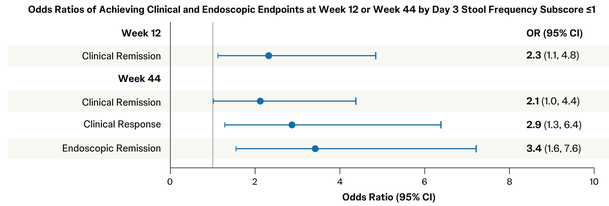
*Data are reported for pts in the guselkumab group only. Symptomatic response: reduction from induction baseline in symptomatic Mayo score (sum of stool frequency and rectal bleeding subscores) by ≥30% and ≥1 point. Symptomatic remission: stool frequency subscore=0 or 1 and rectal bleeding subscore=0. PPV indicates the probability of achieving both symptom remission/response and clinical remission/response. *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*	73%	40%	41%	36%	71%
On Day 14	77%	50%	52%	40%	71%
Symptomatic Response					
Within Day 1–14*	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. *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 Normalization at Day 3 and Clinical and Endoscopic Outcomes at Week 12 and Week 44



Day 3 normalization 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 randomization 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

	IV Induction (QUASAR*)[6]		SC Induction (ASTRO*)[5]	
Proportion of pts at Week 2 (NRI)	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

*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. *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.*

PRESENTED AT: Digestive Disease Week; May 2–5, 2026, Chicago, IL, USA. **REFERENCES: 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. **6.** Lichtenstein GR, et al. Presented at United European Gastroenterology Week (UEGW); October 14–17, 2023.

ACKNOWLEDGMENTS: The authors thank the participants, investigators, and study personnel who made the QUASAR study possible. This presentation was sponsored by Johnson & Johnson. Medical writing support was provided by Erin M Bakes, PhD, of Certara under the direction of the authors in accordance with Good Publication Practice guidelines (*Ann Intern Med.* 2022;175:1298–1304) and was funded by Johnson & Johnson.

DISCLOSURES: AD: Fees for participation in clinical trials, review activities such as data monitoring boards, statistical analysis and end point committees from Abives, 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; payment for lectures including service on speakers bureaus from AbbVie, Alfasigma, Biogen, CED Service GmbH, Celltrion, Falk, Fresenius Kabi, Ferring, Galapagos, Gilead, Hexal, HighCMD, J&J, Materia Prima, MedToday, MSD, Pfizer, Sandoz, Streamed-Up, Takeda, and Vifor Pharma; payment for manuscript preparation from AbbVie, Falk, J&J, Takeda, Thieme, and UniMed Verlag. **FH:** Grant support from AbbVie, Daiichi-Sankyo, EA Pharma Co, Ltd, JMRO, Mitsubishi Tanabe Pharma Corporation, Mochida Pharmaceutical Co., Ltd., Nippon Kayaku Co., Ltd., Pfizer Inc., and Takeda Pharmaceutical Co., Ltd. Consulting fees from Bristol Myers Squibb, EA Pharma Co, Ltd, Eli Lilly, Gilead Sciences, and Johnson & Johnson. Lecture fees from AbbVie, EA Pharma Co, Ltd, Kissei Pharmaceutical Co, Ltd, Mitsubishi Tanabe Pharma Corporation, Mochida Pharmaceutical Co, Ltd, and Takeda Pharmaceutical Co, Ltd. **MS:** Grants or contract from AbbVie GK, CMIC CMO Co, Ltd., Kissei Pharmaceutical Co., Ltd, Mochida Pharmaceutical Co., Ltd., PPD ONBI, K.K., and Zeria Pharmaceutical Co, Ltd. Gilead Sciences K.K., Johnson & Johnson, Pharmaceutical K.K., Kissei Pharmaceutical Co., Ltd., Mitsubishi Tanabe Pharma Corporation, Mochida Pharmaceutical Co., Ltd., Takeda Pharmaceutical Co., Ltd., and Viatris Pharmaceutical Co., Ltd. **KS, YY, JZ, YY,** and **KH:** Employees of Johnson & Johnson. **TH:** Grant support from AbbVie, Daiichi-Sankyo, EA Pharma Co, Ltd, JMRO, Mitsubishi Tanabe Pharma Corporation, Mochida Pharmaceutical Co., Ltd., Nippon Kayaku Co., Ltd., Pfizer Inc., and Takeda Pharmaceutical Co., Ltd. Consulting fees from Bristol Myers Squibb, EA Pharma Co, Ltd, Eli Lilly, Gilead Sciences and Johnson & Johnson. Lecture fees from AbbVie, EA Pharma Co, Ltd., Kissei Pharmaceutical Co., Ltd., Mitsubishi Tanabe Pharma Corporation, Mochida Pharmaceutical Co., Ltd., and Takeda Pharmaceutical Co., Ltd.