

Scan the QR code.
The QR code is intended to provide scientific information for individual reference, and the information should not be altered or reproduced in any way.

Key Takeaways

- ✓ Maintenance PK and efficacy were consistent regardless of induction route (IV or SC), supporting a common maintenance dosing strategy in CD irrespective of route of induction regimen

- ✓ E-R modeling showed efficacy with both maintenance regimens, but exposures with 200 mg q4w were near the plateau of the E-R curves, suggesting that this regimen is more likely to achieve a maximal treatment response

 **Patients with higher residual disease activity after induction may benefit more from the 200 mg maintenance dose**

 There were no associations between GUS concentrations and safety events

Clinical and endoscopic outcome definitions

Endoscopic response

- GALAXI: $\geq 50\%$ improvement from baseline in SES-CD or SES-CD ≤ 2
- GRAVITI: $\geq 50\%$ improvement from baseline in SES-CD

CDAI=Crohn's Disease Activity Index, SES-CD=Simple Endoscopic Score for Crohn's Disease.

Methods

Positive E-R trends were observed between steady-state guselkumab concentration and W48 efficacy (clinical remission and endoscopic response) and remained after accounting for clearance or half-life

**Clinical Remission at Week 48 by
Guselkumab C_{trough, week 48} Quartile (µg/mL)**

**Endoscopic Response at Week 48 by
Guselkumab C_{trough, week 48} Quartile (µg/mL)**

Group	Red Bar (%)	Black Bar (%)
Placebo	5%	8%
[0.01-0.816] µg/mL	29%	37%
[0.816-2.54] µg/mL	65%	51%
(2.54-7.72] µg/mL	51%	43%
(7.72-23.4] µg/mL	66%	63%

Trough Serum GUS Concentration at Week 48

^atrough, week 48 =trough concentration at week 48, GUS=guselkumab, IV=intravenous, SC=subcutaneous

In the E-R model, participants who had not achieved clinical remission by W12, and those with a baseline SES-CD >12 who had not achieved an endoscopic response by W12, were more likely to achieve W48 outcomes when treated with the 200 mg maintenance regimen compared with the 100 mg maintenance regimen

Clinical Remission at W48

Group	Predicted Response Rate at Week 48, % (95% CI)
Not in clinical remission at W12 In endoscopic response at W12	83.1
Not in clinical remission at W12 Not in endoscopic response at W12	55.3
In clinical remission at W12 In endoscopic response at W12	96.8
In clinical remission at W12 Not in endoscopic response at W12	92.3

● 100 mg SC q8w (median C_{trough} : 0.84 $\mu\text{g/mL}$) ● 200 mg SC q4w (median C_{trough} : 7.60 $\mu\text{g/mL}$)

Model-predicted week 48 response rates for SC maintenance treatment groups, stratified by covariates. Response rate was calculated based on model-predicted median $C_{100\text{mg}, \text{week 48}}$ which is 0.84 $\mu\text{g/mL}$ for the 100 mg SC q8w regimen and 7.60 $\mu\text{g/mL}$ for the 200 mg SC q4w regimen. CI=confidence interval, q4w=every 4 weeks, q8w=every 8 weeks, SC=subcutaneous, SES-CD=Simple Endoscopic Score for Crohn's Disease.

Endoscopic Response at W48

Group	Predicted Response Rate at Week 48, % (95% CI)
Baseline SES-CD ≤12, Not in endoscopic response at W12	32.1
Baseline SES-CD ≤12, In endoscopic response at W12	58.9
Baseline SES-CD >12, Not in endoscopic response at W12	58.0
Baseline SES-CD >12, In endoscopic response at W12	77.9

C_{trough}: 7.60 µg/mL)

No associations between guselkumab concentrations and infections, serious infections, serious adverse events, or liver function tests were observed.

- Immunosuppressants did not impact guselkumab concentrations (data not shown)

Baseline SES-CD score >12

Endoscopic Response rate at Week 45

Legend:

- Predicted: Not achieving Week12 Endoscopic response
- Predicted: Achieving Week12 Endoscopic response
- Observed: Not achieving Week12 Endoscopic response
- Observed: Achieving Week12 Endoscopic response

Guselkumab C_{trough} , week 45 ($\mu\text{g/mL}$)

Legend:

- 200 mg Q4W SC
- 100 mg Q8W SC
- Placebo SC

Model-predicted E-R relationships for endoscopic response at week 48 using $C_{\text{trough, week 48}}$ as the PK exposure metric in participants with Crohn's disease, stratified by baseline SES-CD and endoscopic response at week 12.

Figure 1: Baseline SES-CD scores and endoscopic response rates

The figure consists of two panels. The top panel is a Kaplan-Meier plot showing the endoscopic response rate (Y-axis, 0.0 to 1.0) over time (X-axis, 0 to 24 weeks). The plot compares three groups: Predicted: Not achieving Week12 Endoscopic response (dotted line), Predicted: Achieving Week12 Endoscopic response (solid line), and Observed: Achieving Week12 Endoscopic response (triangles). The bottom panel is a bar chart showing the distribution of Guselkumab $C_{rough, \text{ week 48}}$ (X-axis, 0 to 20 $\mu\text{g/mL}$) for three groups: 200 mg Q4W SC (grey bar), 100 mg Q8W SC (dark grey bar), and Placebo SC (white bar).

Table 1: Endoscopic Response Rates (Estimated from Figure 1)

Time (Weeks)	Predicted: Not achieving Week12 Endoscopic response	Predicted: Achieving Week12 Endoscopic response	Observed: Achieving Week12 Endoscopic response
0	0.00	0.00	0.00
1	0.25	0.35	0.45
2	0.25	0.60	0.75
3	0.25	0.65	0.80
4	0.25	0.68	0.80
5	0.25	0.70	0.80
6	0.25	0.70	0.80
7	0.25	0.70	0.80
8	0.25	0.70	0.80
9	0.25	0.70	0.80
10	0.25	0.70	0.80
11	0.25	0.70	0.80
12	0.25	0.70	0.80
13	0.25	0.70	0.80
14	0.25	0.70	0.80
15	0.25	0.70	0.80
16	0.25	0.70	0.80
17	0.25	0.70	0.80
18	0.25	0.70	0.80
19	0.25	0.70	0.80
20	0.25	0.70	0.80
21	0.25	0.70	0.80
22	0.25	0.70	0.80
23	0.25	0.70	0.80
24	0.25	0.70	0.80

Table 2: Guselkumab $C_{rough, \text{ week 48}}$ Distribution (Estimated from Figure 1)

Group	Median $C_{rough, \text{ week 48}}$ ($\mu\text{g/mL}$)	Range ($\mu\text{g/mL}$)
200 mg Q4W SC	~10	~0.5 - 18
100 mg Q8W SC	~1	~0.5 - 4
Placebo SC	~0.5	~0.5 - 1

Any Infection

ALT >3 x ULN

Group	GALAXI 1/2/3: 200 mg IV q4w followed by 100 mg SC q8w or 200 mg SC q4w	200 mg SC q4w
Placebo SC	39.6	19.1
Q1	32.9	39.3
Q2	35.5	40.0
Q3	33.8	22.8
Q4	41.3	32.7

AST >3 x ULN

Group	GALAXI 1/2/3: 200 mg IV q4w followed by 100 mg SC q8w or 200 mg SC q4w	200 mg SC q4w
Placebo SC	5.7	0
Q1	0.7	0

ALT >3 x ULN (100 mg SC q8w)

Group	GALAXI 1/2/3: 200 mg IV q4w followed by 100 mg SC q8w or 200 mg SC q4w	100 mg SC q8w
Placebo SC	1.9	1.8
Q1	2.1	0
Q2	0.7	0
Q4	1.4	1.8
Q4	0.7	0

AST >3 x ULN (100 mg SC q8w)

Group	GALAXI 1/2/3: 200 mg IV q4w followed by 100 mg SC q8w or 200 mg SC q4w	100 mg SC q8w
Placebo SC	1.9	0.9
Q1	0	0

Legend: GALAXI 1/2/3: 200 mg IV q4w followed by 100 mg SC q8w or 200 mg SC q4w

■ GALAXI 1/2/3: 200 mg IV q4w followed by 100 mg SC q8w or 200 mg SC q4w

Serious Infections

ALT Incidence

Group	Incidence (%)
Placebo SC	5.7
Q1	0.7
Q2	1.8
Q3	1.4
Q4	1.8

AST Incidence

Group	Incidence (%)
Placebo SC	1.9
Q1	0.9
Q2	1.8
Q3	2.1
Q4	1.8

q4w ■ GRAVITI: 400 mg SC q4w followed by 100 mg SC q8w or 200 mg SC q4w

Serious Adverse Events

Group	Incidence, %
Placebo SC	18.5
Q1	9.8
Q2	8.5
Q3	3.5
Q4	4.2

followed by 100 mg SC q8w or 200 mg SC q4w

Parameter estimates from the final population PK model for guselkumab in participants with moderately to severely active Crohn's disease
The magnitude of change in the parameter estimate as a result of a continuous covariate was expressed as a range, i.e., percentage change from the median value, when the covariate factor varied from the 25th percentile to the 75th percentile of the population.

$$CL \left(\frac{L}{day} \right) = 0.304 \times \left(\frac{Body\ weight}{70} \right)^{0.618} \times \left(\frac{Albumin}{43} \right)^{-1.23} \times \left(\frac{CRP}{6.4} \right)^{0.021} \times (1.118)^{PK} \times (1.118)^{Q}$$