

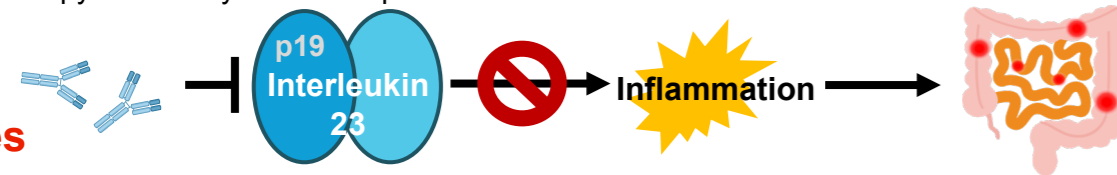
# Efficacy of Guselkumab for Small-Bowel Lesions Using Balloon Assisted Enteroscopy: A Phase 3, Open-label, Multicenter Study

Tepei Omori,<sup>1,2</sup> Kazuo Ohtsuka,<sup>3</sup> Kenji Watanabe,<sup>4</sup> Taku Kobayashi,<sup>5</sup> Naoki Hosoe,<sup>6</sup> Motohiro Esaki,<sup>7</sup> Tomoki Matsuda,<sup>8</sup> Takehiko Sakamoto,<sup>9</sup> Koji Masuda,<sup>9</sup> Madoka Chinen,<sup>10</sup> Hiroshi Horio,<sup>10</sup> Shinichi Yoshigoe,<sup>10</sup> Tadakazu Hisamatsu<sup>11</sup>, on behalf of the guselkumab crohn's disease local study group<sup>\*</sup>  
<sup>1</sup>Department of Gastroenterology and Hepatology, Kyorin University Suganami Hospital, Kyorin University School of Medicine, Tokyo, Japan; <sup>2</sup>Institute of Gastroenterology, Tokyo Women's Medical University, Tokyo, Japan; <sup>3</sup>Department of Gastroenterology and Hepatology, Institute of Science Tokyo, Tokyo, Japan; <sup>4</sup>Department of Internal Medicine for Inflammatory Bowel Disease, University of Toyama, Toyama, Japan; <sup>5</sup>Center for Advanced IBD Research and Treatment, Kitasato University Kitasato Institute Hospital, Tokyo, Japan; <sup>6</sup>Center for Preventive Medicine, Keio University, Tokyo, Japan; <sup>7</sup>Division of Gastroenterology, Department of Internal Medicine, Faculty of Medicine, Saga University, Saga, Japan; <sup>8</sup>Department of Gastroenterology, Sendai Kousei Hospital, Sendai, Japan; <sup>9</sup>Research and Development, Johnson & Johnson, Tokyo, Japan; <sup>10</sup>Medical Affairs, Johnson & Johnson, Tokyo, Japan; <sup>11</sup>Department of Gastroenterology and Hepatology, Kyorin University School of Medicine, Tokyo, Japan

<sup>\*</sup>Hideki Kitada, Hirotugu Sakamoto, Junichi Akiyama, Kaoru Yokoyama, Kazuki Kakimoto, Koichiro Matsuda, Maria Yonezawa, Mikihiro Fujiya, Ryuichi Okamoto, Shingo Kato, Shinichiro Shinzaki, Shun Hattori, Shusaku Yoshikawa, Shunsuke Ogata, Takehiro Arai, Tetsuya Ishida, Toshifumi Ashida, Toshihiro Inokuchi, Toshimitsu Fujii, Toshiro Kamoshida, Toshiyuki Sato, Yohei Furumoto, Yoki Furuta and Yutaka Endo, in alphabetical order

## Background

- Crohn's disease (CD) is a progressive disease with a high surgical resection rate
- The presence or absence of small-bowel lesions affects changes in the disease behavior and long-term prognosis of CD
- Proximal ileum lesions are less responsive to biologic therapy than terminal ileum or colonic lesions
- Guselkumab (GUS) is a human IgG1 monoclonal antibody with efficacy against inflammatory bowel diseases, including CD, as demonstrated in the double-blind, phase 3 GALAXI 2 and GALAXI 3 studies
- However, endoscopic evaluation of the lesions proximal to the reach of conventional ileocolonoscopy has hardly ever been performed.



## Objectives

- To assess the safety and efficacy of GUS in patients with small-bowel lesions, evaluated using retrograde balloon-assisted enteroscopy (BAE), in Japanese patients with moderately to severely active CD

## Results

### Patient demographics and other baseline characteristics

	Total population (N = 38)	Small-bowel assessment group (n = 15)
Sex		
Male, n (%)	24 (63.2)	10 (66.7)
Female, n (%)	14 (36.8)	5 (33.3)
Age, median (range), years	40.5 (20–69)	41.0 (24–69)
Body weight, median (range), kg	57.35 (42.0–99.4)	56.40 (42.5–91.4)
Duration of CD, median (range), years	7.97 (0.4–33.0)	2.92 (0.4–16.9)
CDAI		
Median (range)	240.5 (65–484)	201.0 (65–271)
CRP, median (range), mg/L	4.0 (0.2–104.0)	2.5 (0.4–52.6)
FeCal, median (range), mg/kg	947.0 (43–6321)	712.0 (43–6321)
Gastrointestinal lesion area <sup>a</sup> , n (%)		
Ileum and colon	21 (55.3)	9 (60.0)
Colon only	9 (23.7)	2 (13.3)
Ileum only	8 (21.1)	4 (26.7)
Prior therapies, n (%)		
Corticosteroids	24 (63.2)	10 (66.7)
Immunomodulators	20 (52.6)	7 (46.7)
History of biologic failure, n (%)		
History of failure with any biologic	24 (63.2)	8 (53.3)
History of anti-TNF failure	21 (55.3)	6 (40.0)
Failure with one agent	15 (39.5)	5 (33.3)
Failure with two agents	6 (15.8)	1 (6.7)
SES-CD		
Median (range)	11.5 (4–30)	7.0 (4–22)
mSES-CD SB area <sup>a</sup> , n (%)		
Terminal ileum	—	13 (86.7)
Proximal ileum	—	12 (80)
Jejunum	—	1 (6.7)

<sup>a</sup>Assessed by the central reader  
 Abbreviations: CD, Crohn's disease; CDAI, Crohn's Disease Activity Index; CRP, c-reactive protein; FeCal, fecal calprotectin test; mSES-CD, modified Simple Endoscopic Score for Crohn's Disease; SB, small-bowel; SES-CD, Simple Endoscopic Score for Crohn's Disease; TNF, tumor necrosis factor.

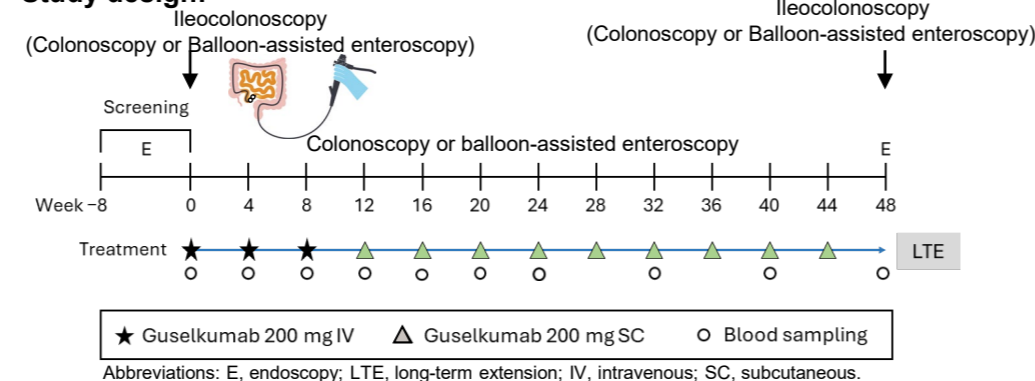
## Safety results

- The mean follow-up 46.6 weeks with a mean of 11.0 GUS administrations
- Overall, 33/38 (86.8%) and 3/38 (7.9%) patients experienced an adverse event (AE) and serious AE, respectively
- Although 11 patients (28.9%) experienced infections, none were serious
- Most AEs were mild or moderate in severity
- No CD-related surgeries or hospitalizations

## Methods

Phase 3, open-label study to evaluate the safety and efficacy of GUS in Japanese patients with moderately to severely active CD who had demonstrated an inadequate response to or were intolerant of their previous therapy (NCT04397263)

### Study design:



**Target patient population:** Adult patients in Japan with moderate to severe CD and endoscopic evidence of active ileocolonic CD (simple endoscopic score for CD [SES-CD score]  $\geq 6$  or  $\geq 4$  for patients with isolated ileal disease) or active small-bowel CD (modified SES-CD [mSES-CD] score  $\geq 5$ )

## Study objectives and endpoints

**Primary:** Safety  
**Major secondary:** Efficacy at week 48  
**Exploratory:** Efficacy in patients with deep small-bowel lesions using retrograde BAE

### Analyses

The small-bowel full analysis set: All patients who received  $\geq 1$  dose of GUS with  $\geq 1$  small-bowel assessment by balloon-assisted enteroscopy after their first dose of GUS

Used partially modified SES-CD and Fisher exact test to explore confounding factors associated with responders/non-responders or ulcer-free/non-ulcer-free

## Modified simple endoscopic score for Crohn's disease (mSES-CD)<sup>1,2</sup>

- Same variables as SES-CD,<sup>3</sup> except presence/type of narrowing/stricture (scored 0–3 in each segment with the max score of 27).
- Target three segments of the small-bowel:
  - Terminal ileum ( $\leq 10$  cm from the ileocecal valve)
  - Proximal ileum (10–300 cm from the ileocecal valve)
  - Jejunum ( $>300$  cm from the ileocecal valve)

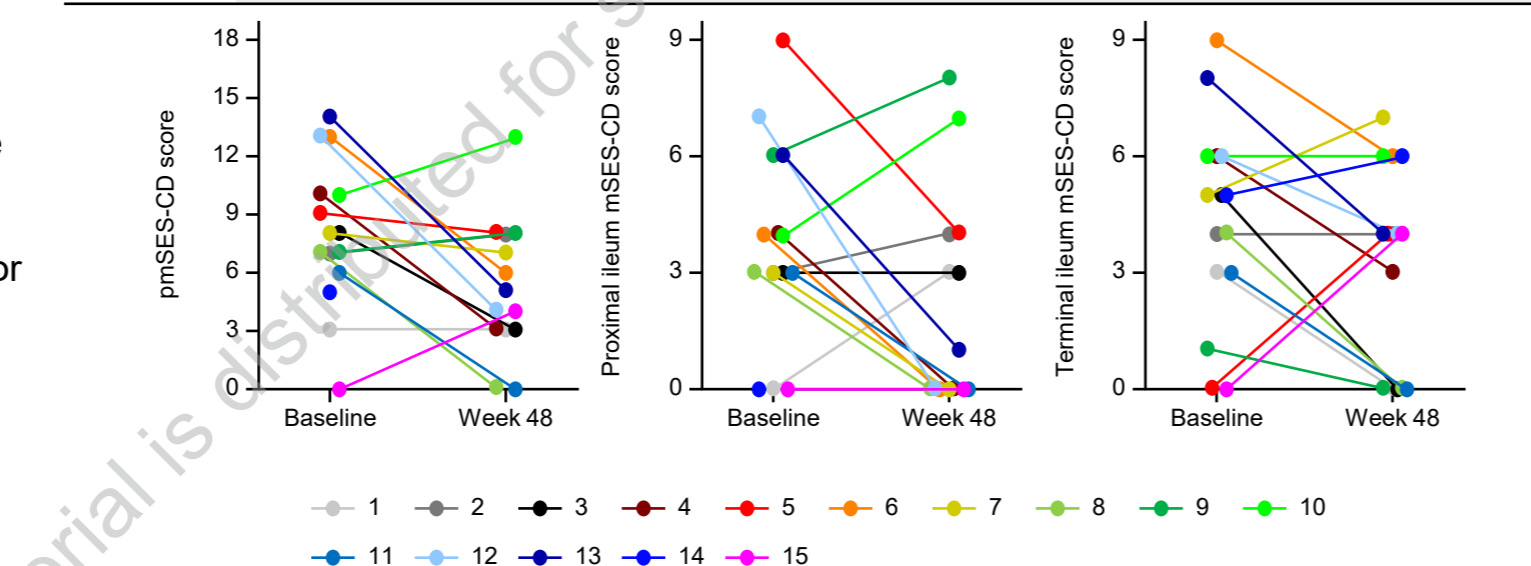
Variables	0	1	2	3
A. Size of ulcers	None	Aphthous ulcers ( $\Phi 0.1$ –0.5 cm)	Large ulcers ( $\Phi 0.5$ –2 cm)	Very large ulcers ( $\Phi > 2$ cm)
B. Ulcerated surface	None	<10%	10–30%	>30%
C. Affected surface	None	<50%	50–75%	>75%

pmSES-CD = Proximal ileum SES-CD + Terminal ileum SES-CD  
 There was no patient with jejunum at week 44.

## Exploratory results

Proximal ileum mSES-CD, terminal ileum mSES-CD, pmSES-CD, and CDAI scores at baseline and Week 48 for individual patients (small-bowel full analysis set)

Patient	L1: ileal-type	Proximal ileum		Terminal ileum		pmSES-CD		CDAI	
		BL	Week 48	BL	Week 48	BL	Week 48	BL	Week 48
1		0	3	3	0	3	3	266	120
2		3	4	4	4	7	8	271	247
3	✓	3	3	5	0	8	3	107	95
4		4	0	6	3	10	3	65	27
5		9	4	0	4	9	8	134	0 <sup>*</sup>
6		4	0	9	6	13	6	201	111
7		3	0	5	7	8	7	248	235
8		3	0	4	0	7	0	139	115
9	✓	6	8	1	0	7	8	143	148
10		4	7	6	6	10	13	186	96
11		3	0	3	0	6	0	233	97
12	✓	7	0	6	4	13	4	224	176
13		6	1	8	4	14	5	162	34
14		0	—	5	6	5	—	213	126
15		0	0	0	4	0	4	261	0 <sup>*</sup>



<sup>\*</sup> Negative CDAIs are displayed as zero.  
 Abbreviations: BL, baseline; CDAI, Crohn's Disease Activity Index; mSES-CD, modified Simple Endoscopic Score for Crohn's Disease; pmSES-CD, partially modified Simple Endoscopic Score for Crohn's Disease.

Summary of pmSES-CDs in the small-bowel group (small-bowel full analysis set, n = 15)

	Measured value					Change from baseline				
	n	Mean	SD	Median	Min Max	n	Mean	SD	Median	Min Max
pmSES-CD										
Baseline	15	8.0	3.8	8.0	0 14					
Week 48 <sup>a</sup>	15	5.2	3.4	5.0	0 13	15	-2.8	4.5	-1.0	-9 4
mSES-CD by location										
Terminal ileum										
Baseline	15	4.3	2.6	5.0	0 9					
Week 48	15	3.2	2.6	4.0	0 7	15	-1.1	2.9	-2.0	-5 4
Proximal ileum										
Baseline	15	3.7	2.6	3.0	0 9					
Week 48 <sup>a</sup>	15	2.0	2.7	0.0	0 8	15	-1.7	3.2	-3.0	-7 3

<sup>a</sup>Missing proximal ileum subscore at Week 48 was imputed by the baseline-observation-carry-forward method prior to calculating the pmSES-CD.  
 Abbreviations: mSES-CD, modified Simple Endoscopic Score for Crohn's Disease; pmSES-CD, partially modified Simple Endoscopic Score for Crohn's Disease; SD, standard deviation factor.

## Key Takeaways

- ✓ No new safety concern with GUS
- ✓ Endoscopic improvement in small-bowel lesions after 48 weeks
  - Decreases in pmSES-CD, proximal ileum and terminal ileum scores, and CDAI

### Small-bowel lesion responses



- ✓ No associations between patient characteristics vs responses to GUS / ulcer-free status based on the pmSES-CD
- ✓ Guselkumab was safe and effective for small-bowel lesions in Japanese patients with moderately to severely active CD
- ✓ Important for physicians to evaluate using enteroscopy to capture a complete picture of disease activity

## Improvement in pmSES-CD at Week 48

pmSES-CD response	Small-bowel assessment group (n = 15)
Endoscopic response <sup>a</sup>	7 (46.7)
Ulcer-free <sup>b</sup>	4 (26.7)
Complete mucosal healing <sup>c</sup>	2 (13.3)

Data are n (%).  
 pmSES-CD-defined outcomes at Week 48.  
<sup>a</sup>Baseline pmSES-CD  $\geq 4$  and 50% decrease in pmSES-CD from baseline.  
<sup>b</sup>Baseline pmSES-CD  $\geq 4$  and pmSES-CD  $< 4$ .  
<sup>c</sup>Baseline pmSES-CD  $\geq 4$  and pmSES-CD of 0.  
 Abbreviation: pmSES-CD, partially modified Simple Endoscopic Score for Crohn's Disease.

- No associations between patient demographics / baseline characteristics and responders / non-responders or ulcer-free / non-ulcer-free patients based on pmSES-CD
- Small-bowel lesion severity did not always align with the patient's CDAI score