P0976

Guselkumab Efficacy and Safety in East Asian Participants with Moderate to Severely Active Crohn's Disease: Subgroup Analysis of the GALAXI 2 & 3 Phase 3 Studies

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Key Takeaways

- **GUS efficacy in the subgroup of East Asian participants from GALAXI 2 & 3 was consistent with that observed in the global study population.**
- **The safety profile of GUS was also favorable in East Asian participants, consistent with previous reports in global populations.**

Background

- Guselkumab (GUS) is a dual-acting interleukin (IL)-23p19 subunit inhibitor that potently neutralizes IL-23 and binds to CD64, a receptor on cells that produce IL-23[1]
- GALAXI 2 & 3 (NCT03466411) are identical 48-week, randomized, double-blind, double-dummy, placebo (PBO)- and active-comparator (ustekinumab; UST)–controlled treat-through trials assessing the efficacy and safety of GUS in participants with moderately to severely active Crohn's disease[2]
- Composite co-primary efficacy endpoints were met for GUS versus PBO in GALAXI 2 & 3[2]
  - Clinical response at Week 12 **and** clinical remission at Week 48
  - Clinical response at Week 12 **and** endoscopic response at Week 48

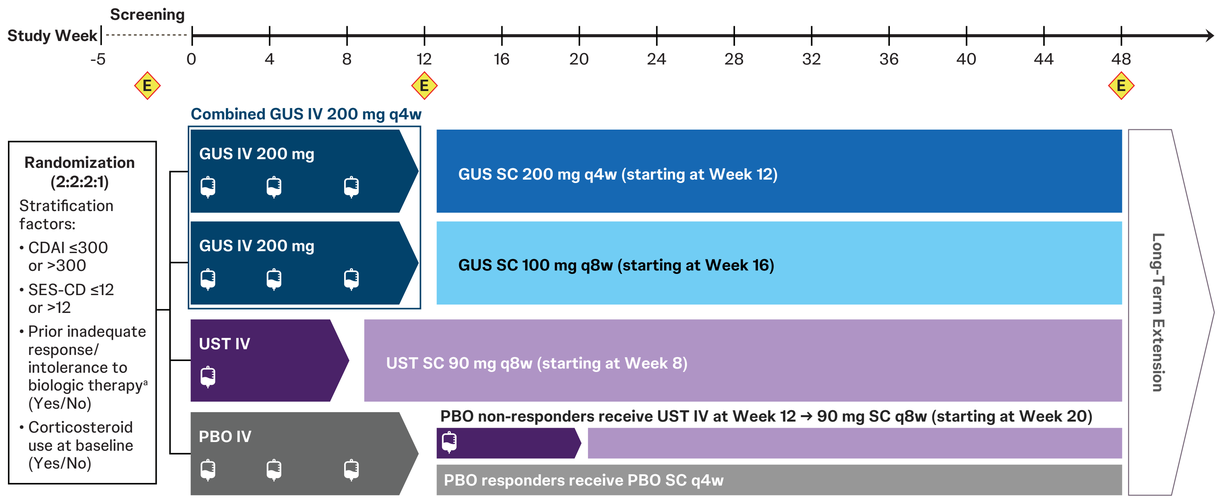
Objective

To report a subgroup analysis of GUS efficacy and safety in East Asian participants from GALAXI 2 & 3

Methods

GALAXI 2 & 3: Identical, Randomized, Double-Blind, Treat-Through Global Clinical Trials

- Key eligibility criteria:
  - Moderately to severely active Crohn's disease (CDAI score 220–450 + mean daily SF count >3 or AP score >1) and SES-CD score ≥6 (or ≥4 for isolated ileal disease)
  - Inadequate response/intolerance to oral corticosteroids or 6-MP/AZA/MTX, or biologic therapies[a]



To maintain treatment masking, all participants received active and/or placebo IV q4w through Week 12 and active and/or placebo SC q4w through Week 48. [a]Biologic therapies: TNF antagonists or vedolizumab. ***AP****=Abdominal pain;* ***CDAI****=Crohn's Disease Activity Index;* ***E****=Endoscopy;* ***IV****=Intravenous;* ***PBO****=Placebo;* ***q4w****=Every 4 weeks;* ***q8w****=Every 8 weeks;* ***SC****=Subcutaneous;* ***SES-CD****=Simple Endoscopic Score for Crohn's Disease;* ***SF****=Stool frequency;* ***UST****=Ustekinumab.*

Subgroup Analysis

- The East Asian subgroup included GALAXI 2 & 3 participants from study sites located in East Asia (China, Japan, Korea, and Taiwan)
- Pooled GALAXI 2 & 3 data are presented
- No statistical comparisons were made between treatment cohorts for this subgroup analysis

Endpoints: short-term and long-term GUS efficacy

Short-term Efficacy Endpoints (GUS vs PBO)	• Clinical remission at W12 • Endoscopic response at W12
Short- and Long-term Composite Efficacy Endpoints (GUS vs PBO)	• Clinical response at W12 **and** clinical remission at W48[a] • Clinical response at W12 **and** endoscopic response at W48[a]
Long-term Efficacy Endpoints (GUS vs UST)	• Endoscopic response at W48 • Endoscopic remission at W48 • Clinical remission **and** endoscopic response at W48 • Deep remission at W48

Clinical remission: CDAI score <150; Endoscopic response: ≥50% improvement from baseline in SES-CD score or SES-CD score ≤2; Clinical response: ≥100-point reduction from baseline in CDAI or CDAI <150; Endoscopic remission: SES-CD score ≤4 and a ≥2-point reduction from baseline and no subscore >1 in any individual component; Deep remission: the composite of clinical remission and endoscopic remission. [a]Co-primary endpoints in the GALAXI 2 and GALAXI 3 trials. ***CDAI****=Crohn's Disease Activity Index;* ***GUS****=Guselkumab;* ***PBO****=placebo;* ***SES-CD****=Simple Endoscopic Score for Crohn's Disease;* ***UST****=Ustekinumab;* ***W****=Week.*

Results

Baseline demographic and disease characteristics were generally similar between East Asian and global participants from GALAXI 2 & 3

Population

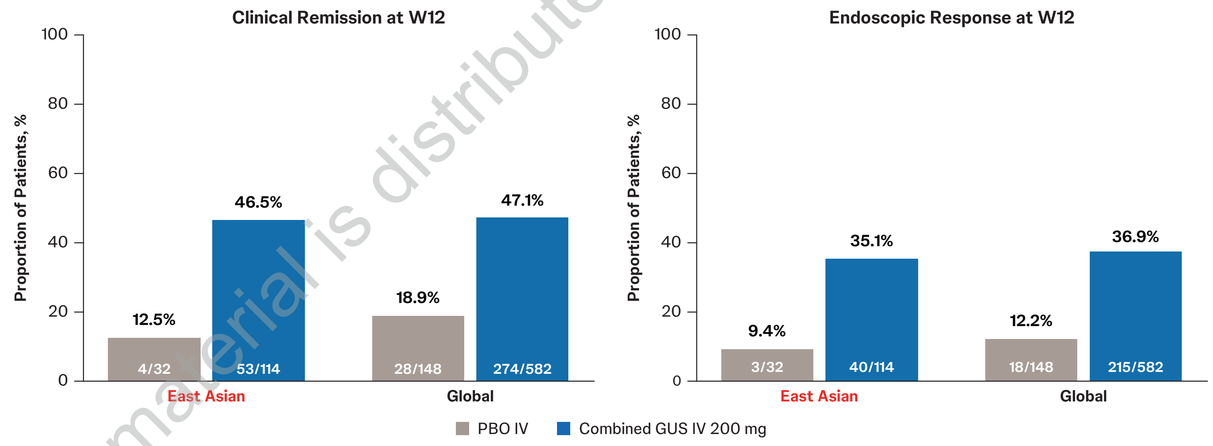
- Of 1021 global participants in the pooled GALAXI 2 & 3 primary analysis set population, **192** were from study sites located in East Asia: China (n=118), Japan (n=48), South Korea (n=23), and Taiwan (n=3)

		East Asian[a] (N=192)	Global (N=1021)
Demographics			
	Age, yrs	33.5 (12.4)	36.5 (12.8)
	Male, n (%)	134 (69.8)	588 (57.6)
	Region: Asia, n (%)	192 (100)	213 (20.9)
	Weight, kg	58.0 (12.6)	68.2 (17.1)
CD Disease Characteristics			
	CD Disease Duration, yrs	6.2 (6.1)	7.2 (7.2)
	CDAI Score	289.6 (52.9)	294.8 (52.9)
	SES-CD Score	14.5 (7.2)	12.9 (7.3)
	Endoscopic Disease Severity (SES-CD Score), n (%)		
	7–16 (Moderate)	97 (50.5)	547 (53.6)
	>16 (Severe)	72 (37.5)	278 (27.2)
	Involved GI Areas by Central Reader, n (%)		
	Ileum Only	22 (11.5)	225 (22.0)
	Colon Only	74 (38.5)	403 (39.5)
	Ileum and Colon	96 (50.0)	393 (38.5)
	CRP, mg/mL	18.0 (24.1)	15.3 (21.5)
	Fecal calprotectin, µg/g	2365.3 (2215.5)[a]	1752.1 (2707.7)[b]

Primary analysis set (pooled GALAXI 2 & 3). Data shown are mean (SD) unless otherwise noted. [a]n=190; [b]n=1008. ***CD****=Crohn's disease;* ***CDAI****=Crohn's Disease Activity Index;* ***CRP****=C-reactive protein;* ***GI****=Gastrointestinal;* ***SD****=Standard deviation;* ***SES-CD****=Simple Endoscopic Score for Crohn's Disease.*

Short-term efficacy of GUS IV induction at Week 12

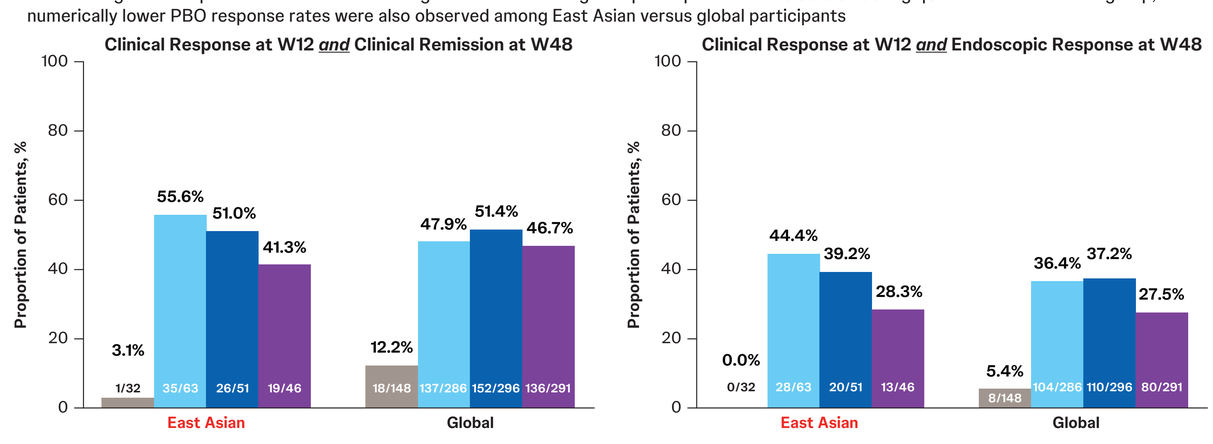
- Rates of clinical remission and endoscopic response at Week 12 were numerically higher with GUS IV 200 mg compared with PBO
- Rates of achieving these endpoints were similar between East Asian and global participants



Primary analysis set (pooled GALAXI 2 & 3 population). Clinical remission: CDAI score <150; Endoscopic response: ≥50% improvement from baseline in SES-CD score or SES-CD score ≤2. ***CDAI****=Crohn's Disease Activity Index;* ***GUS****=Guselkumab;* ***IV****=Intravenous;* ***PBO****=Placebo;* ***SES-CD****=Simple Endoscopic Score for Crohn's Disease;* ***W****=Week.*

Composite endpoints evaluating short-term and long-term efficacy of GUS

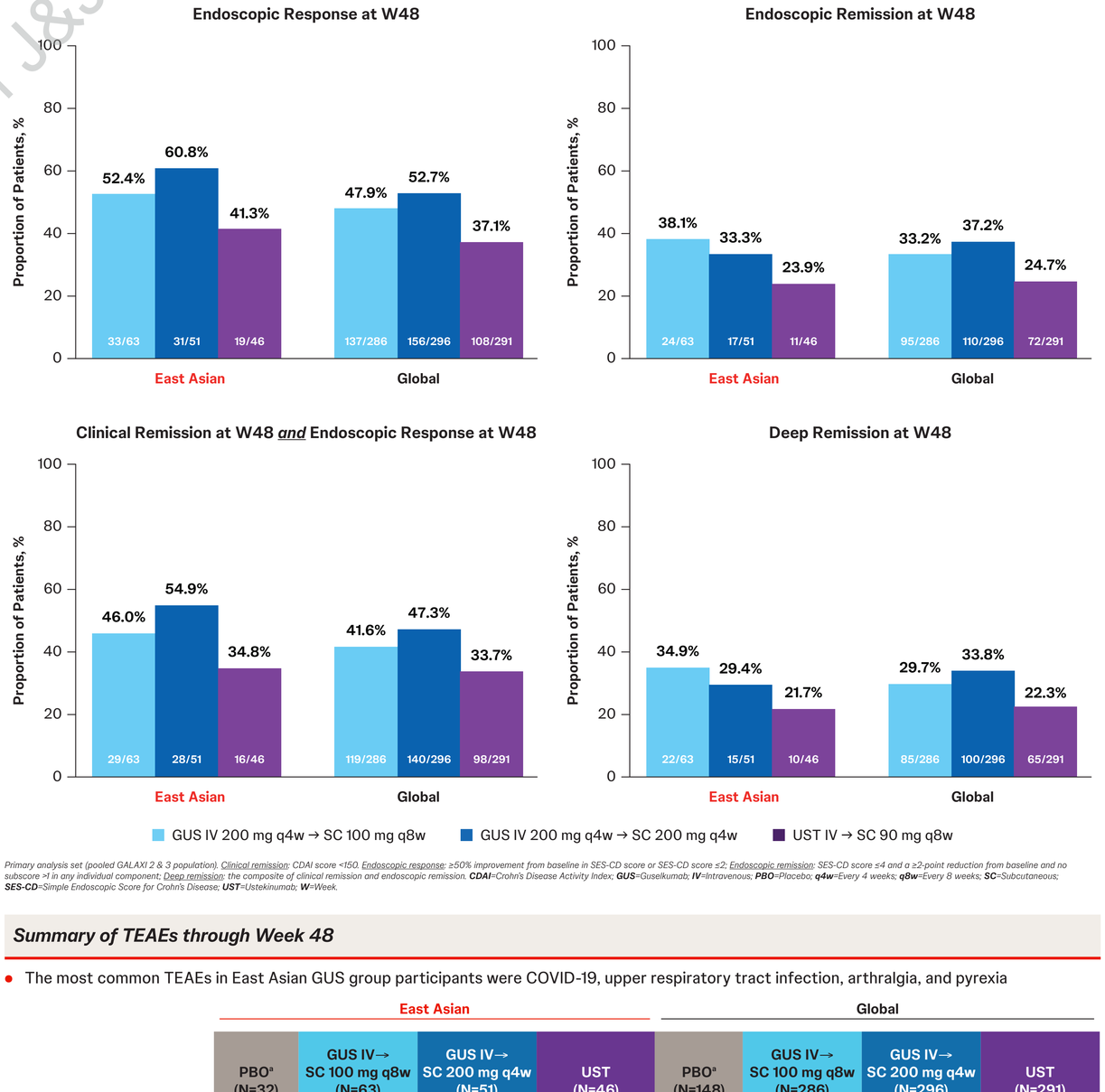
- Rates of achieving co-primary composite efficacy endpoints were numerically higher with both GUS SC maintenance regimens vs PBO
- Similar proportions of East Asian participants achieved these endpoints as observed in the global population; however, numerically higher rates of achieving both endpoints were observed among East Asian versus global participants in the GUS SC 100 mg q8w maintenance dose group; numerically lower PBO response rates were also observed among East Asian versus global participants



Primary analysis set (pooled GALAXI 2 & 3 population). Clinical response: ≥100-point reduction from baseline in CDAI or CDAI < 150; Clinical remission: CDAI score <150; Endoscopic response: ≥50% improvement from baseline in SES-CD score or SES-CD score ≤2. ***CDAI****=Crohn's Disease Activity Index;* ***GUS****=Guselkumab;* ***IV****=Intravenous;* ***PBO****=Placebo;* ***q4w****=Every 4 weeks;* ***q8w****=Every 8 weeks;* ***SC****=Subcutaneous;* ***SES-CD****=Simple Endoscopic Score for Crohn's Disease;* ***UST****=Ustekinumab;* ***W****=Week.*

Long-term efficacy of GUS relative to UST at Week 48

- Numerically higher proportions of GUS group participants achieved endoscopic and clinical endpoints at Week 48 relative to UST participants
- Rates of achieving Week 48 endpoints were generally consistent between East Asian and global participants, with numerically higher rates in the GUS groups among East Asian versus global participants for the endpoints of endoscopic response and the composite of clinical remission *and* endoscopic response



Primary analysis set (pooled GALAXI 2 & 3 population). Clinical remission: CDAI score <150. Endoscopic response: ≥50% improvement from baseline in SES-CD score or SES-CD score ≤2; Endoscopic remission: SES-CD score ≤4 and a ≥2-point reduction from baseline and no subscore >1 in any individual component; Deep remission: the composite of clinical remission and endoscopic remission. ***CDAI****=Crohn's Disease Activity Index;* ***GUS****=Guselkumab;* ***IV****=Intravenous;* ***PBO****=Placebo;* ***q4w****=Every 4 weeks;* ***q8w****=Every 8 weeks;* ***SC****=Subcutaneous;* ***SES-CD****=Simple Endoscopic Score for Crohn's Disease;* ***UST****=Ustekinumab;* ***W****=Week.*

Summary of TEAEs through Week 48

- The most common TEAEs in East Asian GUS group participants were COVID-19, upper respiratory tract infection, arthralgia, and pyrexia

	East Asian				Global			
	PBO[a] (N=32)	GUS IV→ SC 100 mg q8w (N=63)	GUS IV→ SC 200 mg q4w (N=51)	UST (N=46)	PBO[a] (N=148)	GUS IV→ SC 100 mg q8w (N=286)	GUS IV→ SC 200 mg q4w (N=296)	UST (N=291)
Mean duration of follow-up, weeks	18.2	47.7	45.3	45.5	21.4	46.2	46.6	45.4
Total PY follow-up	11.2	57.6	44.3	40.1	60.8	253	264.6	253
Pts w/any TEAEs, %	71.9%	87.3%	90.2%	89.1%	53.4%	76.6%	77.7%	78.7%
TEAEs/100 py	779.6	390.7	444.5	316.5	478.9	321.4	354.2	345.8
Pts w/serious TEAEs, %	15.6%	11.1%	7.8%	13.0%	10.8%	10.5%	7.1%	11.7%
Pts w/TEAEs leading to discontinuation, %	9.4%	4.8%	11.8%	4.3%	8.8%	7.0%	6.4%	7.6%
Pts w/serious infections, %[b]	6.3%	0	0	4.3%	1.4%	0.3%	1.0%	3.8%
Most common TEAEs, n (%)[c]								
Arthralgia	1 (3.1%)	4 (6.3%)	7 (13.7%)	0	4 (2.7%)	22 (7.7%)	25 (8.4%)	20 (6.9%)
COVID-19	2 (6.3%)	13 (20.6%)	15 (29.4%)	11 (23.9%)	9 (6.1%)	43 (15.0%)	53 (17.9%)	37 (12.7%)
Crohn's disease	3 (9.4%)	0	3 (5.9%)	2 (4.3%)	20 (13.5%)	25 (8.7%)	26 (8.8%)	25 (8.6%)
Pyrexia	4 (12.5%)	6 (9.5%)	4 (7.8%)	8 (17.4%)	7 (4.7%)	18 (6.3%)	16 (5.4%)	26 (8.9%)
Upper respiratory tract infection	2 (6.3%)	15 (23.8%)	8 (15.7%)	8 (17.4%)	6 (4.1%)	28 (9.8%)	25 (8.4%)	22 (7.6%)
White blood cell count decreased	1 (3.1%)	2 (3.2%)	7 (13.7%)	2 (4.3%)	3 (2.0%)	4 (1.4%)	8 (2.7%)	2 (0.7%)

Primary safety analysis set (pooled GALAXI 2 & 3 population). [a]Events in this column are attributed to those participants randomized to PBO with one exception: in the case where a participant is randomized to PBO and crosses over to UST, events occurring after receiving UST are not counted in this column. [b]Infections are based on MedDRA system organ class "Infections and Infestations". [c]TEAEs reported in ≥10% of participants in any treatment group. ***GUS****=Guselkumab;* ***IV****=Intravenous;* ***PBO****=Placebo;* ***PY****=Person-years;* ***q4w****=Every 4 weeks;* ***q8w****=Every 8 weeks;* ***SC****=Subcutaneous;* ***TEAE****=Treatment-emergent adverse event;* ***UST****=Ustekinumab.*

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