

MP0297

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Methods

- Patients (Pts) were randomized at W0 to receive GUS 400 mg SC q4w (x3)→GUS 100 mg SC q8w, GUS 400 mg SC q4w (x3)→GUS 200 mg SC q4w, or placebo SC
 - Symptomatic remission, Ulcerative Colitis-Patient-reported outcomes Signs and Symptoms (UC-PRO/SS) assessments of bowel urgency and abdominal pain, and levels of inflammatory biomarkers C-reactive protein (CRP) and fecal calprotectin were assessed through W96 in pts who continued treatment beyond W48. No endoscopic or histologic outcomes were assessed at W96
 - Symptomatic remission is defined as a stool frequency subscore of 0 or 1 and not increased from baseline, and a rectal bleeding subscore of 0 as assessed by two PRO questions from Mayo Score
 - No bowel urgency is defined as a rounded daily average (within 1 week) score of 0 in question Q7 of the UC-PRO/SS. Q7: In the past 24 hours, did you feel the need to have a bowel movement right away?
 - No abdominal pain is defined as a rounded daily average (within 1 week) score of 0 in question Q8 of the UC-PRO/SS. Q8: In the past 24 hours, did you feel pain in your belly?
- Starting from W16, pts meeting the following rescue criteria at W12 received blinded GUS SC treatment*:
 - No improvement in Mayo endoscopic subscore at W12 compared with baseline AND
 - <2 point improvement in partial Mayo score at W12 and W16 compared with baseline
- *Rescue treatment for GUS arms: Sham rescue with matching placebo SC to maintain the blind at W16, W20, and W24. Efficacy and safety data from rescue pts are not reported here.
 - Pts who benefited from treatment at W24 were eligible for the study extension with treatment to be continued through W248
 - Upon study unblinding after W48, placebo pts who were not rescued with GUS discontinued treatment; therefore, placebo efficacy data are not reported
- Statistical Analysis
 - Efficacy analyses were based on pts who were randomized to GUS and continued treatment after W48
 - "As observed" analyses included pts who had data available at the analysis timepoint (no imputation for intercurrent events and missing data)
 - NRI (nonresponder imputation) analyses: pts who, prior to a/the designated timepoint, had an ostomy or colectomy or discontinued study agent due to lack of efficacy or an AE of worsening of UC were considered not to have achieved any of the binary efficacy endpoints at W96. For patients who discontinued study agent due to COVID-19-related reasons (excluding COVID-19 infection) or regional crisis, their observed values were used, if available. Pts who discontinued study agent prior to W96 due to other reasons were considered not to have achieved any of the binary efficacy endpoints at W96. Pts with insufficient data to calculate a binary efficacy endpoint at W96 were considered not to have achieved the endpoint at W96.
 - A cumulative safety analysis W0 through W96 included all treated pts

Here, we report efficacy and safety results of SC maintenance GUS following GUS SC induction through week(W)96 in ASTRO, a randomized, double-blind, placebo-controlled, treat-through phase 3 trial in pts with moderately to severely active UC

Demographics and Baseline Disease Characteristics

	Placebo	GUS 400 mg SC → +100 mg SC q4w	GUS 400 mg SC →200 mg SC q4w
Full analysis set ^a , N	139	139	140
Age in years, mean (SD)	39.5 (13.6)	42.1 (14.6)	43.6 (14.3)
Male, n (%)	90 (64.7%)	79 (56.8%)	87 (62.1%)
UC disease duration in years, mean (SD)	6.61 (6.2)	8.39 (7.3)	7.69 (6.4)
Modified Mayo score ^b (0-9), mean (SD)	6.8 (1.1) ^c	6.8 (1.2)	6.6 (1.2)
Modified Mayo score of 7-9 (severe), n (%)	87 (63.0%) ^c	95 (68.3%)	77 (55.0%)
Mayo endoscopic subscore of 3 (severe), n (%)	78 (56.1%)	78 (56.1%)	78 (55.7%)
Extensive UC, n (%)	73 (52.5%)	69 (49.6%)	82 (58.6%)
C-reactive protein, ^d median in mg/L (IQR)	3.8 (1.2; 10.9)	3.7 (1.3; 7.2)	4.7 (1.7; 9.1)
C-reactive protein ^e >3 mg/L, n (%)	77 (55.8%)	75 (55.1%)	86 (61.4%)
Fecal calprotectin, ^f median in mg/kg (IQR)	1749.0	1351.5	1594.0
Fecal calprotectin ^g >250 mg/kg, n (%)	(617.0; 3202.0)	(609.0; 2805.0)	(838.0; 3336.0)
	119 (90.8%)	107 (84.9%)	119 (93.0%)

*All randomized pts who received at least 1 (partial or complete) dose of study intervention. *Modified Mayo score: 3-component (stool frequency, rectal bleeding, and endoscopy subscores) Mayo score without the physician's global assessment. *Based on N=138. †Based on N=138 for placebo, N=136 for GUS 400 mg SC→100 mg SC q8w, N=140 for GUS 400 mg SC→200 mg SC q4w. ‡Based on N=131 for placebo, N=126 for GUS 400 mg SC→100 mg SC, N=128 for GUS 400 mg SC→200 mg SC q4w. GUS=guselkumab, IQR=interquartile range, q2w=every 2 weeks, q8w=every 8 weeks, SC=subcutaneous, SD=standard deviation.

- A total of 235 pts who were randomized to GUS continued treatment after W48

	Placebo SC	GUS 400 mg SC q4w →100 mg SC q8w	GUS 400 mg SC q4w →200 mg SC q4w	Total
Safety Post W48 Extension Analysis Set^a; N	86	120	115	321
Pts who discontinued study treatment prior to W96, n (%)	47 (54.7%)	15 (12.5%)	9 (7.8%)	71 (22.1%)
Reason for discontinuation, n (%)				
Adverse event - worsening of UC	0	1 (0.8%)	1 (0.9%)	2 (0.6%)
Adverse event – other than worsening of UC	1 (1.2%)	1 (0.8%)	2 (1.7%)	4 (1.2%)
Lack of efficacy	5 (5.8%)	6 (5.0%)	4 (3.5%)	15 (4.7%)
Withdrawal by participant	3 (3.5%)	7 (5.8%)	2 (1.7%)	12 (3.7%)
W48 unblinding	38 (44.2%)	0	0	38 (11.8%)
Lost to follow-up	0	0	0	0
Death	0	0	0	0
Initiated prohibited medication	0	0	0	0
Protocol deviation	0	0	0	0
Other	0	0	0	0

^aPts who received at least one dose of study intervention (including a partial dose) at or after W48. **GUS**=guselkumab, **q4w**=every 4 weeks, **q8w**=every 8 weeks, **SC**=subcutaneous, **UC**=ulcerative colitis, **W**=week.

Stratified Randomization

- BIO/JAK1/SP1-IR status: Yes or No
- Mayo endoscopic subscore at baseline: Moderate (2) or Severe (3)

Screening

Main Treatment Phase

Extension Treatment Phase

Extension Treatment Phase (Safety Assessments Only)

Week

INDUCTION

Rescue at W16*

Correlational Testing

Unblinding after W48 database lock

Current Analysis

Primary Endpoint (Clinical Remission at W12)

Randomization

Histology

Endoscopy

Study unblinding

BIO/JAK1/SP1-IR=Biologic, Janus kinase inhibitor; or Sphingosine 1-phosphate receptor modulator; inadequate response or intolerance; q4w=every 4 weeks; q8w=every 8 weeks; SC=subcutaneous; W=week.

(A) As Observed

Week	48	56	64	72	80	88	96
GUS 400 SC + 100 SC q4w N=47	66.7			80.0			71.4
GUS 400 SC + 200 SC q4w N=45	61.9			74.4			70.6

(B) NRI

Week	48	56	64	72	80	88	96
GUS 400 mg SC q4w → GUS 100 mg SC q4w (N=47)	55.3			61.7			53.3
GUS 400 mg SC q4w → GUS 200 mg SC q4w (N=45)	66.7			71.1			53.3

- No abdominal pain was maintained over time from W48 through W96

(A) As Observed

Week	GUS 400 SC ~ 100 SC q8w (N)	GUS 400 SC ~ 200 SC q4w (N)	GUS 400 SC ~ 100 SC q4w (N)
48	108	111	111
56	114	108	108
64	112	105	105
72	102	105	105
80	97	105	105
88	101	101	101
96	93	98	98

(B) NRI

Week	GUS 400 SC q4w ~ GUS 100 SC q8w (N=12%)	GUS 400 SC q4w ~ GUS 200 SC q4w (N=15%)	GUS 400 SC q4w ~ GUS 100 SC q4w (N=15%)
48	60.0	73.9	73.9
56	73.9	73.9	73.9
64	73.9	73.9	73.9
72	73.9	73.9	73.9
80	73.9	73.9	73.9
88	73.9	73.9	73.9
96	55.8	67	67

As Observed

Median (IQR) fecal calprotectin (mg/kg)

Week

N=

GUS 400 SC → 109
180 SC q6w → 117
200 SC q4w → 116

GUS 400 SC → 109
180 SC q6w → 117
200 SC q4w → 116

Legend:

- GUSekumab 400 mg SC q4w + GUSekumab 100 mg SC q6w
- GUSekumab 400 mg SC q4w + GUSekumab 200 mg SC q6w

Week	GUSekumab 400 mg SC q4w + GUSekumab 100 mg SC q6w (mg/kg)	GUSekumab 400 mg SC q4w + GUSekumab 200 mg SC q6w (mg/kg)
0	1376.0	1376.0
4	1594.0	1594.0
12	232.0	232.0
24	232.0	232.0
48	189.0	189.0
72	114.0	114.0
96	142.0	136.0

- Median CRP biomarker levels were maintained over time from W48 through W96

As Observed

Median (IQR) CRP (mg/L)

Week

0 4 8 12 16 20 24 32 48 72 96

117 120 119 120 119 120 120 119 115 103

GUS 400 SC → 100 SC q8w

115 115 115 115 114 114 114 114 115 107

GUS 400 SC → 200 SC q4w

— Guselkumab 400 mg SC q4w → Guselkumab 100 mg SC q8w

— Guselkumab 400 mg SC q4w → Guselkumab 200 mg SC q4w

Week	Guselkumab 400 mg SC q4w → Guselkumab 100 mg SC q8w (Median CRP mg/L)	Guselkumab 400 mg SC q4w → Guselkumab 200 mg SC q4w (Median CRP mg/L)
0	4.2	3.4
4	2.1	2.1
8	2.1	1.1
12	2.1	1.1
16	1.1	1.1
20	2.1	1.1
24	2.1	1.1
32	1.1	1.1
48	1.9	1.4
72	1.1	1.1
96	1.1	1.1

- Treatment-emergent adverse events per 100 PY through W96 following randomized GUS 100 mg SC q8w and GUS 200 mg SC q4w vs placebo SC treatments

	Placebo SC (n=139)	GUS 400 mg SC q4w + GUS 100 mg SC q8w (n=139)	GUS 400 mg SC q4w + GUS 200 mg SC q4w (n=140)
Average duration of follow-up (weeks)	40.3	861	83.5
Total PY of follow-up	1074	2294	224.0
Number of events per 100 PY of follow up (95% CI)			
AEs	289.45 (258.17, 323.48)	266.34 (245.64, 288.32)	274.05 (252.80, 296.61)
Serious AEs	30.71 (21.4, 43.13)	5.67 (3.02, 9.69)	6.70 (3.75, 11.04)
AEs leading to discontinuation of study agent	14.89 (8.51, 24.18)	3.05 (1.23, 6.29)	3.57 (1.54, 7.04)
Infections*	67.01 (52.43, 84.39)	75.85 (65, 87.99)	62.93 (52.97, 74.22)
Serious infections*	2.79 (0.58, 8.16)	0.87 (0.11, 3.15)	1.34 (0.28, 3.91)
Death	0.93 (0.02, 5.19)	0.44 (0.01, 2.43)	0 (0, 1.34)

CI=confidence interval, GUS=gusekumab, PY=patient years, q4w=every 4 weeks, q8w=every 8 weeks, SC=subcutaneous.
^aInfections are based on MedDRA system organ class "Infections and Infestations."