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 Perianal fistulizing Crohn's disease (PFCD) is a severe and complex complication of Crohn's disease^{1,2}

- Affects ~1/4th of Crohn's disease patients and presence at diagnosis may indicate a more severe clinical course of Crohn's disease³

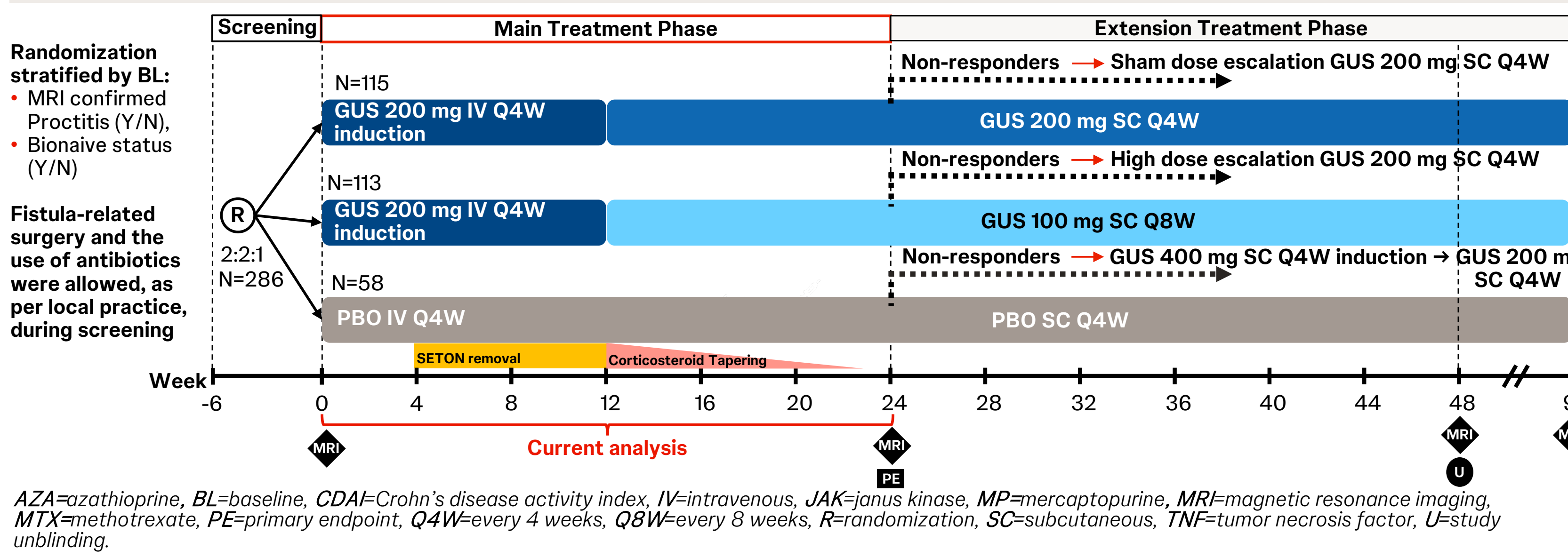
 Guselkumab (GUS) is a dual-acting monoclonal antibody inhibitor of the interleukin (IL)-23p19 subunit that potentially neutralizes IL-23 and binds to CD64, a receptor on cells that produce IL-23. It is approved in adults with moderately-to-severely active Crohn's disease⁴

- **FUZION (NCT05347095)**
- A Phase 3, randomized, placebo-controlled, double-blind, multicenter study in adults with active PFCD
- GUS demonstrated significantly higher Week (W) 24 combined fistula remission vs placebo (PBO), with no new safety signals⁵

 We evaluated additional clinical and radiologic efficacy of GUS through W24 in adults with active PFCD

Key Inclusion Criteria

- ≥18 years of age
- ≥1 active draining perianal fistula confirmed by blinded central MRI
- CDAI score <350
- Inadequate response to oral corticosteroids, immunomodulators (AZA, 6-MP, MTX), antibiotics, or ≤2 advanced-therapy classes (anti-TNF, vedolizumab, JAK inhibitors)



Endpoints

- **Primary:**
 - Combined fistula **remission** at W24 (clinically and radiologically assessed)
- **Multiplicity-Controlled Secondary Endpoints:**
 - Clinically assessed fistula **remission** at W24
 - Clinically assessed fistula **response** at W24
- **Key Secondary Endpoints:**
 - Clinically assessed fistula **response** at W12
 - Change in MAGNIFI-CD score from BL to W24

Statistical Considerations

- GUS 200 mg Q4W dose then the 100 mg Q8W dose were sequentially tested vs PBO for the primary endpoint then for the multiplicity-controlled secondary endpoints
- *p*-values are based on CMH test for binary endpoints and on MMRM for continuous endpoints
- After applying the ICE strategy, missing data were imputed as not having achieved binary endpoints or not having improvement from BL for continuous endpoints

CMH=Cochran-Mantel-Haenszel, ICE=intercurrent event, MAGNIFI-CD=magnetic resonance novel index for fistula imaging in Crohn's disease, MMRM=mixed model for repeated measures

Outcomes

Combined fistula remission	100% closure of all external openings, without development of new fistulas or abscesses and without any drainage by the external openings, occurring spontaneously or after gentle finger compression AND absence of collections >2 cm of the perianal fistulas in at least two of three dimensions, confirmed by a blinded central review of the MRI results
Clinically assessed fistula response	≥50% reduction from BL in number of open or draining perianal fistulas
Clinically assessed fistula remission	100% closure of all external openings, without development of new fistulas or abscesses and without any drainage by the external openings, occurring spontaneously or after gentle finger compression
MAGNIFI-CD score	Score ranges from 0 (no disease activity) to 25 (severe disease activity)

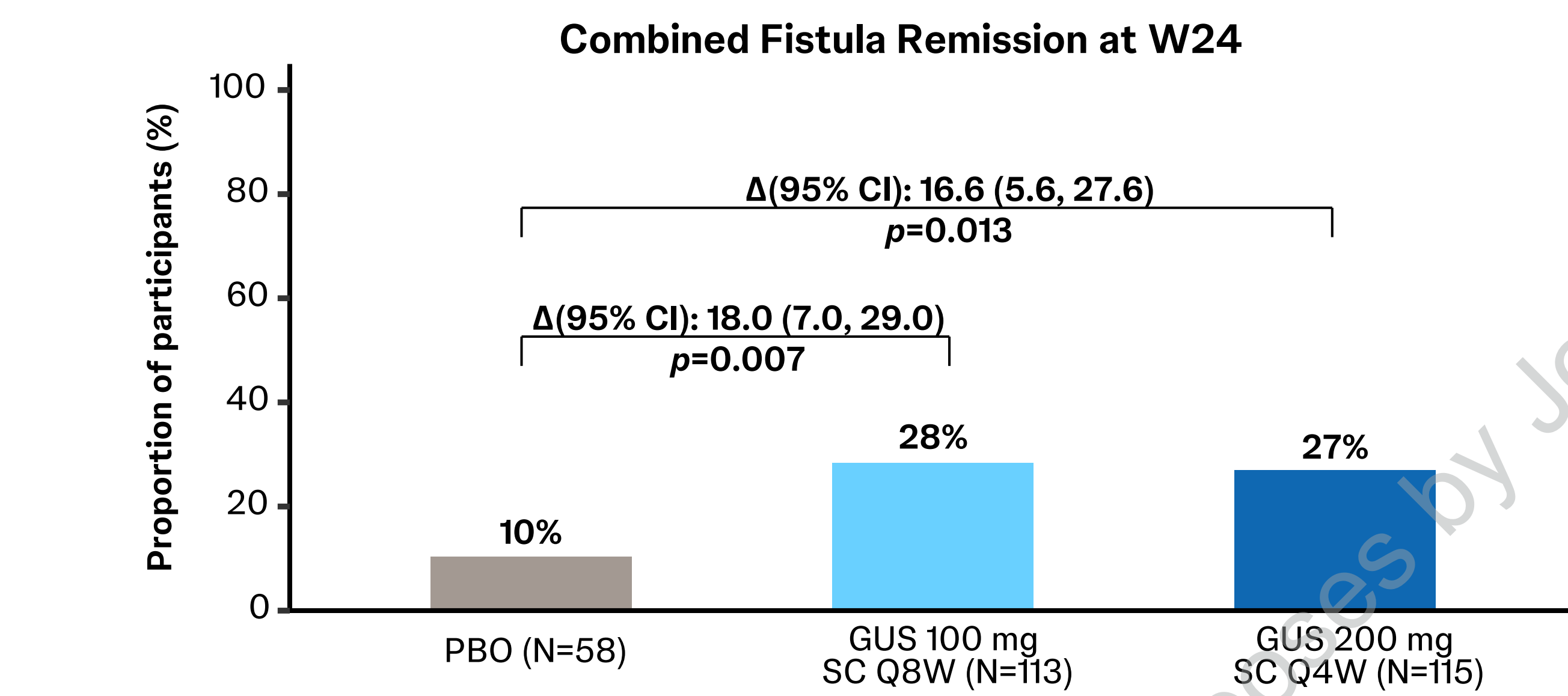
BL characteristics were generally balanced across the arms

- GUS 200mg SC Q4W group had more participants ≥ 2 fistulas at BL

BL Characteristics		GUS 100mg SC Q8W (N = 113)	GUS 200mg SC Q4W (N = 115)	PBO (N = 58)
Demographics				
	Age, yrs	36.2 (12.7)	36.0 (13.0)	38.0 (12.9)
	Male, n (%)	79 (70%)	85 (74%)	41 (71%)
Disease Characteristics				
	Crohn's disease duration, median (IQR), yrs	5.6 (1.9; 15.6)	6.8 (2.1; 15.9)	7.8 (3.4; 17.6)
	CDAI score	154.6 (97.6)	143.2 (84.6) ^a	147.6 (104.3) ^b
	Participants with open or draining fistula, n (%)			
	1 fistula	73 (65%)	60 (52%)	33 (57%)
	≥2 fistulas	40 (35%)	55 (48%)	25 (43%)
	Participants with complex fistula ^c , n (%)	52 (46%)	64 (56%)	30 (52%)
	Previous biologic exposure, n (%)			
	Bio-naïve	43 (38%)	38 (33%)	16 (28%)
	Bio-exposed	70 (62%)	77 (67%)	42 (72%)
	Proctitis, n (%)	31 (27%)	37 (32%)	16 (28%)
	Seton present, n (%)	23 (20%)	21 (18%)	10 (17%)
	≥1 fistula-related surgery during screening, n (%)	17 (15%)	18 (16%)	7 (12%)
	Patients with collections >2 cm, n (%)	0	4 (4%)	2 (3%)
	MAGNIFI-CD score, (0-25)	14.54 (4.8)	15.47 (4.6)	15.05 (5.4)
Inadequate response or intolerance to Crohn's disease medication, n (%)				
	Immunomodulator biologics	70 (62%)	77 (67%)	42 (72%)
	Only 1 anti-TNF agent	43 (38%)	51 (44%)	27 (47%)
	>1 anti-TNF agent	24 (21%)	25 (22%)	14 (24%)
	Only one mechanism of action	62 (55%)	69 (60%)	35 (60%)
Concomitant Crohn's disease medications, n (%)				
	5-ASA	27 (24%)	27 (24%)	19 (33%)
	Corticosteroids	10 (9%)	9 (8%)	3 (5%)
	Immunosuppressants (AZA, 6-MP, MTX)	34 (30%)	35 (30%)	16 (28%)

Data shown are mean (SD) unless otherwise noted. ^aN=108, ^bN=56. ^cFistula complexity was determined by MRI using MAGNIFI-CD "number of fistula tracts" (single/unbranched or complex). ASA=aminosalicylates, IQ=interquartile range, SD=standard deviation.

- Both GUS dose regimens achieved significantly higher W24 combined fistula remission rates vs PBO

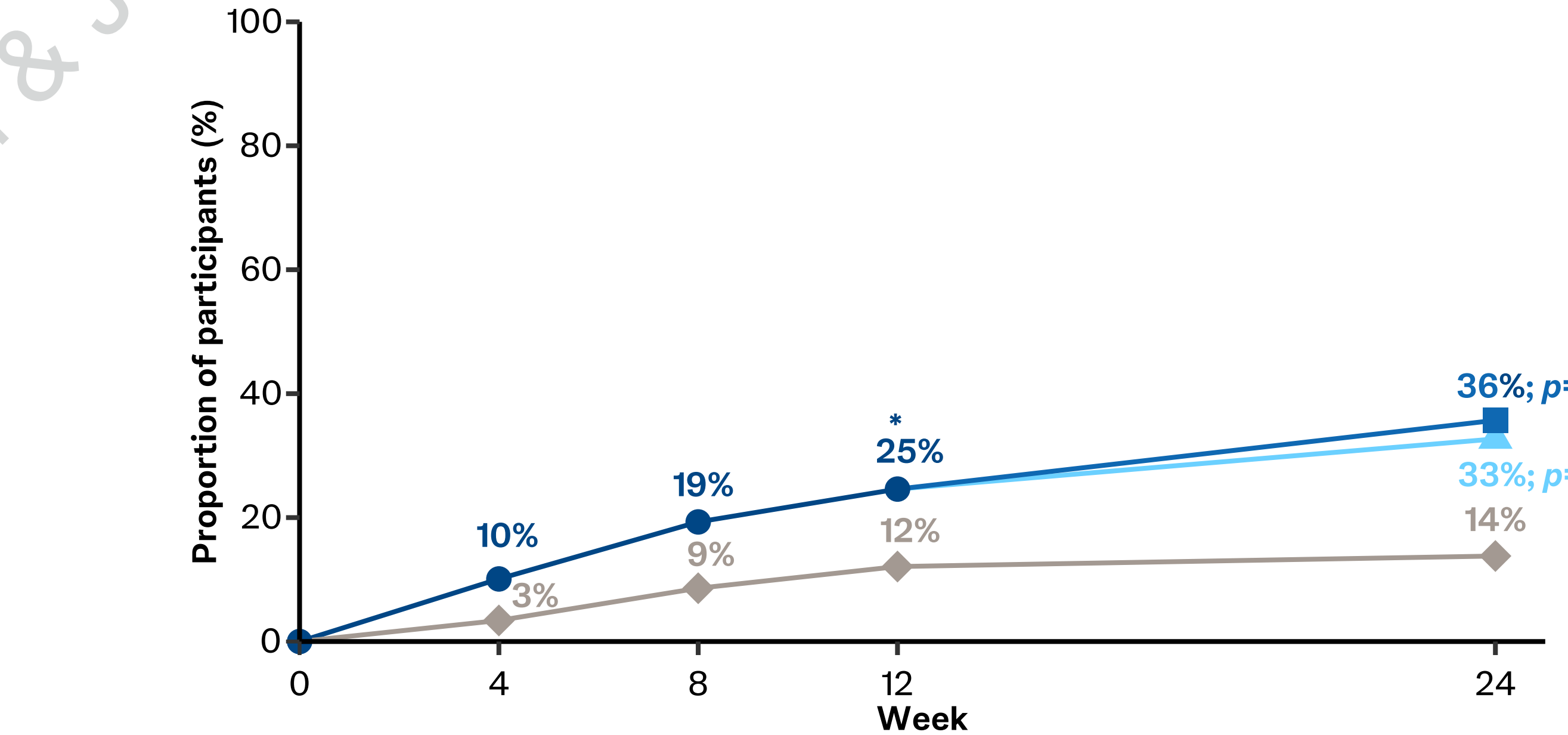


Multiplicity-controlled *p*-values. The adjusted risk difference and CI were based on Wald statistics using Mantel-Haenszel stratum weights stratified by BL proctitis (Y/N) and BL bio-naïve status (Y/N). CI=confidence interval.

Category	Subgroups	GUS combined ^a n/N (%)	PBO n/N (%)	Adjusted rate difference GUS combined vs PBO (%; 95% CI)
Overall	All participants	63/228 (28%)	6/58 (10%)	
BL CDAI	≥220 to ≤450	13/51 (26%)	0/9 (0%)	
	<220	48/170 (28%)	5/46 (11%)	
Biologic exposure	Without prior exposure	26/81 (32%)	4/16 (25%)	
	With prior exposure	37/147 (25%)	2/42 (5%)	
Proctitis at BL	With proctitis	18/68 (26%)	2/16 (12%)	
	Without proctitis	45/160 (28%)	4/42 (10%)	
Number of fistulas	1 fistula	49/133 (37%)	6/33 (18%)	
	≥2 fistulas	14/95 (15%)	0/25 (0%)	
Fistula complexity	Complex fistula	22/116 (19%)	1/30 (3%)	
	Simple fistula	40/110 (36%)	5/28 (18%)	
Infliximab failure	With prior failure	27/110 (24%)	2/32 (6%)	

^aGUS combined includes maintenance combined dose of GUS 100mg SC Q8W and 200mg SC Q4W.

Clinically Assessed Fistula Response



Week	GUS Induction 200 mg IV Q4W (N=228)	GUS 100 mg SC Q8W (N=113)	GUS 200 mg SC Q4W (N=115)	PBO (N=58)
0	0%	0%	0%	0%
4	3%	7%	3%	3%
8	7%	11%	7%	7%
12	9%	17%	9%	9%
24	10%	28%	27%	10%

Nominal $*p < 0.05$. Printed p -values are multiplicity-controlled.

MAGNIFI-CD Score at W24

LSM change from BL (95% CI)

Δ(95% CI): -1.4 (-1.9, -0.8)

Δ(95% CI): -1.7 (-2.3, -1.2)

Δ(95% CI): -0.4 (-1.1, 0.3)

Δ(95% CI): -1.0 (-1.5, -0.5) p=0.004

Δ(95% CI): -0.3 (-0.8, 0.2) p=0.034

Legend:

- GUS 100 mg SC Q8W (N=112)
- GUS 200 mg SC Q4W (N=115)
- PBO (N=58)

Nominal *p*-values. *LSM*=least square mean

Safety Through W24	GUS 100mg SC Q8W (N = 113)	GUS 200mg SC Q4W (N = 115)	PBO (N = 58)
Mean duration of follow-up (weeks)	24.0	24.0	23.8
Mean exposure (number of study agent administrations)	5.7	5.8	5.6
≥1 Adverse event	76 (67%)	80 (70%)	48 (83%)
≥1 Serious adverse event	12 (11%)	7 (6%)	8 (14%)
≥1 Adverse event leading to study agent discontinuation	8 (7%)	3 (3%)	5 (9%)
≥1 Infection	45 (40%)	31 (27%)	27 (47%)
≥1 Serious infection	8 (7%)	2 (2%)	2 (3%)

Data shown are n (%) unless otherwise noted

[illegible]