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- The last successful international, randomized, placebo-controlled trial of an advanced therapy dedicated to evaluating fistulizing Crohn's disease was the ACCENT 2 trial of infliximab, which was published in 2004¹

- Guselkumab:**

- Approved for adults with moderately-to-severely active Crohn's disease³

Key

- ✓ Adults with at least 1 active draining perianal fistula confirmed by blinded central MRI review
- ✓ Active Crohn's disease (CDAI score <350)



Pri

- Combined fistula remission at week 24 (clinically and radiologically assessed)

- Clinically assessed fistula remission at week 24

- Clinically assessed fistula response at

- Clinically assessed fistula response at week 12

MRI=Magnetic Resonance Imaging, **q4w**=every 4 weeks, **q8w**=every 8 weeks.

De

	100 mg SC q8w (N=113)	200 mg SC q4w (N=115)	Combined (N=228)	Placebo (N=58)	Total (N=286)
Age, mean (SD) (years)	36.2 (12.67)	36.0 (13.02)	36.1 (12.82)	38.0 (12.93)	36.5 (12.84)
Male, n (%)	79 (69.9%)	85 (73.9%)	164 (71.8%)	41 (70.7%)	205 (71.7%)
Crohn's disease duration (years)					
Median	5.56	6.77	6.08	7.75	6.29
IQ range	(1.90; 15.64)	(2.07; 15.93)	(1.94; 15.75)	(3.41; 17.59)	(2.07; 15.93)
CDAI Score, N	113	108	221	56	277
Mean (SD)	154.6 (97.57)	143.2 (84.60)	149.0 (91.43)	147.8 (104.26)	148.7 (93.97)
> 220	25 (22.1%)	23 (21.3%)	48 (21.7%)	10 (17.9%)	58 (20.9%)
≤ 220	88 (77.9%)	85 (78.7%)	173 (78.3%)	46 (82.1%)	219 (79.1%)
Participants with open or draining fistula, n (%)					
1 fistula	73 (64.6%)	60 (52.2%)	133 (58.3%)	33 (56.9%)	166 (58.0%)
≥ fistulas	40 (35.4%)	55 (47.8%)	95 (41.7%)	25 (43.1%)	120 (42.0%)
Previous biologic exposure, n (%)					
Bio-naïve	43 (38.1%)	38 (33.0%)	81 (35.5%)	16 (27.6%)	97 (33.9%)
Bio-exposed	70 (61.9%)	77 (67.0%)	147 (64.5%)	42 (72.4%)	189 (66.1%)
Proctitis at baseline, n (%)	31 (27.4%)	37 (32.2%)	68 (29.8%)	16 (27.6%)	84 (29.4%)
Seton present at baseline, n (%)	23 (20.4%)	21 (18.3%)	44 (19.3%)	10 (17.2%)	54 (18.9%)
≥1 fistula-related surgery during screening, n (%)	31 (27.4%)	30 (26.1%)	61 (26.8%)	13 (22.4%)	74 (25.9%)
Patients with collections >2 cm at baseline, n(%)	0	4 (3.5%)	4 (1.8%)	2 (3.4%)	6 (2.1%)

Prior and Concomitant Medications for Crohn's Disease

Participants with prior exposure to IL-12/23 or IL-23 alone were ineligible for study entry. *Participants who were exposed to ustekinumab at its approved labeled dosage AND met the required washout criterion (16 weeks) AND had not demonstrated inadequate response or intolerance to ustekinumab AND received one IV induction dose of ~6 mg/kg and one SC maintenance dose of 90 mg.

	100 mg SC q8w (N=113)	200 mg SC q4w (N=115)	Combined (N=228)	Placebo (N=58)	Total (N=286)
Completed 24 weeks of treatment, n (%)	100 (88.5%)	111 (96.5%)	211 (92.5%)	50 (86.2%)	261 (91.3%)
Discontinued study treatment, n (%)	13 (11.5%)	4 (3.5%)	17 (7.5%)	8 (13.8%)	25 (8.7%)
Reason for discontinuing study treatment, n (%)					
Discontinued due to AE	9 (8.0%)	3 (2.6%)	12 (5.3%)	4 (6.9%)	16 (5.6%)
Adverse event - Other	4 (3.5%)	3 (2.6%)	7 (3.1%)	0	7 (2.4%)
Adverse event - Worsening of Crohn's disease	5 (4.4%)	0	5 (2.2%)	4 (6.9%)	9 (3.1%)
Death	0	0	0	0	0
Lack of efficacy	0	0	0	1 (1.7%)	1 (0.3%)
Lost to follow-up	1 (0.9%)	0	1 (0.4%)	0	1 (0.3%)
Physician decision	1 (0.9%)	0	1 (0.4%)	0	1 (0.3%)
Protocol deviation	0	0	0	0	0
Pregnancy	0	0	0	0	0
Subject refused further study treatment	0	0	0	1 (1.7%)	1 (0.3%)
Withdrawal of consent	2 (1.8%)	0	2 (0.9%)	0	2 (0.7%)
Prohibited Crohn's Disease related surgery	0	0	0	0	0
Other	0	1 (0.9%)	1 (0.4%)	2 (3.4%)	3 (1.0%)

Combined Fistula Remission at Week 24

Group	N	Proportion of participation (%)
Placebo	58	10.3%
100 mg SC q8w	113	28.3%
200 mg SC q4w	115	27%

Δ(95% CI): 16.6 (5.6, 27.6)
P = 0.013

Δ(95% CI): 18.0 (7.0, 29.0)
P = 0.007

Combined Fistula Remission: 100% closure of all treated 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, confirmed by a blinded central review of the MRI results

Missing Data Imputation: After applying the ICE strategy, missing data were imputed as not having achieved a combined fistula remission at week 24. The adjusted risk difference statistics using Mantel-Haenszel stratum weights stratified by baseline proctitis (yes, no) and baseline bio-naïve status (yes, no). The *p*-values are based on the CMH test, stratified by baseline proctitis and baseline bio-naïve status (yes, no).

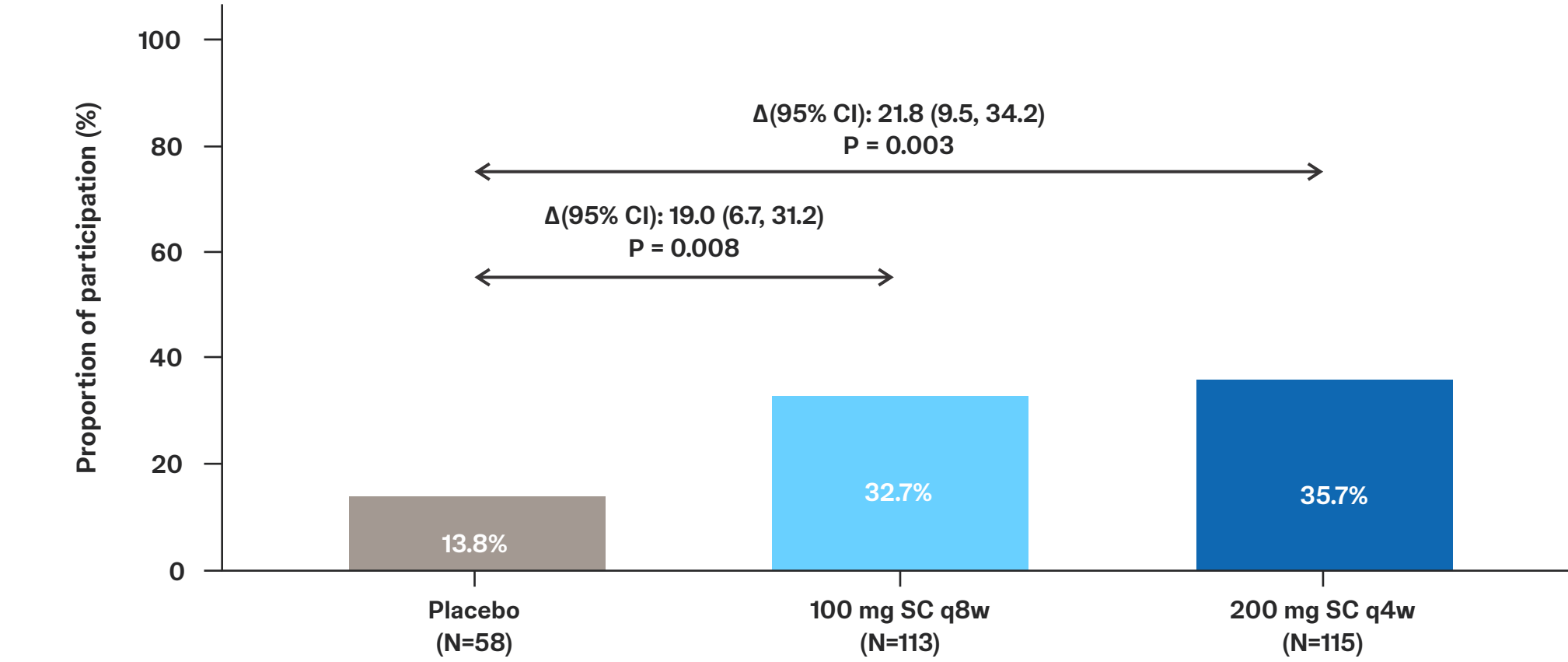
Multiplicity-Controlled Secondary Endpoint

-
- | Group | N | Proportion of participants (%) |
|---------------|-----|--------------------------------|
| Placebo | 58 | 10.3% |
| 100 mg SC q8w | 113 | 28.3% |
| 200 mg SC q4w | 115 | 27% |
- Comparison between 100 mg and 200 mg groups: $\Delta(95\% \text{ CI}): 16.6 (5.6, 27.6)$, $P = 0.013$
- Comparison between Placebo and 200 mg groups: $\Delta(95\% \text{ CI}): 18.0 (7.0, 29.0)$, $P = 0.007$

Clinically Assessed Fistula Remission: 100% closure of all treated external openings, without development of new fistulas or abscesses and without any drainage by the external openings, occurring spontaneously or after gentle finger compression

Missing Data Imputation: After applying the ICE strategy, missing data were imputed as not having achieved a combined fistula remission at week 24. The adjusted risk difference and CI were based on Wald statistics using Mantel-Haenszel stratum weights stratified by baseline proctitis (yes, no) and baseline bio-naïve status (yes, no). The *p*-values are based on the CMH test, stratified by baseline proctitis (yes, no) and baseline bio-naïve status (yes, no).

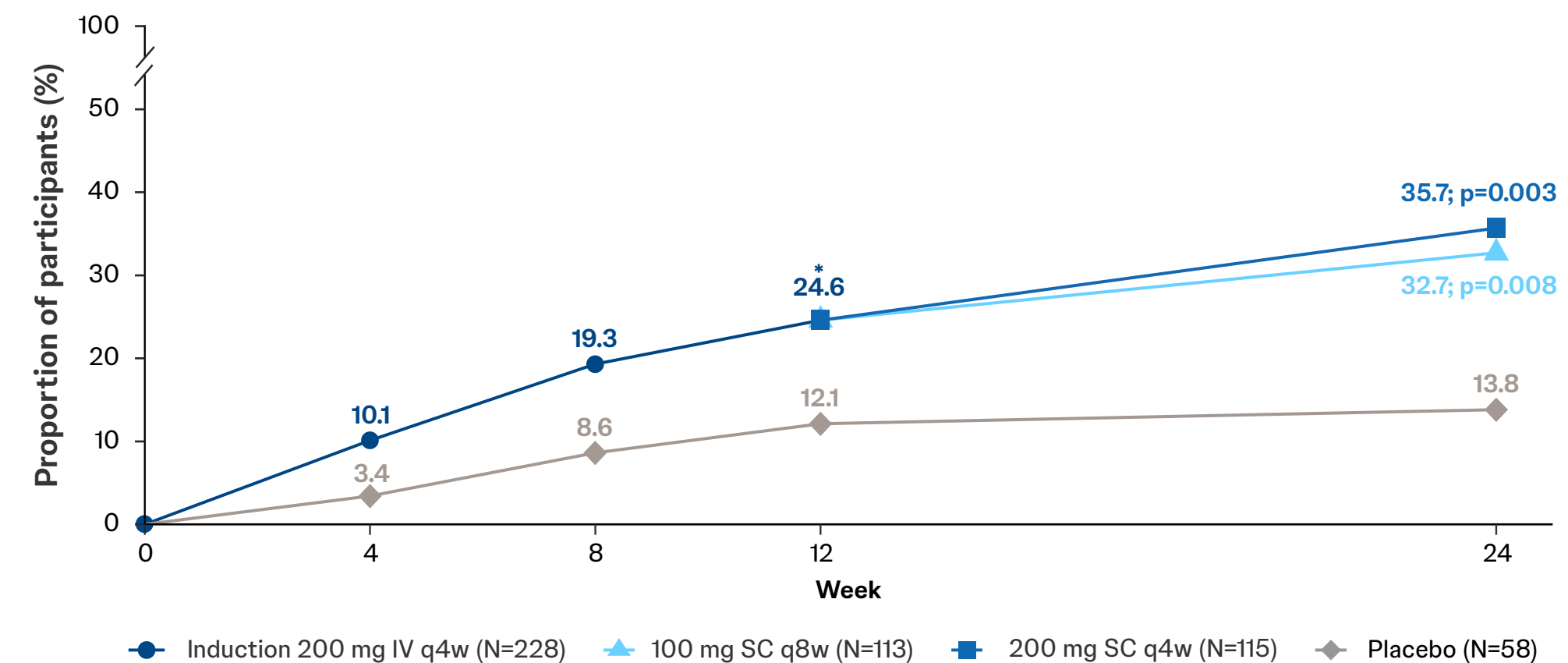
Multiplicity-Controlled Secondary Endpoint



Missing Data Imputation: After applying the ICE strategy, missing data were imputed as not having achieved a combined fistula remission at week 24. The adjusted risk difference and CI were based on Wald statistics using Mantel-Haenszel stratum weights stratified by baseline proctitis (yes, no) and baseline bio-naïve status (yes, no). The *p*-values are based on the CMH test, stratified by baseline proctitis (yes, no) and baseline bio-naïve status (yes, no).

CI=confidence interval, CMH=Cochran-Mantel-Haenszel, ICE=intercurrent event, MRI=magnetic resonance imaging, q4w=every 4 weeks, q8w=every 8 weeks, SC=subcutaneous.

Guselkumab showed meaningful difference versus placebo during induction



Clinically Assessed Fistula Response: $\geq 50\%$ reduction from baseline in number of open or draining perianal fistulas

Nominal $p=0.04$

Missing Data Imputation: After applying the ICE strategy, missing data were imputed as not having achieved a combined fistula remission at Week 24. The adjusted risk difference and CI were based on Wald statistics using Mantel-Haenszel stratum weights stratified by baseline proctitis (yes, no) and baseline bio-naïve status (yes, no). The p-values are based on the CMH test, stratified by baseline proctitis (yes, no) and baseline bio-naïve status (yes, no).

	100 mg SC q8w (N=113)	200 mg SC q4w (N=115)	Combined (N=228)	Placebo (N=58)
Mean duration of follow-up (weeks)	24.0	24.0	24.0	23.8
Mean exposure (number of study agent administrations)	5.7	5.8	5.8	5.6
Subjects with ≥1 adverse event	76 (67.3%)	80 (69.6%)	156 (68.4%)	48 (82.8%)
Subjects with ≥1 serious adverse event	12 (10.6%)	7 (6.1%)	19 (8.3%)	8 (13.8%)
Subjects with ≥1 adverse event leading to discontinuation of study agent	8 (7.1%)	3 (2.6%)	11 (4.8%)	5 (8.6%)
Subjects with ≥1 infection	45 (39.8%)	31 (27.0%)	76 (33.3%)	27 (46.6%)
Subjects with ≥1 serious infection	8 (7.1%)	2 (1.7%)	10 (4.4%)	2 (3.4%)

- The most frequently reported severe events in the guselkumab dose groups were: nasopharyngitis (6.1% guselkumab 200 mg SC q4w; 10.6% guselkumab 100 mg SC q4w) and anal abscess (5.2% guselkumab 200 mg SC q4w; 11.5% guselkumab 100 mg SC q4w)
- No opportunistic infection, anaphylactic reactions or serum sickness reactions, MACe, clinically important host defense disorders and VTE or deaths were reported
- 1 malignancy a B-cell lymphoma was reported through Week 24 (not related to study drug as assessed by investigator)
- Based on the total number of guselkumab injections, the injection site reaction rate was 2.6%, and the majority of the reactions were mild

fections are based on MedDRA system organ class "infections and infestations". Subjects are counted only once for any given event under specific column, regardless of the number of times they actually experienced the event. Adverse events are coded using MedDRA Version 28.0.

ACE=major adverse cardiovascular event, **q4w**=every 4 weeks, **q8w**=every 8 weeks, **SC**=subcutaneous, **VTE**=venous thrombo-embolic event