DOP060

Early disease efficacy of guselkumab therapy in biologic-naïve patients with moderately to severely active Crohn's disease: Post-hoc analysis from the phase 3 GALAXI 2 & 3 studies

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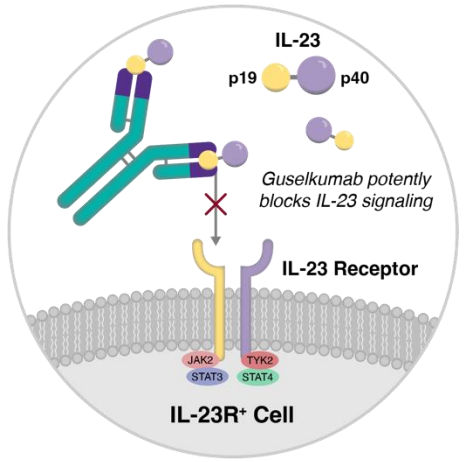
Disclosure of Conflicts of Interest

I, Geert D'Haens, herewith declare the following paid or unpaid consultancies, business interests or sources of honoraria payments for the past three years, and anything else which could potentially be viewed as a conflict of interest:

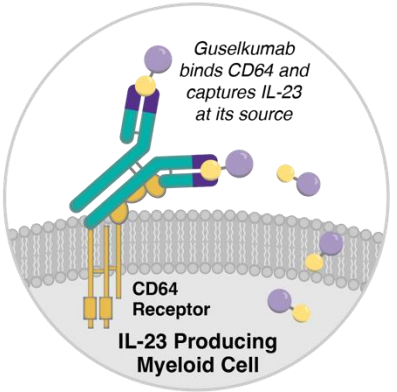
I report consultancy activities for AbbVie, Agomab, Alimentiv, AstraZeneca, AMT, Bristol Meyers Squibb, Boehringer Ingelheim, Celltrion, Eli Lilly, Exeliom, Galapagos, GlaxoSmithKline, Gossamerbio, Immunic, Index, Johnson & Johnson, Kaleido, Origo, Pfizer, Polpharma, Procise Diagnostics, Prometheus Laboratories, Prometheus Biosciences, Progenity, and Protagonist Therapeutics Inc.; speaker's bureau for AbbVie, Bristol Meyers Squibb, Galapagos, Pfizer, and Takeda; and data monitoring board activities for AbbVie, AstraZeneca, Galapagos, and Seres Health.

Background and Objective

- Early biologic treatment is associated with better efficacy outcomes in patients with Crohn's disease (CD)[1]
- Guselkumab is a dual-acting IL-23p19 subunit inhibitor that potently blocks IL-23 and binds to CD64, a receptor on immune cells that produce IL-23[2]
- GALAXI 2 & 3 are identically designed trials assessing the efficacy and safety of guselkumab in participants with moderately to severely active CD, and the efficacy in BIO-naïve participants was previously reported.[3,4,5]
- Here, we present results of a post-hoc analysis of guselkumab efficacy in BIO-naïve participants with disease duration ≤2 years, BIO-naïve participants with disease duration >2 years, and BIO-IR participants (inadequate response/intolerance) using data from the pooled phase 3 GALAXI trials.



Dual-acting IL-23 Inhibitor



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2. Atreya R, Abreu MT, Krueger JG, et al. *J Crohns Colitis.* 2024;18(suppl):S470.
3. Panaccione R, Danese S, Feagan BG, et al. *Gastroenterology*. 2024; 166(5): S1057b.
4. Sands BE, D'Haens G, Danese S, et al. *United European Gastroenterol J*. 2024; 12(S8): 43-4.
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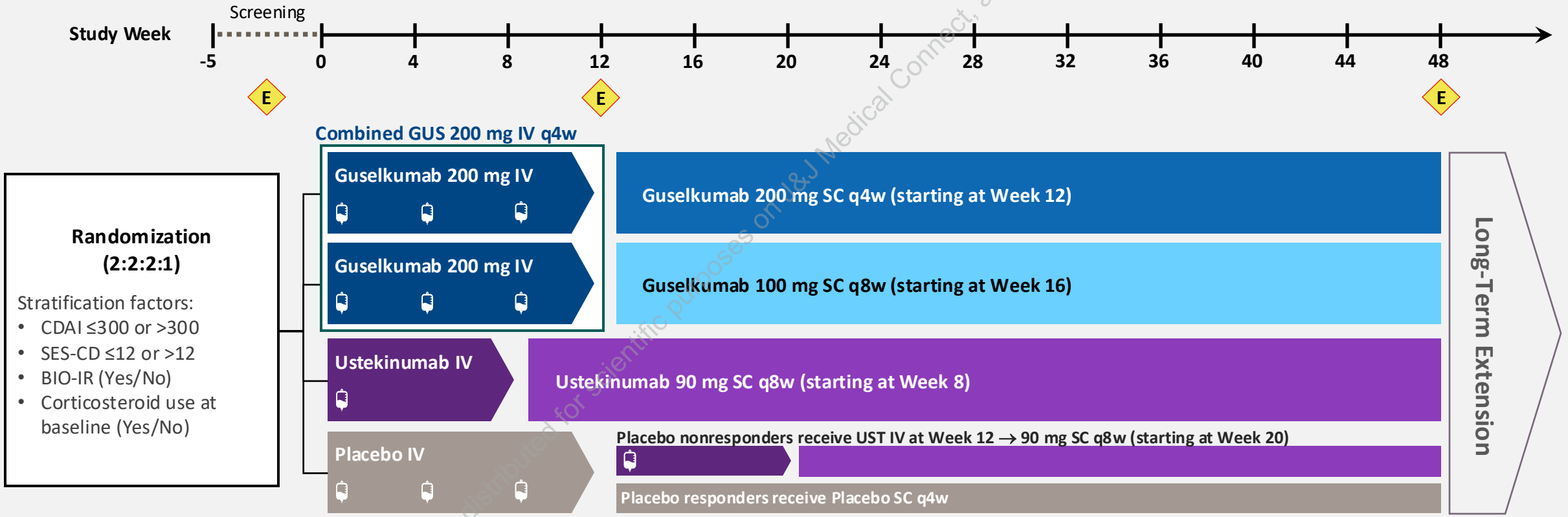
Double-Blind, Treat-Through Design: GALAXI 2 & 3

Key eligibility criteria

- Moderately to severely active CD (CDAI score 220–450 + mean daily Stool Frequency count >3 OR Abdominal Pain score >1) and SES-CD score[a] ≥6 (or ≥4 for isolated ileal disease)
- Inadequate response/intolerance to oral corticosteroids or 6-MP/AZA/MTX, or biologic therapies[b]



a. Scored at screening by central reader with minimum scores of 1 for "size of ulcer" and "ulcerated surface"
b. Biologic therapies: TNF antagonists or vedolizumab
E = Endoscopy
Note: 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

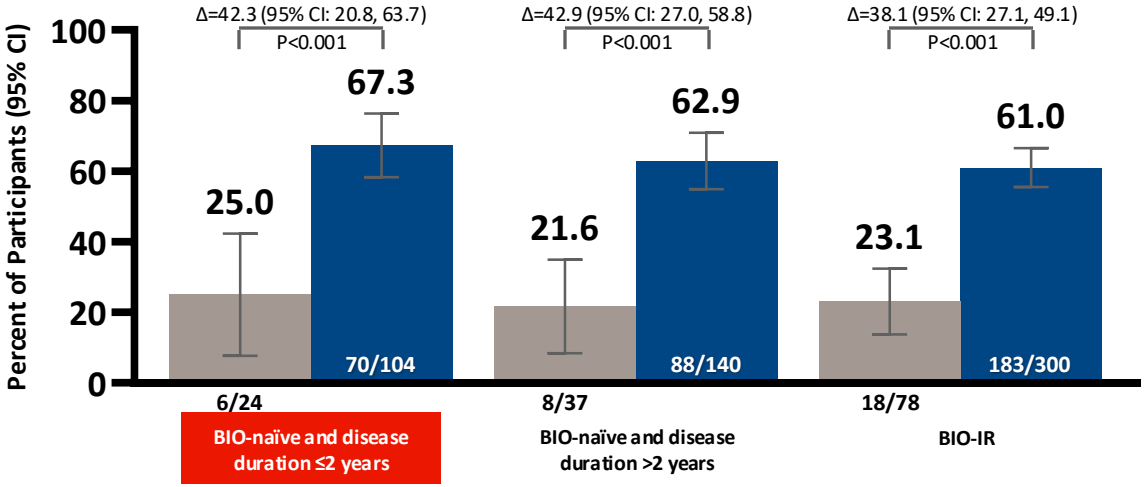
Table 1. Baseline Demographics and Disease Characteristics

Primary analysis set	BIO-naïve and disease duration ≤2 years N=180[a]	BIO-naïve and disease duration >2 years N=246[a]	Total BIO-naïve N=426[a]	BIO-IR N=534[a]
Demographics				
Age in years, mean (SD)	33.6 (13.27)	38.3 (12.76)	36.3 (13.16)	36.9 (12.79)
Male, n (%)	99 (55.0%)	137 (55.7%)	236 (55.4%)	311 (58.2%)
Characteristics				
CD duration in years, mean (SD)	0.88 (0.479)	8.07 (6.447)	5.04 (6.058)	8.54 (7.585)
CDAI score, mean (SD)	292.3 (51.21)	293.4 (52.21)	292.9 (51.73)	294.9 (52.95)
SES-CD score, mean (SD)	11.9 (6.46)	12.0 (6.91)	11.9 (6.72)	13.7 (7.54)
Endoscopic disease severity (SES-CD score), n (%)				
Moderate (7–16)	101 (56.1%)	130 (52.8%)	231 (54.2%)	284 (53.2%)
Severe (>16)	38 (21.1%)	60 (24.4%)	98 (23.0%)	162 (30.3%)
Involved GI areas by central reader, n (%)				
Colon only	68 (37.8%)	101 (41.1%)	169 (39.7%)	213 (39.9%)
Ileum only	44 (24.4%)	64 (26.0%)	108 (25.4%)	104 (19.5%)
Ileum and Colon	68 (37.8%)	81 (32.9%)	149 (35.0%)	217 (40.6%)
Biomarkers				
CRP in mg/L, median (IQR)	5.4 (1.9; 13.6)	4.7 (1.6; 12.8)	4.8 (1.7; 13.0)	8.4 (3.1; 24.7)
Fecal calprotectin in µg/g,[b] median (IQR)	751.0 (278.0; 1790.0)	693.5 (237.0; 1554.0)	728.0 (244.0; 1612.0)	1225.0 (445.0; 2494.0)
Concomitant CD medications at baseline, n (%)				
6-MP/AZA	46 (25.6%)	81 (32.9%)	127 (29.8%)	136 (25.5%)
MTX	1 (0.6%)	0	1 (0.2%)	15 (2.8%)
Oral corticosteroids	83 (46.1%)	109 (44.3%)	192 (45.1%)	158 (29.6%)

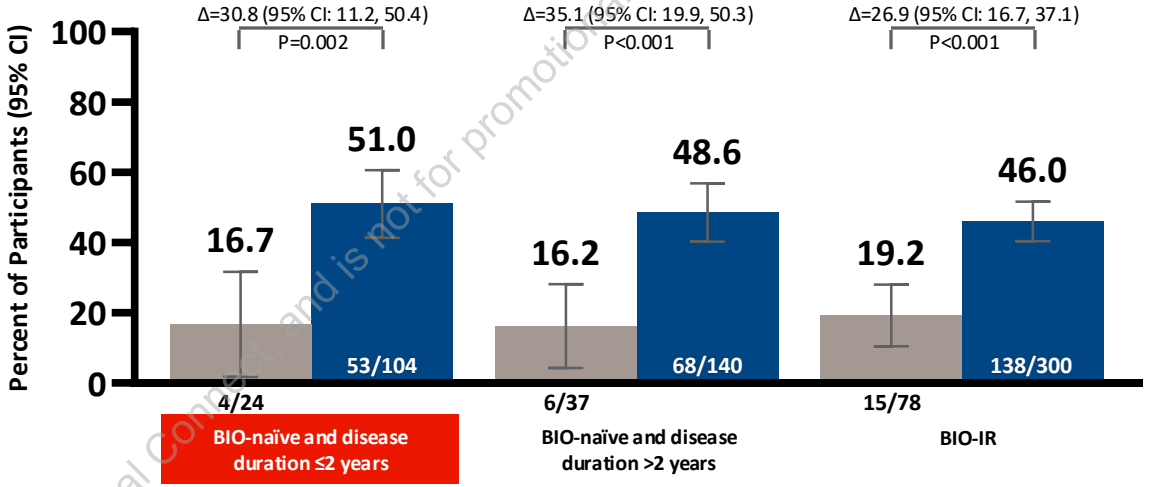
6-MP= 6-mercaptopurine. AZA= azathioprine. BIO= biologic. CDAI= Crohn's disease activity index. CRP= C-reactive protein. IQR= interquartile range. IR= inadequate response/intolerance. MTX= methotrexate. SC= subcutaneous. SD= standard deviation. SES-CD= simple endoscopic score for Crohn's disease.

[a] Includes all participants (including those randomly assigned to ustekinumab) in the BIO-naïve or BIO-IR subpopulation of the primary analysis set (all randomized participants who received at least 1 partial or complete dose of study intervention and had a screening SES-CD score ≥6 [or ≥4 for participants with isolated ileal disease]). [b] Based on N=179 for disease duration ≤2 years, N=242 for disease duration >2 years, N=421 for total BIO-naïve, and N=526 for BIO-IR.

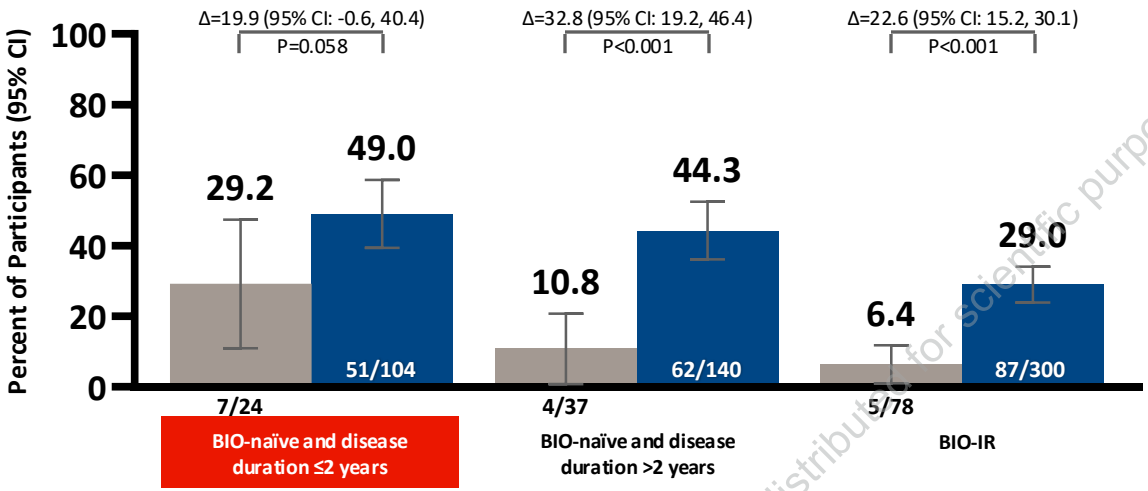
Clinical Response at Wk 12



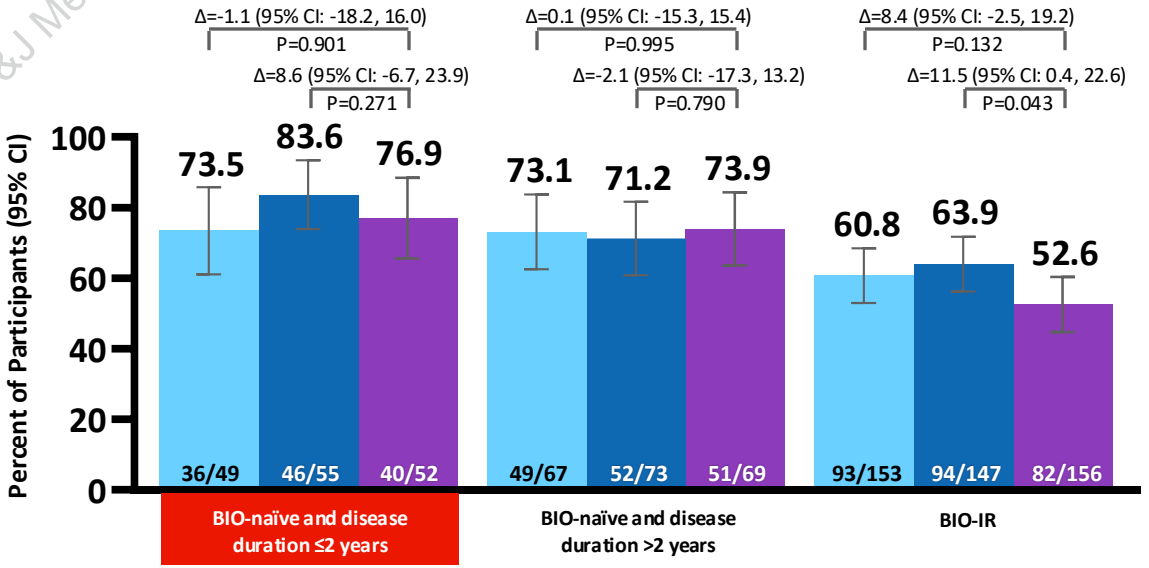
Clinical Remission at Wk 12



Endoscopic Response at Wk 12



Clinical Remission at Wk 48



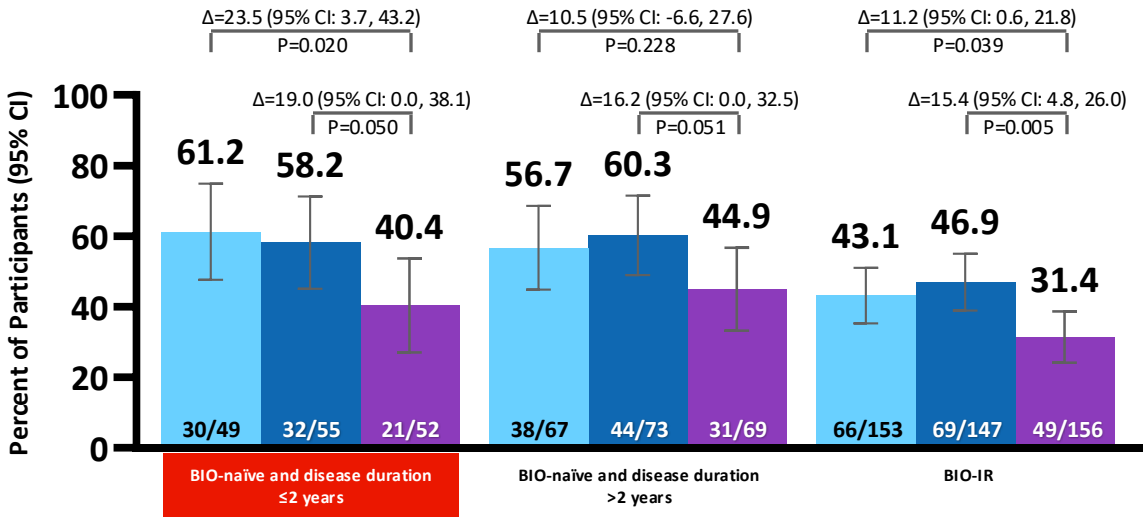
Placebo | GUS 200 mg IV q4w | GUS 200 mg IV q4w → GUS 100 mg SC q8w | GUS 200 mg IV q4w → GUS 200 mg SC q4w | UST ~6 mg/kg IV → UST 90 mg SC q8w

Clinical remission: CDAI score <150
Endoscopic response: ≥50% improvement from baseline in SES-CD or SES-CD ≤ 2
Clinical response: ≥100-point reduction from baseline CDAI or CDAI<150

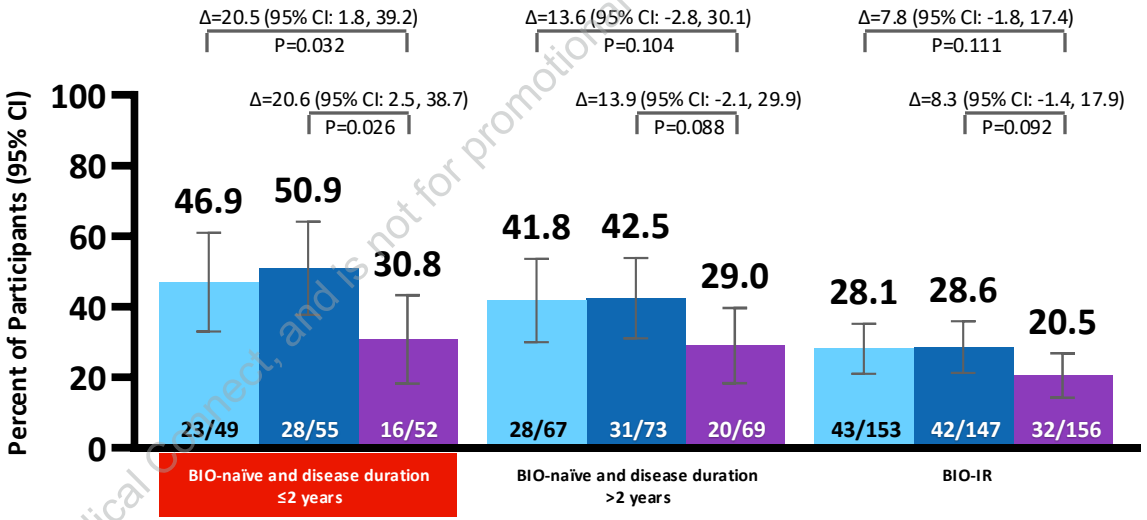
All p-values are nominal.

Note: Participants who had a CD-related surgery, a prohibited change in CD medication, or discontinued study agent due to lack of efficacy, an AE of worsening CD or Week 20/24 non-responder or discontinued study agent for any reason (other than COVID-19 related reasons [excluding COVID-19 infection] or regional crisis) were considered not to have met the endpoint at the designated timepoint. Participants who discontinued study intervention due to COVID-19 related reasons (excluding COVID-19 infection) or regional crisis had their observed data used, if available. After accounting for the aforementioned data handling rules, participants who were missing data pertaining to an endpoint at a designated timepoint were considered not to have achieved the endpoint. The adjusted treatment difference(s), confidence interval(s), and p-value(s) were based on the common risk difference by use of Mantel-Haenszel stratum weights and the Sato variance estimator. The stratification factors are baseline CDAI score (≤300 or >300), baseline SES-CD score (≤12 or >12), and baseline corticosteroid use (Yes or No).

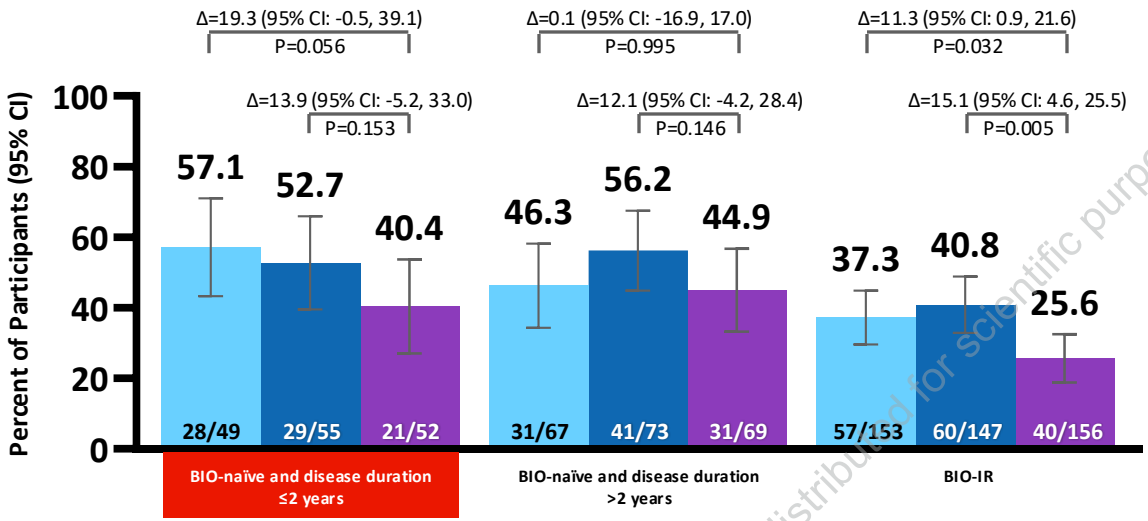
Endoscopic Response at Week 48



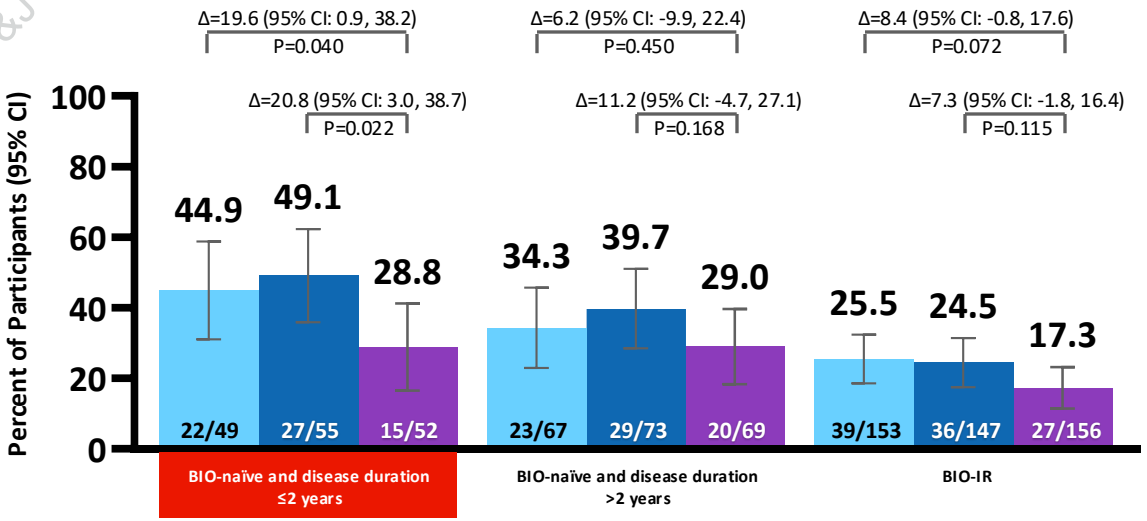
Endoscopic Remission at Week 48



Clinical Remission **AND** Endoscopic Response at Week 48



Deep Remission at Week 48



GUS 200 mg IV q4w → GUS 100 mg SC q8w

GUS 200 mg IV q4w → GUS 200 mg SC q4w

UST ~6 mg/kg IV → UST 90 mg SC q8w

Endoscopic response: ≥50% improvement from baseline in SES-CD or SES-CD ≤ 2

Endoscopic remission: SES-CD ≤ 4 and a ≥2-point reduction from baseline and no subscore greater than 1 in any individual component

Clinical remission: CDAI score <150

Deep remission: Clinical remission **AND** endoscopic remission

All p-values are nominal.

Note: Participants who had a CD-related surgery, a prohibited change in CD medication, or discontinued study agent due to lack of efficacy, an AE of worsening CD or Week 20/24 non-responder or discontinued study agent for any reason (other than COVID-19 related reasons [excluding COVID-19 infection] or regional crisis) were considered not to have met the endpoint at the designated timepoint. Participants who discontinued study intervention due to COVID-19 related reasons (excluding COVID-19 infection) or regional crisis had their observed data used, if available. After accounting for the aforementioned data handling rules, participants who were missing data pertaining to an endpoint at a designated timepoint were considered not to have achieved the endpoint. The adjusted treatment difference(s), confidence interval(s), and p-value(s) were based on the common risk difference by use of Mantel-Haenszel stratum weights and the Sato variance estimator. The stratification factors are baseline CDAI score (≤300 or >300), baseline SES-CD score (≤12 or >12), and baseline corticosteroid use (Yes or No).

Key Takeaways

- In GALAXI, guselkumab-treated BIO-naïve participants with disease duration ≤2 years achieved clinical and endoscopic endpoints in greater proportions compared with placebo and endoscopic endpoints in greater proportions compared with ustekinumab

- Clinical and endoscopic improvements in BIO-naïve participants were greater than those with prior BIO-IR

- For the more stringent endpoints at 1 year, such as endoscopic remission and deep remission, BIO-naïve participants with disease duration ≤2 years who received guselkumab achieved higher rates compared to those with disease duration >2 years
  - This trend was observed for both guselkumab doses, but not ustekinumab

- Overall, these robust results highlight the benefit of early biologic treatment and support the use of guselkumab as an early therapeutic choice in CD

Acknowledgments

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