The Efficacy of Maintenance Treatment with Guselkumab in Patients with Moderately to Severely Active Ulcerative Colitis: Phase 3 QUASAR Maintenance Study Results at Week 44 by Biologic/Janus Kinase Inhibitor History

P2580

J.R. Allegretti,[1] J. Panés,[2] L. Peyrin-Biroulet,[3] B.E. Sands,[4] S. Yarandi,[5] K.-H.G. Huang,[5] M. Germinaro,[5] J. Zhan,[5] H. Zhang,[5] J. Begun,[6] J. Kierkuś,[7] T. Kravchenko,[8] T. Hisamatsu,[9] D.T. Rubin,[10] B. Bressler,[11] and A. Dignass[12] on behalf of the QUASAR Investigators

[1]Brigham and Women's Hospital Crohn's and Colitis Center, Boston, MA, USA; [2]Hospital Clínic de Barcelona, IDIBAPS, CIBERehd, Barcelona, Spain; [3]Nancy University Hospital, Université de Lorraine, Nancy, France; [4]Icahn School of Medicine at Mount Sinai, New York City, NY, USA; [5]Janssen Research & Development, LLC, Spring House, PA, USA; [6]Mater Hospital, Brisbane, Australia; [7]Children's Memorial Health Institute, Warsaw, Poland; [8]National Medical University, Kyiv, Ukraine; [9]Kyorin University, Tokyo, Japan; [10]University of Chicago Medicine Inflammatory Bowel Disease Center, Chicago, IL, USA; [11]University of British Columbia, Vancouver, BC, Canada; [12]Agaplesion Markus Hospital, Frankfurt, Germany

Background

Guselkumab (GUS) is a dual-acting IL-23p19 subunit inhibitor that blocks IL-23 and binds to CD64, a receptor on cells that produce IL-23[1]

The Phase 3 QUASAR Maintenance Study was a randomized-withdrawal, double-blind, placebo-controlled design that evaluated the efficacy and safety of GUS SC maintenance treatment in patients with moderately to severely active UC who achieved clinical response to GUS IV induction

– Positive results for the QUASAR Phase 3 Maintenance Study and the QUASAR Phase 2b/3 Induction Studies (IV GUS) in UC have been previously presented[2,3,4]

– A Phase 3 guselkumab SC Induction Study in UC is ongoing (ASTRO, NCT05528510)

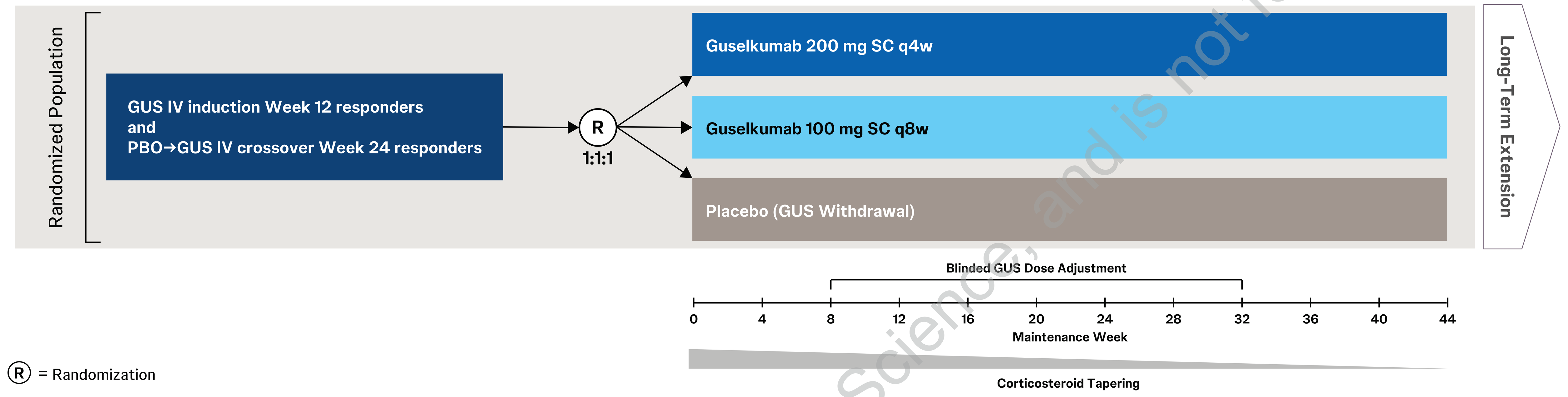
Objective

Here, we report Week 44 efficacy and safety results for GUS maintenance treatment compared with placebo (GUS withdrawal) by history of treatment with biologics and/or Janus kinase (JAK) inhibitors

Methods

QUASAR Maintenance Study Design

Target Patient Population:
Adults with moderately to severely active UC (defined as induction baseline modified Mayo score of 5 to 9 with a Mayo rectal bleeding subscore ≥ 1 and a Mayo endoscopic subscore ≥ 2 as obtained during central review of the screening endoscopy) who had inadequate response/intolerance to conventional therapy and/or biologic and/or JAK inhibitor therapy



Conclusions

Regardless of prior history of treatment with a biologic and/or JAK inhibitor

– **Maintenance treatment with GUS resulted in greater improvements compared with placebo (GUS withdrawal) across key clinical, endoscopic, and histologic endpoints at Week 44**

– **Maintenance treatment with both GUS SC dose regimens was efficacious in patients with UC**

Safety results for both GUS maintenance dose regimens were

– **Comparable across subpopulations by biologic/JAK inhibitor history**

– **Consistent with the known and favorable safety profile of GUS in approved indications**

Results

Demographics and Disease Characteristics at Induction Baseline by Biologic/JAK Inhibitor History

	Induction Guselkumab IV Responders					
	BIO/JAK-Naïve			BIO/JAK-IR		
	Placebo (GUS Withdrawal) N=108	GUS 100 mg q8w N=105	GUS 200 mg q4w N=96	Placebo (GUS Withdrawal) N=75	GUS 100 mg q8w N=77	GUS 200 mg q4w N=88
Age in years, mean (SD)	40.5 (13.38)	39.1 (12.34)	38.1 (14.29)	42.8 (13.88)	42.5 (13.88)	42.7 (14.61)
Male, n (%)	67 (62.0%)	56 (53.3%)	41 (42.7%)	38 (50.7%)	43 (55.8%)	55 (62.5%)
UC disease duration in years, mean (SD)	6.13 (5.702)	5.44 (7.264)	6.77 (7.755)	9.03 (7.019)	11.04 (9.219)	9.76 (8.937)
Extensive UC, n (%)	54 (50.0%)	40 (38.1%)	43 (44.8%)	41 (54.7%)	37 (48.1%)	38 (43.2%)
Modified Mayo score (0-9), mean (SD)[a]	6.8 (1.13)	6.8 (1.19)	6.9 (1.16)	7.3 (0.98)	6.7 (1.12)	7.0 (1.06)
Modified Mayo score of 7-9 (severe), n (%)	60 (55.6%)	64 (61.0%)	61 (63.5%)	61 (81.3%)	45 (58.4%)	60 (68.2%)
Mayo endoscopic subscore of 3 (severe), n (%)	64 (59.3%)	58 (55.2%)	52 (54.2%)	60 (80.0%)	62 (80.5%)	69 (78.4%)
C-reactive protein, median in mg/L (IQR)[b]	4.1 (1.5; 7.9)	2.9 (1.1; 8.0)	3.2 (1.2; 7.7)	4.3 (1.8; 14.0)	4.9 (2.1; 15.3)	4.1 (1.5; 10.1)
Fecal calprotectin, median in mg/kg (IQR)[c]	1680.0 (554.0; 3392.5)	1693.5 (477.0; 3077.0)	1362.0 (570.0; 2481.0)	1631.5 (831.0; 3741.0)	1647.0 (1003.0; 4834.0)	1605.5 (751.0; 3434.0)
Oral corticosteroid use at baseline, n (%)	41 (38.0%)	41 (39.0%)	34 (35.4%)	32 (42.7%)	30 (39.0%)	39 (44.3%)
Immunosuppressant use at baseline, n (%)[d]	29 (26.9%)	21 (20.0%)	24 (25.0%)	13 (17.3%)	18 (23.4%)	18 (20.5%)

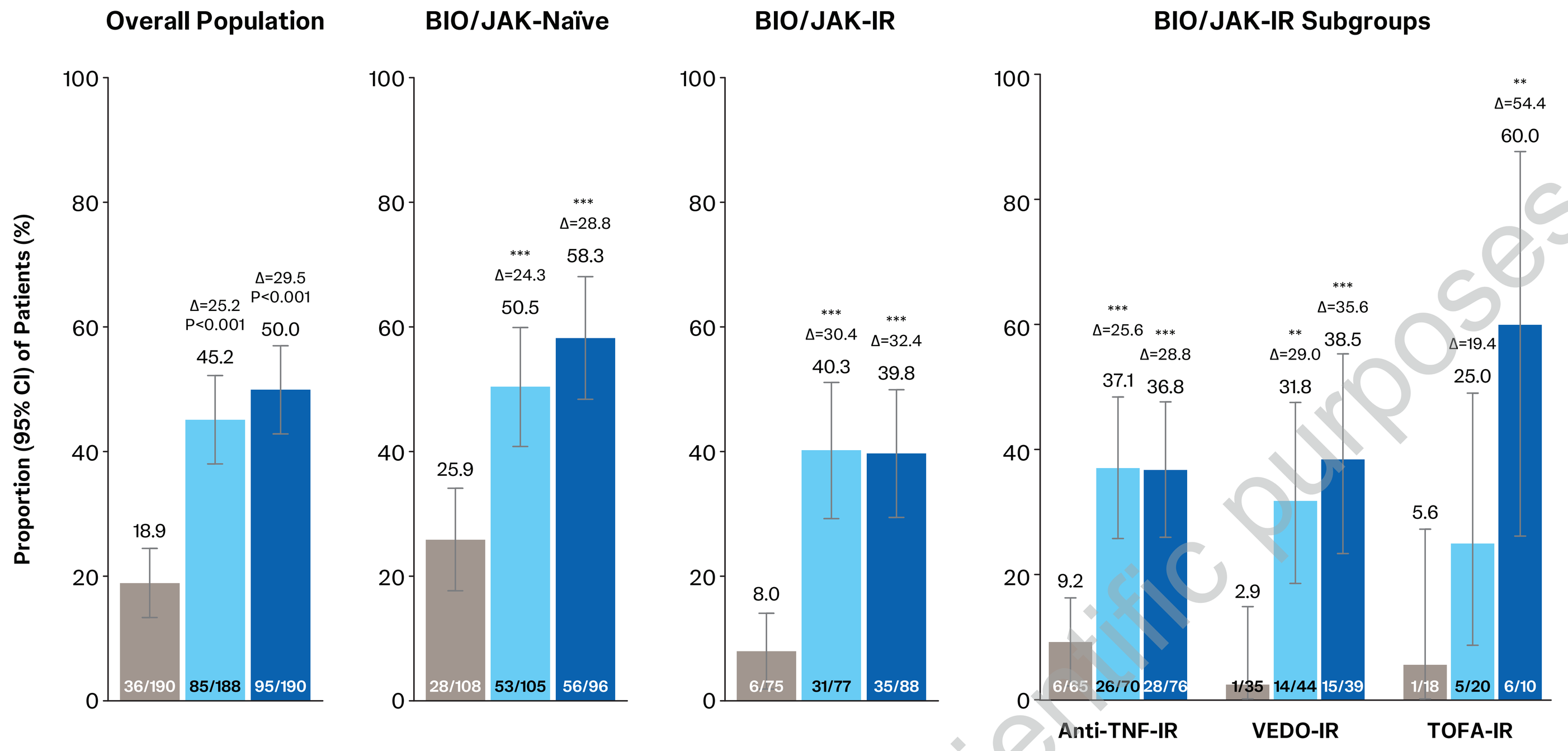
[a]Modified Mayo score: 3-component (stool frequency, rectal bleeding, and endoscopic subscores) Mayo score without the physician's global assessment. [b]Based on PBO, N=108; GUS 100 mg, N=103; GUS 200 mg, N=95, for BIO/JAK-naïve and PBO, N=75; GUS 100 mg, N=76; GUS 200 mg, N=86 for BIO/JAK-IR. [c]Based on PBO, N=100; GUS 100 mg, N=90; GUS 200 mg, N=87, for BIO/JAK-naïve and and PBO, N=70; GUS 100 mg, N=64; GUS 200 mg, N=78 for BIO/JAK-IR. [d]Immunosuppressants included azathioprine, 6-mercaptopurine, and methotrexate. Randomized Full Analysis Set.

Summary of Adverse Events Through Week 44 by Biologic/JAK Inhibitor History

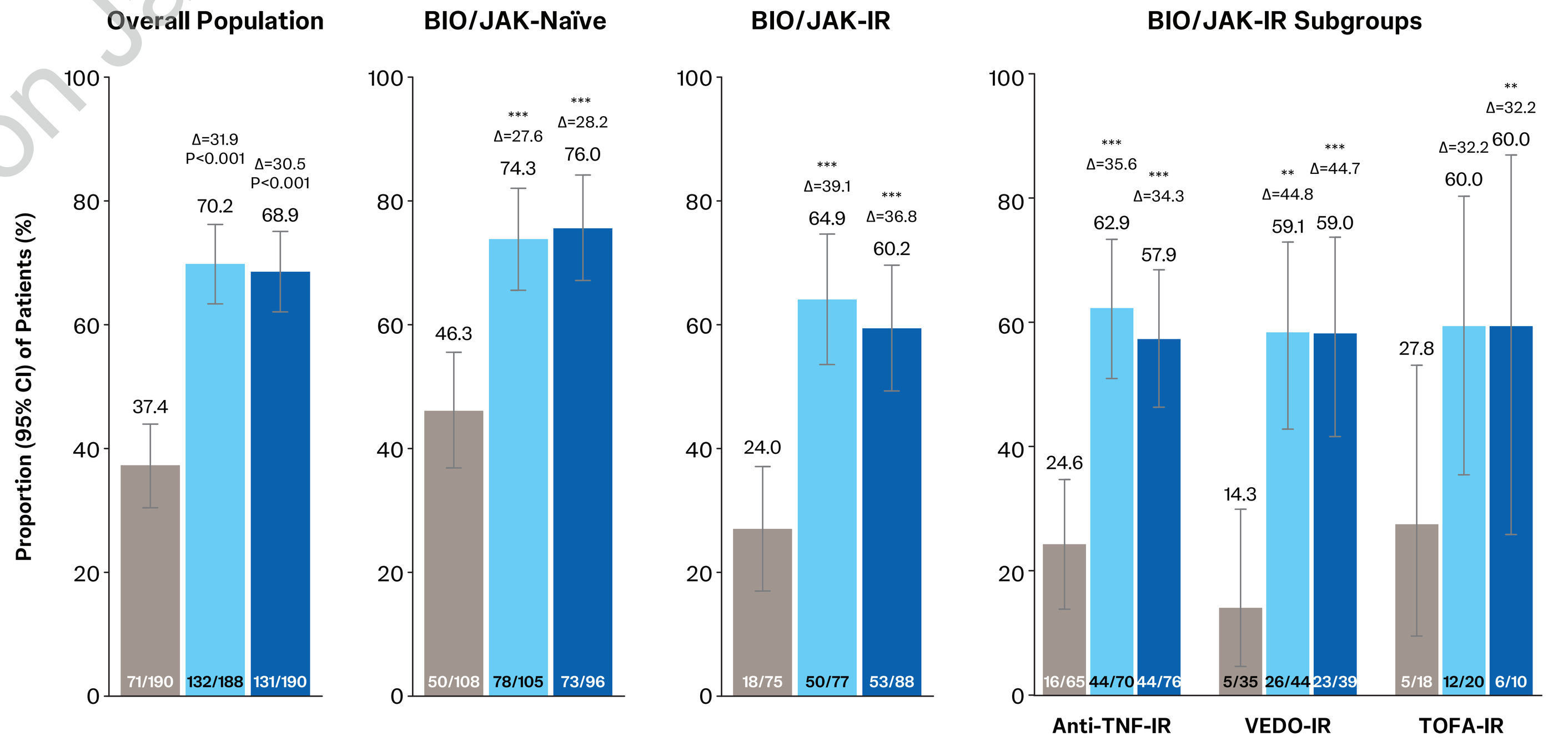
	Induction Guselkumab IV Responders					
	Overall Population		BIO/JAK-Naïve		BIO/JAK-IR	
	Randomized Placebo (GUS Withdrawal)	Randomized GUS	Randomized Placebo (GUS Withdrawal)	Randomized GUS	Randomized Placebo (GUS Withdrawal)	Randomized GUS
Randomized safety analysis set, N	192	376	109	200	76	164
Average duration of follow-up (weeks)	34.0	39.8	37.0	41.1	29.1	38.2
Average exposure (number of administrations)	8.2	9.8	31.9	35.0	24.5	32.1
Patients with 1 or more:						
Deaths	0	0	0	0	0	0
Adverse events	131 (68.2%)	253 (67.3%)	70 (64.2%)	124 (62.0%)	57 (75.0%)	122 (74.4%)
Serious adverse events	1 (0.5%)	17 (4.5%)	1 (0.9%)	8 (4.0%)	0	8 (4.9%)
Adverse events leading to discontinuation	13 (6.8%)	12 (3.2%)	6 (5.5%)	4 (2.0%)	7 (9.2%)	7 (4.3%)
Infections	63 (32.8%)	118 (31.4%)	36 (33.0%)	56 (28.0%)	26 (34.2%)	59 (36.0%)

Includes patients with modified Mayo score 5-9 at induction baseline who were randomized in the Maintenance study and data up to the time of dose adjustment for patients who had a dose adjustment.

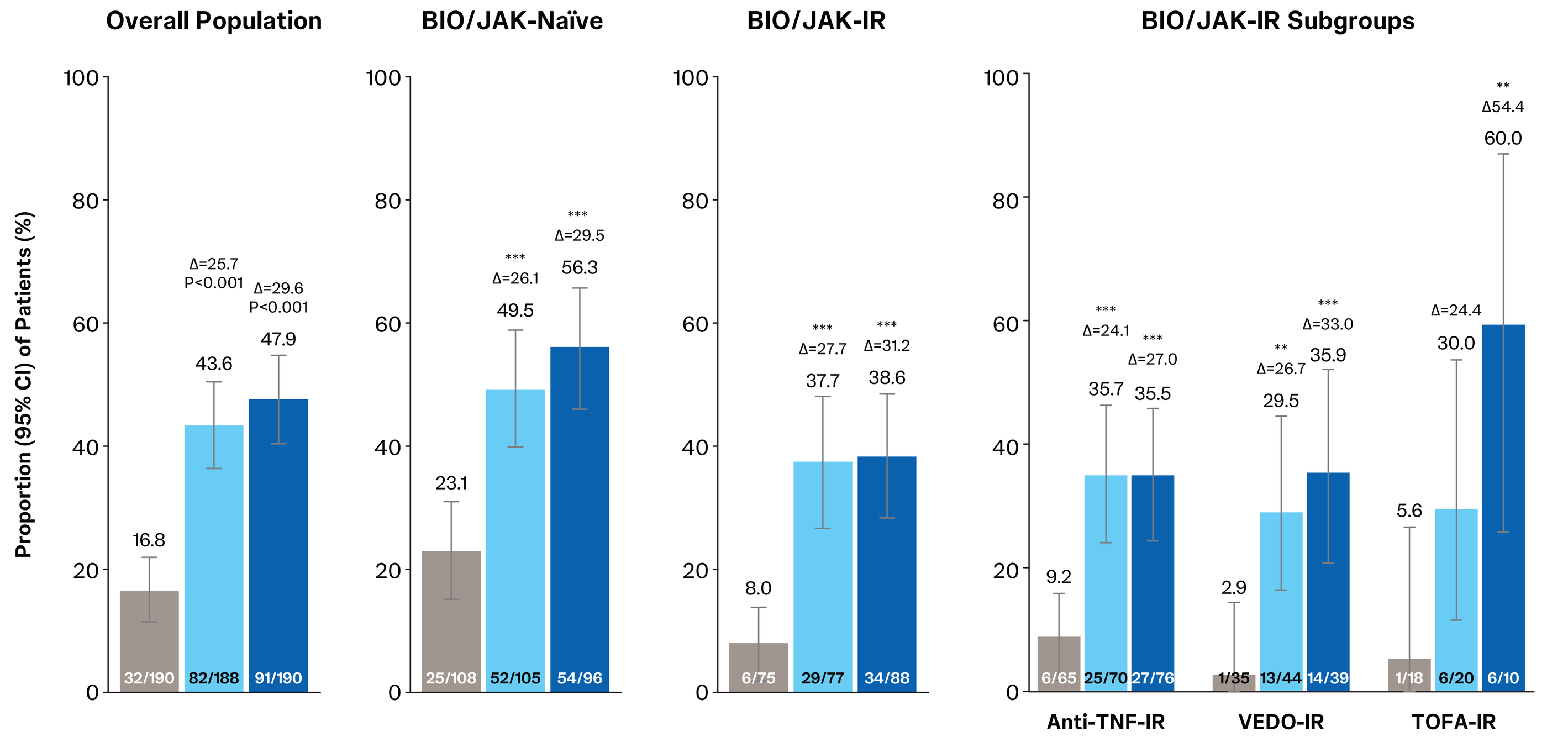
Cinical Remission at Week 44



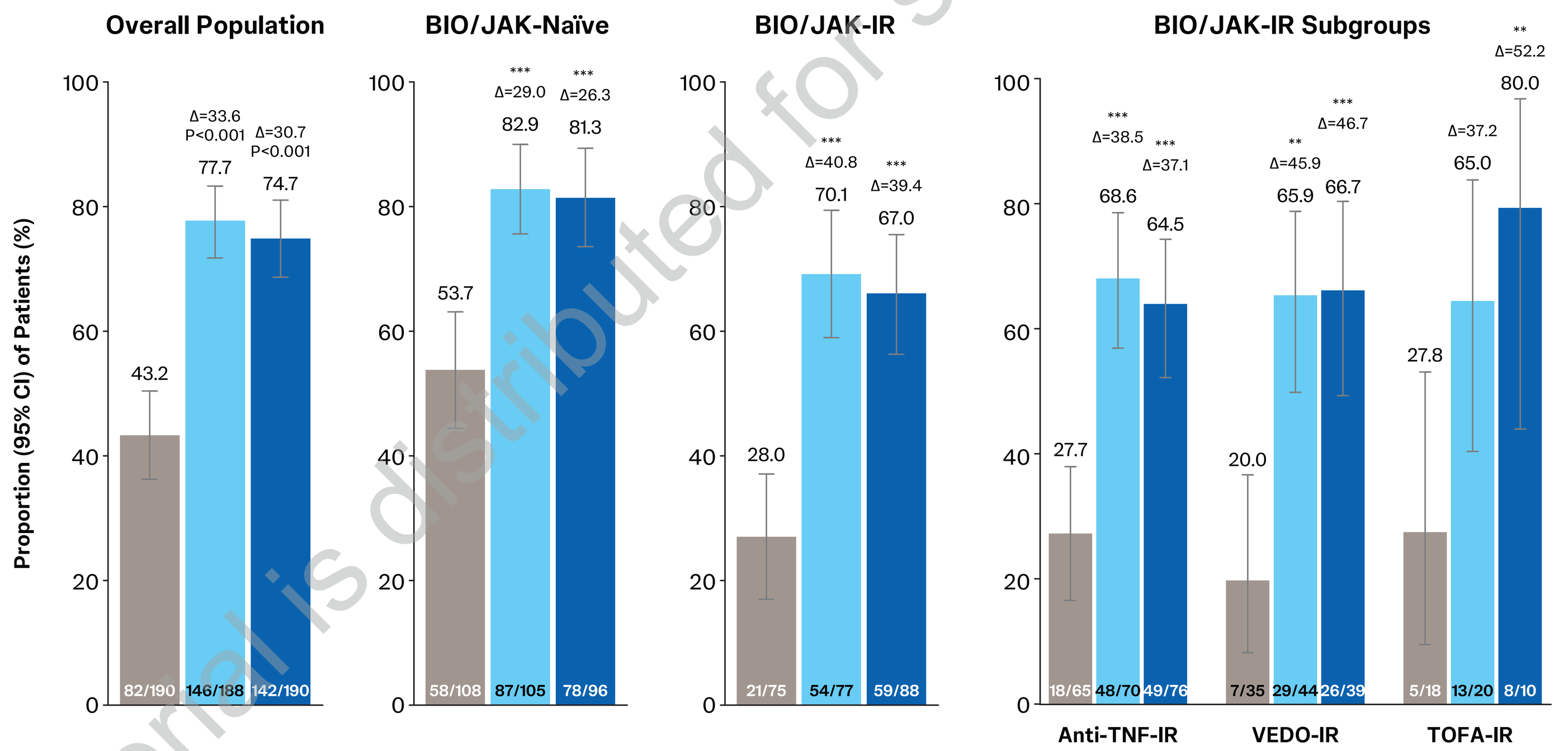
Symptomatic Remission at Week 44



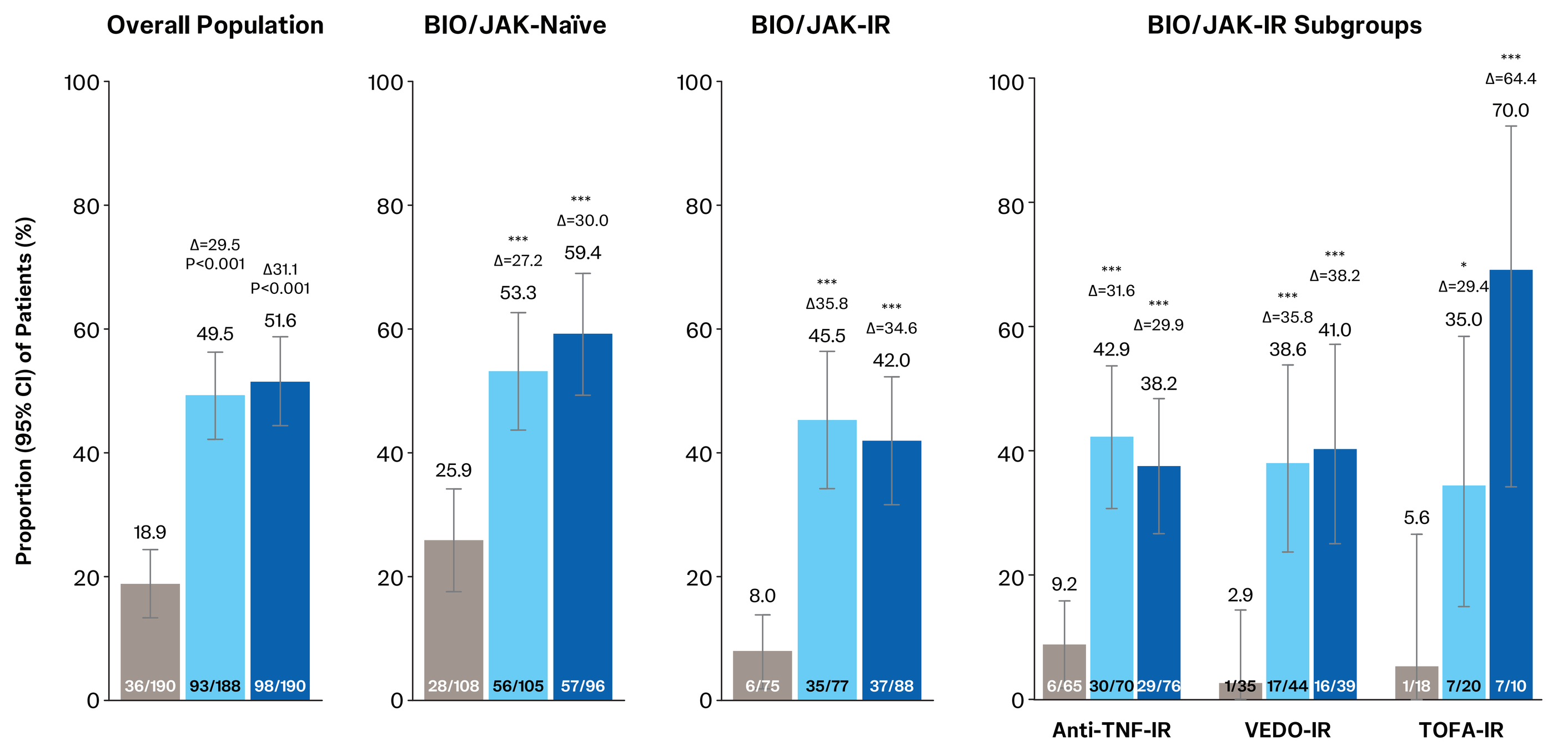
Histo-Endoscopic Mucosal Improvement at Week 44



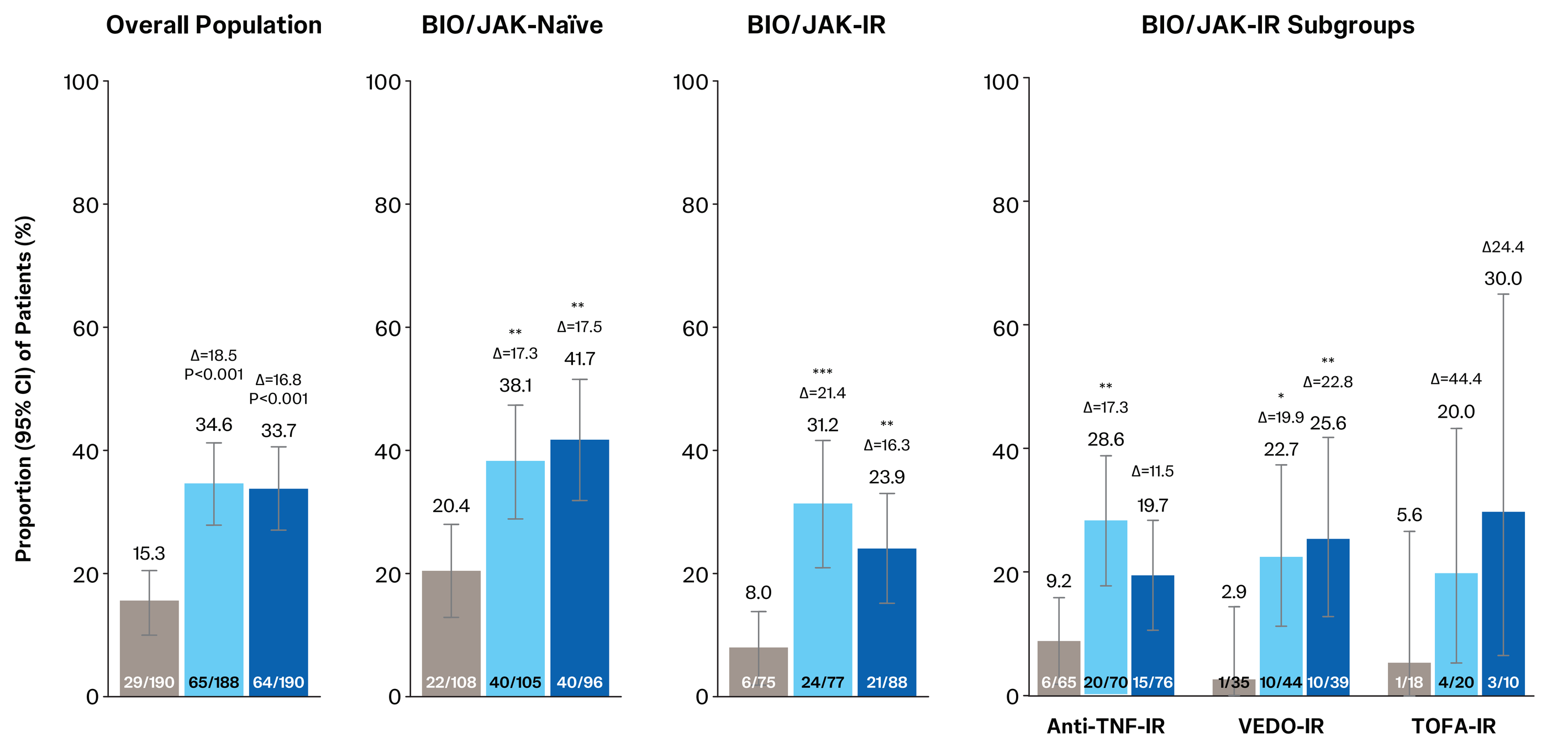
Maintenance of Clinical Response at Week 44



Endoscopic Improvement at Week 44



Endoscopic Remission at Week 44



PBO (GUS Withdrawal) | GUS 100 mg SC q8w | GUS 200 mg SC q4w

Clinical remission: A Mayo stool frequency subscore of 0 or 1 and not increased from baseline, a Mayo rectal bleeding subscore of 0, and a Mayo endoscopic subscore of 0 or 1 with no friability. **Maintenance of clinical response:** Clinical response at Week 44 among patients in clinical response at maintenance baseline. **Symptomatic remission:** A stool frequency subscore of 0 or 1 and not increased from induction baseline, and a rectal bleeding subscore of 0. **Endoscopic improvement:** An endoscopic subscore of 0 or 1 with no friability. **Histo-endoscopic mucosal improvement:** Achieving a combination of histologic improvement (neutrophil infiltration in <5% of crypts, no crypt destruction, and no erosions, ulcerations or granulation tissue according to the Geboes grading system) and endoscopic improvement (endoscopic subscore of 0 or 1, with no friability). **Endoscopic remission (normalization):** MES=0.
Randomized Full Analysis Set. Δ=Treatment difference compared with placebo. *Nominal P<0.05. **Nominal P<0.01. ***Nominal P<0.001. MES=Mayo endoscopic subscore.

PRESENTED AT: the American College of Gastroenterology (ACG) 2024; October 25-30, 2024; Philadelphia, PA, USA. This data was originally presented at United European Gastroenterology Week (UEGW) 2024.

REFERENCES: 1. BAtreya R, Abreu MT, Krueger JG, et al. *J Crohns Colitis.* 2024;18(suppl):S470. **2.** Rubin DT, Allegretti JR, Panes J, et al. *Gastroenterology.* 2024;166(suppl):S180. **3.** Peyrin-Biroulet L, Allegretti JR, Rubin DT, et al. *Gastroenterology.* 2023;165(6):1443-1457. **4.** Allegretti JR, Peyrin-Biroulet L, Feagan BG, et al. *Gastroenterology.* 2023;164(suppl):S1572.

ACKNOWLEDGMENTS: The authors thank the patients, investigators, and study personnel who made the QUASAR study possible. This work was supported by Janssen Research & Development, LLC. Under the direction of the authors and in accordance with Good Publication Practices, Nichole Orlowsky of Janssen Scientific Affairs, LLC provided writing and editorial assistance. **DISCLOSURES: JRA** is a consultant for Finch Therapeutics, Artugen, Pfizer, Takeda, Janssen, and Iterative Scopes and receives research support from Merck. Consultant and speaker for BMS. **JP** received consultancy fees/honorarium from AbbVie, Alimentiv, Athos, Atomwise, Boehringer Ingelheim, Celsius, Ferring, Galapagos, Genentech/Roche, GlaxoSmithKline, Janssen, Mirum, Nimbus, Pfizer, Progenity, Prometheus, Protagonist, Revolo, Sanofi, Sorriso, Surrozen, Takeda, and Wasserman, and has served on a data safety monitoring board for Alimentiv, Mirum, Sorriso, Sanofi, and Surrozen. **LPB** reports personal fees from AbbVie, Allergan, Alma, Amgen, Applied Molecular Transport, Arena, Biogen, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Celltrion, Enterome, Enthera, Ferring, Fresenius, Genentech, Gilead, Hikma, Index Pharmaceuticals, Janssen, Lilly, MSD, Mylan, Nestlé, Norgine, Oppilan Pharma, OSE Immunotherapeutics, Pfizer, Pharmacosmos, Roche, Samsung Bioepis, Sandoz, Sterna, Sublimity Therapeutics, Takeda, Tillots and Vifor; grants from AbbVie, MSD and Takeda; stock options from CTMA. **BES** reports consulting fees from Abbvie, Alimentiv, Amgen, Arena Pharmaceuticals, Artugen Therapeutics, Astra Zeneca, Boehringer Ingelheim, Boston Pharmaceuticals, Calibr, Celgene, Celltrion, ClostraBio, Equillium, Enthera, Evommune, Fresenius Kabi, Galapagos, Genentech (Roche), Gilead Sciences, GlaxoSmithKline, Gossamer Bio, Index Pharmaceuticals, Innovation Pharmaceuticals, Inotrem, Kaleido, Kallyope, Merck, Morphic Therapeutics, MRM Health, Progenity, Prometheus Biosciences, Prometheus Laboratories, Protagonist Therapeutics, Q32 Bio, Sun Pharma, Surrozen, Target RWE,Teva, TLL Pharmaceutical, Ventyx Biosciences; consulting and speaking fees from Abivax; consulting and speaking fees and other support from Lilly; research grants, consulting and speaking fees and other support from Bristol Myers Squibb, Janssen, Pfizer, Takeda; research grants and consulting fees from Theravance Biopharma; and stock options from Ventyx Biopharma. **SY, KGH, MG, JZ, HZ** are employees of Johnson & Johnson and owns company stock/stock options. **JB** received grant support from AbbVie, Janssen, Pfizer and Ferring. Consulting fees from Janssen, Pfizer, Abbvie, Takeda, Ferring, Microba, Anatara, DrFalk, Bristol Meyers Squibb, Glaxo Smith Klein and Chieisi, and lecture fees from AbbVie, Janssen, Pfizer, Takeda, and Ferring. **JK** reports personal fees from Bristol-Myers Squibb, Celltrion, Ferring, Fresenius, Janssen, Lilly, Nestlé. **TK** is a clinical investigator and consultant for Janssen. **TH** received grant support from AbbVie, Daiichi-Sankyo, EA Pharma Co, Ltd. JIMRO, Mitsubishi Tanabe Pharma Corporation, Mochida Pharmacuetical Co., Ltd., Nippon Kayaku Co., Ltd., Pfizer Inc., Takeda Pharmaceutical Co., Ltd., consulting fees from EA Pharma Co, Ltd., Janssen Research & Development, LLC., and lecture fees from AbbVie, EA Pharma Co, Ltd, Mitsubishi Tanabe Pharma Corporation, Takeda Pharmaceutical Co., Ltd. **DTR** reports research funding from Takeda, and has served as a consultant to Abbvie, Altrubio, Apex, Avalo Therapeutics, Bristol-Myers Squibb, Buhlmann Diagnostics Corp, Celgene, Connect BioPharma, Intouch Group, Iterative Health, Janssen Pharmaceuticals, Lilly, Pfizer, Samsung Neurologica, and Takeda; Board of Trustees for the Crohn's & Colitis Foundation; Co-Founder and Board of Directors for Cornerstones Health. **BB** is an advisor/speaker for Abbvie, BMS, Ferring, Janssen, Merck, Novartis, Organon, Pfizer, Sandoz, Takeda; advisor for Alimentiv, Allergan, AMT, Bausch Health, BMS, Celgene, Celltrion Healthcare, Eupraxia, Fresenius Kabi, Genentech, Gilead, Iterative Scopes, Jamp Pharma, Merck Amgen, Microbiome Insights, Mylan, Pendopharm, Protagonist, Viatris; received research support from Abbvie, Amgen, BI, BMS, Genentech, GSK, Janssen, Merck, Qu Biologic; and reports stock options for Qu Biologic. **AD** reports received fees for participation in clinical trials, review activities such as data monitoring boards, statistical analysis and end point committees from Abivax, AbbVie, Bristol Myers Squibb, Dr Falk Foundation, Galapagos, Gilead, Janssen, and Pfizer; consultancy fees from AbbVie, Amgen, Arena Pharmaceuticals, Biogen, Boehringer Ingelheim, Bristol Myers Squibb, Celltrion, Dr Falk Foundation, Ferring Pharmaceuticals, Fresenius Kabi, Galapagos, Janssen, Lilly, MSD, Pfizer, Pharmacosmos, Roche, Sandoz,; Stada, Takeda, Tillotts, and Vifor Pharma; payment for lectures including service on speakers bureaus from AbbVie, Biogen, CED Service GmbH, Celltrion, Falk Foundation, Ferring, Galapagos, Gilead, High5MD, Janssen, Materia Prima, MedToday, MSD, Pfizer, Sandoz, Takeda, Tillotts, and Vifor Pharma; payment for manuscript preparation from Abbvie, Falk Foundation, Janssen, Takeda, Thieme, and UniMed Verlag.