

Efficacy and Safety of the First Co-Antibody Therapy, JNJ-78934804, in Patients with Moderately to Severely Active Crohn's Disease Refractory to Two or More Systemic Therapy Mechanisms

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Background

 Despite therapeutic advances, substantial unmet need remains in Crohn's disease (CD), as many patients develop disease refractory to systemic therapies (STs; biologics and novel oral agents), with diminishing efficacy after each treatment

 We previously reported results from the DUET-CD study of JNJ-78934804 (JNJ-4804), the first fixed-dose, co-antibody therapy with guselkumab (GUS) and golimumab (GOL) targeting the complementary IL-23 and TNF pathways

 In DUET-CD, JNJ-4804 high dose showed the most substantial and clinically meaningful benefit vs GUS and GOL monotherapies in the subpopulation of participants with CD refractory to ≥ 2 ST mechanisms (anti-TNFs, anti-IL-12/23s, anti-IL-23p19s, anti-integrins, and JAK inhibitors)

Objective

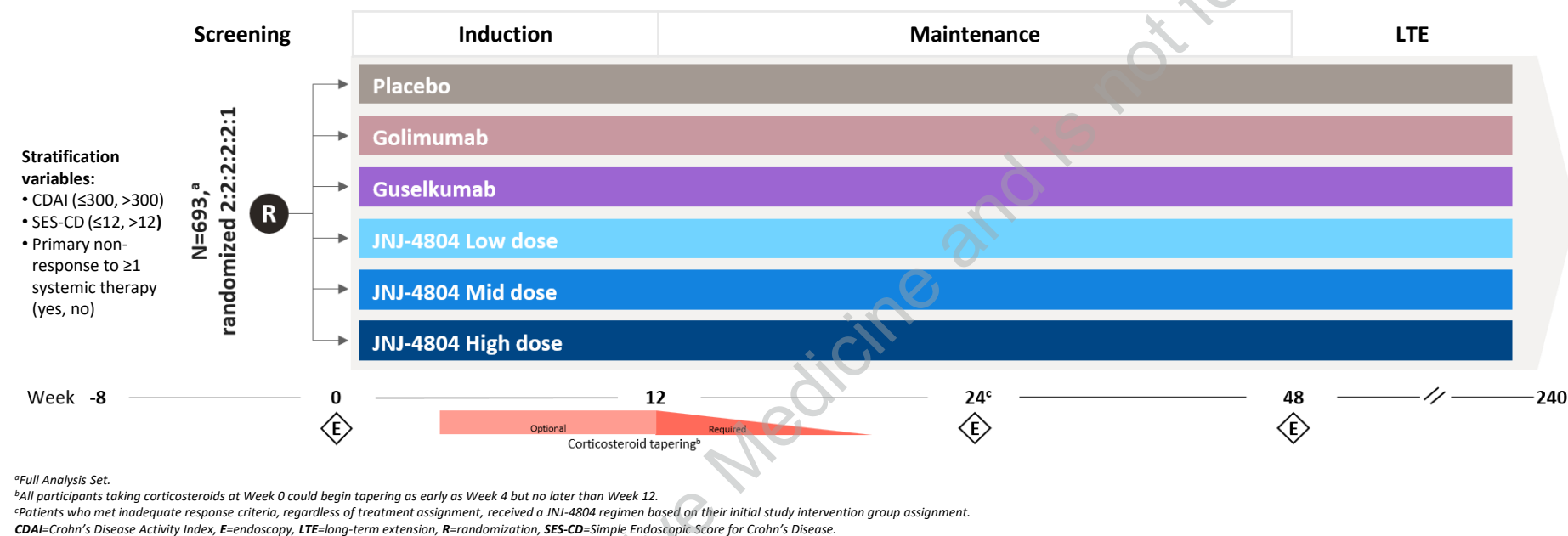
 Here, we present efficacy data from this treatment-refractory subpopulation as well as additional fecal calprotectin and safety data

Methods

- In this Phase 2b, randomized, double-blind, dose-ranging, active- and placebo (PBO)-controlled, parallel-group, multicenter study, participants were randomized 1:2:2:2:2:2 to PBO, GOL, GUS, or JNJ-4804 (low dose, mid dose, or high dose)

- Co-primary endpoints were clinical remission at Week 48 and endoscopic response at Week 48
 - Clinical remission: CDAI score of ≤ 150
 - Endoscopic response: $>50\%$ improvement from baseline in SES-CD or an SES-CD ≤ 2 , per central endoscopy
- Key Week 48 endpoints included endoscopic remission, deep remission, and corticosteroid-free clinical remission
 - Endoscopic remission: SES-CD ≤ 4 , with a ≥ 2 -point reduction from baseline and no subscore ≥ 1 on any component
 - Deep remission: both clinical remission and endoscopic remission
 - Corticosteroid-free (60-day) clinical remission: clinical remission with no corticosteroids received for ≥ 60 days

- Fecal calprotectin concentrations over time were also evaluated
 - Data are as-observed, log-transformed, and exclude inadequate responders after Week 24 treatment escalation



Results

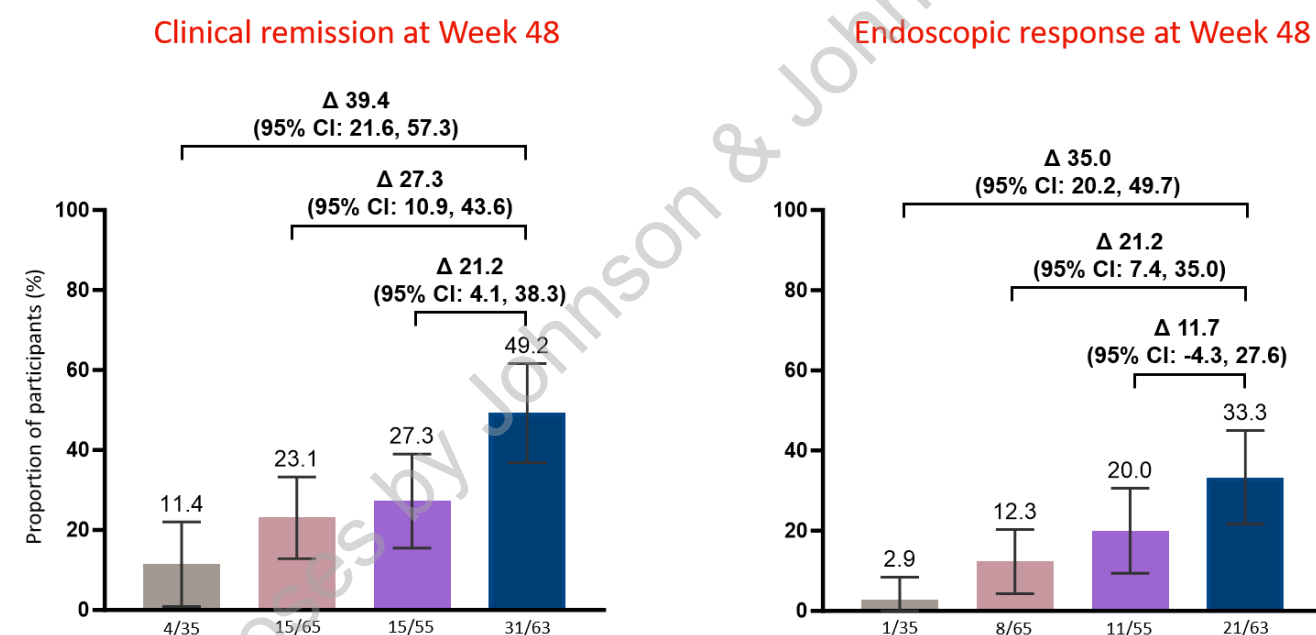
Baseline demographics and disease characteristics show that DUET-CD evaluated one of the most treatment-refractory CD populations studied to date

			Placebo	Golimumab	Guselkumab	JNJ-4804 Low dose	JNJ-4804 Mid dose	JNJ-4804 High dose
Full analysis set			64	126	127	127	123	126
Participants with IR to ≥2 ST mechanisms			35	65	55	73	55	63
Demographics								
	Age in years, mean (SD)		35.9 (13.62)	39.0 (12.82)	35.7 (11.22)	37.8 (12.34)	37.5 (10.84)	37.4 (12.62)
	Sex, n (%)	Male	26 (74.3%)	38 (58.5%)	27 (49.1%)	37 (50.7%)	33 (60.0%)	23 (36.5%)
	Crohn's disease duration in years, mean (SD)		12.04 (9.916)	11.29 (7.389)	13.17 (8.125)	13.47 (9.235)	11.68 (8.291)	13.91 (9.286)
Disease characteristics								
	Disease location, n (%)	Ileum only	7 (20.0%)	22 (33.8%)	15 (27.3%)	14 (19.2%)	12 (21.8%)	14 (22.2%)
	CDAI score, mean (SD) ^a		325.57 (61.583)	324.14 (61.661)	338.22 (49.532)	324.75 (60.935)	312.26 (53.835)	335.52 (64.701)
	SES-CD, mean (SD)		14.46 (8.023)	13.28 (8.020)	14.67 (8.367)	15.03 (8.617)	13.98 (8.038)	14.38 (9.042)
Concomitant medications								
	Immunomodulators, n (%)		6 (17.1%)	7 (10.8%)	8 (14.5%)	14 (19.2%)	4 (7.3%)	10 (15.9%)
	Oral corticosteroids, n (%)		13 (37.1%)	20 (30.8%)	18 (32.7%)	23 (31.5%)	16 (29.1%)	22 (34.9%)
Inflammatory pharmacodynamic markers								
	CRP (mg/L), median ^b		8.70	7.50	10.70	10.80	8.10	8.90
	Fecal calprotectin (mg/kg), median ^c		1705.00	1133.40	1373.35	1747.80	978.00	1145.00
Prior ST inadequate response history								
	2 ST mechanisms, n (%)		24 (68.6%)	45 (69.2%)	37 (67.3%)	49 (67.1%)	37 (67.3%)	39 (61.9%)
	>2 ST mechanisms, n (%)		11 (31.4%)	20 (30.8%)	18 (32.7%)	24 (32.9%)	18 (32.7%)	24 (38.1%)
	Anti-IL-12/23 and anti-TNF, n (%)		21 (60.0%)	37 (56.9%)	26 (47.3%)	35 (47.9%)	28 (50.9%)	31 (49.2%)

*Means are based on the following numbers of participants with non-missing data: 35 (PBO), 63 (GOL), 54 (GUS), 73 (JINI-4804 low dose), 54 (JINI-4804 mid dose), 63 (JINI-4804 high dose).
 †Medians are based on the following numbers of participants with non-missing data: 35 (PBO), 62 (GOL), 55 (GUS), 73 (JINI-4804 low dose), 55 (JINI-4804 mid dose), 63 (JINI-4804 high dose).
 ‡Medians are based on the following numbers of participants with non-missing data: 31 (PBO), 57 (GOL), 46 (GUS), 66 (JINI-4804 low dose), 49 (JINI-4804 mid dose), 55 (JINI-4804 high dose).
 CD4I=Crohn's Disease Activity Index, CRP=C-reactive protein, R=Inadequate response or intolerance, n=number, SD=standard deviation, SES-CD=Simple Endoscopic Score for Crohn's Disease, ST=systemic therapy.

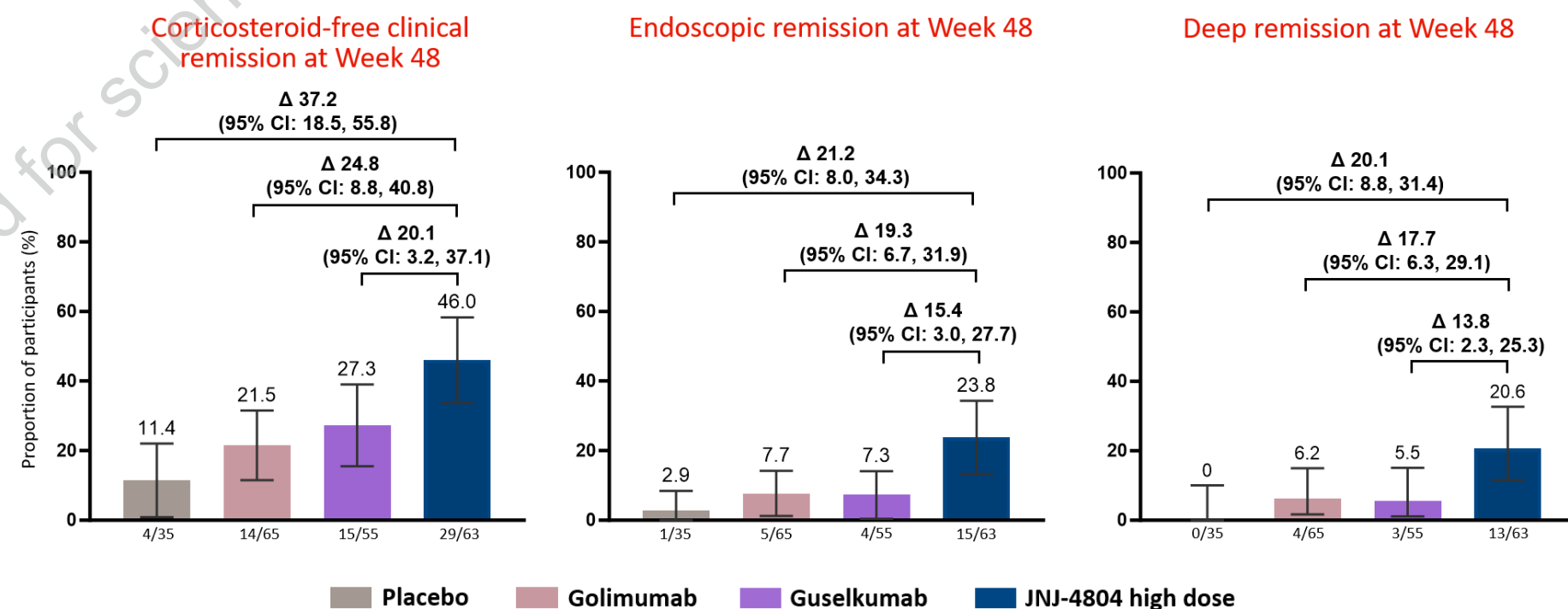
Among participants with CD refractory to ≥ 2 ST mechanisms, JNJ-4804 high dose led to clinically meaningful differences at Week 48 in rates of clinical remission and endoscopic response vs GOL, GUS, and placebo

Co-primary endpoints: ≥ 2 systemic therapy mechanisms-IR



Notably, rates of meeting high-bar outcomes, including endoscopic remission and deep remission, with JNJ-4804 high dose exceeded the sum of the rates in the individual monotherapy arms, suggesting a synergistic effect

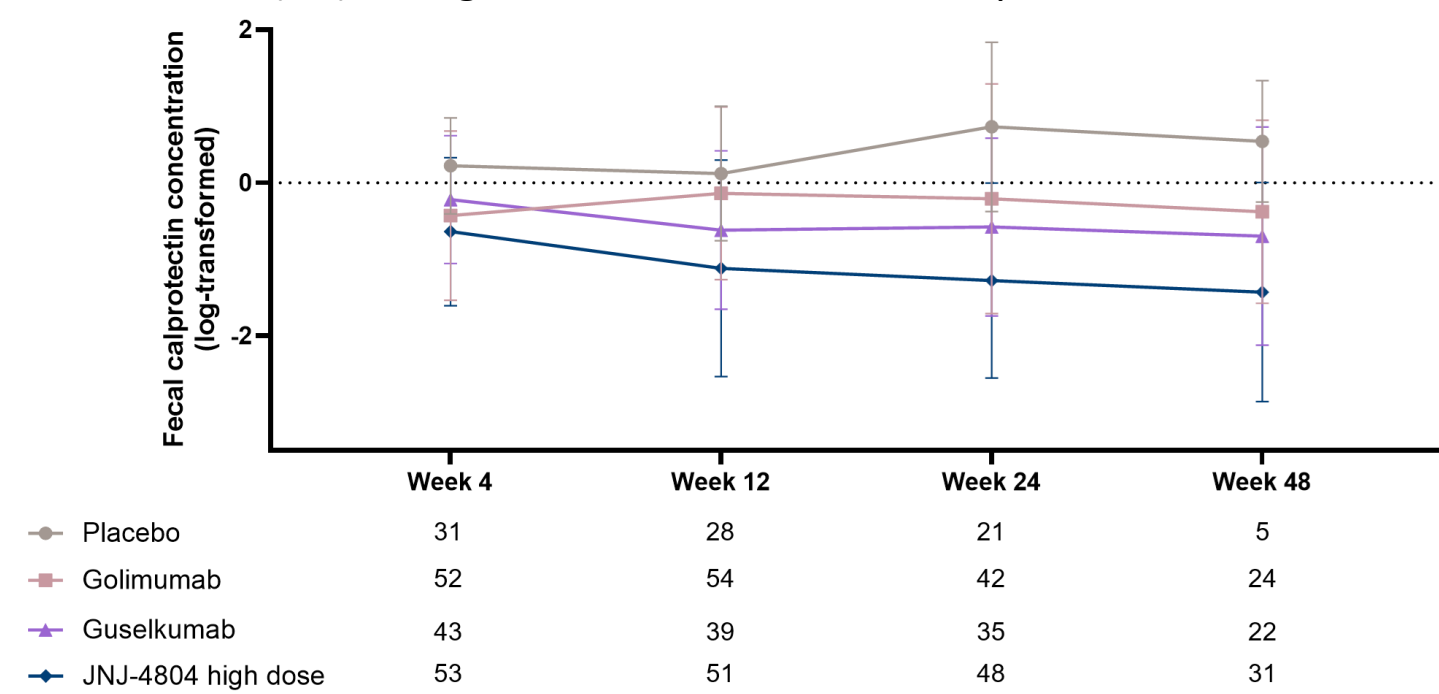
Key endpoints: ≥ 2 systemic therapy mechanisms-IR



CI=confidence interval, IR=inadequate response or intolerance

Mean change from baseline in fecal calprotectin was greater with JNJ-4804 high dose vs the other groups in participants with CD refractory to ≥ 2 ST mechanisms

Mean (SD) change from baseline in fecal calprotectin concentration



Exposure-adjusted safety event rates with JNJ-4804 in the subpopulation were overall similar to or lower than those with placebo, GOL, or GUS and were similar to those in the overall population^a

	Placebo	Golimumab	Guselkumab	JNJ-4804 Low dose	JNJ-4804 Mid dose	JNJ-4804 High dose	JNJ-4804 Combined
Full analysis set	64	126	127	127	123	126	376
Participants with IR to ≥2 ST mechanisms	35	65	55	73	55	63	191
Total patient-years of follow-up	20.5	44.9	38.9	54.2	42.6	50.0	146.8
Event rate per hundred patient-years [number of events] (95% CI)							
AEs	606.0 [124]	695.1 [312]	798.8 [311]	631.4 [342]	615.4 [262]	585.6 [293]	611.2 [897]
	(504.02, 722.51)	(620.08, 776.64)	(712.50, 892.72)	(566.27, 702.02)	(543.17, 694.66)	(520.46, 656.64)	(571.82, 652.51)
SAEs	24.4 [5]	44.6 [20]	20.5 [8]	42.5 [23]	18.8 [8]	24.0 [12]	29.3 [43]
	(7.93, 57.02)	(27.22, 68.81)	(8.87, 40.49)	(26.92, 63.72)	(8.11, 37.03)	(12.39, 41.89)	(21.20, 39.46)
AEs leading to discontinuation of study treatment	53.8 [11]	29.0 [13]	23.1 [9]	11.1 [6]	11.7 [5]	10.0 [5]	10.9 [16]
	(26.83, 96.18)	(15.42, 49.53)	(10.57, 43.88)	(4.07, 24.11)	(3.81, 27.41)	(3.24, 23.32)	(6.23, 17.70)
Infections	102.6 [21]	151.5 [68]	120.7 [47]	155.1 [84]	133.9 [57]	143.9 [72]	145.1 [213]
	(63.53, 156.87)	(117.64, 192.05)	(88.70, 160.54)	(123.70, 192.01)	(101.41, 173.48)	(112.59, 181.22)	(126.29, 165.98)
Serious infections	4.9 [1]	2.2 [1]	7.7 [3]	11.1 [6]	4.7 [2]	2.0 [1]	6.1 [9]
	(0.12, 27.23)	(0.06, 12.41)	(1.59, 22.52)	(4.07, 24.11)	(0.57, 16.97)	(0.05, 11.14)	(2.80, 11.64)
Deaths	0.0 [0]	0.0 [0]	0.0 [0]	0.0 [0]	0.0 [0]	0.0 [0]	0.0 [0]
	(0.00, 14.64)	(0.00, 6.67)	(0.00, 7.69)	(0.00, 5.53)	(0.00, 7.04)	(0.00, 5.99)	(0.00, 2.04)

AE=adverse event, CI=confidence interval, IR=inadequate response or intolerance, SAE=serious adverse event, ST=systemic therapy. ^aAbreu, et al. DDW 2026