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Obj

Results

Flowchart of the Study Design:

- Screening:** Week -8 to 0. Stratification variables: CD4I (≤ 300 , >300), SES-CD (≤ 12 , >12), Primary non-response to ≥ 1 systemic therapy (yes, no). N=693, randomized 2:2:2:2:1.
- Main Treatment Phase:**
 - Induction:** Week 0 to 12. Corticosteroid tapering: Optional (Week 0-12), Required (Week 12-24).
 - Maintenance:** Week 12 to 48.
- Groups:** Placebo, Golimumab, Guselkumab, JUN-4804 Low dose, JUN-4804 Mid dose, JUN-4804 High dose.
- End of Study:** Week 48 (LTE).

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

Clinical remission at Week 48

Endoscopic response at Week 48

Clinical remission at Week 48

Treatment Group	Proportion of Participants (%)
Placebo	11.4
Golimumab	23.1
Guselkumab	27.3
JNJ-4804 High dose	49.2

Endoscopic response at Week 48

Treatment Group	Proportion of Participants (%)
Placebo	2.9
Golimumab	12.3
Guselkumab	20.0
JNJ-4804 High dose	33.3

Pairwise Comparisons (Clinical remission at Week 48)

Comparison	Delta (%)	95% CI (%)
Placebo vs JNJ-4804 High dose	39.4	(21.6, 57.3)
Golimumab vs JNJ-4804 High dose	27.3	(10.9, 43.6)
Guselkumab vs JNJ-4804 High dose	21.2	(4.1, 38.3)

Pairwise Comparisons (Endoscopic response at Week 48)

Comparison	Delta (%)	95% CI (%)
Placebo vs JNJ-4804 High dose	35.0	(20.2, 49.7)
Golimumab vs JNJ-4804 High dose	21.2	(7.4, 35.0)
Guselkumab vs JNJ-4804 High dose	11.7	(-4.3, 27.6)

remission at Week 48

Time Point	Placebo	Golimumab	Ustekinumab	JNJ-4804 High dose
4/35	11.4			
14/65		21.5		
15/55			27.3	
29/63				46.0

at Week 48

Time Point	Placebo	Golimumab	Ustekinumab	JNJ-4804 High dose
1/35	2.9			
5/65		7.7		
4/55			7.3	
15/63				23.8

at Week 28

Time Point	Placebo	Golimumab	Ustekinumab	JNJ-4804 High dose
1/35	0			
5/65		6.2		
4/55			5.5	
15/63				20.6

CI=confidence interval, **IR**=inadequate response or intolerance.

Mean (SD) change from baseline in fecal calprotectin concentration

Fecal calprotectin concentration (log-transformed)

Week 4 Week 12 Week 24 Week 48

Placebo 31 28 21 5

Golimumab 52 54 42 24

Guselkumab 43 39 35 22

JNJ-4804 high dose 53 51 48 31

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 [24] (504.02, 722.51)	695.1 [312] (620.08, 776.64)	798.8 [311] (712.50, 892.72)	631.4 [342] (566.27, 702.02)	615.4 [262] (543.17, 694.66)	585.6 [293] (520.46, 656.64)	611.2 [897] (571.82, 652.51)
SAEs	24.4 [5] (7.93, 57.02)	44.6 [20] (27.22, 68.81)	20.5 [8] (8.87, 40.49)	42.5 [23] (26.92, 63.72)	18.8 [8] (8.1, 37.03)	24.0 [12] (12.39, 41.89)	29.3 [43] (21.20, 39.46)
AEs leading to discontinuation of study treatment	53.8 [11] (26.83, 96.18)	29.0 [13] (15.42, 49.53)	23.1 [9] (10.57, 43.88)	11.1 [6] (4.07, 24.11)	11.7 [5] (3.81, 27.41)	10.0 [5] (3.24, 23.32)	10.9 [16] (6.23, 17.70)
Infections	102.6 [21] (63.53, 156.87)	151.5 [68] (117.64, 192.05)	120.7 [47] (88.70, 160.54)	155.1 [84] (123.70, 192.01)	133.9 [57] (101.41, 173.48)	143.9 [72] (112.59, 181.22)	145.1 [213] (126.29, 165.98)
Serious infections	4.9 [1] (0.12, 27.23)	2.2 [1] (0.06, 12.41)	7.7 [3] (1.59, 22.52)	11.1 [6] (4.07, 24.11)	4.7 [2] (0.57, 16.97)	2.0 [1] (0.05, 11.14)	6.1 [9] (2.80, 11.64)
Deaths	0.0 [0] (0.00, 14.64)	0.0 [0] (0.00, 6.67)	0.0 [0] (0.00, 7.69)	0.0 [0] (0.00, 5.53)	0.0 [0] (0.00, 7.04)	0.0 [0] (0.00, 5.99)	0.0 [0] (0.00, 2.04)

AE=adverse event, **CI**=confidence interval, **IR**=inadequate response or intolerance, **SAE**=serious adverse event, **ST**=systemic therapy.