The UNITI Jr Study: Safety and Efficacy Results of Ustekinumab in Paediatric Patients With Crohn's Disease

OP18

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Disclosure of Conflicts of Interest

I, Dan Turner, 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 having received consultation fees, research grant, royalties, or honorarium from Johnson & Johnson, Pfizer, Shaare Zedek Medical Center, Hospital for Sick Children, Ferring, AbbVie, Takeda, Prometheus Biosciences, Lilly, SorrisoPharma, Boehringer Ingelheim, Galapagos, BMS, Alfasigma, and Merck.

The study presented herein was sponsored by Johnson & Johnson

Background and Objective

Infliximab and adalimumab are the only approved compounds for the treatment of Crohn's disease (CD) in children 6 to 18 years of age, with no new compounds approved in the last 11 years

Ustekinumab, an interleukin-12/23p40 antagonist, has been approved in the European Union for moderately-to-severely active CD in children weighing ≥40 kg[1-3]

In a Phase 1 study, mg/kg dosing did not consistently result in similar exposures in the lowest body weight subgroups, prompting the adoption of body surface area (BSA)-based dosing[1]

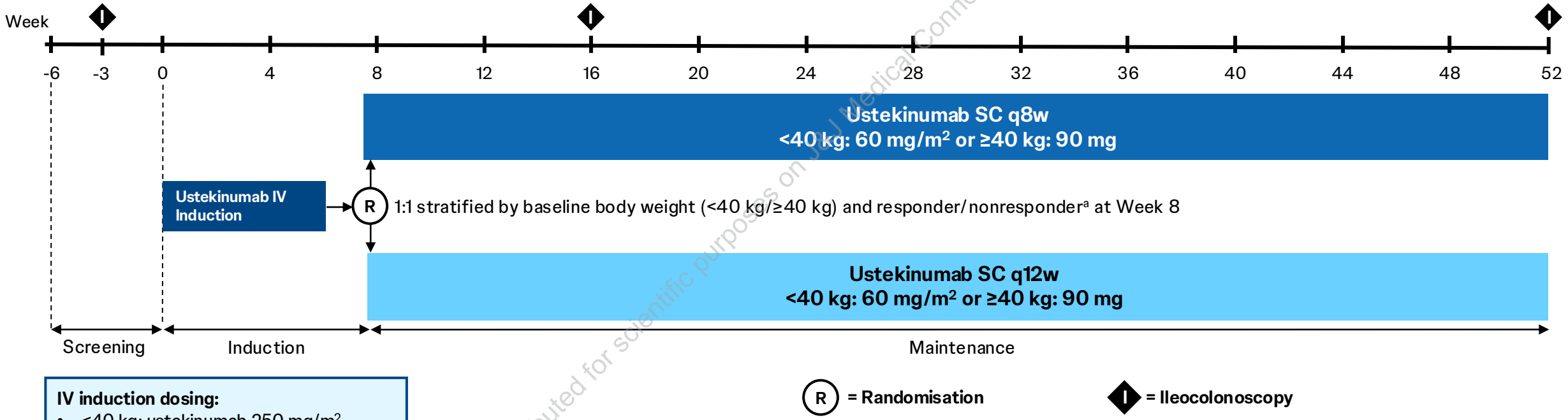
Study Objective: UNITI Jr is a Phase 3, randomised, controlled trial (NCT04673357) evaluating the efficacy and safety of ustekinumab in paediatric patients with moderately-to-severely active CD

1. Rosh JR, et al. *J Crohn's Colitis*. 2021;15(11):1931–42; 2. Turner D, et al. *J Pediatr Gastroenterol Nutr*. 2024;79:315–24; 3. Stelara (Ustekinumab). European Commission Decision. URL: https://www.ema.europa.eu/en/medicines/human/EPAR/stelara.

UNITI Jr Study Design

Key Eligibility Criteria:

- Children ≥2 to <18 years old with a PCDAI score of >30
- Inadequate response/intolerance to biologic therapies, corticosteroids, or immunosuppressants (thiopurines/MTX)
- Ileocolonoscopic ulceration or increased CRP (>3.0 mg/L) or fecal calprotectin (≥250 µg/g)



IV induction dosing:

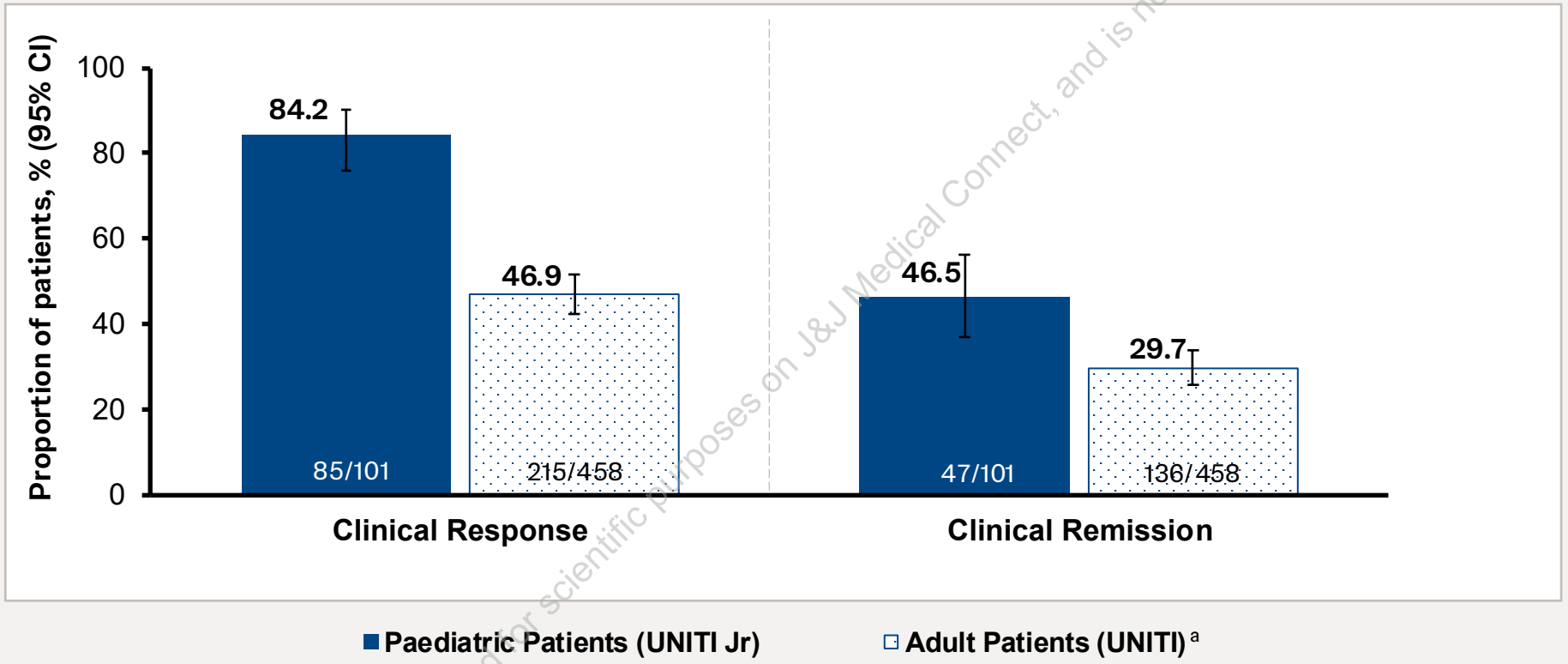
- <40 kg: ustekinumab 250 mg/m²
- ≥40 kg to ≤55 kg: ustekinumab 260 mg
- >55 kg to ≤85 kg: ustekinumab 390 mg
- >85 kg: ustekinumab 520 mg

[a]Response was defined as a PCDAI decline ≥12.5 points with a total PCDAI score ≤30 and nonresponse as a PCDAI decline <12.5 points. CRP, C-reactive protein; IV, intravenous; MTX, methotrexate; PCDAI, Paediatric Crohn's Disease Activity Index; q8w, every 8 weeks; q12w, every 12 weeks; SC, subcutaneous.

Baseline Characteristics

	Ustekinumab		
	q8w (n=48)	q12w (n=49)	Total[a] (N=101)
Demographics			
Age, years, median (IQR)	14.0 (12.0; 15.0)	14.0 (12.0; 16.0)	14.0 (12.0; 15.0)
Female	37.5%	42.9%	40.6%
Race, Asian/Black/White	8.3/2.1/89.6%	20.1/4.1/85.7%	8.9/3.0/87.1%
BMI Z-score, median (IQR)	-0.37 (-0.87; 0.43)	-0.48 (-0.82; 0.35)	-0.46 (-0.84; 0.35)
Weight, <30 kg/≥30-<40 kg/≥40 kg	6.3/22.9/70.8%	16.3/10.2/73.5%	10.9/17.8/71.3%
Disease Characteristics			
CD disease duration, years	2.6 (2.0)	2.8 (2.5)	2.6 (2.2)
PCDAI score, median (IQR)	40.0 (35.0; 45.0)	40.0 (35.0; 47.5)	40.0 (35.0; 45.0)
CDAI score, mean (SD)	359.4 (135.9)	371.5 (105.7)	365.2 (120.6)
CRP, mg/L	18.2 (25.5)	20.5 (26.9)	19.2 (25.8)
Fecal calprotectin, mg/kg	2818.8 (3577.0)	2776.2 (2780.7)	2765.7 (3121.2)
Biologic naïve	37.5%	46.9%	42.6%
Biological failure	62.5%	49.0%	56.4%
Concomitant Medications			
Corticosteroids	27.1%	20.4%	24.8%
Immunomodulatory drugs	37.5%	46.9%	42.6%
5-Aminosalicylate	33.3%	32.7%	31.7%

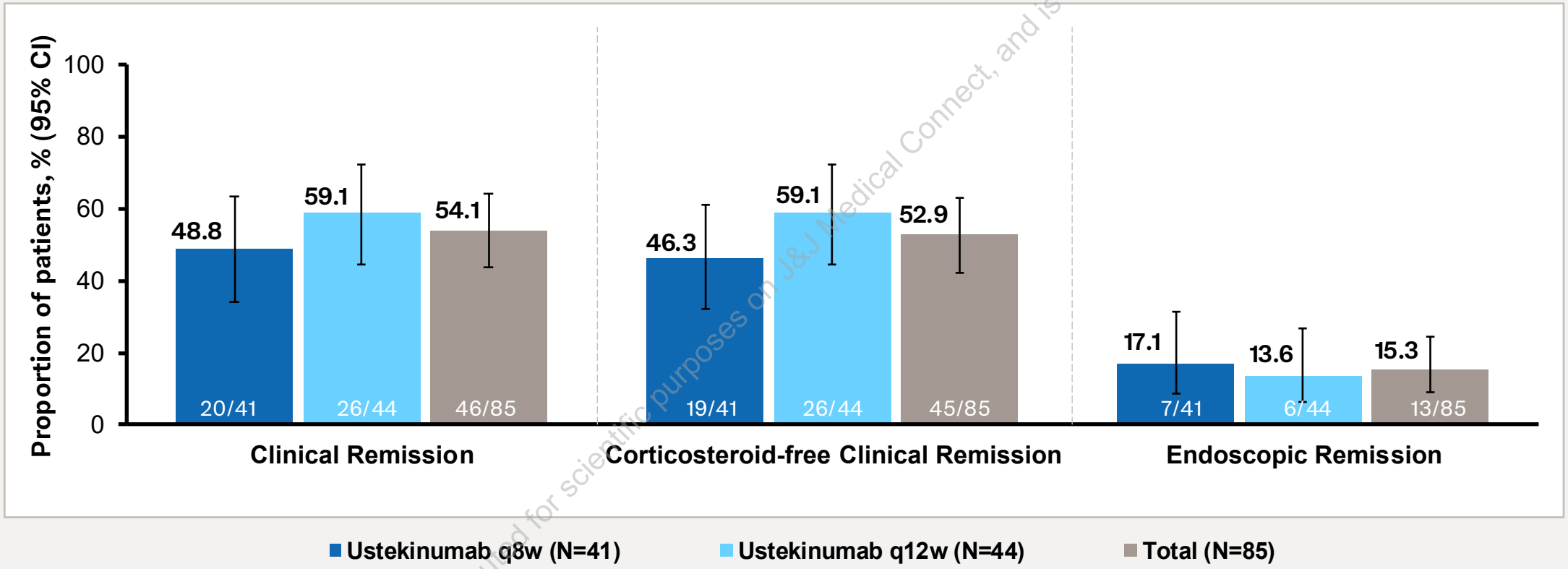
Week 8 Clinical Response and Clinical Remission Rates in Paediatric Patients vs Historical Rates in Adults



Paediatric clinical response: reduction from baseline in the PCDAI of ≥12.5 points with total PCDAI ≤30
Adult clinical response: reduction from baseline in the CDAI of ≥100 points or total CDAI score ≤150
Paediatric clinical remission: PCDAI ≤10
Adult clinical remission: CDAI <150

[a]Adult patients received ustekinumab IV 6 mg/kg (Feagan BJ, et al. *N Engl J Med*. 2016;375(20):1946–60). CI, confidence interval.

Remission Rates in Paediatric Patients Were Maintained at Week 52[a]



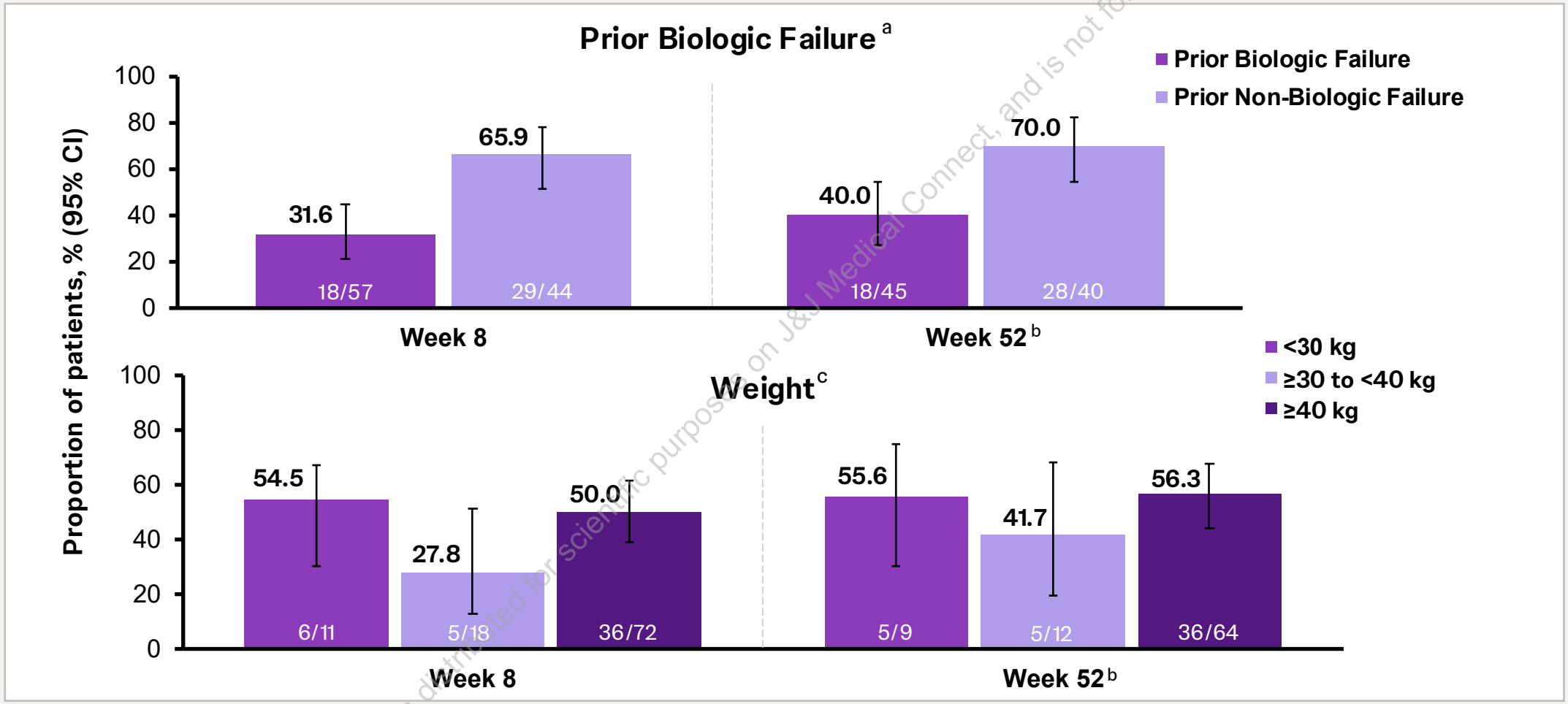
Clinical remission: PCDAI ≤10

Corticosteroid-free clinical remission: PCDAI ≤10 and not receiving corticosteroids for at least 90 days before Week 52

Endoscopic remission: SES-CD score of ≤2 in patients with a baseline SES-CD score of ≥3

[a]Among Week 8 clinical responders, defined as PCDAI reduction from baseline of ≥12.5 points with total PCDAI ≤30. SES-CD, Simple Endoscopic Score for Crohn's Disease.

Clinical Remission in Paediatric Patients by Prior Biologic Failure and Weight



Clinical remission: PCDAI ≤10

[a]At baseline, median CD duration was 2.7 years for the prior biologic failure group and 1.1 years for the prior non-biologic failure group; [b]Among Week 8 clinical responders, defined as PCDAI reduction from baseline of ≥12.5 points with total PCDAI ≤30; [c]**The proportion of patients with prior biologic failure at Week 8 was 64% for the <30 kg group, 72% for the ≥30-<40 kg group, and 51% for the ≥40 kg group, and at Week 52 was 56% for the <30 kg group, 67% for the ≥30-<40 kg group, and 50% for the ≥40 kg group.**

No New Safety Signals Were Observed Through Week 52

	Ustekinumab		
	q8w (n=48)	q12w (n=49)	Total[a] (N=97)
Weeks of follow-up, mean	36.5	36.2	36.4
Patients with ≥1			
AE	40 (83.3%)	44 (89.8%)	84 (86.6%)
SAE	7 (14.6%)	6 (12.2%)	13 (13.4%)
Serious infection	2 (4.2%)	2 (4.1%)	4 (4.1%)
AE leading to discontinuation	2 (4.2%)	3 (6.1%)	5 (5.2%)[b]
Most common AEs (≥10%)[c]			
CD exacerbation	19 (39.6%)	17 (34.7%)	36 (37.1%)
Upper respiratory tract infection	7 (14.6%)	16 (32.7%)	23 (23.7%)
COVID-19	8 (16.7%)	7 (14.3%)	15 (15.5%)[d]
Nasopharyngitis	5 (10.4%)	7 (14.3%)	12 (12.4%)[d]
Anemia	5 (10.4%)	7 (14.3%)	12 (12.4%)

[a]Four patients who were not randomised were excluded; [b]All were exacerbated CD; [c]AEs that were considered to be reasonably related to the study drug included nasopharyngitis, upper respiratory tract infection, and rash in the q12w group (n=2) and headache in the q8w group (n=1); [d]One patient who underwent dose adjustment was included. AE, adverse event; SAE, serious adverse event.

Key Takeaways

- Overall, ustekinumab was effective in inducing and maintaining remission in children with moderately-to-severely active CD
- Clinical response and remission rates trended higher in children with CD compared to adults
- Among patients with clinical response at induction Week 8, similar proportions of patients in the q8w and q12w groups achieved remission at Week 52
- Clinical remission rates were lower among patients with prior biologic failure, and there was as a trend toward lower clinical remission rates in the ≥30-<40 kg group possibly due to higher biologic experience rates
- Ustekinumab was well-tolerated with no new safety signals. No deaths, malignancy, active tuberculosis, opportunistic infections, or injection-site reactions were reported.

Acknowledgments

- We would like to thank the UNITI Jr study participants and their families, and the investigators and staff at each study site

- This study was supported by Johnson & Johnson

- Medical writing support was provided by Cindy C. Taylor, PhD of Certara, under the direction of the authors in accordance with Good Publication Practice guidelines and was funded by Johnson & Johnson