ID #406

Dose Escalation in Participants With Primary/Secondary Loss of Response to Conventional Dosing of Ustekinumab in Pediatric Crohn's Disease (UNITI Jr Study)

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SPEAKER DISCLOSURE

I, **Omoniyi J. Adedokun**, disclose the following financial relationships with a commercial interest:

- Employee of Johnson & Johnson; owns stock/stock options in Johnson & Johnson.

Background and Objective

Ustekinumab therapy induced and maintained response and remission in adult patients with moderate-to-severe CD in the IM-UNITI program[1,2]
Data from IM-UNITI demonstrated that steady-state serum trough concentrations of ≥1.4 µg/mL ustekinumab were associated with clinical remission[3]

The shortening of ustekinumab dosing intervals is regularly utilized in clinical practice and has been shown to be effective in real-world pediatric studies[4]

UNITI Jr was a phase 3 multicenter study in pediatric patients (≥2 to <18 years) with one open-label IV ustekinumab dose followed by randomized double-blind SC maintenance dosing q8w or q12w starting at Week 8[5]

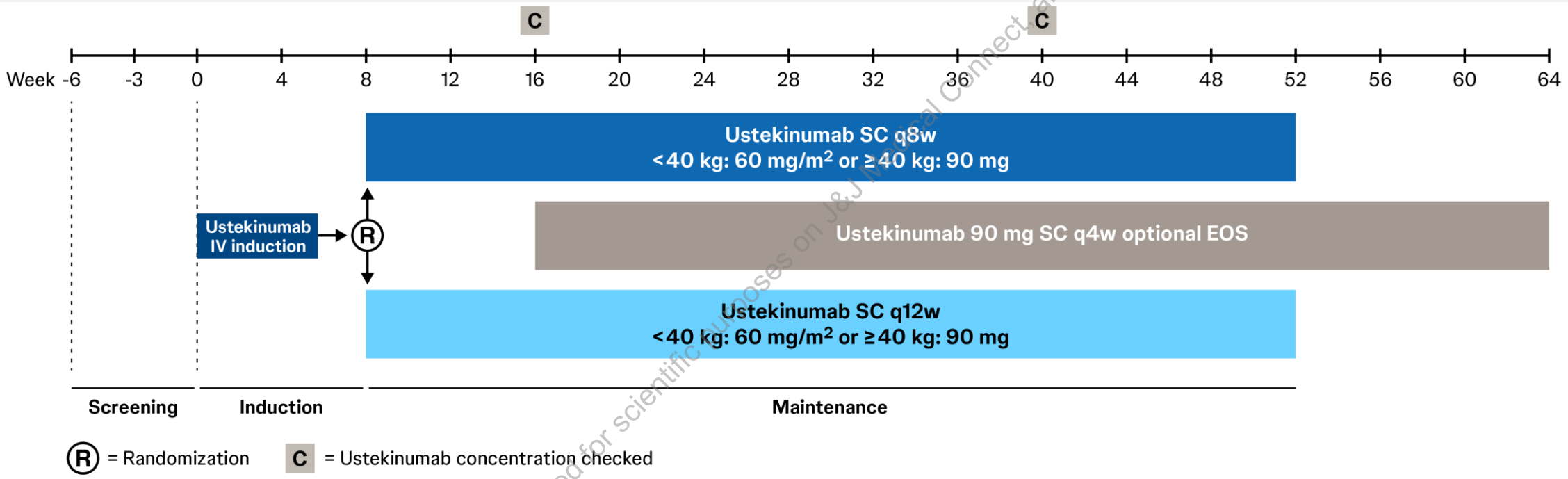
Objective: To examine efficacy, safety, and pharmacokinetics of ustekinumab q4w dosing for a minimum of 16 weeks in pediatric participants (≥2 to <18 years) with moderate-to-severe CD in the UNITI Jr (NCT04673357) EOS

1. Feagan BJ, et al. *N Engl J Med*. 2016;375:1946-60. 2. Sandborn WJ, et al. *Clin Gastroenterol Hepatol*. 2022;20:578-90. 3. Adedokun OJ, et al. *Gastroenterology*. 2018;154:1660-71. 4. Pujol-Muncunill G, et al. *Eur J Pediatr*. 2024;183:3253-62. 5. ClinicalTrials.gov; https://www.clinicaltrials.gov/study/NCT04673357. Accessed September 10, 2025. **CD**=Crohn's disease; **EOS**=exposure optimization substudy; **IV**=intravenous; **PK**=pharmacokinetics; **q4w**=every 4 weeks; **q8w**=every 8 weeks; **q12w**=every 12 weeks; **SC**=subcutaneous.

UNITI Jr EOS Study Design

Key Eligibility Criteria for UNITI Jr:

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



IV induction dosing:
- <40 kg: ustekinumab 250 mg/m^2
- ≥40 kg to ≤55 kg: ustekinumab 260 mg
- >55 kg to ≤85 kg: ustekinumab 390 mg
- >85 kg: ustekinumab 520 mg

EOS eligibility criteria: Participants who were induction non-responders and had low steady-state trough ustekinumab concentrations (<1.4 µg/mL) at Week 16 or participants losing response after Week 16 and who had corresponding low steady-state trough ustekinumab concentrations at Week 16 or Week 40[a]

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[a]Participants could enter the EOS at various times. **CD**=Crohn's disease; **CRP**=C-reactive protein; **EOS**=exposure optimization substudy; **IV**=intravenous; **PCDAI**=Pediatric Crohn's Disease Activity Index; q4w=every 4 weeks; **q8w**=every 8 weeks; **q12w**=every 12 weeks; **SC**=subcutaneous.

Outcomes / Assessments and Analyses for the EOS

EOS (Weeks 1-16)	• **Major endpoints**
	  • Clinical remission at EOS Week 16
	  • Clinical response at EOS Week 16
	  • Pharmacokinetics during EOS
	  • Safety (Occurrence and severity of AEs, SAEs, and laboratory values)
	• **Analyzed population**
	  • All participants who entered the EOS and had data at/through Week 16

AE=adverse events; **EOS**=exposure optimization substudy; **SAE**=serious adverse event.

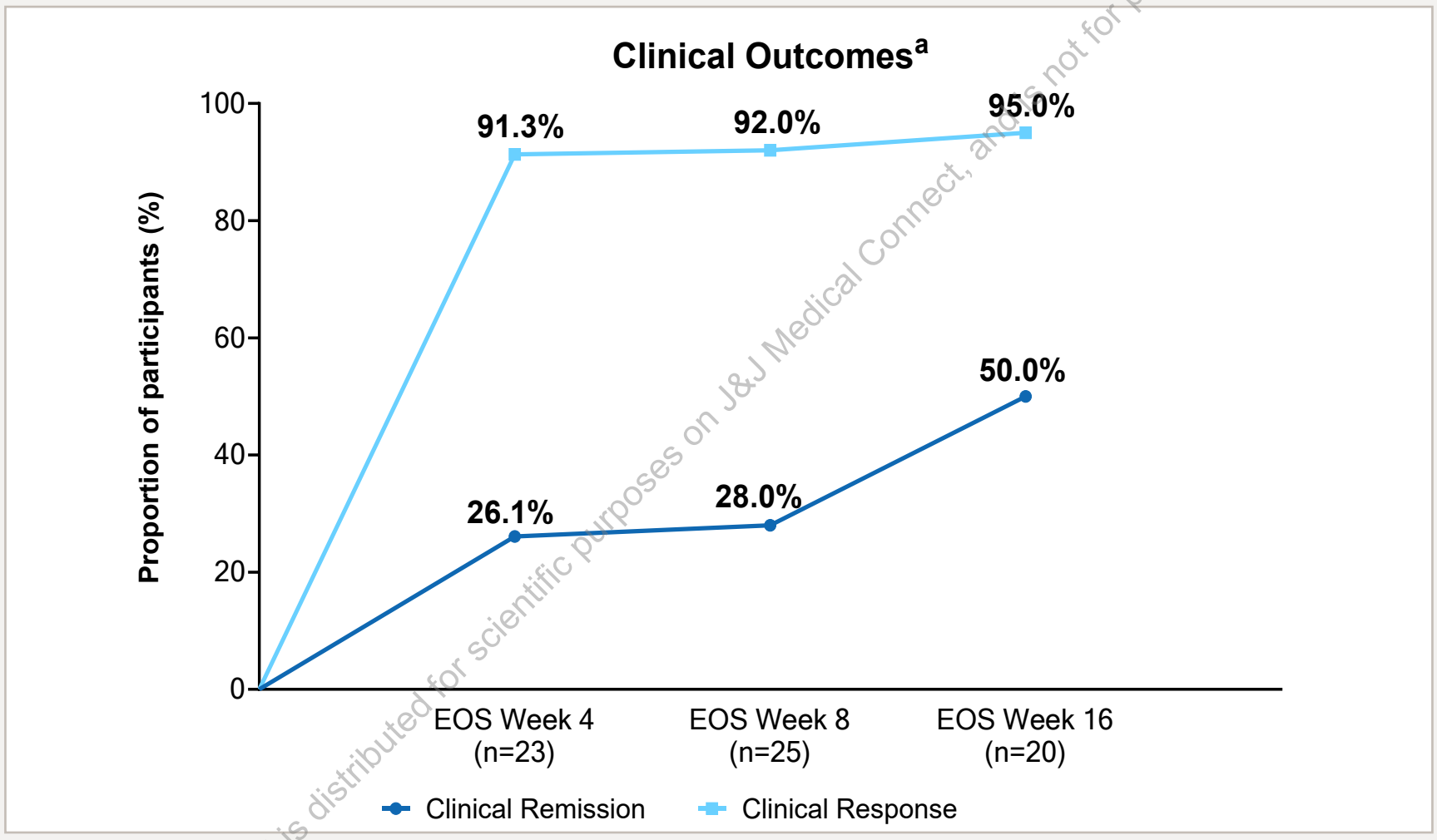
Results

Baseline Characteristics

Baseline Characteristics		Total (N = 26)
Demographics		
	Age, yrs, median (IQR)	14.0 (12.0, 16.0)
	Female, %	46.2%
	Race, Asian/Black/White, %	7.7/3.8/88.5%
	Weight, kg, median (IQR)	48.8 (39.6, 59.8)
	BMI-Z score, median (IQR)	-0.16 (-0.82, 0.44)
Disease Characteristics, mean (SD)		
	CD disease duration, yrs	3.0 (2.0)
	PCDAI score	42.6 (8.0)
	sPCDAI score	56.0 (12.2)
	sPCDAI score at EOS Week 0	49.2 (14.1)
	CRP, mg/L	21.5 (27.0)
	CRP at EOS Week 0, mg/L	20.3 (27.2)
	Fecal calprotectin, mg/kg	2741.3 (1853.6)
Prior CD Treatments, n (%)		
	Prior biologic failure	21 (80.8%)
	≥1 anti-TNF (not vedolizumab)	20 (76.9%)
	Prior corticosteroid failure	13 (50.0%)
	Prior immunomodulator failure	16 (61.5%)

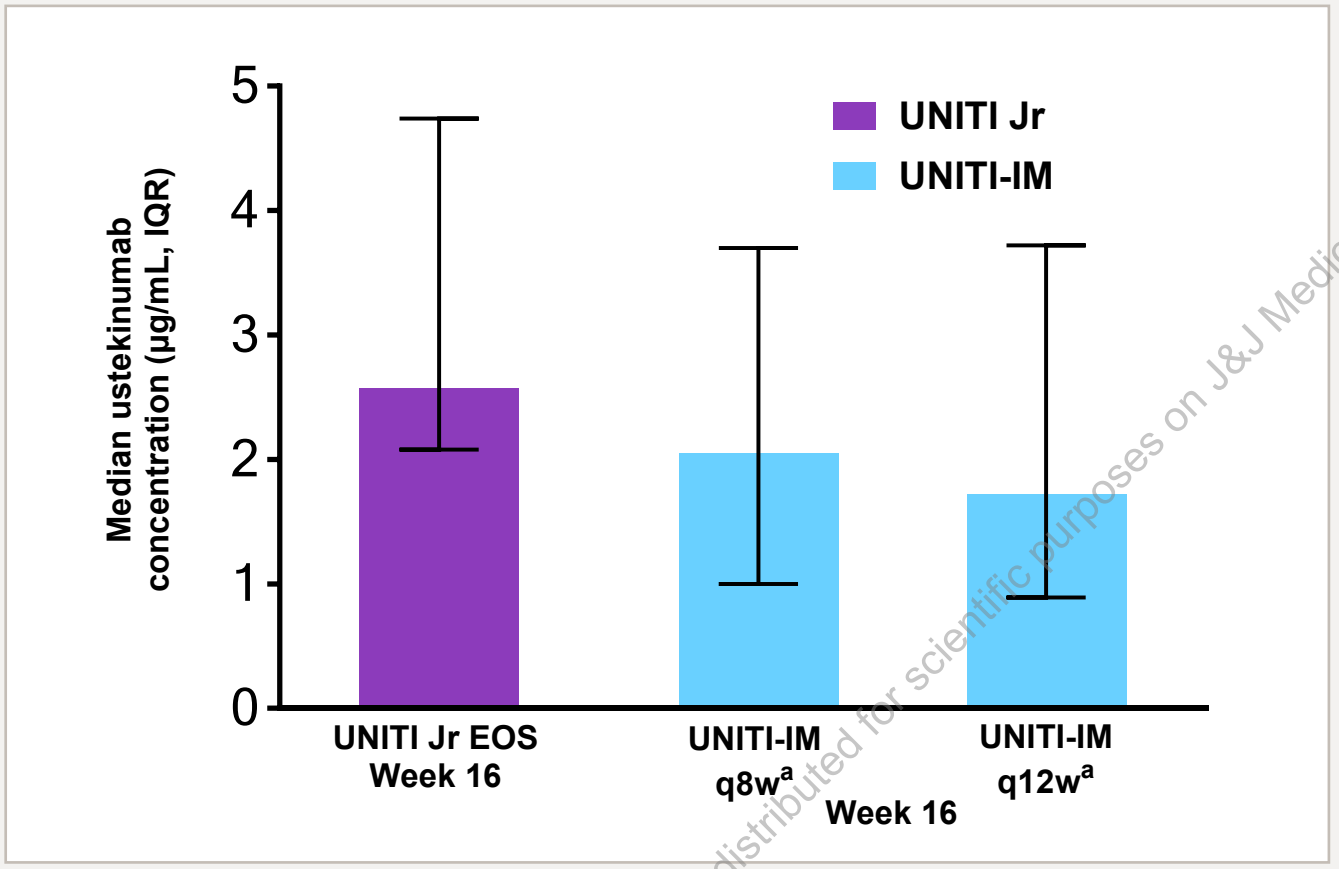
BMI=body mass index, **CD**=Crohn's disease, **CRP**=C-reactive protein, **EOS**=exposure optimization substudy, **IQR**=interquartile range, **PCDAI**=Pediatric Crohn's Disease Activity Index, **sPCDAI**=short Pediatric Crohn's Disease Activity Index, **TNF**=tumor necrosis factor.

Clinical Outcomes Improved Over Time During the EOS



[a]Observed data were used. Clinical remission is defined as PCDAI score ≤10 points. Clinical response is defined as a reduction from baseline in the PCDAI score of ≥12.5 points with a total PCDAI score not more than 30. **EOS**=exposure optimization substudy, **PCDAI**=Pediatric Crohn's Disease Activity Index.

Serum Ustekinumab Concentrations at EOS WK16 Were Similar to the Concentrations Observed in the Adult CD Study



Steady-state ustekinumab concentration at EOS Week 16

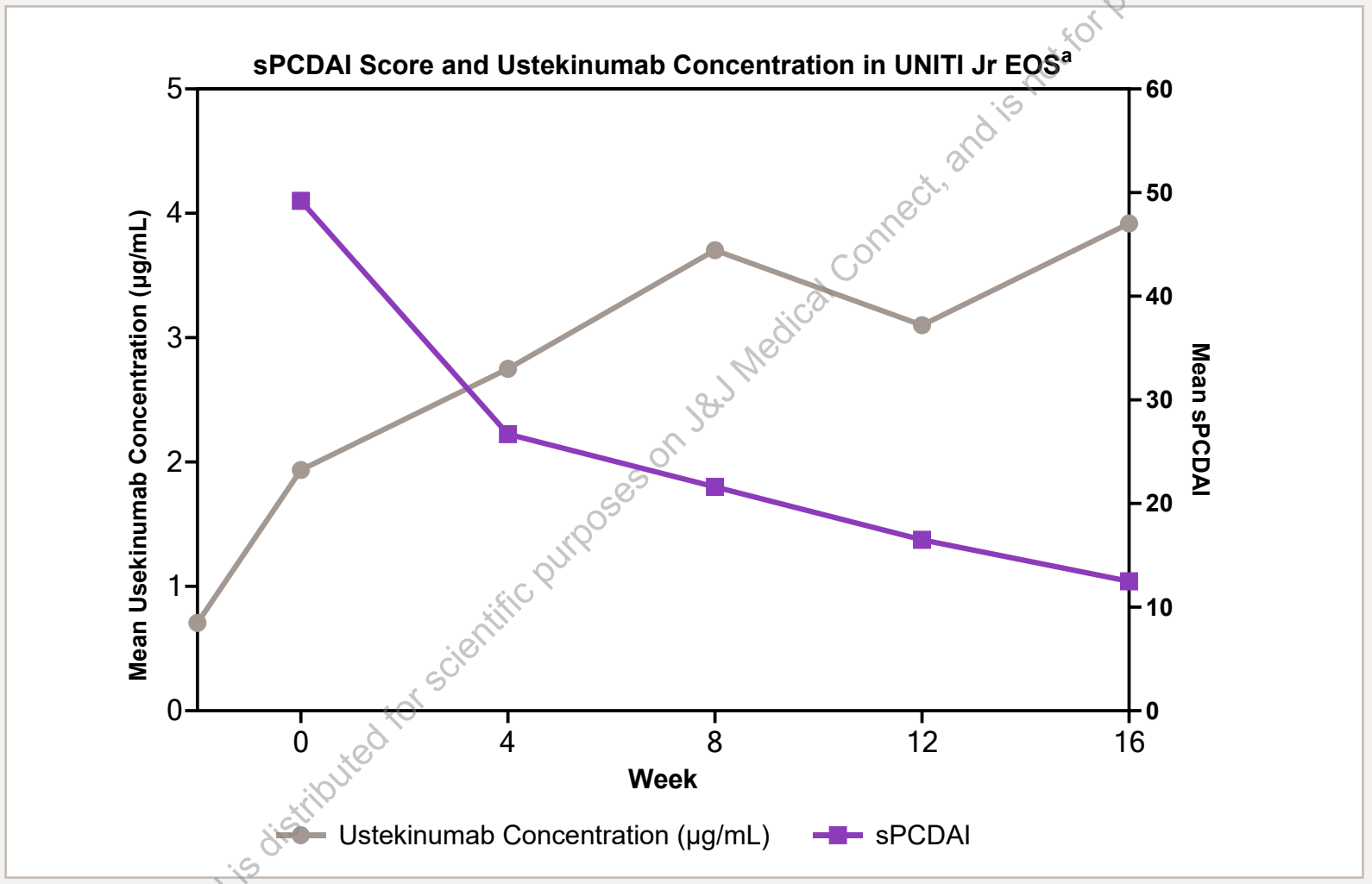
- q4w dosing: (median) 2.57 µg/mL (IQR: 2.08, 4.74)

Historically, in the UNITI-IM study, steady-state ustekinumab concentrations in adults at Week 16[a]

- q8w dosing: (median) 2.05 µg/mL (IQR: 1.00, 3.70)
- q12w dosing: (median) 1.72 µg/mL (IQR: 0.89, 3.72)

[a]Data from Feagan BJ, et al. *N Engl J Med*. 2016;375:1946-60. **EOS**=exposure optimization substudy, **IQR**=interquartile range, **q4w**=every 4 weeks, **q8w**=every 8 weeks, **q12w**=every 12 weeks.

Increased Serum Ustekinumab Concentration Was Associated with Improved sPCDAI Scores



[a]Time point prior to EOS Week 0 is mean ustekinumab concentration prior to the start of the EOS. **EOS**=exposure optimization substudy, **sPCDAI**=short Pediatric Crohn's Disease Activity Index.

No New Safety Signals Were Observed Through the End of the EOS

Safety Through the End of the EOS	EOS (N=26)
Mean Weeks of Follow-Up	20.4
Any AE	19 (73.1%)
Any SAE	3 (11.5%)
Infections	12 (46.2%)
Serious infections[a]	3 (11.5%)
Opportunistic infections[b]	1 (3.8%)
Discontinuations due to AE	2 (7.7%)
Most Common AEs (≥5%)[c]	
Crohn's disease	4 (15.4%)
Upper respiratory tract infection	3 (11.5%)
Fatigue	3 (11.5%)
Nausea	2 (7.7%)
Rhinitis	2 (7.7%)
Pyrexia	2 (7.7%)
Rhinitis allergic	2 (7.7%)
Iron deficiency anemia	2 (7.7%)

[a]1 participant reported events of terminal ileitis with abscess formation; 1 participant reported pyrexia post-ileocolonoscopy; 1 participant reported gastroenteritis aeromonas (reported term of "worsening gastroenteritis with aeromonas species"). [b]Cytomegalovirus colitis. [c]2 participants reported AEs reasonably related to the study drug. **AE**=adverse event, **EOS**=exposure optimization study, **SAE**=serious adverse event.

Laboratory Values and Change from EOS baseline (Week 16) Were Similar to the UNITI Jr Main Study (Week 52)

Mean (range)	EOS Week 16 [CFB]	UNITI Jr Main Study Week 52 [CFB][a]
CRP, mg/L	2.75 (0.1-7.8) [-9.22 (64.5-0)]	6.07 (0.1-57.2) [-10.74(-102.5-11.6)]
Hematocrit	0.380 (0.30-0.43) [0.011 (-0.02-0.05)]	0.392 (0.32-0.49) [0.028 (-0.06-0.12)]
Platelets, $x10^9$/L	353.1 (238-655) [-48.9 (-136-29)]	330.8 (154-542) [-77.3 (-389-211)]
Albumin, g/L	43.5 (36-48) [1.9 (-4-8)]	45.1 (34-55) [3.4 (-4-16)]
ESR, mm/hr	28.3 (3-83) [-4.4 (-28-38)]	21.9 (2-73) [-16.1 (-75-30)]
Fecal lactoferrin, µg/g	423.9 (1.8-1000.0) [-115.4 (-998.2-794.9)]	182.63 (0.41-1000.0) [-59.06 (-996.38-420.61)]

[a]Change from maintenance period baseline at Week 8. **CFB**=change from baseline, **EOS**=exposure optimization substudy, **ESR**=erythrocyte sedimentation rate.

Key Takeaways

The majority of pediatric participants with CD in the UNIFI Jr EOS were in clinical response, and half achieved clinical remission, 16 weeks after switching to ustekinumab q4w dosing

- ✓ Switching to q4w dosing in pediatric participants resulted in higher serum concentrations of ustekinumab
- ✓ Ustekinumab exposures in participants in the EOS fell within the safe and effective exposure range observed in adult CD ustekinumab studies

- ✓ Improvements in inflammatory markers were seen after 16 weeks
- ✓ The safety profile of ustekinumab administered to participants q4w was consistent with the safety profile in the main UNITI Jr study
- ✓ No new safety issues were identified

CD=Crohn's disease, **EOS**=exposure optimization substudy, **q4w**=every 4 weeks,