TU1439

Ustekinumab Pharmacokinetics and Exposure-Response Relationships in Pediatric Patients With Moderately to Severely Active Crohn's Disease: Results From UNITI Jr. Phase 3 Study

Omoniyi J Adedokun, Jingyun Li, Richard S Strauss, Edaire Cheng, Els Van Limbergen, Sheri Volger, Lilianne Kim, An Vermeulen

Johnson & Johnson, Spring House, PA, USA

Background

- Ustekinumab is a fully human IL-12 and IL-23 antagonist indicated for the treatment of moderately to severely active Crohn's disease (CD) in adults[1,2]
- 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[3]
- The double-blind Phase 3 UNITI Jr (NCT04673357) study evaluated the efficacy, safety, and pharmacokinetics (PK) of ustekinumab in pediatric participants with moderately to severely active CD
- Approved pharmacologic treatment options for pediatric patients with CD remain limited

Objective

The PK and exposure-response (E-R) relationships of ustekinumab were characterized in pediatric patients with CD based mainly on data from the Phase 3 UNITI Jr study, and results were compared with those in adults with CD

Methods

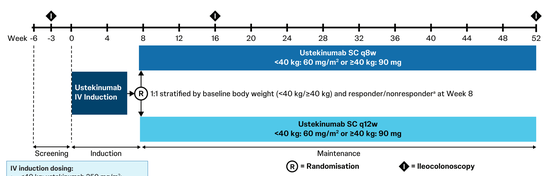
PK & E-R Analyses

- Blood samples from the Phase 3 UNITI Jr study were collected for evaluation of serum ustekinumab concentrations and antibodies to ustekinumab
  - Blood samples for ustekinumab concentrations were collected at:
    - Induction: Week 0 (pre- and 1-hour post-infusion), Week 3, Week 6, and Week 8
    - Maintenance: Week 12, Week 16, Week 20, Week 24, Week 32, Week 40, Week 44, Week 48, and Week 52
  - Serum ustekinumab concentrations were measured using a validated assay (Gaithersburg, Maryland, US); the lowest quantifiable concentration in a sample for the MSD Electrochemiluminescence Immunoassay (ECLIA) method was 0.1688 µg/mL
  - Antibodies to ustekinumab were evaluated using a validated drug-tolerant ECLIA assay
- Relationships between serum ustekinumab concentrations and efficacy and safety were assessed graphically
  - An E-R analysis for efficacy was performed: clinical remission at induction Week 8 in relation to $C_{trough,week8}$ and clinical remission at Week 52 in relation to $C_{trough,week52}$
  - The E-R analyses for safety were based on combined data from: UNITI Jr and UniStar, a Phase 1 pediatric CD PK study (NCT02968108)
- Results were compared with a reference adult CD population who received ustekinumab in the UNITI-1 (NCT01369329), UNITI-2 (NCT01369342), and IM-UNITI (NCT01369355) studies

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

*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**=Pediatric Crohn's Disease Activity Index; **q8w**=every 8 weeks; **q12w**=every 12 weeks; **SC**=subcutaneous.

Results

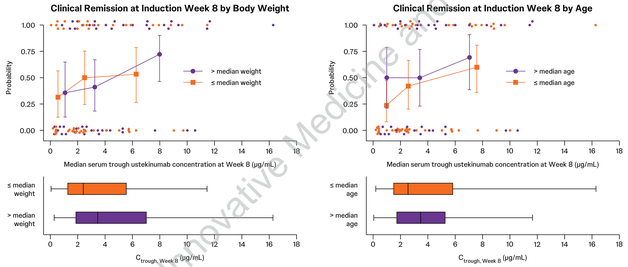
Baseline Characteristics: UNITI Jr

		Ustekinumab q8w (n=48)	Ustekinumab q12w (n=49)	Ustekinumab Total* (N = 101)
Demographics				
	Age, yrs, median (IQR)	14.0 (12.0; 15.0)	14.0 (12.0; 16.0)	14.0 (12.0; 15.0)
	Female, n (%)	18 (37.5%)	21 (42.9%)	41 (40.6%)
	Race, Asian/Black/White, n (%)	8.3/2.1/89.6%	10.2/4.1/85.7%	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, <30kg/≥30-<40kg/≥40kg, n (%)	6.3/22.9/70.8%	16.3/10.2/73.5%	10.9/17.8/71.3%
Disease Characteristics				
	CD disease duration, yrs, mean (SD)	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, mean (SD)	18.2 (25.5)	20.4 (26.9)	19.2 (25.8)
	Fecal calprotectin, mg/kg, mean (SD)	2818.8 (3577.0)	2776.2 (2780.6)	2765.7 (3121.2)
	Biologic naïve, n(%)	18 (37.5%)	23 (46.9%)	43 (42.6%)
	Biologic failure, n (%)	30 (62.5%)	25 (51.0%)	57 (56.4%)
Concomitant Medications				
	Corticosteroids, n (%)	13 (27.1%)	10 (20.4%)	25 (24.8%)
	Immunomodulatory drugs, n (%)	18 (37.5%)	23 (46.9%)	43 (42.6%)
	5-Aminosalicylate, n (%)	16 (33.3%)	16 (32.7%)	32 (31.7%)

Baseline characteristics were similar across the treatment groups and were representative of pediatric patients with moderate-to-severe CD

*Four participants received induction therapy but were not randomized.
BMI=body mass index; **CD**=Crohn's disease; **CDAI**=Crohn's disease activity index; **CRP**=C-reactive protein; **IQR**=interquartile range; **PCDAI**=Pediatric Crohn's Disease Activity Index; **q8w**=every 8 weeks; **q12w**=every 12 weeks.

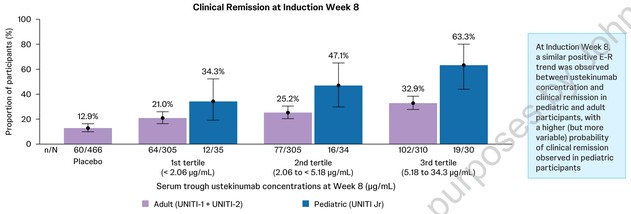
Age and body weight had no apparent effect on the E-R relationship for clinical remission at induction Week 8



Note: Connected dots with error bars are the observed mean and 95% CIs of probability in the respective exposure tertile groups. Dots at the lower and upper part of the plotting area represent the individual model-predicted exposure metrics in nonresponders and responders, respectively, which were predicted based on the actual dose regimen and individual PopPK model parameter estimates in pediatric participants who have measurable ustekinumab concentrations after receiving ustekinumab 250 mg/m² (weight <40 kg) or ~6 mg/kg (weight ≥40 kg) at Week 1-0 from UNITI Jr
Note: Stratification for age was as follows: 2 to 5 years vs >4 to 17 years. Stratification for weight was as follows: 12.6 to 47.2 kg vs >47.2 to 87.6 kg.
***$C_{trough,\ Week\ 8}$**=trough concentration for IV induction dose at Week 8; **CI**=confidence interval; **E-R**=exposure-response; **IV**=intravenous; **N**=number of participants; **PopPK**=population pharmacokinetic(s).*

Induction

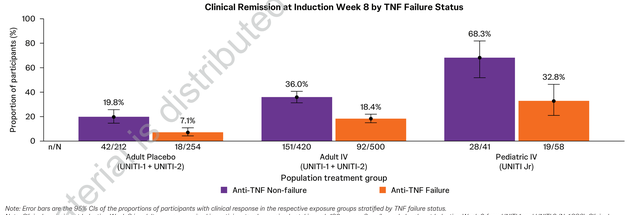
Serum ustekinumab concentrations were positively associated with clinical remission at induction Week 8, and these relationships were generally comparable between pediatric and adult participants



At Induction Week 8, a similar positive E-R trend was observed between ustekinumab concentration and clinical remission in pediatric and adult participants, with a higher (but more variable) probability of clinical remission observed in pediatric participants

Note: Error bars are the 95% CIs of the proportions of participants with clinical response in the respective exposure tertile groups.
Note: E-R relationship in adults was summarized in participants who received ustekinumab 130 mg or ~6 mg/kg and placebo at Week 1-0 from UNITI-1 and UNITI-2 (N=1386). E-R relationship in pediatric participants was summarized in participants who have measurable ustekinumab concentrations after receiving ustekinumab 250 mg/m² (weight <40 kg) or ~6 mg/kg (weight ≥40 kg) at Week 1-0 from UNITI Jr (N=99). Exposure tertile cutoffs for $C_{trough,week8}$ were based on pooled data from pediatric UNITI Jr and adult Studies UNITI-1 and UNITI-2.
***CI**=confidence interval; **$C_{trough,week8}$**=trough concentration for IV induction dose at induction Week 0-8; **E-R**=exposure-response; **IV**=intravenous; **N**=number of participants.*

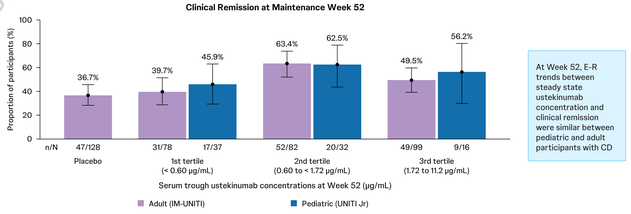
Similar to adult participants, at a given ustekinumab concentration at induction Week 8, the proportions of pediatric participants in clinical remission were higher in the anti-tumor necrosis factor (TNF) non-failure population vs the anti-TNF failure population



Note: Error bars are the 95% CIs of the proportions of participants with clinical response in the respective exposure groups stratified by TNF failure status.
Note: Clinical remission at Induction Week 8 in adults was summarized in participants who received ustekinumab 130 mg or ~6 mg/kg and placebo at Induction Week 0 from UNITI-1 and UNITI-2 (N=1386). Clinical remission at Induction Week 8 in pediatric participants was summarized in participants who have measurable ustekinumab concentrations after receiving ustekinumab 250 mg/m² (body weight <40 kg) or ~6 mg/kg (body weight ≥40 kg) at Week 1-0 from UNITI Jr (N=99).
***CI**=confidence interval; **IV**=intravenous; **N**=number of participants; **TNF**=tumor necrosis factor.*

Maintenance and Durability

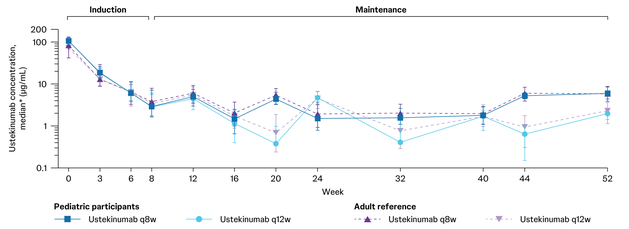
Serum ustekinumab concentrations were positively associated with clinical remission at Week 52 during maintenance treatment, and these relationships were generally comparable between pediatric and adult participants



At Week 52, E-R trends between steady state ustekinumab concentration and clinical remission were similar between pediatric and adult participants with CD

Note: Error bars are the 95% CIs of the proportions of participants with clinical response in the respective exposure tertile groups.
Note: The E-R relationship in adults was summarized in participants who were randomized to receive SC maintenance regimens of placebo, ustekinumab 90 mg q8w, or 90 mg q12w in IM-UNITI. E-R relationship in pediatric participants was summarized in participants who were induction responders and randomized to receive SC maintenance regimens of ustekinumab 60 mg/m² (body weight <40 kg) or 90 mg (body weight ≥40 kg) q8w or q12w in UNITI Jr (N=80). Exposure tertile cutoffs for $C_{trough,\ Week\ 52}$ (last trough ustekinumab concentration prior to Week 52) were based on pooled data from pediatric UNITI Jr and adult IM-UNITI Study.
***CI**=confidence interval; **E-R**=exposure-response; **N**=number of participants; **qXw**=every X weeks; **SC**=subcutaneous.*

Serum ustekinumab concentrations were similar between pediatric and adult participants with CD



- Ninety-nine patients received at least 1 dose of ustekinumab and had at least 1 blood sample evaluated for ustekinumab PK
- Median serum ustekinumab concentrations were similar between pediatric and adult participants following induction (from Week 0 to Week 8) and following maintenance treatment (from Week 8 to Week 52)

*Error bars represent IQR.

Safety and Immunogenicity

No association between serum ustekinumab concentrations and safety events was observed

	Phase 3 UNITI Jr and Phase 1 UniStar Pediatric Studies			
	1st Quartile	2nd Quartile	3rd Quartile	4th Quartile
Induction*	N=33	N=32	N=33	N=32
Mean weeks of follow-up	8.14	7.97	8.05	8.06
Avg exposure (administrations, n)	1	1	1	1
Participants with ≥1 TEAEs, n (%)	7 (21.2%)	6 (18.8%)	13 (39.4%)	8 (25.0%)
Participants with ≥1 serious infections, n (%)	0	0	0	1 (3.1%)
Participants with ≥1 SAEs, n (%)	3 (9.1%)	2 (6.3%)	0	1 (3.1%)
Maintenance†	N=25	N=25	N=25	N=24
Mean weeks of follow-up	41.47	43.57	42.29	41.36
Avg exposure (administrations, n)	8.64	8.96	7.64	6.63
Participants with ≥1 TEAEs, n (%)	18 (72.0%)	15 (60.0%)	13 (52.0%)	18 (75.0%)
Participants with ≥1 serious infections, n (%)	1 (4.0%)	1 (4.0%)	0	0
Participants with ≥1 SAEs, n (%)	2 (8.0%)	4 (16.0%)	1 (4.0%)	2 (8.3%)

- There was no effect of ustekinumab concentration on rates of serious infections and SAEs in the pediatric study populations
- Safety data were similar between the pediatric and adult study populations (data not shown)

Note: Participants are counted only once for any given event, regardless of the number of times they actually experienced the event. Adverse events are coded using MedDRA Version 27.1. For induction, quartiles are calculated based on ustekinumab concentration at Week 1-8 (Week 8) for all participants from UNITI Jr and UniStar studies regardless of the induction doses received. For maintenance, quartiles are calculated based on ustekinumab concentration at steady-state visits for all participants from UNITI Jr and UniStar studies regardless of the induction doses received.
¹st quartile=≤1.98 µg/mL, 2nd quartile=>1.98 to ≤2.96 µg/mL, 3rd quartile=>2.96 to ≤5.09 µg/mL, 4th quartile is >5.09 µg/mL
†1st quartile=≤0.37 µg/mL, 2nd quartile=>0.37 to ≤1.21 µg/mL, 3rd quartile=>1.21 to ≤2.15 µg/mL, 4th quartile is >2.15 µg/mL
***PK**=pharmacokinetics; **SAE**=serious adverse events; **TEAE**=treatment emergent adverse event.*

- Immunogenicity of ustekinumab was similar through 1 year between pediatric and adult participants with CD: anti-ustekinumab antibodies occurred in 3 (3.3%) [n=91] for pediatric UNITI Jr vs 9 (3.1%) [n=287] for the adult reference

Key Takeaways

- **Serum ustekinumab concentrations in pediatric participants with CD were generally comparable to those observed in a reference adult population with CD**
- **E-R trends were similar between pediatric and adult participants with CD**
- **The incidence of antibodies to ustekinumab was low in pediatric participants with CD consistent with the immunogenicity profile of ustekinumab in adult CD participants**

PRESENTED AT: Digestive Disease Week, May 2–5, 2026, Chicago, IL, USA. **REFERENCES: 1.** Stelara (ustekinumab): Prescribing information. Johnson & Johnson; 2025. https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/125261s167lbl.pdf **2.** Stelara (ustekinumab): Summary of Product Characteristics. Johnson & Johnson; 2025. **3.** Rosh JR, et al. *J Crohn's Colitis.* 2021;15(11):1931–1942. **ACKNOWLEDGMENTS:** Medical writing support was provided by Teresa Tartaglione, PharmD, of Certara under the direction of the authors in accordance with Good Publication Practice guidelines (*Ann Intern Med.* 2022;175:1298–1304). This presentation was sponsored by Johnson & Johnson.
DISCLOSURES: OJA, JL, RSS, EC, EVL, SV, LK, and **AV:** Employees of Johnson & Johnson; may own stock/stock options in Johnson & Johnson.