OP41

Ustekinumab Open-label Induction and Randomized Blinded Maintenance Therapy in Pediatric Participants with Moderately to Severely Active Crohn's Disease: The Phase 3 UNITI Jr Study

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Disclosure information

Jeffrey S. Hyams

I disclose the following financial relationship(s) with a commercial interest

I have served on an advisory board for Janssen and AbbVie; and served as a consultant for Pfizer, Eli Lilly, Boehringer Ingelheim, Bristol Myers Squibb, and Genentech.

Background and Objective

Ustekinumab is an IL-12/23p40 subunit inhibitor that is indicated for Crohn's disease, ulcerative colitis, plaque psoriasis, and psoriatic arthritis in adults and plaque psoriasis and psoriatic arthritis in pediatric patients (≥6 years)

UNITI Jr is a study evaluating open-label ustekinumab intravenous induction followed by randomized, double-blind subcutaneous maintenance therapy (q12w or q8w) in pediatric participants (<18 yrs) with moderately to severely active Crohn's disease

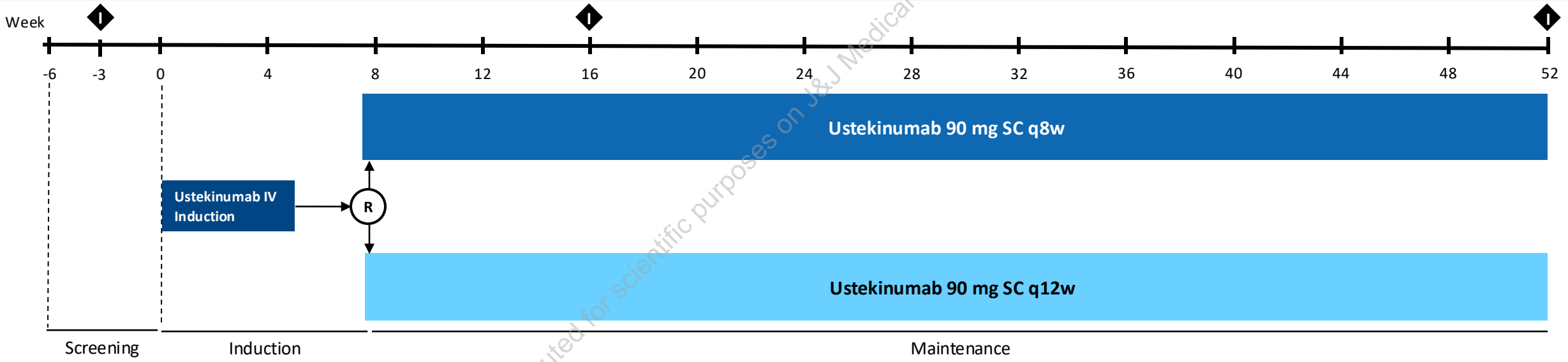
An interim analysis of participants weighing ≥40 kg was conducted to support an earlier regulatory submission to the EMA before the enrollment of younger participants (weighing <40 kg) was complete

Study Objective: Here we report interim efficacy and safety results from UNITI Jr through Week 52 in pediatric participants ≥40 kg

UNITI Jr Study Design

Key Eligibility Criteria:

- Pediatric participants <18 years old with a body weight of ≥40 kg and a Pediatric Crohn's Disease Activity Index (PCDAI) score of >30
- Inadequate response/intolerance to biologic therapies (TNFα antagonist or vedolizumab), IV or oral corticosteroids (including corticosteroid dependence), or immunosuppressants (6-MP/AZA/MTX)
- Ileocolonoscopy with evidence of active Crohn's disease defined as presence of ulceration during screening



Weight-tiered IV dosing:

- ≥40 kg to ≤55 kg: ustekinumab 260 mg
- >55 kg to ≤85 kg: ustekinumab 390 mg
- >85 kg: ustekinumab 520 mg

Responders who lost response and had low ustekinumab trough concentrations (<1.4 µg/mL) were eligible to enroll in the **open-label Exposure Optimization Substudy** and dose adjust to q4w (N=12)

IV, intravenous; SC, subcutaneous

R = Randomization

I = Ileocolonoscopy

Baseline Demographics and Clinical Characteristics

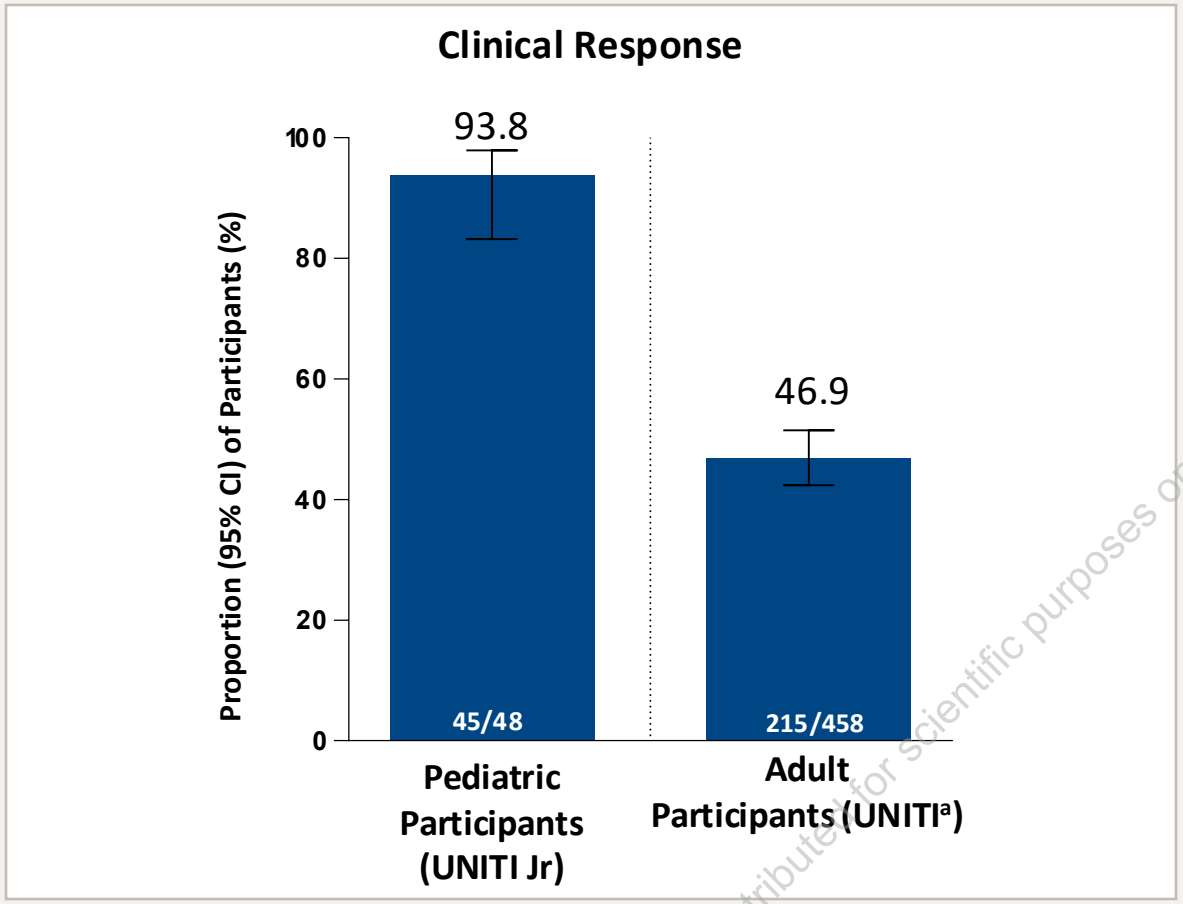
	Ustekinumab IV→SC q12w (N=25)	Ustekinumab IV→SC q8w (N=23)
Demographics		
Age, yrs, mean (SD)	14.7 (1.52)	14.7 (1.76)
Male, n (%)	11 (44.0)	16 (69.6)
White, n (%)	22 (88.0)	22 (95.7)
Weight, kg, median (range)	47.8 (41; 83)	55.4 (42; 85)
Height z-score, median (range)	0.67 (-1.4; 1.5)	0.47 (-1.3; 2.3)
BMI z-score, median (range)	-0.26 (-1.7; 2.6)	0.08 (-1.3; 4.1)
Clinical Characteristics		
Age at diagnosis, yrs, mean (SD)	12.1 (3.11)	12.2 (2.50)
Disease duration, yrs, mean (SD)	2.7 (2.65)	2.6 (1.91)
C-reactive protein, mg/L, median (IQR)	10.70 (5.60; 41.20)	13.10 (2.20; 41.90)
Fecal calprotectin, mg/kg, median (IQR)	1971.0 (1739; 3725.0)	1874.5 (966.0; 3780.0)
PCDAI score, mean (SD)	42.00 (9.043)	41.20 (6.024)
sPCDAI score, mean (SD)	56.0 (12.08)	55.0 (11.58)
CDAI score, mean (SD)	431.22 (121.108)	392.62 (106.482)
SES-CD score, mean (SD)	12.5 (6.33)	12.1 (7.43)

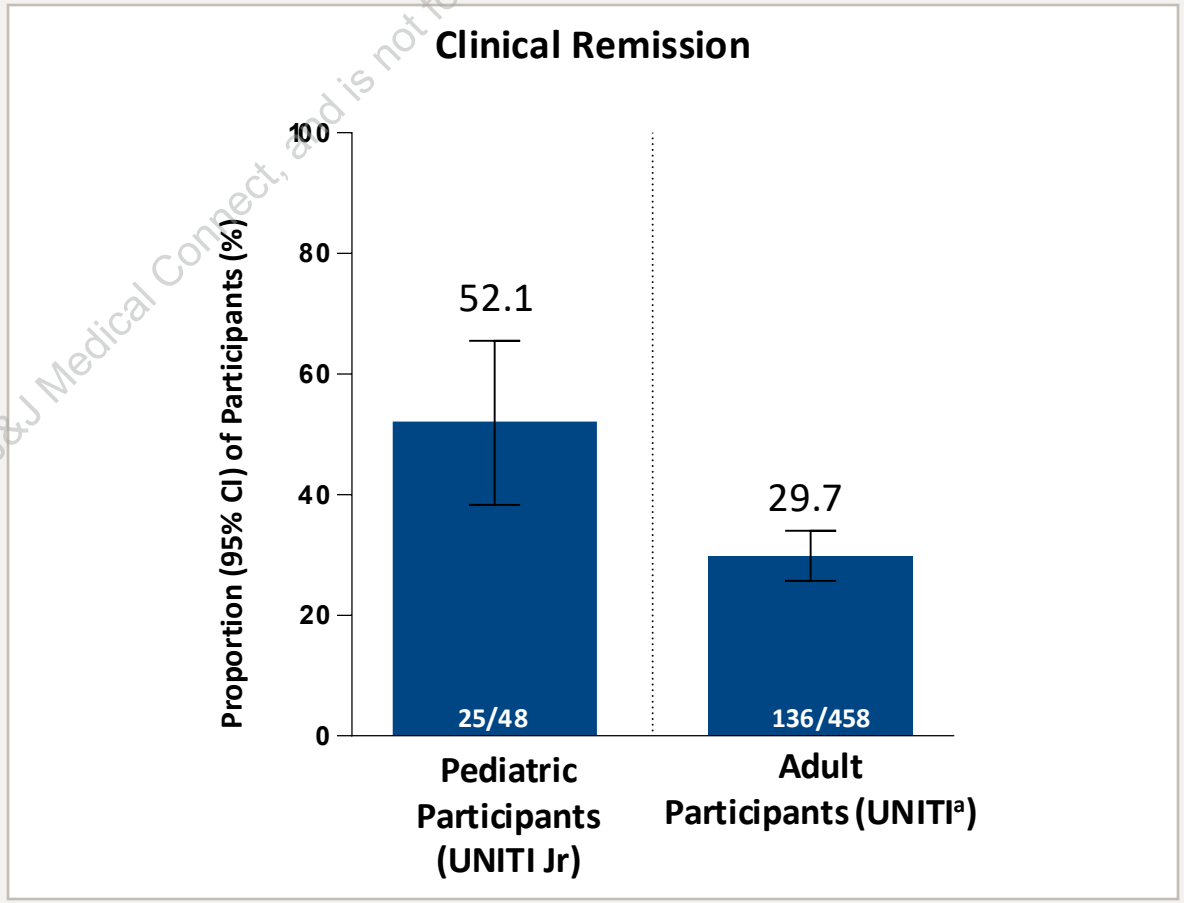
BMI, body mass index; CDAI, Crohn's Disease Activity Index; IQR, interquartile range; PCDAI, Pediatric Crohn's Disease Activity Index; SES-CD, Simple Endoscopic Score for Crohn's Disease; SD, standard deviation; sPCDAI, short Pediatric Crohn's Disease Activity Index

Crohn's Disease-Related Medications and Therapies

	Ustekinumab IV→SC q12w (N=25)	Ustekinumab IV→SC q8w (N=23)
Prior history of biologics, n (%)		
Inadequate response or intolerance to biologics	9 (36.0)	10 (43.5)
Biologic-naïve	15 (60.0)	12 (52.2)
Prior history of exclusive enteral nutrition as primary therapy, n (%)	11 (44.0)	9 (39.1)
Baseline Crohn's disease-related concomitant medications, n (%)	18 (72.0)	17 (73.9)
Corticosteroids	6 (24.0)	8 (34.8)
Immunomodulators	9 (36.0)	9 (39.1)
5-Aminosalicylates (5-ASA)	11 (44.0)	10 (43.5)
Baseline exclusive enteral nutrition, n (%)	2 (8.0)	3 (13.0)

Clinical Response and Clinical Remission at Week 8





Pediatric clinical response: reduction from baseline in the PCDAI score ≥12.5 with total PCDAI score not more than 30

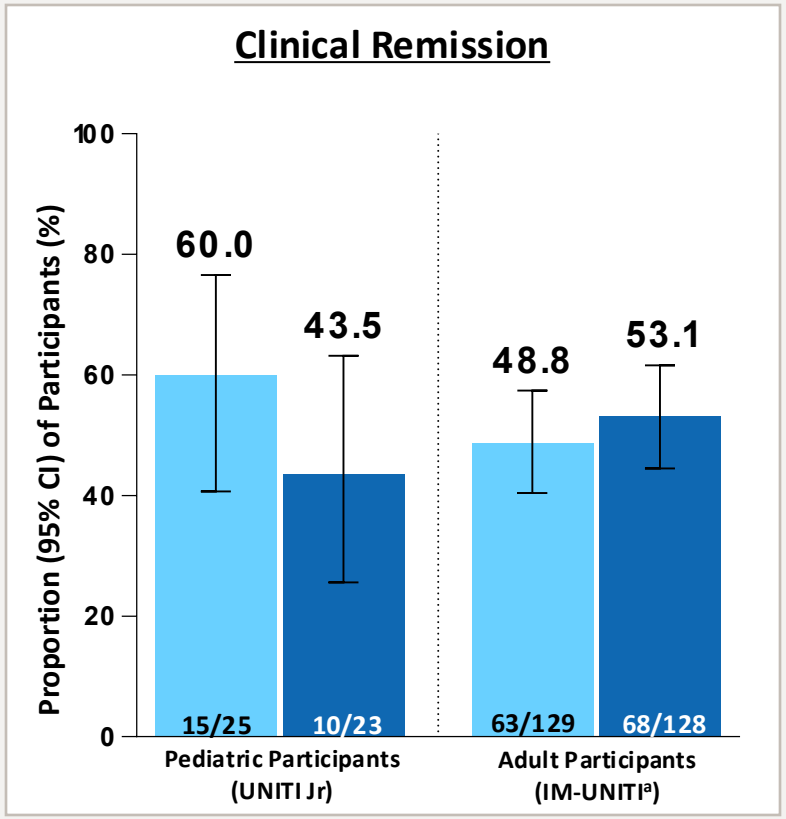
Adult clinical response: reduction from baseline in the CDAI score ≥100 points or total CDAI score not more than 150

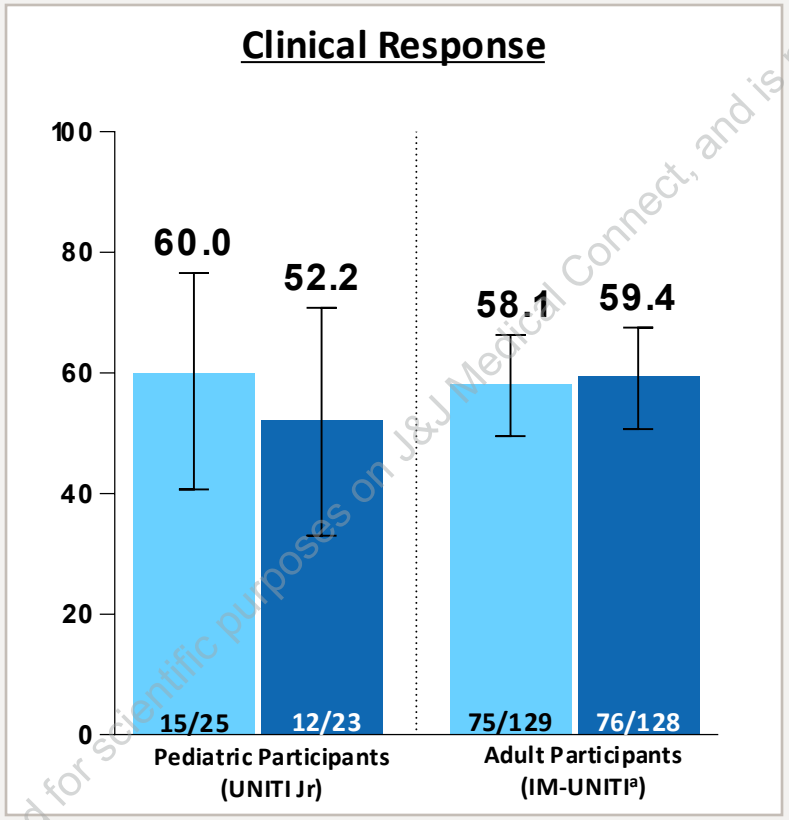
Pediatric clinical remission: PCDAI score ≤10

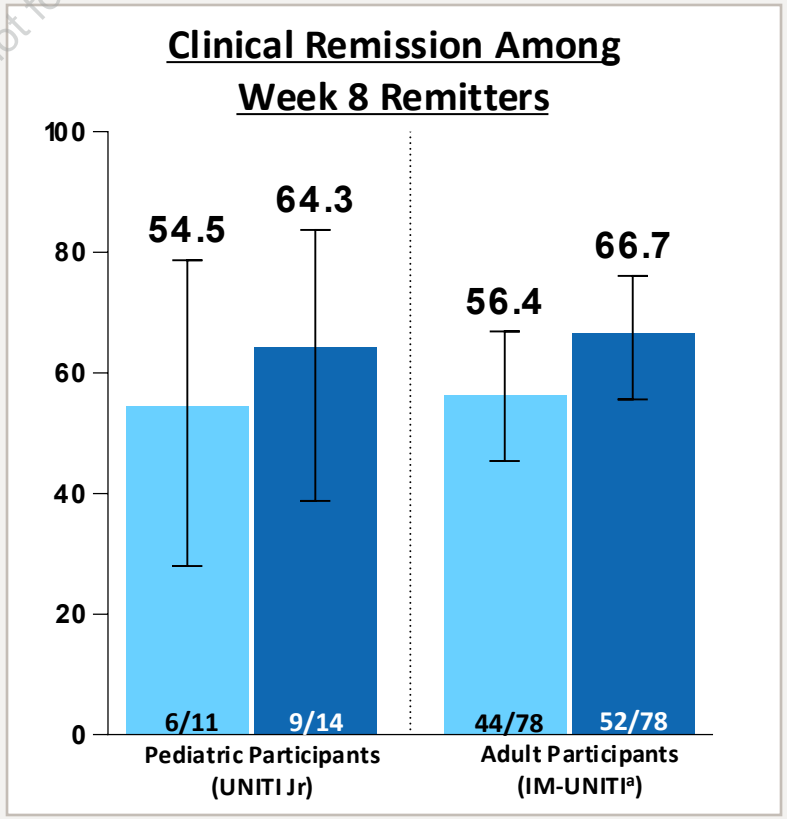
Adult clinical remission: CDAI score <150

[a]Feagan, B. et al. NEJM; 2016

Clinical Outcomes at Week 52







Pediatric clinical remission: PCDAI score ≤10

Clinical response: reduction from baseline in the PCDAI reduction of ≥12.5 with total score of ≤30

Adult clinical remission: CDAI score <150

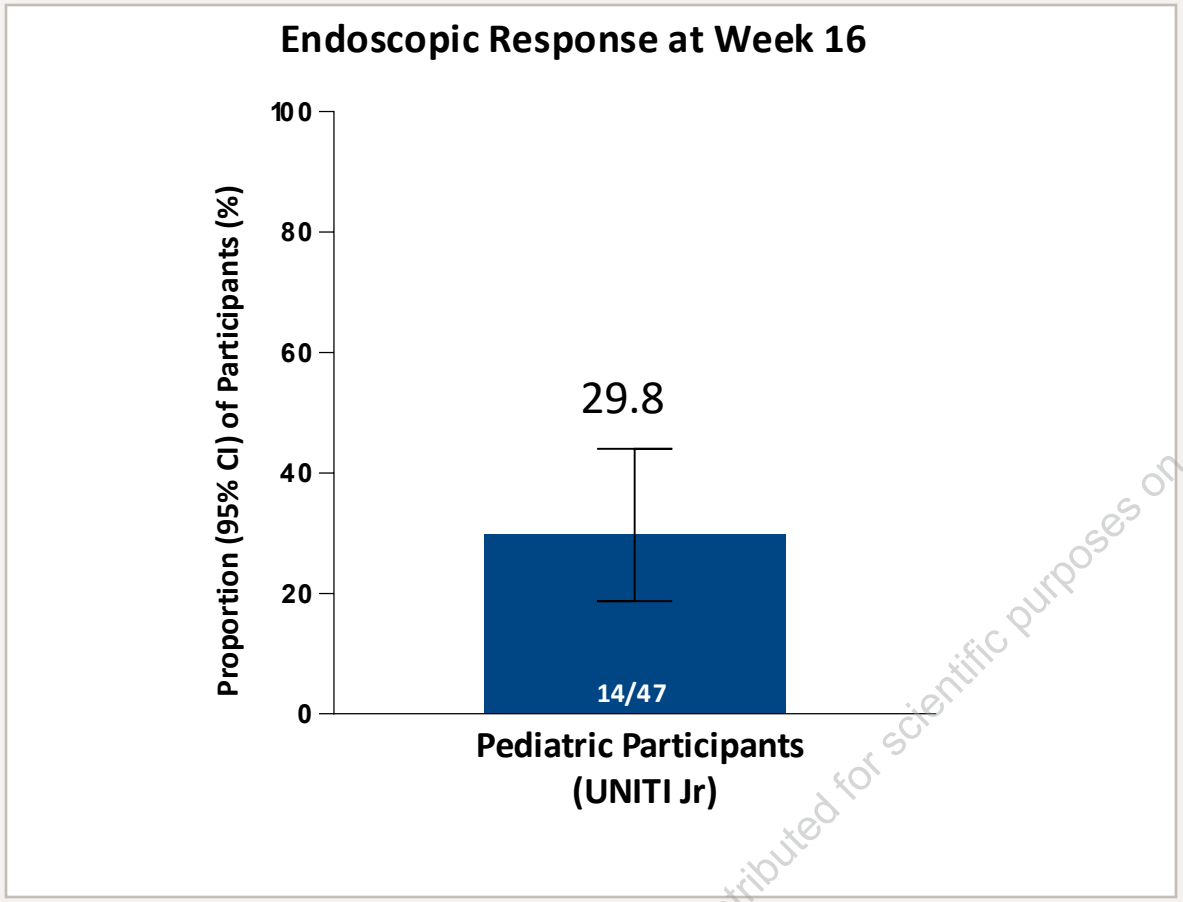
Adult clinical response: reduction from baseline in the CDAI score ≥100 points or total CDAI score not more than 150

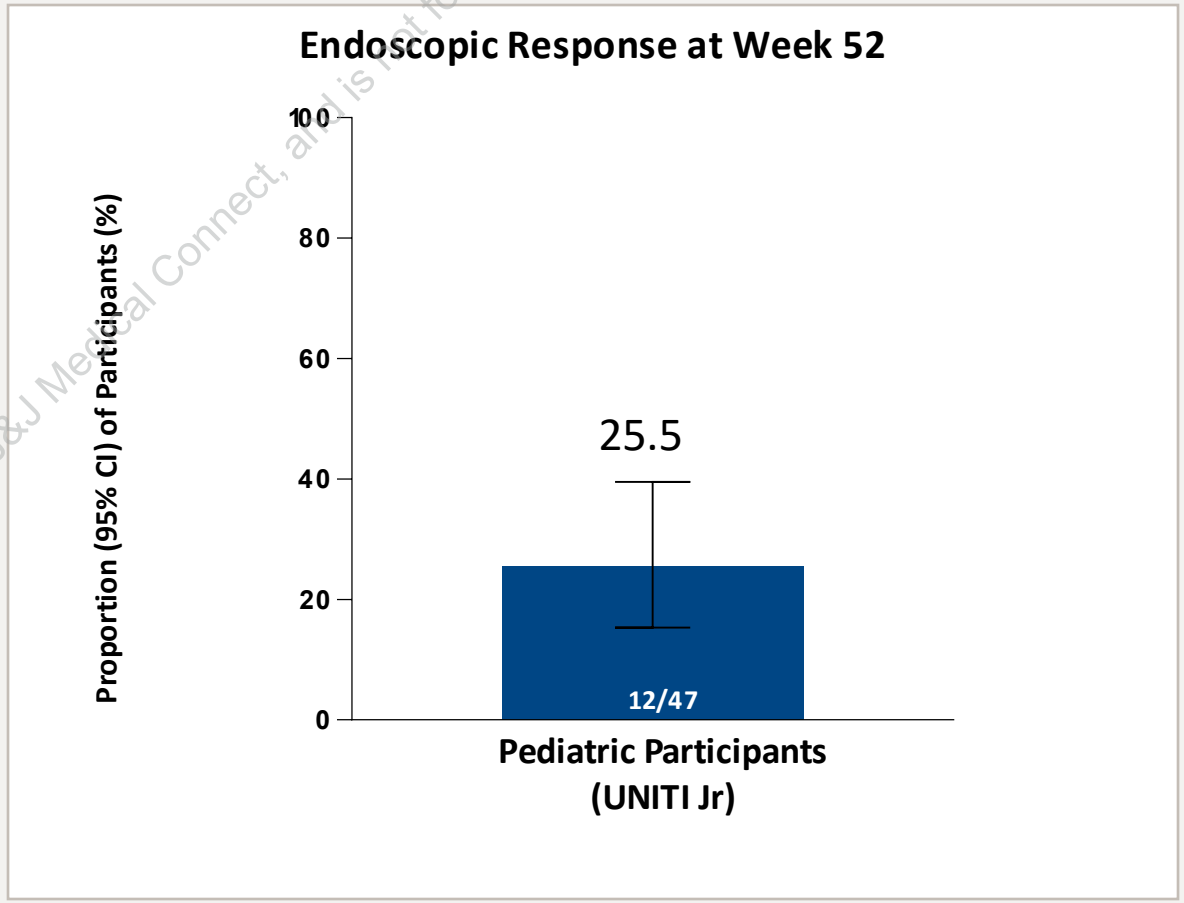
All pediatric participants who were in clinical remission at Week 52 were corticosteroid free

[a]Feagan, B. et al. NEJM; 2016

Ustekinumab SC q12w Ustekinumab SC q8w

Endoscopic Response at Week 16 and Week 52





Pediatric endoscopic response: reduction from baseline in SES-CD score ≥50% or SES-CD score ≤2 in subjects with a baseline SES-CD score of ≥3

Adverse Events From Week 0 Through Week 52

	Ustekinumab IV→SC q12w (N=25)	Ustekinumab IV→SC q8w (N=23)
Average duration of follow-up (weeks)	43.7	47.5
Average number of administrations	7.3	7.8
Participants with 1 or more, n (%):		
Adverse events	23 (92.0)	21 (92.3)
Serious adverse events	5 (20.0)	4 (17.4)
Death	0	0
Adverse events leading to discontinuation	1 (4.0)	1 (4.3)
Infections	18 (72.0)	17 (73.9)
Serious infections	0	0
Infections requiring oral and/or parenteral antimicrobial treatment	3 (12.0)	7 (30.4)
Malignancy	0	0
Active tuberculosis infection	0	0
Opportunistic infections	0	0
Injection-site reactions[a]	0	0

Note: Includes any final safety visit data which occurs prior to the database lock in participants who discontinued study intervention.

[a] Injection-site reaction is any reaction at an SC study intervention injection site that was recorded as an injection-site reaction by the investigator.

Serious Adverse Events

During the Induction Period: 1 participant experienced an Serious Adverse Event (SAE) of nephrolithiasis, with a prior history of nephrolithiasis.

During the maintenance period: 8 participants (16.7%) experienced 1 or more SAE.

SAEs included:

- Crohn's disease exacerbation
- Bloody diarrhea
- Excision of a perianal fistula
- Worsening of gastritis due to Aeromonas infection
- Suicide attempt
- Elevated liver enzymes
- Broken right collarbone
- Syncope

No participants experienced SAEs during the substudy.

Key Takeaways

- Ustekinumab induction and maintenance therapy was effective and safe through 52 weeks in pediatric participants weighing ≥40 kg with moderately to severely active Crohn's disease
- Clinical response and remission rates through Week 52 were consistent with those observed in adult patients with Crohn's disease
- No new safety issues were identified through Week 52. No deaths, malignancy, active tuberculosis, opportunistic infections, or injection-site reactions were reported.

Future Direction

- On March 31, 2025, Stelara was approved in the EU for pediatric Crohn's Disease for children ≥40 kg based upon this interim data, with supportive real-world evidence from the ImproveCareNow network
- The UNITI Jr study has concluded, with data collection complete for all pediatric patients aged 2 to <18 years who have moderately to severely active Crohn's disease (including children weighing <40 kg)
- Regulatory submissions to FDA and EMA for label extensions are planned

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