Endoscopic and Histologic Results From the UNITI Jr Study of Ustekinumab in Pediatric Crohn's Disease

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Key Takeaways

- **Endoscopic, histologic, and histo-endoscopic response and remission were induced with ustekinumab treatment and maintained with maintenance treatment**
- **Endoscopic and histo-endoscopic remission rates at Week 52 were comparable when analyzed by dose group and weight, with overlapping CIs; however, the sample sizes were small**
- **Although these histology and combined histo-endoscopic measures have not yet been validated for pediatric CD, these data suggest that treatment with ustekinumab can improve endoscopic and histologic outcomes in pediatric patients with moderately to severely active CD**

Background

Endoscopic and histological healing are treatment targets in adults with inflammatory bowel disease (IBD), but more research is needed to identify validated outcomes for endoscopic and histologic response and remission in pediatric patients[1]

UNITI Jr is a study evaluating open-label intravenous (IV) ustekinumab induction followed by randomized, double-blind subcutaneous (SC) every 8 weeks (q8w) or every 12 weeks (q12w) maintenance therapy in pediatric patients (≥2 to <18 years) with moderately to severely active Crohn's disease (CD)

Objectives

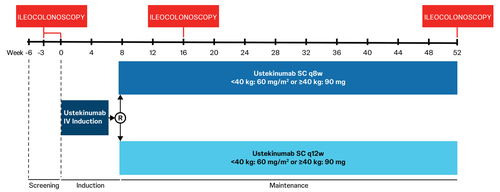
This study evaluated the efficacy of ustekinumab for the induction and maintenance of endoscopic healing and histological response in pediatric patients with moderately to severely active CD

Methods

UNITI Jr – Study Design

Key inclusion criteria

- ✓ Pediatric patients ≥2 to <18 years old with a 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)
- ✓ Ileocolonoscopic ulceration or increased CRP (≥3.0 mg/L) or 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

- UNITI Jr was a Phase 3, multicenter, interventional study consisting of an open-label induction period with a single IV ustekinumab induction dose followed by a maintenance period with a randomized, double-blind, parallel-group, 2-arm study design
- Patients underwent 3 ileocolonoscopies at Screening, Week 16, and Week 52

***6-MP**=6-mercaptopurine, **AZA**=azathioprine, **CRP**=C-reactive protein, **MTX**=methotrexate, **PCDAI**=Pediatric Crohn's Disease Activity Index, **TNFα**=tumor necrosis factor alpha. Ⓡ=Randomization*

Analysis Methods

- Efficacy endpoints were evaluated at Week 16 in randomized patients and at Week 52 in induction clinical responders, defined as a PCDAI reduction from baseline of ≥12.5 points with a total PCDAI score not more than 30 at induction Week 8
- Intercurrent Events (ICEs)
  - Patients who had a CD-related surgery (with the exception of percutaneous drainage of an abscess or seton placement) thought to be a result of lack of efficacy of study intervention, discontinued study intervention due to lack of efficacy or an adverse event (AE) of worsening of CD, had prohibited changes in CD medications, or discontinued study intervention due to reasons other than worsening of CD or COVID-19 infection were considered as a nonresponder for binary endpoints after this event
  - Patient who discontinued study intervention due to COVID-19-related reasons (excluding COVID-19 infections) were considered to have missing data after the event occurred

Statistical Considerations

- Summary statistics were computed
- No formal statistical testing was performed but confidence intervals (CIs) were compared
- Both observed data and ICE data are reported
- For observed data: All observed histologic response/remission data were included. ICE strategies were not used. Patients who had missing histologic response/remission data were not included in the summaries.

Endoscopic and Histologic Outcome Definitions[a]

Outcome	Definition
SES-CD endoscopic response	Reduction in the SES-CD score of ≥50% or SES-CD score ≤2 in patients with a baseline SES-CD score of ≥3
SES-CD endoscopic remission	SES-CD score ≤2 in patients with a baseline SES-CD score of ≥3
RHI histologic response	≥50% reduction in RHI score from baseline or a score ≤3 with subscores of lamina propria neutrophils and neutrophils in epithelium must be equal to 0, with no ulcers or erosions
RHI histologic remission	RHI score ≤3 with subscores of lamina propria neutrophils, and neutrophils in epithelium must be equal to 0, with no ulcers or erosions
RHI histo-endoscopic response	A combination of histologic response and endoscopic response (described above), among patients with histologic disease at baseline based on RHI score
RHI histo-endoscopic remission	A combination of histologic remission and endoscopic remission (described above), among patients with histologic disease at baseline based on RHI score

*[a]Endoscopic and histologic response and remission (using SES-CD scores RHI indices [derived from Geboes]) were evaluated by blinded central readers at Week 16 in randomized patients and at Week 52 in induction responders. **RHI**=Riboarta Histopathology Index, **SES-CD**=Simple Endoscopic Score for Crohn's Disease.*

Results

Baseline Characteristics

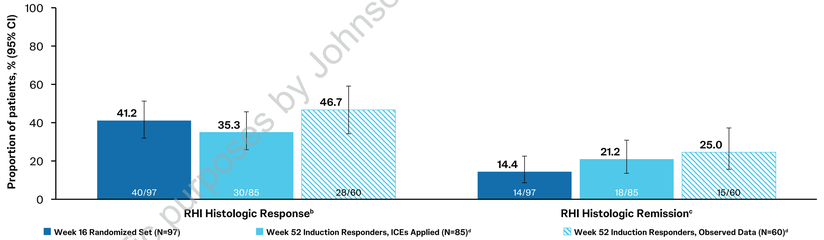
	TOTAL (N = 97[a])
Demographics	
Age, yrs, median (IQR)	14.0 (12.0, 16.0)
Female	40.2%
Race, Asian/Black/White	9.3/3.1/87.6%
BMI, kg/m²	18.5 (3.6)
Weight <40 kg, n	27
Disease Characteristics	
PCDAI Score, median (IQR)	40.0 (35.0, 45.0)
SES-CD Score, median (IQR)	12.0 (6.5, 18.5)
SES-CD ≥3, n	94
Location, n	
Ileal only	9
Colonic only	17
Ileocolonic	57
RHI histologic disease activity	82/95, 86.3%

*[a]Combined q8w and q12w groups. **BMI**=body mass index, **IQR**=interquartile range.*

Patient Disposition

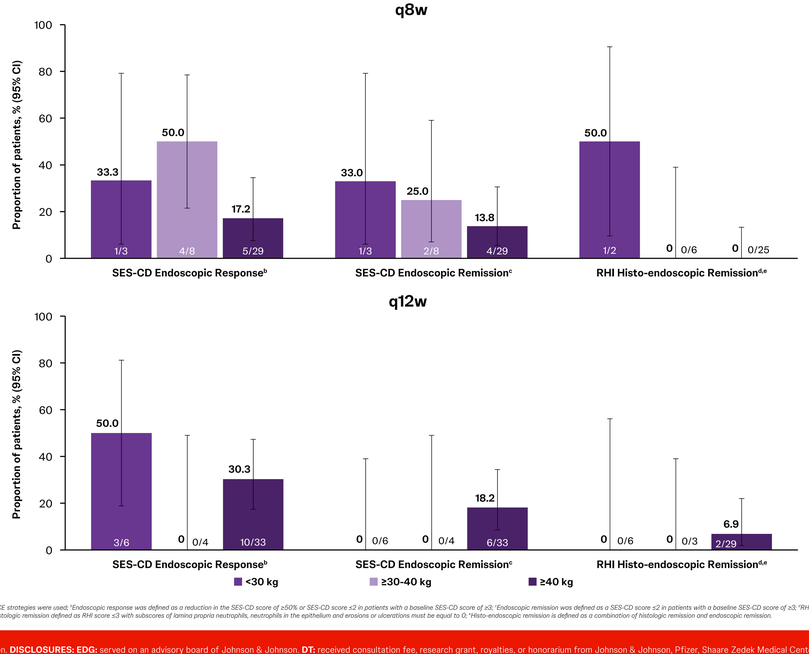
- Overall, 101 patients enrolled and received open-label IV ustekinumab induction dose
- 97/101 patients were randomized into two treatment groups (q12w and q8w) for maintenance therapy
- 95 patients completed baseline ileocolonoscopy with biopsy
- 94 patients had baseline SES-CD ≥3
- 85/101 patients (84.2%) achieved clinical response to induction therapy at Week 8

Histologic response and remission were induced and maintained with ustekinumab maintenance treatment[a]



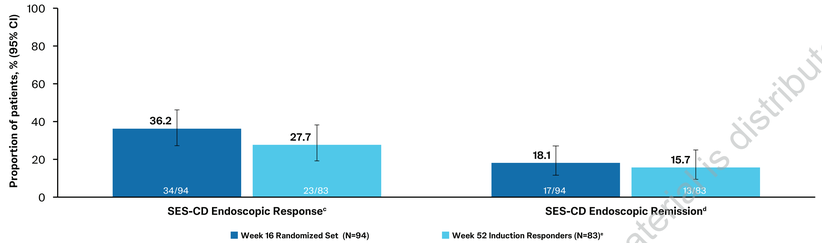
[a]Combined q8w and q12w maintenance groups; [b]Histologic response was defined as ≥50% reduction in RHI score from baseline or a score ≤3 with subscores of lamina propria neutrophils and neutrophils in epithelium must be equal to 0, with no ulcers or erosions; [c]Histologic remission was defined as RHI score ≤3 with subscores of lamina propria neutrophils, neutrophils in the epithelium and erosions or ulcerations must be equal to 0; [d]Achieved clinical response based on reduction from baseline in the PCDAI score of ≥12.5 points with a total PCDAI score not more than 30 at induction Week 8.

At Week 52, endoscopic and histo-endoscopic remission rates were comparable when analyzed by dose group and weight[a]



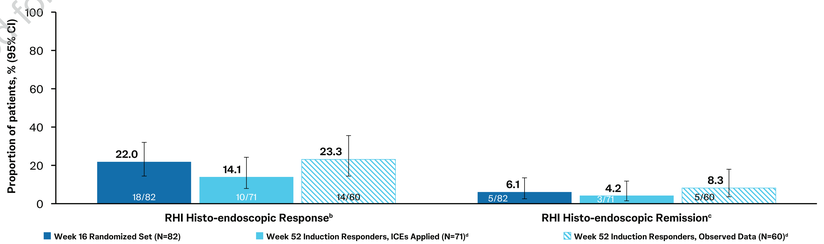
[a]ICE strategies were used; [b]Endoscopic response was defined as a reduction in the SES-CD score of ≥50% or SES-CD score ≤2 in patients with a baseline SES-CD score of ≥3; [c]Endoscopic remission was defined as a SES-CD score ≤2 in patients with a baseline SES-CD score of ≥3; [d]RHI histologic remission defined as RHI score ≤3 with subscores of lamina propria neutrophils, neutrophils in the epithelium and erosions or ulcerations must be equal to 0; [e]Histo-endoscopic remission is defined as a combination of histologic remission and endoscopic remission, among patients with histologic disease at baseline based on RHI score.

Endoscopic response and remission were induced and maintained with ustekinumab maintenance treatment[a,b]



[a]ICE strategies were used; [b]Combined q8w and q12w maintenance groups; [c]Endoscopic response was defined as a reduction in the SES-CD score of ≥50% or SES-CD score ≤2 in patients with a baseline SES-CD score of ≥3; [d]Endoscopic remission was defined as a SES-CD score ≤2 in patients with a baseline SES-CD score of ≥3; [e]Achieved clinical response based on reduction from baseline in the PCDAI score of ≥12.5 points with a total PCDAI score not more than 30 at induction Week 8.

Histo-endoscopic response and remission were induced with ustekinumab treatment[a]



[a]Combined q8w and q12w maintenance groups; [b]Histo-endoscopic response was defined as a combination of histologic response and endoscopic response, among patients with histologic disease at baseline based on RHI score; [c]Histo-endoscopic remission is defined as a combination of histologic remission and endoscopic remission, among patients with histologic disease at baseline based on RHI score; [d]Achieved clinical response based on reduction from baseline in the PCDAI score of ≥12.5 points with a total PCDAI score not more than 30 at induction Week 8.

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