Assessment of IBD-Specific Quality of Life (IMPACT-III) Symptoms After Treatment With Ustekinumab in Paediatric Crohn's Disease

Robert Fieo[1], Sheri Volger[2], Richard Strauss[2], Anne M. Griffiths[3*], Lilianne Kim[4]

[1]Division of Patient-Reported Outcomes, Johnson & Johnson, Raritan, NJ, USA; [2]Department of Immunology, Johnson & Johnson, Spring House, PA, USA; [3]Division of Gastroenterology, The Hospital for Sick Children, University of Toronto, Toronto, Canada; [4]Statistics and Decision Sciences, Johnson & Johnson, Spring House, PA, USA

Presenting Author

P0548

Key Takeaways

- **Ustekinumab-treated paediatric participants with moderately-to-severely active CD experienced clinically meaningful improvements in HRQoL as measured by IMPACT-III**
- **Symptom-related domains within IMPACT-III were more responsive than other domains measuring concepts such as emotional status, social functioning, and body image**
- **The inclusion of fatigue-related content into paediatric IBD symptom scales does not appear to diminish responsiveness to change**

Background

- Ustekinumab is an IL–12/23p40 subunit inhibitor indicated for Crohn's disease (CD), ulcerative colitis (UC), plaque psoriasis (Ps), and psoriatic arthritis (PsA) in adults, and Ps and PsA in paediatric patients ≥ 6 years in the United States[1]
  - Ustekinumab is also indicated for CD in paediatric patients weighing ≥40 kg in Europe[2]
- The safety and efficacy of ustekinumab was assessed in the UNITI Jr study in paediatric participants with moderately-to-severely active CD[3]
  - Open-label intravenous (IV) ustekinumab induction, followed by randomized, double-blind subcutaneous (SC) maintenance therapy ([ustekinumab every 12 weeks (Q12W) or every 8 weeks (Q8W)]
- Assessment of CD-related health-related quality of life (HRQoL) was a predefined tertiary endpoint in UNITI Jr
- The symptoms of CD can have a profound effect on HRQoL of patients with CD (**Figure 1**)

Figure 1A. Most Important Concerns of Adolescents (13–17 years of age) with CD (N=66)[4*]

Treatment	Emotional	Bowel	Functional/social
Taking medication	Having flareups	GI pain/cramps	Not doing things
Needing surgery	Chronicity	Food limitations due to symptoms	Too tired for preferred activities
Body Image	Future health problems	Bloody stools	Missing school
Weight	Unfairness of IBD	Loose/frequent stools	Impaired ability to play sports
Height	Frustration	Flatulence	Travel difficulties
Physical appearance	Not improving	Awareness of bathroom locations away from home	Public bathrooms
Systemic	Anger		
Tired			
Fatigue			

*Items represent concerns, worries, or negative feelings.
***CD**=Crohn's disease, **IBD**=inflammatory bowel disease, **N**=population size.*

Figure 1B. Differences in Concerns Between Adolescents (13-17 years of age; N=66) and Children (≤ 12 years of age; N=20) with CD[4*]

More Important to Adolescents	More Important to Children
Impaired ability to play sports	Hospital admission
Stress	Food limitations
Bad mood	Missing fun
Misunderstood	Social stigma
	Public bathrooms
	Nausea/being sick to stomach
	Bloody stools

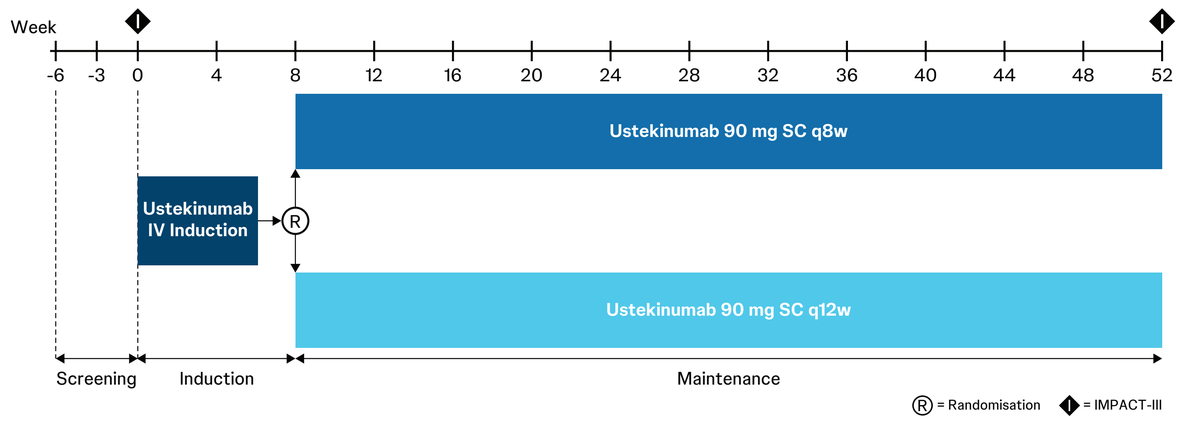
Objective

To evaluate the effect of ustekinumab on CD-related HRQoL in paediatric participants enrolled in UNITI Jr using the IMPACT-III assessment, with an emphasis on the symptom facets of the "Well-being" subdomain

Methods

- Study design is shown in **Figure 2**

Figure 2. UNITI Jr (NCT04673357) Study Design



Weight-tiered IV 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 8-week open-label induction period with a single IV ustekinumab induction dose followed by a 44-week maintenance period with a randomised, double-blind, parallel-group, 2-arm study design.
- The IMPACT-III questionnaire was self-administered at Week 0 (Induction baseline) and Week 52 (Maintenance Week 44)

Key inclusion criteria
- ✓Pediatric participants <18 years old with a Paediatric 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)
- ✓Ileocolonoscopic ulceration or increased C-reactive protein (≥3.0 mg/L) or calprotectin (≥250 µg/g)

***AZA**=azathioprine, **IV**=intravenous, **6-MP**=6-mercaptopurine, **MTX**=methotrexate, **PCDAI**=Paediatric Crohn's Disease Activity Index, **Q8W**=every 8 weeks, **Q12W**=every 12 weeks, **SC**=subcutaneous, **TNFα**=tumor necrosis factor alpha.*

IMPACT-III General Information

- Measure of disease-specific HRQoL[5-8]
- Applicable for children/adolescents with inflammatory bowel disease (IBD) aged ≥9 years[5,6,8]

Total scores

- Questions scored on a 5-point Likert scale (1 to 5)[8]
- Total scores represent summed responses from 35 questions over 6 domains (range: 35-175)[7]
  - Higher score represents better HRQoL[7]

Table 1. IMPACT-III Domains

	Items, n
IMPACT-III Domains (original 6-domains)[5,6]	
Bowel symptoms	7
Systemic symptoms	3
Emotional functioning	7
Social functioning	12
Body image	3
Tests and treatments	3
IMPACT-III (revised 4-factor model)[8]	
Well-being	12
Facets of Well-being domain (impacts)	5
Facets of Well-being domain (symptoms)	7
Modified Well-being symptom facets	6
Social	11
Emotional	7
Body image	4

*Key stakeholders involved in HRQoL validation have previously endorsed delineating HRQoL content into broad categories of "symptoms" vs. "impacts". Based on face validity, we classified 5 of 12 Well-being items as "impacts" of CD and 7 items as "symptoms" of CD. To align with regulatory recommendations (ie, avoiding redundant/overlapping patient-reported outcome content across trial endpoints), we removed the IMPACT-III "stomach hurting" item, as this item was clearly overlapping with content from the PCDAI endpoint. Thus, the final modified "Well-being Symptom Facets" endpoint comprised 6 items. **n**=number.*

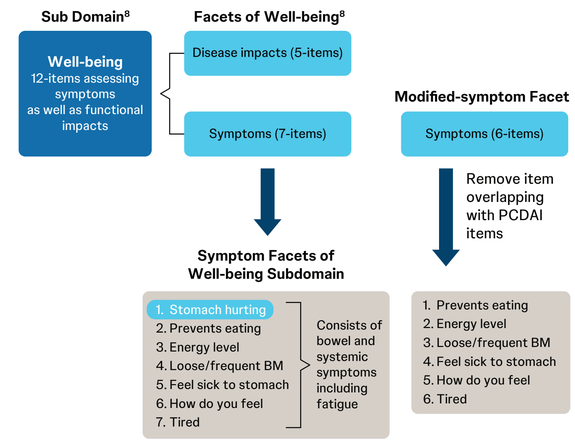
Domains (Table 1)

- In 2020, the original 6-domain version was updated to 4-domains while the questions were unchanged[8] (**Table 1**)
- **Transformed Scores:** Likert scores were linearly transformed to a range of 1-100 to obtain transformed total and domain scores[8]

Distribution-based Methodology

- 0.5 standard deviation (SD) is proposed as reasonable minimum threshold for establishing clinically meaningful improvement in HRQoL concepts[9,10]
- The Well-being subdomain and associated facets are shown in **Figure 3**

Figure 3. IMPACT-III Well-being Subdomain



***BM**=bowel movement, **PCDAI**=Paediatric Crohn's Disease Activity Index.*

- In UNITI Jr, the IMPACT-III was self-administered by participants ≥ 10 years of age at Week (W)0 and W52 (home or study site) with a 2-week recall period

Results

UNITI Jr Paediatric Population

- Demographics and disease characteristics at baseline are shown in **Table 2**

Table 2. Baseline Demographics and Characteristics (Full Analysis Set)

Baseline Characteristics	Total (N=101)*
Demographics	
Age, median, yrs	14.0
IQR range	12.0; 15.0
Female, n (%)	41 (40.6%)
Race, Asian/Black/White/Not reported, %	8.9/3.0/87.1/1.0%
BMI Z score¥, median	-0.46
IQR range	-0.84; 0.35
Weight <40 kg, n (%)	29 (28.7%)
Disease Characteristics	
PCDAI Score, median (n=101)	40.0
IQR range	35.0; 45.0
SES-CD Score, median (n=100)	12.0
IQR range	6.5; 18.5
Location, n (%) (n=99)	
Ileal only	11 (11.1%)
Colonic only	18 (18.2%)
Ileocolonic	58 (58.6%)
Proximal small intestine, stomach, and/or oesophagus	39 (39.4%)
Perianal	33 (33.3%)

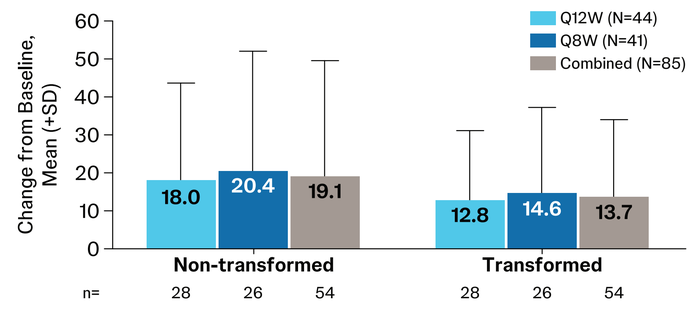
- At baseline, median (IQR) IMPACT total score was 101.0 (84.0, 123.0), n=77 of 101 participants

Four participants received induction therapy but were not randomized. ¥age and sex-specific. **BMI=body mass index, **CD**=Crohn's disease, **IQR**=interquartile range, **n**=number in group, **N**=population size, **PCDAI**=Paediatric Crohn's Disease Activity Index, **SES-CD**=Simple Endoscopic Score for Crohn's Disease, **SD**=standard deviation.*

IMPACT-III Total Score

- At W52, ustekinumab-treated participants reported improved HRQoL as measured by IMPACT-III total scores (**Figure 4**):
  - Mean (SD) change from baseline = 19.1±27.99 (non-transformed)
  - Mean (SD) change from baseline = 13.7±19.99 (transformed)
- HRQoL was similar in both dose groups (**Figure 4**)
- Because stakeholders identified 0.5 SD as a reasonable minimum threshold for establishing clinically meaningful improvement in HRQoL concepts[9,10] the improvement in IMPACT-III observed here is considered clinically meaningful

Figure 4. IMPACT-III Total Score



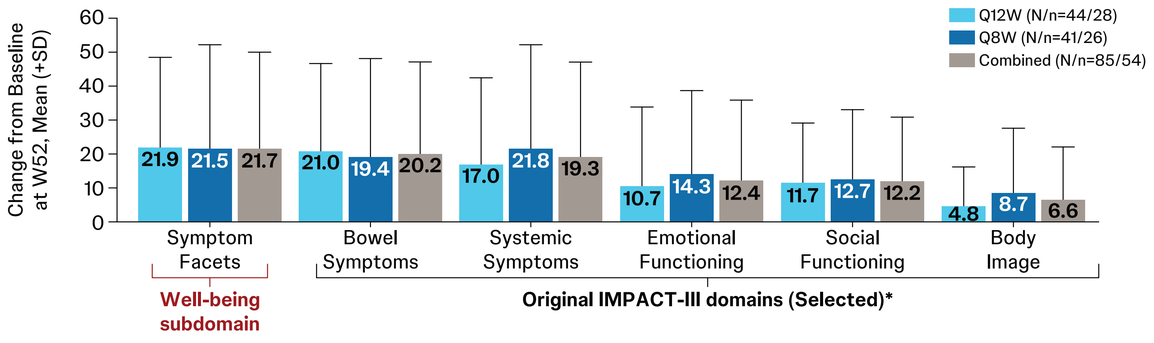
***n**=number in group, **N**=population size, **Q8W**=every 8 weeks, **Q12W**=every 12 weeks, **SD**=standard deviation.*

***Notes:** Baseline was defined as the last observation prior to or at the time of the first study intervention.*
ICEs included: (1) Participants who had a CD-related surgery thought to be a result of lack of efficacy of study intervention, (2) Discontinued study intervention due to lack of efficacy or an AE of worsening of CD, (3) Had prohibited changes in CD medications, (4) Used rescue medication for treatment of LOR after Week 16 for responders and Week 24 for delayed responders, (5) Were eligible for dose adjustment after Week 16, (6) Discontinued study intervention due to COVID-19 related reasons, (7) Discontinued study intervention due to reasons other than ICEs 2 or 6.
*ICEs strategies: Participants that had ICEs 1-5, and 7 prior to a visit were considered to have had no CFB for that endpoint at that visit and subsequent visit. Participants with ICE 6 had their data assumed missing after the ICE 6 occurred. **AE**=adverse event, **CD**=Crohn's disease, **ICE**=intercurrent event, **LOR**=loss of response.*

IMPACT-III Domains and Subdomains

- At W52, ustekinumab-treated participants reported improved CD-related HRQoL concepts (**Figure 5**)
  - Mean change from baseline domains/subdomains exceeded the 0.5 SD threshold for clinically meaningful improvement
- Mean change from baseline (improvement) in the 6-item Symptom Facets of the "Well-being" subdomain was 21.7 (SD 28.32), which exceeded the 0.5 SD threshold
- Symptom-based subdomains ("Well-being" symptom facets, "Bowel Symptoms," and fatigue-related "Systemic Symptoms") thought to be more proximal to IBD were most responsive to treatment, followed by subdomains representing distal impacts of IBD (**Figure 5**)
- Symptom-related concepts were more sensitive to change than emotional status, social function, and body image (**Figure 5**)

Figure 5. IMPACT-III Domains and Subdomains



***N**=population size, **n**=number in group, **Q8W**=every 8 weeks, **Q12W**=every 12 weeks, **SD**=standard deviation, **W**=week.*

***Notes:** Baseline was defined as the last observation prior to or at the time of the first study intervention. *Tests and Treatments domain data were excluded from this figure because the content is somewhat distinct from other IMPACT-III domains broadly grouped into IBD symptoms and impacts and may not be commonly reported across HRQoL metrics. However, we acknowledge that this domain captures important health concepts relevant to patients and its inclusion in the broader assessment process serves to enhance the comprehensiveness of HRQoL assessment.*
ICEs included: (1) Participants who had a CD-related surgery thought to be a result of lack of efficacy of study intervention, (2) Discontinued study intervention due to lack of efficacy or an AE of worsening of CD, (3) Had prohibited changes in CD medications, (4) Used rescue medication for treatment of LOR after Week 16 for responders and Week 24 for delayed responders, (5) Were eligible for dose adjustment after Week 16, (6) Discontinued study intervention due to COVID-19 related reasons, (7) Discontinued study intervention due to reasons other than ICEs 2 or 6.
*ICEs strategies: Participants that had ICEs 1-5, and 7 prior to a visit are considered to have no change from baseline for that endpoint at that visit and subsequent visit. Participants with ICE 6 had their data assumed missing after the ICE 6 occurred. **AE**=adverse event, **CD**=Crohn's disease, **ICE**=intercurrent event, **LOR**=loss of response.*

PRESENTED AT: 21st Congress of ECCO, February 18–21, 2026, Stockholm, Sweden. **REFERENCES: 1.** STELARA® (ustekinumab). Prescribing Information, Johnson & Johnson and its affiliates, 2025; https://www.janssenlabels.com/package-insert/product-monograph/prescribing-information/STELARA-pi.pdf. Accessed September 10, 2025. **2.** STELARA (ustekinumab). European Medicines Agency. Stelara: EPAR-Product Information, 2025; https://www.ema.europa.eu/en/documents/product-information/stelara-epar-product-information_en.pdf. Accessed September 10, 2025. **3.** ClinicalTrials.gov; https://www.clinicaltrials.gov/study/NCT04673357. Accessed September 10, 2025. **4.** Griffiths AM, et al. *J Pediatr Gastroenterol Nutr.* 1999;28:S46–S52. **5.** Otley AR, et al. *J Pediatr Gastroenterol Nutr.* 2002;35(4):557–563. **6.** Otley AR, et al. *Inflamm Bowel Dis.* 2006;12(8):684–691. **7.** Otley AR, et al. *J Pediatr Gastroenterol Nutr* 2006;43(Suppl 2):S49. **8.** Grant A, et al. *J Pediatr Gastroenterol Nutr* 2020;71(4):494-500. **9.** Homco J, et al. *J Patient Cent Res Rev.* 2019;6(2):135–147. **10.** Norman GR, et al. *Med Care.* 2003;41:582–592. **ACKNOWLEDGMENTS:** Medical writing support was provided by Lori Kornberg, PhD (System One) and Doyel Mitra, PhD, CMPP (Johnson & Johnson) under the direction of the authors in accordance with Good Publication Practice guidelines (*Ann Intern Med.* 2022;175:1298–1304). The poster layout was provided by Amit Kavle from SIRO Medical Writing Pvt. Ltd. (funded by Johnson & Johnson). This presentation was sponsored by Johnson & Johnson. **DISCLOSURES: RF, RS, LK, and SV:** Employees of Johnson & Johnson; may hold stock/stock options in Johnson & Johnson. **AMG:** In the last 3 years, received consultation fee, research grant, royalties or honorarium from AbbVie, Alfasigma, Janssen, Lilly, Merck, Pfizer, Shaare Zedek Medical Centre, SickKids Hospital, and Takeda.