

Assessment of Inflammatory Bowel Disease-Specific Quality of Life (IMPACT-III) Symptoms After Treatment With Ustekinumab in Pediatric Ulcerative Colitis

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Background

- Ustekinumab is a fully human IL-12 and IL-23 antagonist indicated for the treatment of moderately to severely active ulcerative colitis (UC) in adults and children ≥2 years of age^{1,2}
- The symptoms of UC can impair the quality of a child's life
- In pediatric patients with UC, restoration and normalization of health-related quality of life (HRQoL) is a recommended long-term treatment target
- Assessment of HRQoL in pediatric UC was a predefined tertiary endpoint in UNIFI Jr

Objectives

The aim of this study was to examine the effects of ustekinumab treatment on HRQoL in pediatric patients with UC

- To evaluate the effect of ustekinumab on UC-related HRQoL in UNIFI Jr using the IMPACT-III questionnaire
- To explore the responsiveness to change for individual IMPACT-III variables, including a newly proposed domain structure

Methods

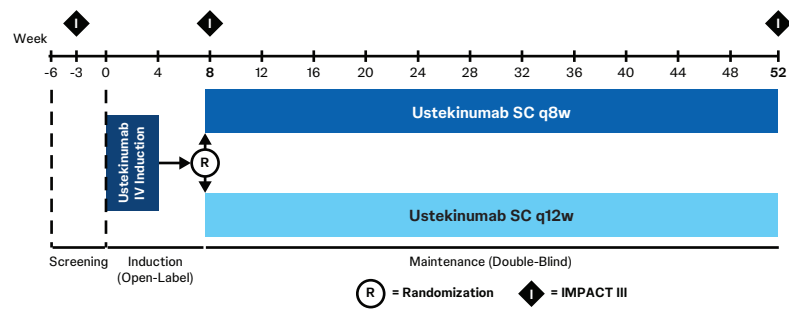
UNIFI Jr – Study Design

IMPACT-III questionnaire

Participants ≥10 years of age self-administered the IMPACT-III at home using electronic patient reported outcome at Week 0 (Baseline), Week 8 (end of induction) and Week 52 (Maintenance Week 44) with a 2-week recall period

Key inclusion criteria:

- Age 2 to <18 years
- Weight ≥10 kg
- Moderately to severely active UC³
- Inadequate response or intolerant to conventional/biologic therapy or corticosteroid-dependent



Weight-tiered ustekinumab dosing

- IV induction:**
- <40 kg: 250 mg/m²
 - ≥40 to <55 kg: 260 mg
 - >55 to <85 kg: 390 mg
 - >85 kg: 520 mg
- SC maintenance:**
- <40 kg: 60 mg/m²
 - ≥40 kg: 90 mg

IMPACT-III

- Measure of disease-specific HRQoL³⁻⁶ applicable for children/adolescents with inflammatory bowel disease (IBD) aged ≥9 years³⁻⁶
- Development included item generation and item reduction based on patient reporting and physician expert opinion^{3,6}
- Questions scored on a 5-point Likert scale (1 to 5)^{5,6}
 - Total scores represent summed responses from 35 questions over 6 domains (range: 35-175)
 - Higher scores indicate better HRQoL⁴⁻⁶
- The efficacy endpoint was mean change from baseline in raw, transformed, and subdomain scores through Week 52

IMPACT-III (6 Domains) ^{3,4}	Items, n
Bowel Symptoms	7
Systemic Symptoms	3
Emotional Functioning	7
Social Functioning	12
Body Image	3
Tests and Treatments	3

Revised IMPACT-III

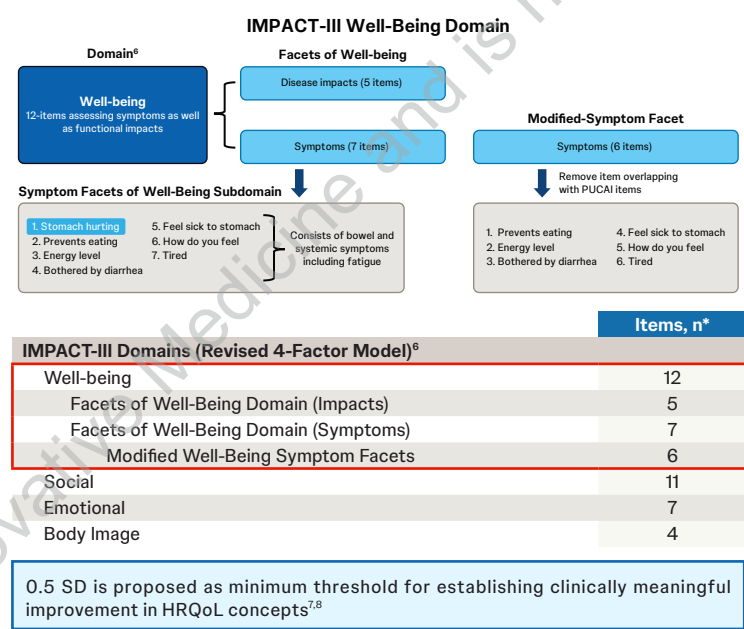
- In 2020, the 6-domain structure was revised to a 4-factor domain structure based on a large pool of pediatric IBD patients with diverse age, sex distribution, disease type, treatments, and disease activity; questions were unchanged⁴
- The revised 4-factor model was tested to further explicate IMPACT-III measurement properties, i.e., structural validity and scoring models
 - The Well-being subdomain consists of questions related to overall daily functioning and disease symptoms

IMPACT-III (Original 6 Domains) ^{3,4}	Items, n
Bowel Symptoms	7
Systemic Symptoms	3
Emotional Functioning	7
Social Functioning	12
Body Image	3
Tests and Treatments	3

IMPACT-III Domains (Revised 4-Factor Model) ⁶	Items, n*
Well-being	12
Social	11
Emotional	7
Body Image	4

Likert scores were linearly transformed to a range of 1-100 to obtain transformed total and domain scores⁶

Revised IMPACT-III: Modified Well-Being Symptom Facets



*The 4-factor model retained all 35 items from the original model, but 1 item (abdominal pain) was excluded from the domain structure. n=number, PUCAI=Pediatric Ulcerative Colitis Activity Index, SD=standard deviation.

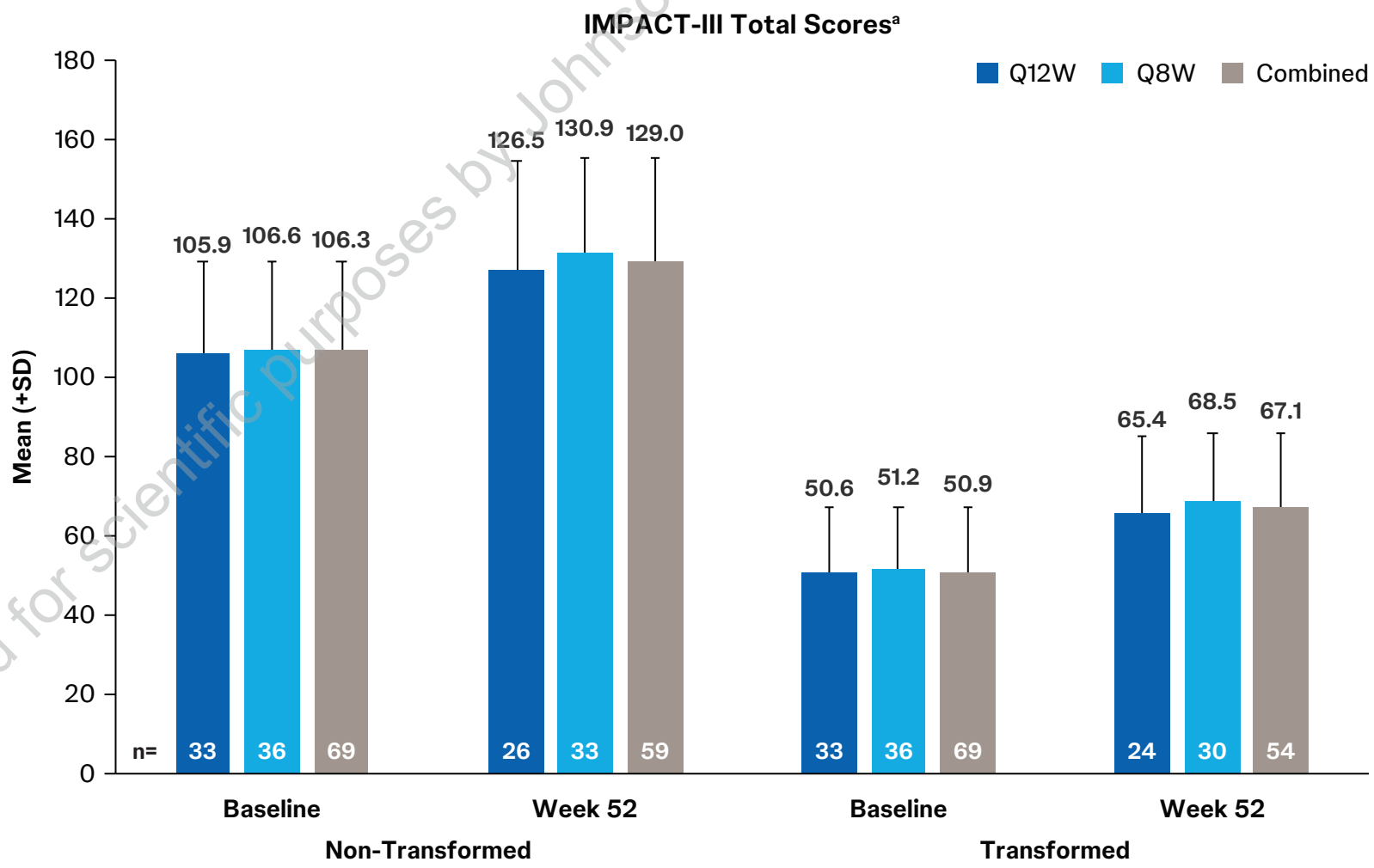
Results

Baseline Characteristics

Baseline Characteristics (participants ≥ 10 years of age)*		Total (N = 82)
Demographics		
Age, yrs, mean (SD)		14.3 (2.0)
Median (IQR) yrs		14.0 (13.0, 16.0)
Females, %		60%
Race, % Asian/Black/White/not reported or unknown		11.0%/2.4%/84.1%/2.4%
Weight, kg, mean (SD)		51.2 (12.6)
Median (IQR) kg		50.0 (42.5, 60.1)
Range, kg		28–80
<40 kg, %		19.5%
Disease Characteristics		
UC disease duration, yrs mean (SD)		2.1 (2.1)
Extensive UC, %		63%
Mayo score, mean (SD)		8.5 (1.5)
Moderate (Mayo score 6–10), %		90%
Severe (Mayo score >10), %		10%
PUCAI score, mean (SD)		53.0 (14.0)

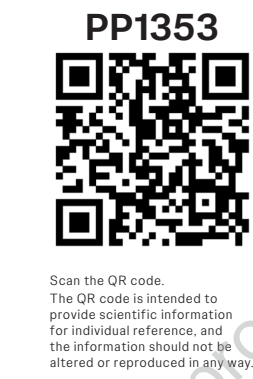
*Participants eligible to complete IMPACT-III questionnaire. IQR=interquartile range.

Changes in IMPACT-III Total Scores at Week 52



- At Week 52, the improved mean change IMPACT-III total score (transformed) of 15.3 (SD 15.1) for combined dose groups exceeded 0.5 SD threshold

*35-item. Among participants ≥10 years of age at baseline who completed the IMPACT-III questionnaire. Baseline was defined as the last observation prior to or at the time of the first study intervention. Intercurrent event criteria were applied. n=number with available data, Q8W=every 8 weeks, Q12W=every 12 weeks.

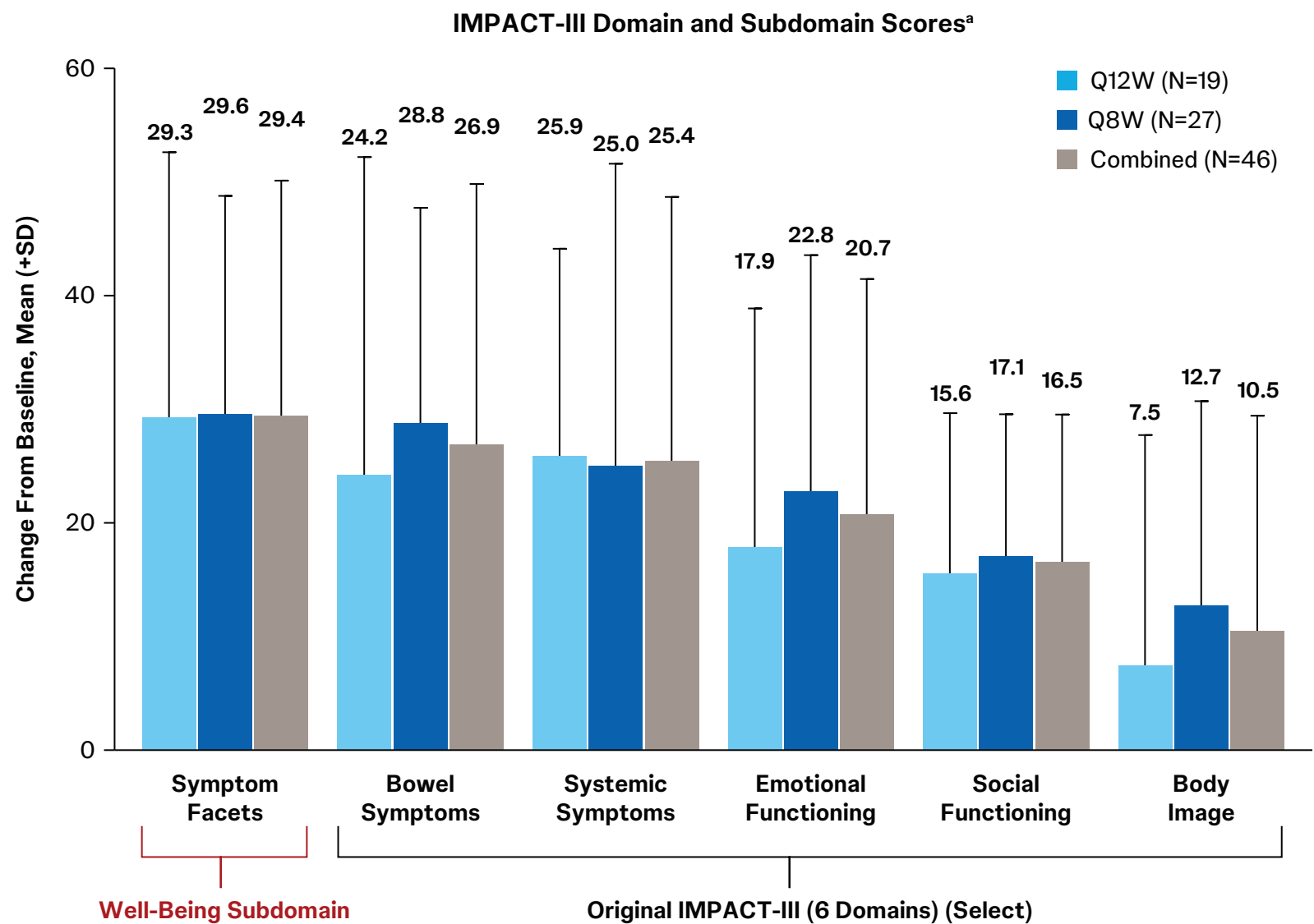


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Key Takeaways

- In pediatric patients with UC, 52 weeks of ustekinumab treatment (both q8w and q12w dosing regimens) presented with distribution-based clinically meaningful improvement of UC-related HRQoL concepts
- The symptom facets of “Well-being” and other IBD-related symptoms domains were the most responsive HRQoL concepts
- Symptom-related domains within IMPACT-III were more responsive than other domains measuring concepts such as emotional status, social functioning, and body image
- The modified-symptom facets from the Well-being subdomain appeared particularly responsive to change

Changes in IMPACT-III Domains and Subdomains at Week 52



*Transformed. Among participants ≥10 years of age at baseline who completed the IMPACT-III questionnaire. Baseline was defined as the last observation prior to or at the time of the first study intervention. Intercurrent event criteria for treatment failure were applied.