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Upadacitinib for Induction of Remission in Pediatric Ulcerative Colitis: An International Multicenter Study

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Author Contributions

A.Y.-F., S.C.: Conception of the work, design of the work, data interpretation, taking the lead in writing the manuscript. All authors: Data collection, critical revision of the article.

Conflict of Interest

These authors disclose the following:

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Abstract

Background and Aims: Data on upadacitinib therapy in children with ulcerative colitis (UC) or unclassified inflammatory bowel disease (IBD-U) are scarce. We aimed to evaluate the effectiveness and safety of upadacitinib as an induction therapy in pediatric UC or IBD-U.

Methods: In this multicenter retrospective study, children treated with upadacitinib for induction of remission of active UC or IBD-U from 30 centers worldwide were enrolled. Demographic, clinical, and laboratory data, as well as adverse events (AEs), were recorded at Week 8 post-induction.

Results: One hundred children were included (90 UC and 10 IBD-U, median age 15.6 [interquartile range 13.3–17.1] years). Ninety-eight were previously treated with biologic therapies, and 76 were treated with ≥2 biologics. At the end of the 8-week induction period, clinical response, clinical remission, and corticosteroid-free clinical remission (CFR) were observed in 84%, 62%, and 56% of the children, respectively. Normal C-reactive protein and fecal calprotectin (FC) <150 mcg/g were achieved in 75% and 50%, respectively. Combined CFR and FC remission was observed in 18/46 (39%) children with available data at 8 weeks. Adverse events were recorded in 37 children, including 1 serious AE of an appendiceal neuroendocrine tumor. The most frequent AEs were hyperlipidemia (n = 13), acne (n = 12), and infections (n = 10, 5 of whom with herpes viruses).

Conclusions: Upadacitinib is an effective induction therapy for refractory pediatric UC and IBD-U. Efficacy should be weighed against the potential risks of AEs.

Keywords

Inflammatory bowel disease; JAK inhibitors; children

1. Introduction

Current guidelines recommend antitumor necrosis factor agents in children with ulcerative colitis (UC) who fail 5-aminosalicylic acid (5-ASA) and thiopurines therapy, or do not respond to systemic steroids.[1] Real-world data support the use of other biologics, approved for adults but not yet for the pediatric population, such as vedolizumab and ustekinumab,

in refractory cases.[2,3] Tofacitinib, a nonselective Janus kinase (JAK) inhibitor, was the first small molecule therapy approved for adults with moderate-to-severe UC. Although not yet approved for the pediatric population, a retrospective international study of children with biologic refractory UC reported a corticosteroid-free clinical remission (CFR) rate of 16% and 23% at Weeks 8 and 24, respectively.[4]

Upadacitinib is an oral selective JAK1 inhibitor[5] that has demonstrated superiority over placebo in both 8-week induction and maintenance Phase 3 studies for clinical, endoscopic, and histologic endpoints in adult populations with UC[6–8] and Crohn's disease.[9,10] Upadacitinib studies revealed a relatively high efficacy in patients who were refractory to prior advanced therapies.[6–10] While upadacitinib has not been approved for pediatric inflammatory bowel disease (IBD), it is often used as off-label in children with refractory disease. Efficacy data in pediatric IBD are limited to a single-center retrospective case series of 20 adolescents, of whom 15 achieved CFR at Week 12 of therapy with no new safety signals.[11] Safety data for upadacitinib in the pediatric population are derived mostly from studies on atopic dermatitis; however, AEs with upadacitinib are commonly dose dependent, and dosing in atopic dermatitis is lower than in IBD.[12]

This study aimed to evaluate effectiveness, safety, and dosing of upadacitinib for induction of remission in pediatric UC and IBD-U.

2. Methods

2.1. Study design and population

This was a retrospective cohort study from 30 centers in Europe and the Middle East, affiliated with the Pediatric IBD Interest and Porto group of the European Society for Paediatric Gastroenterology, Hepatology, and Nutrition (ESPGHAN), as well as centers in North America (including patients from the Mt. Sinai cohort[11]). Included were children and adolescents (≤18 years of age) diagnosed with UC or unclassified IBD (IBD-U) according to the revised Porto criteria and current guidelines[1,13] who were treated with upadacitinib for the induction of remission due to active disease between January 2022 and April 2024, and had a follow-up of at least 8 weeks. To allow for intention-to-treat (ITT) analyses and avoid selection bias, we included all patients who received an upadacitinib dose.

2.2. Data collection

We collected demographic and clinical data on disease characteristics according to the Paris classification[14] and on disease activity as measured by the Pediatric Ulcerative Colitis Activity Index (PUCAI),[15] past and concomitant therapy, surgeries, and laboratory results at the initiation of upadacitinib therapy (up to 1 week before) and during 8 weeks of follow-up (±2 weeks). Data at 4 weeks of follow-up (±1 week) were also collected, when available. All adverse events (AEs) that were potentially related to therapy according to the judgment of the treating physician were recorded. Serious AEs were defined as those that were life-threatening or resulting in hospitalization, disability, or discontinuation of therapy.

2.3. Outcomes

The primary outcome of the study was CFR at the end of the 8-week induction period of upadacitinib therapy. Secondary outcomes included Week 8 clinical remission, clinical response, normalization of C-reactive protein (CRP), decrease of fecal calprotectin (FC) to <150 mcg/g, combined CFR and FC remission (CFR and decrease of FC to <150 mcg/g), need for IBD-related surgery during follow-up, durability of therapy, and AEs.

Clinical remission was defined as PUCAI < 10. Clinical response was defined as PUCAI reduction of >20 points from baseline. Normalization of CRP was defined as a CRP level <5 mg/L. Hyperlipidemia was defined according to the recommendations of the Integrated Guidelines for Cardiovascular Health and Risk Reduction in Children and Adolescents: Serum low-density lipoprotein cholesterol ≥130 mg/dL or total cholesterol ≥200 mg/dL or triglycerides ≥100 mg/dL at 0–9 years or ≥130 mg/dL above 10 years of age.[16]

2.4. Statistical analysis

Continuous variables were expressed as median and interquartile range (IQR). Categorical variables were presented as frequency and percentage. Categorical variables were compared by chi-square test or the Fisher exact test, as appropriate, while continuous variables were compared with the Mann–Whitney test. A generalized estimating equations model was applied for repeated measures analysis. The analyses of the primary outcome were performed under the ITT principle. Data on clinical outcomes at Week 8 were available for all patients unless therapy had been discontinued earlier. Missing outcome data at Week 8 were imputed by the nonresponse imputation approach. Imputation to missing laboratory data was not performed. The number of patients with available data for each determinant was detailed in the appropriate tables. All the statistical tests were 2-tailed. A p-value <0.05 was considered statistically significant. SPSS (version 27; IBM Corporation) was used for all statistical analyses.

2.5. Ethical considerations

This study was approved by the Ethics Committee of the Tel Aviv Sourasky Medical Center (TLV-23–0723) and equivalent committees of the contributing centers.

3. Results

A total of 100 children were included, of whom 90 were diagnosed with UC and 10 with IBD-U. Their median [IQR] age was 15.6 [13.3–17.1] years (range 5.5–18 years) at the initiation of upadacitinib therapy (Table 1), and their median [IQR] disease duration was 2.5 [1.4–5.1] years. Before receiving upadacitinib therapy, 98 children had been treated with biologic agents: 94 with anti-TNFα agents (84 with infliximab, 35 with adalimumab, 1 with golimumab), 55 with vedolizumab, 38 with ustekinumab, and 1 with risankizumab (Table 1). Twenty-one patients were treated with tofacitinib. One patient who had no prior biologic therapy had failed steroids and azathioprine and due to a concomitant diagnosis of atopic dermatitis was then started upadacitinib therapy, and the second patient with no prior biologic therapy was treated with ozanimod prior to upadacitinib. All patients had an active

UC at the initiation of upadacitinib therapy. Based on the PUCAI, 25% of the patients had mild disease, 53% had moderate disease, and 22% had severe disease.

3.1. Upadacitinib dosing and combination therapies

The induction doses of upadacitinib are presented in Table 2. Most of the patients (87%) received an upadacitinib daily dose of 45 mg. In children who weighed <40 kg, the median daily dose was 35.5 (27.4–40.5) mg/m^2 or 1.26 (0.97–1.4) mg/kg (Table 2). At the end of induction, 32 children underwent dose reduction from 45 to 30 mg and 2 from 30 to 15 mg; 1 patient's dose was increased from 30 to 45 mg. Upadacitinib was provided as combination therapy in 59 children as follows: corticosteroids (n = 32), 5-ASA (n = 22), biologic agents (n = 22: 14 ustekinumab, 5 vedolizumab, 2 risankizumab, 1 infliximab), methotrexate (n = 1), and tacrolimus (n = 1). In all cases of a combination of upadacitinib and biologic agent, upadacitinib therapy was added to an ongoing biologic therapy that was continued after the initiation of upadacitinib.

3.2. Study outcomes

At the end of the induction period, 90 (90%) children were still receiving upadacitinib therapy. The shortest exposure time was 2 weeks. The majority of patients who discontinued therapy (9/10) did so due to nonresponse, 8 of whom underwent colectomy after a median duration of 7 [2–8] weeks, and 1 child was denied insurance coverage. Clinical response, clinical remission, and CFR at Week 8 were observed in 84 (84%), 62 (62%), and 56 (56%) children, respectively (Figure 1). The median PUCAI decreased from 45 [33–60] to 0 [0–20] at Week 8 (p < .001; Table 3, Figure 2A). Of the 32 children treated with corticosteroids at the initiation of upadacitinib therapy, 14 (44%) weaned off steroids by Week 8.

A total of 22 patients with acute severe colitis were treated with upadacitinib after failure of steroids and infliximab. Clinical response, clinical remission, and CFR in this group were observed in 18 (82%), 13 (59%), and 12 (55%) patients, respectively. Six patients underwent colectomy after a median of 4.5 (1–8) weeks of therapy. Among the 9 patients with severe UC who did not achieve clinical remission, 1 patient had mild disease post-induction, 4 patients had moderate disease, and 4 patients showed no response.

At baseline, 53/98 (54%) and 61/64 (95%) patients with available data had elevated CRP and FC >150 mcg/g levels, respectively. CRP and FC levels were available in 87 and 46 children, respectively at Week 8. Normal CRP levels and an FC level of <150 mcg/g post-induction were observed in 65 (75%) and 23 (50%), respectively. The median FC level declined from 1645 [628–2263] mcg/g at baseline to 140 [33–669] mcg/g at Week 8 (p < 0.001) (Figure 2B). Combined CFR and FC remission was observed in 18/46 (39%) children whose data were available (Figure 1). The longitudinal changes in laboratory measures are presented in Table 3.

Data at 4 weeks of follow-up were available for 69 patients. Clinical response, clinical remission, and CFR were observed in 44 (64%), 29 (42%), and 25 (36%) patients, respectively, with available data (44%, 29%, and 25%, respectively, of the ITT population).

3.3. Predictors of outcomes

Several baseline variables were associated with failure to achieve CFR at Week 8. These variables included a higher PUCAI at the initiation of upadacitinib therapy, and steroid therapy at baseline (Table 1). The previous failure of vedolizumab therapy was also associated with failure to achieve CFR. Notably, 53/55 patients who had been treated with vedolizumab were treated with ≥2 biologics. Higher CRP levels at the initiation of therapy were also associated with failure to achieve CFR at Week 8 (7 [2.4–17.2] vs 3 [0.6–7.9] mg/L, $p = 0.011$). While the daily dose/body surface area (BSA) was higher among children who weighed <40 kg, this was not associated with the primary outcome (week 8 CFR of 67% vs 54% in patients below and above 40 kg, respectively, $p = 0.367$). Clinical response at 4 weeks was an additional predictor of Week 8 CFR [odds ratio = 31, 95% confidence interval 3.7–262.1, $p < 0.001$]. Overall, 31/44 (70%) patients who had responded to therapy at 4 weeks of follow-up achieved CFR post-induction. Among 25 children who had not experienced clinical response at Week 4, only 1 (4%) patient achieved CFR by Week 8. Additional Week 4 clinical and laboratory variables that were associated with Week 8 CFR are presented in Supplementary Table 1. Other variables, such as age, sex, disease duration and phenotype, extraintestinal manifestations, past therapies (except vedolizumab), the dosing regimen, and combination therapy (except steroids) were not associated with clinical outcomes.

3.4. Adverse events

Adverse events that were potentially related to upadacitinib therapy were reported in 37 children (Table 4). The most frequent AEs were hyperlipidemia ($n = 13$), acne ($n = 12$), and infections ($n = 10$, including 4 cases of herpes simplex infections and 1 case of herpes zoster infection). Two of the 10 patients who sustained infectious AEs were treated with a combination of immunosuppressive agents. One patient who was treated with upadacitinib and vedolizumab developed an Epstein–Barr virus infection, and 1 patient treated with upadacitinib and steroids developed a herpes simplex infection. The baseline and follow-up lipid status data of the patients are presented in Supplementary Table 2. The median low-density lipoprotein of patients with hyperlipidemia at the end of induction was 140 [136–150] mg/dL. The 1 serious AE of an appendiceal neuroendocrine tumor that was reported after colectomy did not require specific therapy. There were no thromboembolic events or malignancies, and no AE led to discontinuation of the drug.

4. Discussion

This is the first multicenter analysis of a cohort of children with refractory UC and IBD-U treated with upadacitinib for the induction of remission. Corticosteroid-free clinical remission and combined CFR and FC remission were demonstrated by Week 8 in 56% and 39% of the children, respectively.

The rates of clinical remission with upadacitinib 45 mg in Phase 3 induction trials among adults were 26% and 34%.[6] Clinical response was reported for 73% and 74% of the patients.[6] A prospective analysis of 105 adults with IBD (44 UC) who were treated with upadacitinib reported that clinical remission and response were achieved at 8 weeks in

81% and 85% of the UC patients, respectively.[17] Comparable rates of 64% for CFR and 84% for clinical response were reported in a retrospective study on 76 adults with UC.[18] Meta-analyses of clinical studies on upadacitinib in the treatment of IBD reported clinical remission rates of 25%–55% and clinical response rates of 42%–65%,[19] with corresponding rates of 25% and 73% in a UC population.[20] The efficacy rates for upadacitinib 45 mg daily were highest for all efficacy induction outcomes in a network meta-analysis that included 23 studies on advanced therapies for moderate–severe UC.[21] The main clinical endpoints in our current pediatric study (clinical response, clinical remission, and CFR of 84%, 62%, and 56%, respectively) are comparable to those in the real-life adult population. Notably, employing the ITT approach may lead to varying degrees of underestimation of the assessed clinical outcomes. The single pediatric case series from the Mt. Sinai cohort on upadacitinib therapy for IBD reported post-induction CFR in all 11 UC/IBD-U patients, who are also included in the current study.[11]

The rate of steroid withdrawal in our pediatric study was 44%. Raine et al.[22] reported similar rates of 57% in adults. Notably, several adult case series have shown the potential effectiveness of upadacitinib as a salvage therapy for acute severe colitis. As demonstrated in our study, most of the patients in those series (67%–88%) avoided colectomy and achieved clinical remission with upadacitinib therapy.[23–25]

The vast majority of the patients in our cohort received an induction dose of 45 mg daily. In addition, 53% and 71% of those weighing less than 40 and 30 kg, respectively, received reduced dosage; however, their dose for BSA or weight was higher compared to patients who weighed above 40 kg. Nevertheless, the dosing regimen was not associated with clinical outcomes. The association between dosing, plasma exposure, and efficacy of upadacitinib has been established in adults.[26] Several studies have shown that a dose of 45 mg maximizes efficacy for clinical and endoscopic outcomes.[26,27] Twenty-two children in our study were treated with a combination of 2 advanced therapies, and no difference in clinical outcomes was observed between them and the children who had been treated with upadacitinib as monotherapy. In their pediatric cohort, Spencer et al. reported that all seven patients under combined upadacitinib and ustekinumab therapy achieved CFR following induction.[11] Importantly, the potential efficacy of combining advanced therapies should be weighed against the risks of serious AEs.[28]

The respective rates of clinical response, clinical remission, and CFR were 64%, 42%, and 36% after 4 weeks of therapy. These data are supported by other studies that reported improvement in symptoms and quality of life as early as Week 2 in adult populations.[6,7,17,27] The authors of a post-hoc analysis of data from 2 Phase 3 induction trials ($n = 969$) observed improvement of symptoms as early as Day 1.[29] The rapid onset of response makes upadacitinib therapy particularly promising for patients with severe or steroid-dependent UC, facilitating rapid withdrawal from steroids.

The effectiveness of upadacitinib in our study was superior to that reported for tofacitinib in the largest pediatric study published by Ledder et al. (CFR and clinical response rates of 16% and 30%, respectively).[4] Improved clinical effectiveness of upadacitinib compared to tofacitinib was also demonstrated in adult populations with UC.[30,31] The effectiveness

of upadacitinib compared to previous studies of tofacitinib should be interpreted with caution, due to differences in populations, study designs, and interpretation of the results. Importantly, our study findings showed no difference in the response or remission rates between tofacitinib-naïve or tofacitinib-experienced children, comparable to the results observed in several pediatric and adult studies.[11,17,32] These data may support the beneficial use of upadacitinib in patients who have been previously exposed to tofacitinib.

Consistent with clinical outcomes, improvements in CRP and FC post-induction were reportedly observed in patients treated with upadacitinib.[6,17,18] The rates of normal CRP values (75%) and FC < 150 mcg/g (50%) in our study were high, and the decline in FC from a median of 1645 at baseline to 140 mcg/g at Week 8 was also significant. Notably, all patients with UC/IBD-U achieved normalization of CRP post-induction in Spencer et al.'s study on adolescents with refractory IBD.[11]

Our study findings support the association between Week 4 clinical response and improvement in FC to Week 8 remission, which was also reported by Loftus et al. in adults.[29] In our study, 31/44 (70%) patients who had already responded to therapy at 4 weeks achieved CFR by the end of induction. The observation that only 1 of 25 children who had not experienced clinical response at Week 4 achieved CFR by Week 8 emphasizes the importance of early monitoring.

The most frequent AEs in our study were hyperlipidemia, acne, and infections (including 4 children with herpes simplex infections and 1 child with herpes zoster infection). No thromboembolic events or malignancies were reported. There was 1 patient with an appendiceal neuroendocrine tumor detected after colectomy that was listed as a serious AE. The most commonly reported AEs associated with upadacitinib in a Phase 3 induction study on adults were nasopharyngitis (5%), creatine phosphokinase elevation (4%), and acne (5%–7%).[6] The rates of serious AEs and AEs leading to treatment discontinuation were lower in the upadacitinib 45 mg group compared to placebo in both induction studies.[6] In their prospective study, Friedberg et al. reported that the most common AE was acne, occurring in 23% of their adult patients.[17] Notably, the rate of AE was higher in Raine et al.'s adult patients treated with upadacitinib in combination with steroids.[22] No AEs during induction were reported in a population of 20 adolescents studied by Spencer et al.[11] Importantly, the warning by the European Medicines Agency regarding the increased risk of venous thromboembolism, cancer, and major cardiovascular conditions requires careful consideration.[33]

This is the largest and the first multicenter study on a cohort of children with UC treated with upadacitinib. However, the study is limited by its retrospective design, which prevented a structured follow-up, and specifically lacked an organized reporting of Week 4 outcomes and AEs. The lack of systematic monitoring of AEs in our study should be acknowledged, and potential AEs should be discussed with the patients and families throughout the decision-making process. Another limitation is the absence of endoscopic and imaging follow-up data because these endpoints were available for only a small subset of patients during induction. An additional limitation is the short-term follow-up and the clear need for long-term data on the efficacy and safety of upadacitinib in children.

In conclusion, the findings of this study suggest that upadacitinib therapy was effective for children with refractory UC, improving clinical and biomarker outcomes. The data support the beneficial use of upadacitinib in children who have previously failed tofacitinib. While the safety profile was generally favorable, the efficacy of upadacitinib should be weighed against the potential risk of AEs.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Data Availability

The data underlying this study are available in the paper and in its online supplementary material. The data will be shared on reasonable request to the corresponding author.

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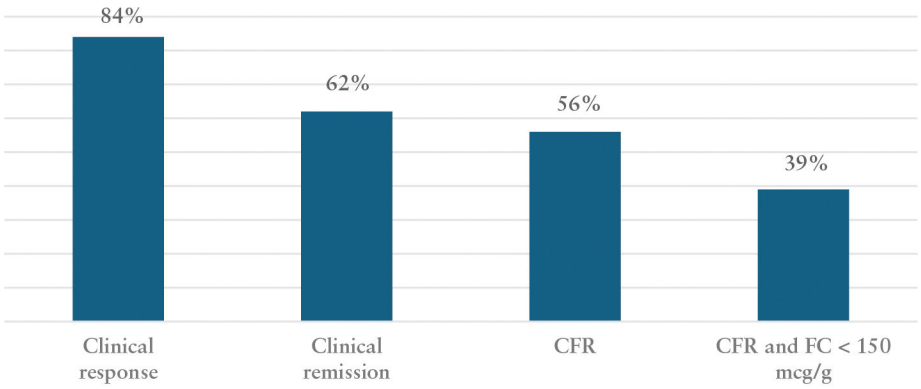
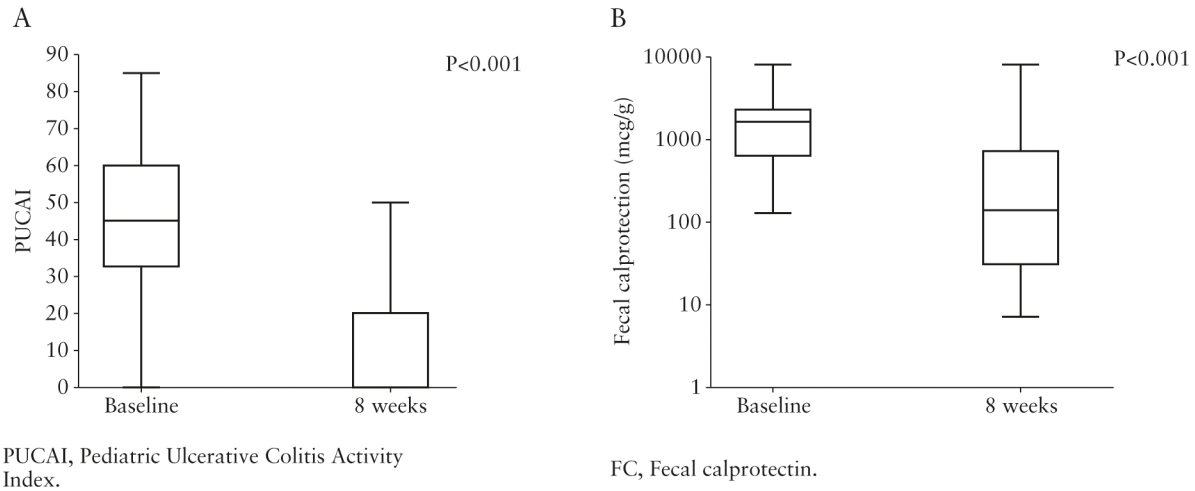


CFR, Corticosteroid-free clinical remission; FC, fecal calprotectin.

Figure 1.
Main study outcomes.



PUCAI, Pediatric Ulcerative Colitis Activity Index.

FC, Fecal calprotectin.

Figure 2.

A: Pediatric Ulcerative Colitis Activity Index (PUCAI) at baseline and at Week 8. B: Fecal calprotectin (FC) at baseline and at Week 8.

Table 1

Demographic and clinical data of the study cohort.

	All cohort (*n* = 100)	Absence of CFR at Week 8 (*n* = 44)	CFR at Week 8 (*n* = 56)	*p*-Value
Age at diagnosis of UC (years)	12.5 (8.6–14.7)	12.8 (8.5–14.7)	11.5 (8.8–14.9)	0.708
Age at upadacitinib therapy (years)	15.6 (13.3–17.1)	16 (13.6–17.6)	15.1 (12.3–16.9)	0.143
Duration of UC (years)	2.5 (1.4–5.1)	2.9 (1.4–5.1)	2.3 (1.3–5)	0.435
Males	53 (53%)	21 (47.7%)	32 (57.1%)	0.349
UC extent:				0.109
Proctitis	2 (2%)	2 (4.5%)	0	
Left-sided colitis	15 (15%)	8 (18.2%)	7 (12.5%)	
Extensive colitis	17 (17%)	4 (9.1%)	13 (23.2%)	
Pancolitis	66 (66%)	30 (68.2%)	36 (64.3%)	
UC severity:				0.063
Never severe	35 (35%)	11 (25%)	24 (42.9%)	
Ever severe	65 (65%)	33 (75%)	32 (57.1%)	
Extraintestinal manifestations	23 (23%)	12 (27.3%)	11 (19.6%)	0.368
Previous therapy				
Corticosteroids (*n* = 56)	53 (94.6%)	28 (100%)	25 (89.3%)	0.236
5-ASA (*n* = 56)	49 (87.5%)	25 (89.3%)	24 (85.7%)	>0.999
Thiopurines	37 (37%)	18 (40.9%)	19 (33.9%)	0.473
Methotrexate	12 (12%)	5 (11.4%)	7 (12.5%)	0.862
Infliximab	84 (84%)	38 (86.4%)	46 (82.1%)	0.568
Adalimumab	35 (35%)	15 (34.1%)	20 (35.7%)	0.866
Golimumab	1 (1%)	0	1 (3.6%)	>0.999
Vedolizumab	55 (55%)	31 (70.5%)	24 (42.9%)	**0.006**
Ustekinumab	38 (38%)	16 (36.4%)	22 (39.3%)	0.765
Risankizumab	1 (1%)	1 (2.3%)	0	0.44
Tofacitinib	21 (21%)	10 (22.7%)	11 (19.6%)	0.707
Tacrolimus	6 (6%)	5 (11.4%)	1 (1.8%)	0.084
Cyclosporin	1 (1%)	1 (2.3%)	0	0.44
Ozanimod	4 (4%)	2 (4.5%)	2 (3.6%)	>0.999

	All cohort (*n* = 100)	Absence of CFR at Week 8 (*n* = 44)	CFR at Week 8 (*n* = 56)	*p*-Value
Number of failed biologics:				0.144
0	2 (2%)	1 (2.3%)	1 (1.8%)	
1	22 (22%)	7 (15.9%)	15 (26.8%)	
2	44 (44%)	19 (43.2%)	25 (44.6%)	
3	25 (25%)	13 (29.5%)	12 (21.4%)	
4	7 (7%)	4 (9.1%)	3 (5.4%)	
PUCAI at baseline	45 (33–60)	50 (40–65)	40 (25–60)	**0.024**
Corticosteroids at baseline	32 (32%)	21 (47.7%)	11 (19.6%)	**0.003**
Biologics at baseline	22 (22%)	9 (20.5%)	13 (23.2%)	0.741

Abbreviations: 5-ASA, 5-aminosalicylic acid; CFR, corticosteroid-free clinical remission; PUCAI, Pediatric Ulcerative Colitis Activity Index; UC, Ulcerative colitis.

Bold denotes significant. Data are presented as median (interquartile range) for continuous variables and number (%) for categorical variables.

J Crohns Colitis. Author manuscript; available in PMC 2025 October 23.

Table 2

Induction doses of upadacitinib.

Daily dose	All cohort (*n* = 100)	Weight <40 kg (*n* = 15)	Weight <30 kg (*n* = 7)
45 mg	87 (87%)	7 (47%)	2 (29%)
30 mg	10 (10%)	7 (47%)	4 (57%)
15 mg	3 (3%)	1 (7%)	1 (14%)
Dose in mg/m^2 BSA *	28.2 (25.9–30.8)	35.5 (27.4–40.5)	33 (29.1–39.8)
Dose in mg/kg *	0.83 (0.73–0.94)	1.26 (0.97–1.40)	1.26 (1.09–1.48)

Abbreviations: m^2 BSA, per square meter of body surface area.

* Data are presented as median (interquartile range).

J Crohns Colitis. Author manuscript; available in PMC 2025 October 23.

Table 3

Clinical and laboratory measures during follow-up.

	Baseline	Follow-up at 4 weeks	Follow-up at 8 weeks	*p*-Value
PUCAI	45 (33–60) *n* = 100	5 (0–23) *n* = 69	0 (0–20) *n* = 100	**<0.001**
Hemoglobin (g/dL)	11.9 (10.2–12.5) *n* = 99	12.4 (11.5–13.4) *n* = 38	12.4 (11.8–13.5) *n* = 88	0.079
CRP (mg/L)	2.3 (1–12.1) *n* = 98	1 (0.5–1.9) *n* = 37	1 (0.5–2) *n* = 87	**0.021**
ESR (mm/h)	26 (9–46) *n* = 84	8 (3–15) *n* = 28	10 (6–18) *n* = 73	**<0.001**
Albumin (g/L)	40 (33–44) *n* = 100	45 (42–48) *n* = 39	45 (42–48) *n* = 89	**<0.001**
Fecal calprotectin (mcg/g)	1645 (628–2263) *n* = 64	240 (87–963) *n* = 20	140 (33–669) *n* = 46	**<0.001**

Abbreviations: CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; PUCAI, Pediatric Ulcerative Colitis Activity Index.

Bold denotes significant. Data are presented as median (interquartile range).

Table 4

Adverse events

Serious adverse events	Number of patients
Neuroendocrine tumor in appendix	1
Other adverse events	
Hyperlipidemia	13
Acne	12
Infections:	
Herpes simplex	4
Upper respiratory tract	2
Herpes zoster	1
Acute gastroenteritis	1
Epstein–Barr virus	1
Clostridium difficile	1
Headache	3
Fatigue	1
Elevated serum creatine phosphokinase	1
Neutropenia	1
Transient increase in serum lipase	1