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Brief Report - Clinical

Clinical and Endoscopic Outcomes After Upadacitinib Induction for Ulcerative Colitis: A Multicenter Retrospective Cohort Study

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Introduction

Medical therapies for ulcerative colitis (UC) have recently expanded to include small molecule inhibitors of Janus-kinase (JAK).[1–3] Upadacitinib is the newest oral selective JAK1 inhibitor that was approved for the treatment of UC in 2022.[2,4] Randomized controlled trials have demonstrated the superiority of upadacitinib to induce remission of UC at 8 weeks compared with placebo.[2] However, treatment efficacy observed in clinical trial settings may not reflect real-world clinical practice.

Recent real-world studies reported clinical remission rates up to 82% after upadacitinib induction for UC.[5,6] However, these studies were limited by small sample sizes.[5,6] Additionally, no postinduction endoscopic data have been reported in real-world settings to date. In this multicenter retrospective cohort study, we assessed both clinical and endoscopic outcomes after 8 weeks of upadacitinib induction for UC.

Methods

This retrospective cohort study included adults who initiated upadacitinib for UC between March 1, 2022 and February 1, 2023, at Brigham and Women's Hospital (Boston, MA, USA), Massachusetts General Hospital (Boston, MA, USA), and the University of North Carolina at Chapel Hill (Chapel Hill, NC, USA). Electronic health records were manually reviewed, and those who were prescribed upadacitinib primarily for non-UC indications (eg, Crohn's disease, rheumatoid arthritis) and those with prior colectomies were excluded. Upadacitinib start dates were extracted from gastroenterology and prior authorization documentation.

Baseline characteristics included patient demographics, prior IBD therapies, concomitant IBD therapies, disease severity (eg, serum albumin, C-reactive protein [CRP], and simple clinical colitis activity index [SCCAI] or partial [9-point] Mayo scores documented within 12 weeks prior to upadacitinib initiation, last endoscopic extent and severity, and any UC hospitalization within 12 months prior to upadacitinib initiation).

The primary outcome was steroid-free clinical remission (SFCR) assessed at the first gastroenterology follow-up visit 8 to 16 weeks after upadacitinib initiation. Steroid-free clinical remission was defined using the following criteria in order of preference based on data availability: (1) SCCAI ≤2; (2) partial (9 point) Mayo score ≤2; or (3) provider documentation of clinical remission. Patients were also required to be off of oral and intravenous corticosteroids at the time of assessment. Secondary outcomes also assessed at 8 to 16 weeks were clinical response (improvement in the SCCAI or Mayo score by ≥3 points or provider documentation of clinical response with the intent to continue upadacitinib therapy while tapering or off corticosteroids), biochemical remission (CRP <10 mg/L), and improvement in baseline arthralgia (if present). Additional outcomes assessed during all available follow-up through April 1, 2023, (not limited to 16 weeks) included endoscopic response (improvement in Mayo endoscopic subscore by ≥1 point from baseline), endoscopic remission (Mayo endoscopic subscore = 0), drug-related adverse events (AEs), UC hospitalization, and treatment discontinuation.

We also reported the distribution of upadacitinib doses at clinical follow-up among those who achieved SFCR and clinical response and the proportion of patients with prior tofacitinib exposure who achieved SFCR and clinical response.

Categorical data were reported using fractions and percentages, and continuous data were reported using medians and interquartile ranges (IQRs). StataSE 17 (College Station, TX) was used for data analyses. This study was

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Key Messages

What is already known?
In clinical trials, upadacitinib was effective in inducing clinical remission of ulcerative colitis. Real-world clinical and endoscopic outcomes of upadacitinib are not well-described.

What is knew here?
In this bio-exposed cohort of ulcerative colitis patients, 48 of 75 achieved steroid-free clinical remission, 64 of 76 achieved clinical response, 16 of 26 achieved endoscopic response, and 9 of 26 achieved endoscopic remission.

How can this study help patient care?
Upadacitinib may be an effective therapeutic option to induce steroid-free clinical remission in a bio-exposed population of patients with ulcerative colitis.

approved by the institutional review boards of Brigham and Women's Hospital and the University of North Carolina.

Results

Seventy-six patients initiated upadacitinib for UC, with median available follow-up of 34.1 weeks (IQR, 21.3-44.5 weeks). Forty-seven percent were female, 87% were Caucasian, 54% were on concomitant oral corticosteroids (prednisone or oral budesonide at maximum doses of 40 mg and 9 mg, respectively), and all patients were previously exposed to biologics or small molecules: 91% were anti-TNF-exposed, 74% were vedolizumab-exposed, 30% were ustekinumab-exposed, and 30% were tofacitinib-exposed (Table 1).

At 8 to 16 weeks after upadacitinib initiation, 64.0% (48 of 75; 1 patient had insufficient documentation) achieved SFCR, 84.2% (64 of 76) achieved clinical response, 88.2% (45 of 51) achieved biochemical remission, and 62.5% (10 of 16) reported improvement in arthralgia (Figure 1). The median CRP improved from 4.3 to 0.3 mg/L pre vs postupadacitinib initiation. Endoscopic evaluations were performed in 26 patients at a median of 23.3 weeks (IQR, 13.1-30.8 weeks) after upadacitinib initiation, among which 61.5% (16 of 26) achieved endoscopic response, and 34.6% (9 of 26) achieved endoscopic remission.

During median follow-up of 34.1 weeks, 14 AEs were reported among 11 patients, including bacteremia, cellulitis, diverticulitis, pneumonia, streptococcal pharyngitis, photosensitive rash, pruritic rash, acne, anemia, nausea, neutropenia, peripheral edema, angina, and elevated liver enzymes. The case of angina was attributed to worsening anemia rather than an acute thromboembolic event. Ulcerative colitis hospitalizations occurred in 6.6% (5 of 76) and upadacitinib was discontinued in 11.8% (9 of 76) of patients. Reasons for discontinuation included nonresponse (6 of 9, 3 of which required colectomy for refractory disease), AEs (2 of 9, angina and elevated liver enzymes), and colectomy for dysplasia (1 of 9). The 3 patients who required colectomy for refractory disease had 1, 3, and 5 prior biologic exposures.

Among 48 patients who achieved SFCR, 25.0% were receiving 15 mg, 62.5% were receiving 30 mg, and 12.5% were receiving 45 mg at follow-up. Among 64 patients who achieved clinical response, 20.3% were receiving 15 mg, 64.1% were receiving 30 mg, and 15.6% were receiving 45 mg at follow-up. Among patients receiving 45 mg who achieved SFCR ($n = 6$), 2 were receiving 45 mg for at least 16 weeks, and the remaining 4 patients received 45 mg for 8 to

Table 1. Baseline characteristics.

Characteristic	Value (N = 76 unless specified)
Demographics	
Female sex, *n* (%)	36 (47%)
Age at induction, y, median (IQR)	39.6 (29.1, 49.1)
UC duration, y, median (IQR)	9.5 (3.3, 14.3)
Race, *n* (%)	
Caucasian	66 (87%)
Black	3 (4%)
Asian, Pacific Islander, or Native Hawaiian	6 (8%)
Native American	1 (1%)
Hispanic ethnicity, *n* (%)	2 (3%)
BMI, kg/m^2, median (IQR)	25.0 (22.1, 28.0)
Arthralgia, *n* (%)	17 (22%)
Current smoking, *n* (%)	1 (1%)
Prior IBD therapies	
Thiopurine or methotrexate, *n* (%)	37 (49%)
Prior biologic or small molecule failure, *n* (%)	76 (100%)
Number of prior anti-TNFs, *n* (%)	
0	7 (9%)
1	40 (53%)
2	25 (33%)
3	3 (4%)
4	1 (1%)
Vedolizumab, *n* (%)	56 (74%)
Ustekinumab, *n* (%)	23 (30%)
Tofacitinib, *n* (%)	23 (30%)
Concomitant IBD therapies	
Prednisone or oral budesonide, *n* (%)	41 (54%)
Thiopurine or methotrexate, *n* (%)	3 (4%)
Vedolizumab, *n* (%)	4 (5%)
Ustekinumab, *n* (%)	1 (1%)
Risankizumab, *n* (%)	1 (1%)
Disease severity	
Albumin, g/dL, median (IQR), N = 71	4.1 (3.8, 4.4)
C-reactive protein ≥10 mg/L, *n* (%), N = 68	23 (34%)
SCCAI score, median (IQR), N = 72	6 (3, 9)
Partial Mayo score, median (IQR), N = 14	5 (3, 6)
Last disease extent (> proctitis), *n* (%)	56 (74%)
Last Mayo endoscopic subscore, *n* (%)	
0 (remission)	7 (9%)
1 (mild)	11 (15%)
2 (moderate)	33 (44%)
3 (severe)	24 (32%)
UC hospitalization within 12 months, *n* (%)	24 (32%)

Abbreviations: IQR, interquartile range; TNF, tumor necrosis factor; CRP, C-reactive protein; SCCAI, simple clinical colitis activity index.

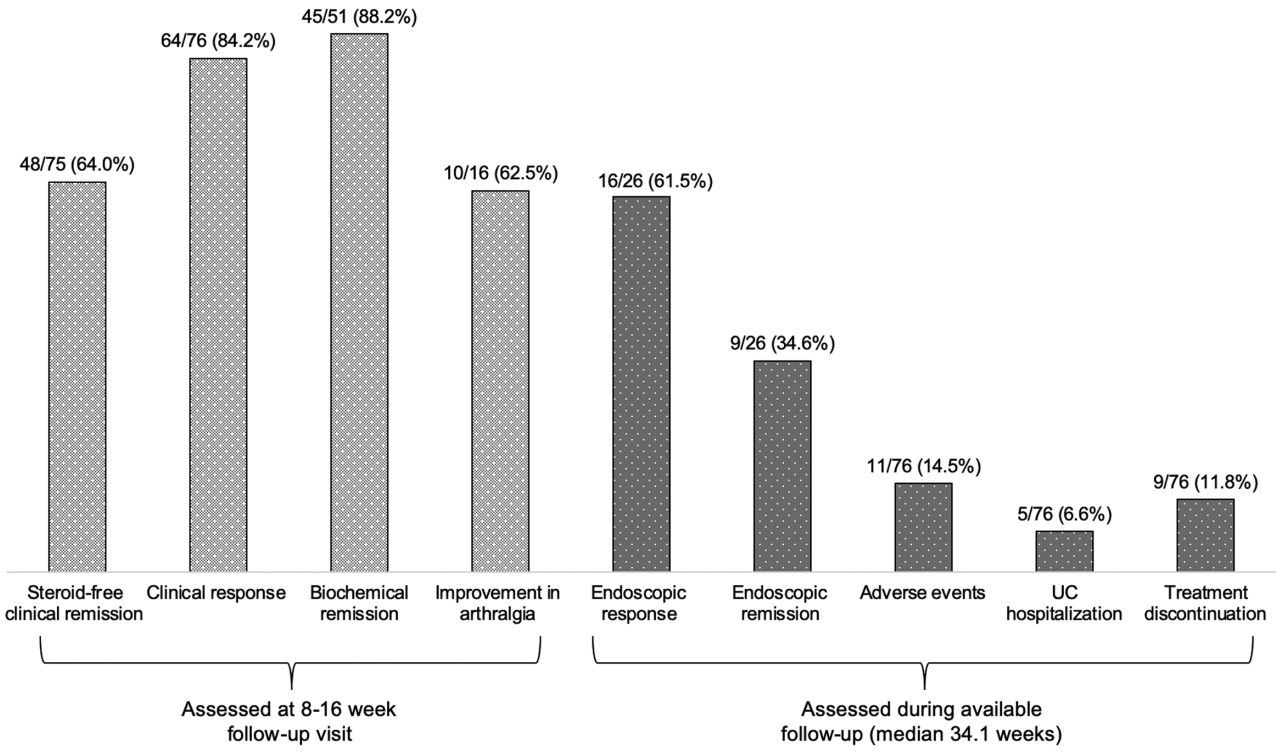

Figure 1. Clinical and endoscopic outcomes. Denominators vary due to one patient with insufficient documentation for steroid-free clinical remission and subsets of patients with baseline elevated CRP, arthralgia, and available endoscopic data.

12 weeks; no AEs were reported for this group. Patients with prior tofacitinib exposure ($n = 22$) had similar rates of SFCR (54.5%) and clinical response (82.6%) as those without prior tofacitinib exposure ($P = .30$ and $P = 1.00$, respectively, by Fisher's exact test).

Discussion

Real-world data describing clinical and endoscopic outcomes after upadacitinib induction are needed to guide therapeutic decision-making for UC. In this multicenter cohort, the majority of patients were previously exposed to anti-TNFs and vedolizumab. Nevertheless, most patients achieved SFCR and clinical response 8 to 16 weeks after upadacitinib initiation, including the subgroup with prior tofacitinib exposure. The majority of patients with postinduction endoscopic evaluations also achieved endoscopic response. Adverse events were consistent with the known safety profile of upadacitinib and rarely led to treatment discontinuation.[2,7,8]

The strengths of this study include reporting of granular data such as disease activity and endoscopic assessments, AEs, and specific reasons for treatment discontinuation. Limitations include the retrospective design, potential omissions in clinical documentation, relatively small sample size precluding additional subgroup and multivariable analyses, and subjectivity inherent to SCCAI and Mayo score assessments. The limited follow-up time also does not allow for assessment of the durability of upadacitinib, for which additional studies are needed.

In summary, upadacitinib appears to be an effective and safe treatment option in a real-world, biologic-refractory population. Larger studies with long-term follow-up and comparative effectiveness data are needed to determine the optimal positioning of upadacitinib relative to other therapeutic agents approved for moderate to severe UC.

Author Contributions

R.S.D.: study concept and design, acquisition of data, analysis and interpretation of data, and drafting of manuscript.

G.K., H.C., and S.B.: acquisition of data and critical revision of the manuscript for important intellectual content.

E.B.: study concept and design, analysis and interpretation of data, and critical revision of the manuscript for important intellectual content.

J.R.A.: study concept and design, analysis and interpretation of data, critical revision of the manuscript for important intellectual content, and study supervision.

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Conflicts of Interest

J.R.A. serves as a consultant for Janssen, Pfizer, Abbvie, Iterative Scopes, Finch Therapeutics, Seres Therapeutics, Ferring, Merck, Bristol Myer Squibb, and Adiso, serves as a speaker for BMS, Abbvie, Janssen, and has research support from Pfizer, Merck, and Janssen. R.S.D. has served as a consultant for Centaur Labs and Janssen and has grant support from Pfizer and Janssen. E.L.B. has served as a consultant for Bristol-Meyers Squibb and Target RWE. All other authors have no conflicts of interest to disclose.

Data Availability

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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