BMC Gastroenterology

RESEARCH

Open Access

Upadacitinib induction therapy in Crohn's disease: a retrospective real-world study in biologic-refractory patients

Xiaoyu Fu[1], Lei Tu[1], Yu Fu[1], Huan Wang[1], Yidong Chen[1], Xiaopeng Zhang[1], Qi Yu[1], Fang Liu[1,2], Yiyu Cheng[1], Jiamin Li[1], Qianxi Xia[1], Rong Lin[1*] and Liangru Zhu[1*]

Abstract

Background and aims Upadacitinib, a selective Janus kinase 1 (JAK1) inhibitor, has demonstrated efficacy in clinical trials for Crohn's disease (CD) but real-world evidence remains limited. This study aimed to evaluate the effectiveness and safety of upadacitinib as induction therapy in a Chinese cohort with active CD.

Methods We conducted a retrospective, single-center cohort study of CD patients who received upadacitinib at Union Hospital (Wuhan, China) between June 2023 and February 2025. Clinical and endoscopic outcomes and safety events were systematically assessed. Multivariate analyses were performed to identify predictors of therapeutic response.

Results 94 patients met inclusion criteria, endoscopic response and remission were achieved in 50.00% and 38.89%, while mucosal healing occurred in 27.78% by week 12. 53.25% achieved clinical response and 42.86% achieved clinical remission. Biomarker normalization was observed in 62.71% (CRP), 70.91% (ESR), and 29.63% (fecal calprotectin). Adverse events were recorded in 34.0% of patients, with lymphopenia being the most frequent. Lower baseline CDAI and SES-CD scores were associated with higher remission rates.

Conclusion This real-world study demonstrates that upadacitinib is effective and generally well tolerated in biologic-experienced Chinese patients with active CD. Our findings support the clinical utility of JAK1 inhibition in a real-world setting.

Keywords Crohn's disease, Upadacitinib, JAK1 inhibitor, Real-world evidence, Endoscopic remission

*Correspondence:
Rong Lin
linrong@hust.edu.cn
Liangru Zhu
zhuliangru@hust.edu.cn
[1]Division of Gastroenterology, Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, 1277 Jiefang Ave, Wuhan 430022, China
[2]Division of Gastroenterology, The First Affiliated Hospital of Shihezi University, Shihezi, China

Introduction

Crohn's disease (CD) is a chronic, relapsing-remitting inflammatory disorder of the gastrointestinal tract characterized by transmural inflammation, mucosal ulceration, and progressive structural damage [1]. Once considered rare in East Asia, CD has become increasingly prevalent in China, where rapid industrialization, urbanization, and changing dietary patterns have been paralleled by a striking rise in disease incidence [2]. As the epidemiological shift unfolds, clinicians are increasingly confronted with a heterogeneous population of patients exhibiting complex disease behavior, treatment resistance, and heightened healthcare needs.

Conventional therapeutic strategies for CD–anchored by corticosteroids, immunomodulators, and biologic agents–are often insufficient for long-term disease control. Corticosteroids remain the cornerstone of induction therapy but are associated with a high burden of systemic toxicity, including metabolic, skeletal, and infectious complications [3, 4]. Immunosuppressants such as azathioprine and methotrexate exhibit delayed onset of action and unpredictable therapeutic windows [5, 6]. Although biologics targeting tumor necrosis factor (TNF), integrins, or interleukin pathways have improved patient outcomes and reshaped the treatment algorithm, clinical response is far from universal. A substantial proportion of patients demonstrate primary non-response, while others gradually lose efficacy due to immunogenicity or mechanistic escape [7]. Furthermore, the need for parenteral administration, high treatment costs, and cumulative immune suppression pose barriers to adherence and long-term disease management [8, 9].

Against this backdrop, there is a growing clinical interest in orally administered small-molecule drugs that provide targeted immunomodulation without the drawbacks of biologics. The Janus kinase (JAK)–signal transducer and activator of transcription (STAT) pathway plays a central role in the transduction of cytokine-mediated inflammatory signals that underlie the pathogenesis of CD [10, 11]. Among the JAK family members, JAK1 is particularly integral to pro-inflammatory cytokine signaling, including interferon-γ and interleukin-6 [12]. Upadacitinib, a highly selective JAK1 inhibitor, has been developed to achieve potent blockade of these pathways while minimizing off-target effects associated with pan-JAK inhibition [13, 14]. Phase 2 and 3 clinical trials have demonstrated its capacity to induce rapid clinical and endoscopic improvement in CD, along with a manageable safety profile [15]. However, pivotal trials are often conducted under tightly controlled conditions and may not fully capture treatment effectiveness or tolerability in broader patient populations.

Real-world studies are therefore essential to complement trial data by evaluating therapeutic performance under routine clinical conditions. Unlike randomized controlled trials, real-world analyses capture a broader spectrum of disease behavior, comorbidities, and treatment histories, offering insights that are directly applicable to everyday clinical decision-making. This is particularly important in the context of Crohn's disease, where therapeutic response is shaped by numerous hosts, microbial, and environmental factors. Despite the growing clinical interest in JAK1 inhibition, there remains a paucity of data from Asian populations, where genetic susceptibility, treatment access, and disease phenotype may differ substantially from Western cohorts [16–18].

To address this gap, we conducted a retrospective, real-world cohort study of biologic-experienced patients with active Crohn's disease who initiated upadacitinib at a tertiary referral center in Central China. Our objectives were fourfold: (1) to evaluate clinical, endoscopic, and biomarker-based responses during the 12-week induction phase; (2) to characterize the safety and tolerability profile of upadacitinib in real-world practice; (3) to identify baseline predictors associated with therapeutic response; and (4) to generate regionally relevant evidence to inform individualized treatment strategies. These findings aim to support the integration of JAK1 inhibitors into precision medicine approaches for CD management in rapidly evolving healthcare settings.

Methods

Study design and patient selection

This retrospective, single-center cohort study enrolled adult patients with CD treated with upadacitinib at Union Hospital, Tongji Medical College, Huazhong University of Science and Technology (Wuhan, China) between June 2023 and February 2025. Eligible patients were aged 18–75 years, had endoscopic or histological confirmation of active CD, had previously failed or were intolerant to ≥ 1 biologic agent, or had elected upadacitinib therapy based on informed patient preference. All included patients completed at least 12 weeks of induction therapy with upadacitinib. Exclusion criteria were incomplete baseline data, follow-up duration < 12 weeks, loss to follow-up, presence of severe comorbidities, or concurrent use of other biologic therapies. The study was approved by the Union Hospital Ethics Committee. Clinical data were extracted from electronic medical records.

Endpoints

The primary endpoints were

(1) Endoscopic response, defined as a ≥ 50% reduction in the Simple Endoscopic Score for Crohn's Disease (SES-CD) from baseline;

(2) Endoscopic remission, defined as SES-CD ≤ 4 with a ≥ 2-point reduction from baseline and no subscore > 1.

The secondary endpoints included

(1) Mucosal healing, defined as an ulcerated surface subscore of 0 in patients with baseline subscore ≥ 1;
(2) Clinical response, defined as a ≥100-point reduction in the Crohn's Disease Activity Index (CDAI);
(3) Clinical remission, defined as CDAI < 150;
(4) Biomarker remission, defined as normalization of serum C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), and fecal calprotectin (FC) levels.

Safety assessment

All adverse events (AEs) occurring during the 12-week induction period were recorded. Laboratory abnormalities were documented regardless of clinical symptoms. Serious adverse events (SAEs) were defined as events leading to treatment discontinuation, hospitalization, or life-threatening complications.

Statistical analysis

Descriptive statistics were presented as frequencies and percentages for categorical variables, and as mean (± standard deviation) or median (interquartile range, IQR) for continuous variables. Between-group comparisons of categorical data employed the χ^2 test or Fisher's exact test, as appropriate. Continuous data were analyzed using the Wilcoxon rank-sum test or independent two-sample t-test for unpaired comparisons, and Wilcoxon signed-rank test or paired t-test for longitudinal data. Multivariate logistic regression models were applied to assess baseline predictors of therapeutic outcomes. Statistical significance was defined as a two-tailed $P < 0.05$. Analyses were performed using SAS (v9.4; SAS Institute), and data visualization was conducted using GraphPad Prism (v9.0).

Results

Patient characteristics and baseline clinical features

A total of 117 patients with CD initiated upadacitinib therapy at our center between June 2023 and February 2025. After excluding two patients with incomplete baseline documentation and 21 patients who did not complete 12 weeks of therapy yet, 94 patients were included in the final efficacy and safety analyses (Fig. 1). The cohort was predominantly male (64.9%, 61/94), with a median age of 30 years (interquartile range [IQR], 24–39), and a median disease duration of 44.4 months (IQR, 31.0–71.1).

Based on the Montreal classification, most patients were categorized as A2 (diagnosed between 16 and 40 years; 77.7%). Ileocolonic involvement (L3) was the most common disease distribution (60.6%), followed by non-stricturing, non-penetrating behavior (B1; 55.3%). Perianal manifestations, including fistulas and abscesses, were

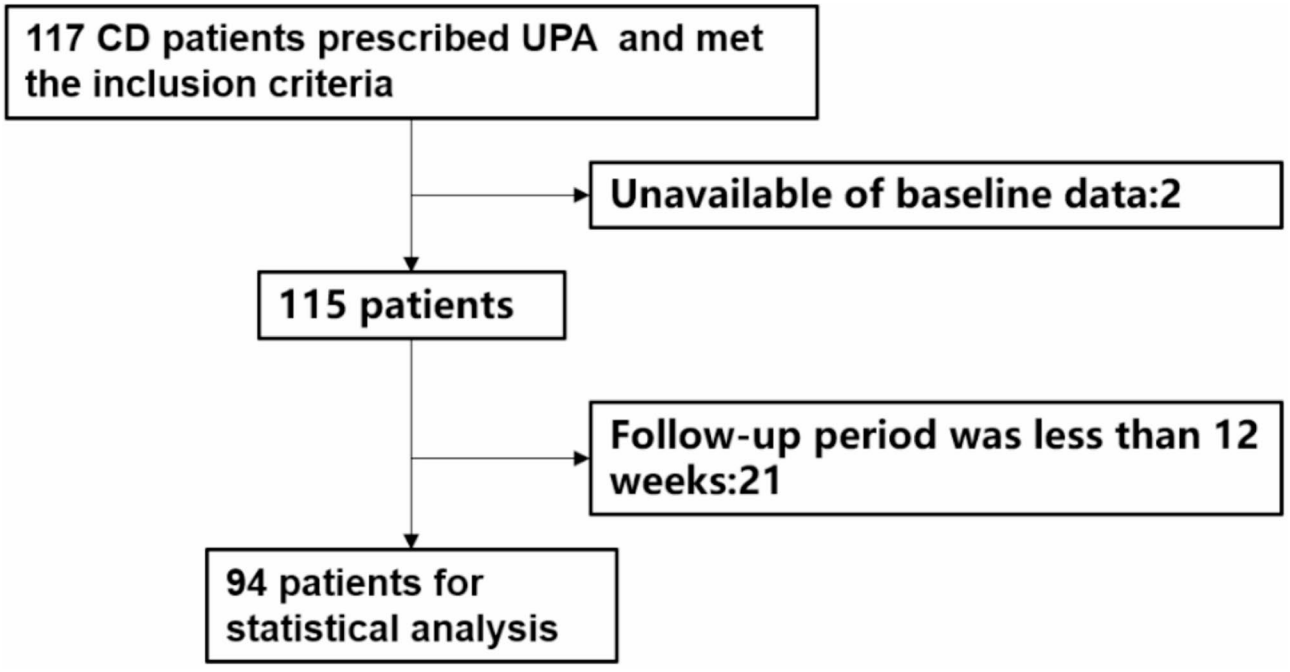

Fig. 1 Study cohort selection flowchart. Flow diagram showing patient screening and selection. Among 117 Crohn's disease (CD) patients who initiated upadacitinib between June 2023 and February 2025, 2 were excluded due to missing baseline data, and 21 hadn't completed 12 weeks of therapy yet. The final efficacy analysis included 94 patients, all of whom were also assessed for safety outcomes

present in 61.7% of patients. A history of gastrointestinal surgery was reported in 23.4% (22/94), while 36.2% had undergone at least one perianal surgery. Comorbidities were reported in 9.6%, most commonly hypertension and ankylosing spondylitis. All patients received baseline screening prior to upadacitinib initiation, including T-SPOT testing and chest CT scans for tuberculosis (TB) risk assessment, testing for viral hepatitis, herpes zoster, cytomegalovirus (CMV), EB virus (EBV) infections and venous thromboembolism ultrasound as well. The abnormal screening results are as follows: 4 patients tested positive for T-SPOT at upadacitinib initiation and received concomitant anti-TB treatment by isoniazide for oral administration. 2 patients with baseline hepatitis B infection were on entecavir therapy. Detailed baseline characteristics are provided in Table 1.

All but one patient had been previously treated with at least one biologic agent. Infliximab (64.9%), adalimumab (40.4%), and ustekinumab (33.0%) were the most commonly used therapies. Upadacitinib was initiated after documented failure of infliximab in 39.8%, adalimumab in 29.0%, and ustekinumab in 31.2% of patients. For the reason of therapy conversion, inadequate response to anti-TNF agents accounted for 57.4% (54/94), while 9.6% (9/94) reported allergic reactions or side effects to anti-TNF agents. For anti-IL-12/IL-23 agents, 19.1% (18/94) of patients had inadequate response or loss of response, and 8.5% (8/94) experienced allergic reactions or adverse effects. Notably, 39.4% (37/94) had prior exposure to two or more biologic agents. Additionally, 4.3% (4/94) switched to oral upadacitinib due to poor adherence to injective therapies. Besides, 5 patients received glucocorticoids at baseline, in which 3 patients were tapered gradually and discontinued, but 2 patients continued low dose glucocorticoids during the induction phase due to inadequate symptom improvement. 4 patients were on azathioprine and 2 patients were on oral mesalazine at baseline; and these medications were discontinued after symptom was controlled. Patients with perianal lesions did not receive antibiotics at baseline.

At baseline, 67.7% of patients undergoing endoscopic evaluation (63/93) demonstrated moderate-to-severe mucosal disease activity (SES-CD ≥ 7), with a median SES-CD of 10.0 (IQR, 6–10) (Fig. 2A). Clinically, 75.5% (71/94) of patients met criteria for moderate-to-severe disease (CDAI > 220), with a mean baseline CDAI of 291.53 ± 99.26 (Fig. 2B). Inflammatory biomarkers were elevated in a majority of patients: CRP in 70.8% (63/89), ESR in 44.7% (38/85), and fecal calprotectin (FC) in 90.3% (65/72). Nutritional parameters indicated a median body mass index (BMI) of 19.7 kg/m² (IQR, 18.1–23.4), and serum albumin levels were < 35 g/L in 21.5% of patients, consistent with systemic inflammation and undernutrition.

These findings characterize a predominantly young, biologic-refractory CD population with elevated inflammatory markers and complex disease phenotypes at the time of upadacitinib initiation.

Endoscopic outcomes following induction therapy

Endoscopic reassessment at week 12 was performed in 36 of the 94 patients (38.3%) who completed induction therapy. The comparison of baseline characteristics between those who had follow-up endoscopy and those who did not was shown in supplementary material 6. In this subset, treatment with upadacitinib led to a significant reduction in endoscopic disease activity. The median SES-CD score declined from 13.5 (IQR, 8.0–17.0) at baseline to 6.0 (IQR, 2.0–10.5) at week 12, corresponding to a median reduction of 4.5 points (95% confidence interval [CI], 3.0–7.0; $P < 0.001$) (Fig. 3A).

Half of the patients (50.0%, 18/36) achieved an endoscopic response, defined as a ≥ 50% reduction in SES-CD from baseline. Endoscopic remission, defined as SES-CD ≤ 4 with a ≥ 2-point reduction and no subscore > 1, was achieved in 38.9% (14/36). Mucosal healing—defined as the complete resolution of ulcerated mucosal surfaces—was observed in 27.8% (10/36) of patients with documented ulcerations at baseline.

Although the proportion of patients undergoing post-treatment endoscopy was limited, those who completed the evaluation represent a clinically relevant subset of the cohort with moderate-to-severe endoscopic disease at baseline. The observed rates of response and remission are consistent with previously reported induction-phase outcomes for JAK1 inhibition in CD, supporting the mucosal efficacy of upadacitinib under real-world conditions.

Clinical response and remission rates

At the end of the 12-week induction phase, clinical disease activity was evaluable in 77 of 94 patients (81.9%) who completed upadacitinib therapy. Treatment was associated with a significant reduction in CDAI scores, with mean values decreasing from 282.4 ± 95.4 at baseline to 184.7 ± 84.7 at week 12 (mean change: −97.7; 95% CI, − 84.4 to − 111.0; $P < 0.001$) (Fig. 3B).

A clinical response–defined as a reduction of at least 100 points from baseline CDAI—was achieved in 53.2% (41/77) of patients. Clinical remission, defined as CDAI < 150, was attained in 42.9% (33/77) of patients. Notably, 31.2%(24/77)of patients met criteria for both clinical response and remission, reflecting both a reduction in disease burden and normalization of clinical symptoms.

Although CDAI is partially subjective and influenced by patient-reported outcomes, the observed response rates are consistent with objective biomarker

Table 1 Baseline demographic, clinical, and laboratory characteristics of the study cohort

Variable	Median (P25, P75)/number (%)
Gender	
Male	61 (64.89%)
Female	33 (35.11%)
Age(years)	30(24,39)
Disease duration(months)	44.42(30.98,71.06)
Smoking	
Current smoker	3 (3.19%)
Former smoker	3 (3.19%)
Never	88 (93.62%)
Drinking	
Current drinker	1 (1.06%)
Former drinker	0(0.00%)
Never	93 (98.94%)
Montreal classification	
A1	5 (5.32%)
A2	73 (77.66%)
A3	16 (17.02%)
L1	13 (13.83%)
L2	10 (10.64%)
L3	57 (60.64%)
L2 + 4	1 (1.06%)
L3 + 4	13 (13.83%)
B1	52 (55.32%)
B2	28 (29.79%)
B3	6 (6.38%)
B2 + 3	8 (8.51%)
P	58 (61.70%)
Gastrointestinal operation history	
None	72 (76.60%)
1	11 (11.70%)
2	7 (7.45%)
≥ 3	4 (4.26%)
Perianal operation history	
None	60 (63.83%)
1	30 (31.91%)
2	3 (3.19%)
≥ 3	1 (1.06%)
Prior biologics therapy	
IFX	61 (64.89%)
ADA	38 (40.43%)
UST	31 (32.98%)
VDZ	2 (2.13%)
None	1 (1.06%)
Last biologics before upadacitinib therapy	
IFX	37(39.78%)
ADA	27(29.03%)
UST	29(31.18%)
Baseline disease severity	
SES-CD ($n = 93$)	10.00 (6.00, 17.00)
CDAI ($n = 94$)	291.53 ± 99.26
BMI (kg/m^2) ($n = 94$)	19.68(18.07,23.43)
CRP (mg/L) ($n = 89$)	6.72 (3.18, 21.36)
ESR (mm/h) ($n = 85$)	16.00 (7.00, 33.00)

Table 1 (continued)

Variable	Median (P25, P75)/number (%)
FC (μg/g) (*n* = 72)	264.64 (133.97, 463.01)
WBC (*10^9/L) (*n* = 93)	6.93 ± 2.14
RBC (*10^{12}/L) (*n* = 93)	4.66 ± 0.62
HB (g/L) (*n* = 93)	129.00 (114.00, 141.00)
PLT (*10^9/L) (*n* = 93)	298.00 (221.00, 353.00)
Lymphocyte (*10^9/L) (*n* = 75)	1.55 (1.23, 2.01)
ALB (g/L) (*n* = 79)	39.90 (35.45, 44.40)
Comorbidity	
Hypertension	3 (3.19%)
Ankylosing Spondylitis	3 (3.19%)
Hyperlipidemia	1 (1.06%)
IgA nephropathy	1 (1.06%)
Psoriasis	1 (1.06%)

IFX Infliximab, *ADA* Adalimumab, *UST* Ustekinumab, *VDZ* Vedolizumab, *SES-CD* Simple Endoscopic Score for Crohn's Disease, *CDAI* Crohn's Disease Activity Index, *BMI* Body Mass Index, *CRP* C-Reactive Protein, *ESR* Erythrocyte Sedimentation Rate, *FC* Fecal Calprotectin, *WBC* White Blood Cell, *RBC* Red Blood Cell, *HB* Hemoglobin, *HCT* Hematocrit, *PLT* Platelet, *ALB* Albumin

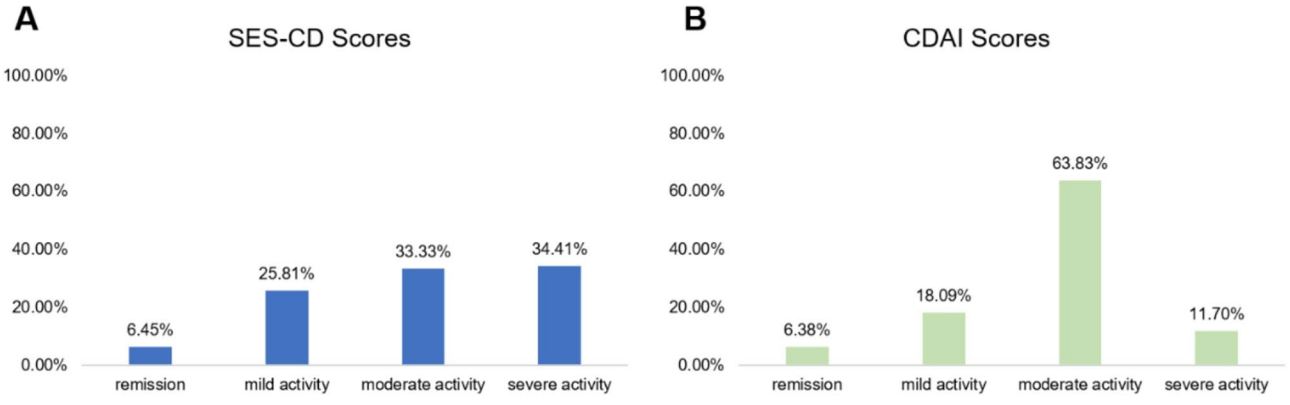

Fig. 2 Baseline endoscopic and clinical status of the cohort. At baseline, 67.7% (63/93) of patients demonstrated moderate-to-severe mucosal disease activity (SES-CD ≥ 7) **A**. Clinically, 75.5% (71/94) of patients met criteria for moderate-to-severe disease (CDAI > 220) **B**

improvements and endoscopic findings, reinforcing the therapeutic benefit of upadacitinib in this biologic-refractory CD population.

Biomarker dynamics during treatment

Upadacitinib induction therapy resulted in significant reductions in systemic and intestinal inflammatory biomarkers over the 12-week treatment period. Among patients with available paired data, serum CRP levels decreased from a median of 6.57 mg/L (IQR, 2.81–22.77) at baseline. The median reduction was 3.87 mg/L (96.37% CI, 1.66–6.99; $P < 0.001$). CRP normalization was observed in 62.7% (37/59) of patients by week 12 (Fig. 4A).

Erythrocyte sedimentation rate (ESR) also declined significantly, with a median reduction of 2.5 mm/h (95.98% CI, 1.0–7.0; $P = 0.003$). ESR normalization was achieved in 70.9% (39/55) of patients (Fig. 4B).

Fecal calprotectin (FC), a sensitive biomarker of intestinal inflammation, decreased significantly from a median of 267.97 μg/g (IQR, 131.64,466.18) at baseline. The median reduction was 142.8 μg/g (97.07% CI, 68.27–222.9; $P < 0.001$). Despite this improvement, only 29.6% (16/54) of patients achieved normalization of FC (< 60 μg/g), suggesting residual mucosal inflammation in a subset of patients (Fig. 4C).

Other laboratory indices reflected favorable systemic trends. White blood cell (WBC) counts declined modestly but significantly (mean change: -0.35×10^9/L; $P < 0.001$), while serum albumin levels increased by a mean of + 2.4 g/L ($P < 0.001$), indicating improvements in both inflammatory burden and nutritional status (supplementary material 1).

Together, these biomarker trajectories provide robust objective evidence of the anti-inflammatory effects of upadacitinib during induction therapy and support its concordant clinical and endoscopic efficacy.

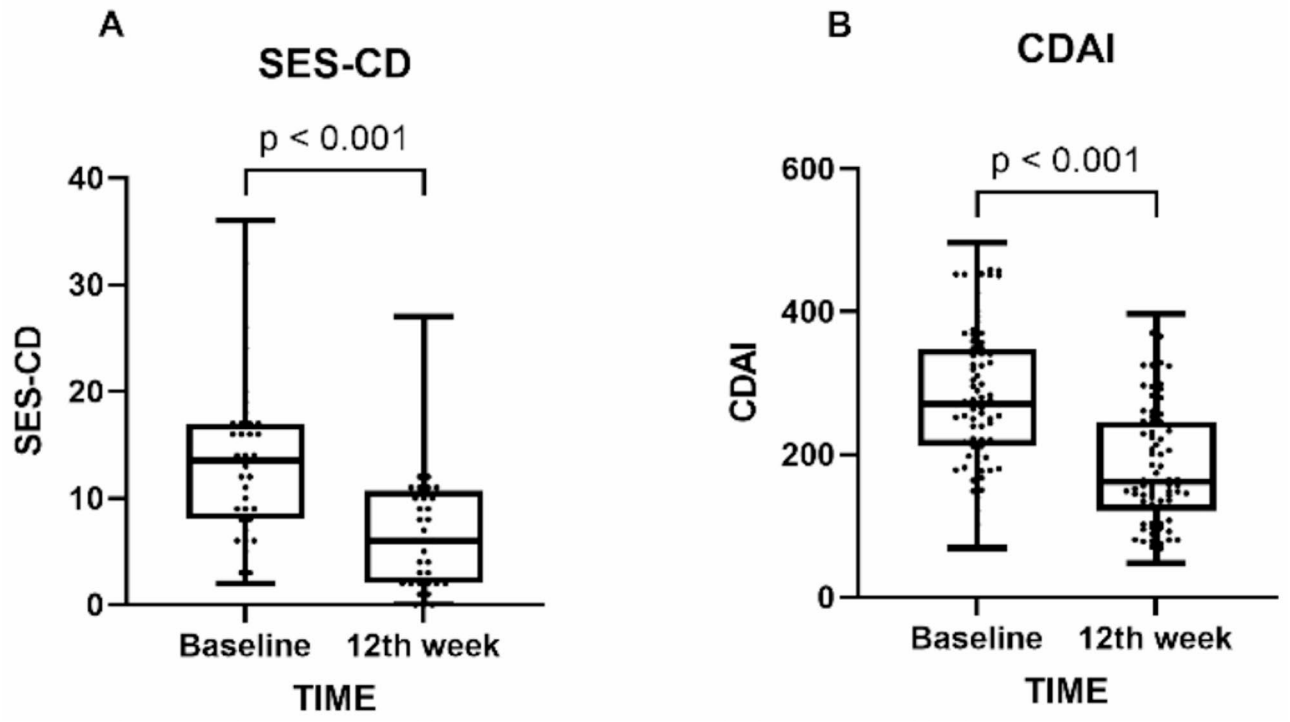

Fig. 3 Endoscopic response and clinical response following 12-week upadacitinib induction therapy. At the end of 12-week induction therapy, the Median SES-CD reduction was 4.5 points (95% CI: 3.0–7.0, $P < 0.001$) **A**. Mean CDAI reduction was 97.69 points (95% CI: 84.42–111.0, $P < 0.001$) **B**

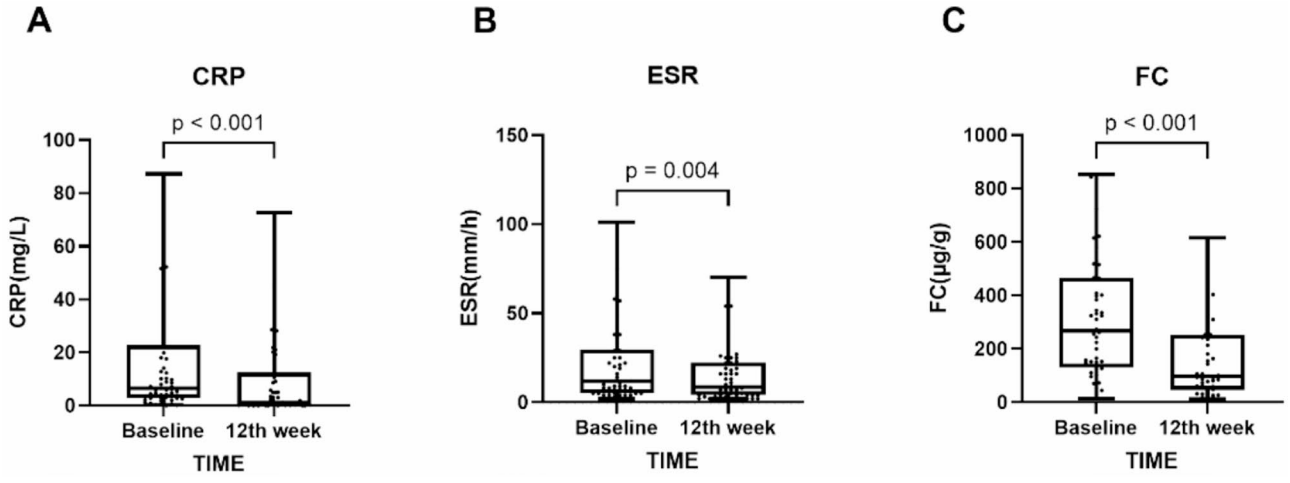

Fig. 4 Longitudinal changes in inflammatory biomarkers during upadacitinib induction. Serial measurements of CRP ($n = 59$), ESR ($n = 55$), and fecal calprotectin (FC; $n = 54$) from baseline to week 12. CRP decreased by a median of 3.87 mg/L (95.37% CI: 1.66–6.99, $P < 0.001$) **A**, ESR by 2.5 mm/h (95.98% CI: 1.0–7.0, $P = 0.003$) **B**, and FC by 142.80 μg/g (97.07% CI: 68.27–222.90, $P < 0.001$) **C**. Normalization was achieved in 62.71% (CRP), 70.91% (ESR), and 29.63% (FC) of patients, respectively

Safety profile and adverse events

All 94 patients who completed the 12-week induction phase were included in the safety analysis. A total of 41 treatment-emergent adverse events were documented in 32 patients (34.0%), the majority of which were mild to moderate in severity and self-limiting.

Lymphopenia was the most frequently observed events, reported in 10.6% (10/94). Elevations in hepatic transaminases were observed in 9.6% (9/94) of patients. One individual required hepatoprotective therapy, whereas others continued upadacitinib with routine liver function monitoring. Dermatologic adverse events were noted in 8.5% of patients, including acne ($n = 6$) and herpes zoster ($n = 2$); both cases of zoster were treated with antiviral agents. Hyperlipidemia was detected in 5.3% (5/94) and managed with lipid-lowering therapy.

Table 2 Treatment-emergent adverse events during upadacitinib induction therapy

Adverse events	Number(percentage%)
Serious adverse events	
Tuberculosis	1(1.06%)
Others	
Lymphopenia	10(10.64%)
Hepatic disorder (transaminase elevation)	9(9.57%)
Acne	6(6.38%)
Hyperlipidemia	5(5.32%)
Opportunistic infections	5(5.32%)
Constipation	3(3.19%)
Herpes zoster	2(2.13%)

Opportunistic infections were recorded in 5.3% (5/94) of patients, comprising 2 enteric infections, 1 respiratory tract infection, 1 folliculitis and 1 uncomplicated urinary tract infection, although the direct causal relationship with upadacitinib could not be definitively established. All cases were managed with culture-directed antimicrobial therapy but 2 of them discontinued upadacitinb temporarily. Gastrointestinal adverse events were infrequent, with early-onset constipation reported in 3 patients and resolved spontaneously.

Serious adverse events occurred in 1 patient (1.1%) and led to permanent discontinuation of upadacitinib. This patient was found active pulmonary tuberculosis after 12 weeks of upadacitinb treatment. Following definite tuberculosis diagnosis, upadacitinib was promptly discontinued with concurrent initiation of antitubercular therapy, currently ongoing. No cases of malignancy, thromboembolic events, or death occurred during the study period.

A summary of all treatment-emergent adverse events is presented in Table 2. Overall, the safety profile of upadacitinib in this biologic-experienced CD population was consistent with prior clinical trial findings. Most adverse events were manageable with standard supportive care, and no unexpected toxicities were identified.

Baseline predictors of therapeutic response

To explore clinical factors associated with therapeutic outcomes, baseline characteristics were compared between responders and non-responders across multiple endpoints. Variables examined included demographic factors, disease duration, clinical activity indices (CDAI, SES-CD), inflammatory biomarkers (CRP, ESR, and fecal calprotectin), prior biologic exposure, and disease phenotype based on the Montreal classification.

Endoscopic response at week 12 was significantly associated with longer disease duration. Responders had a median disease duration of 77.4 months, compared to 31.4 months in non-responders ($P=0.020$), suggesting that patients with a more prolonged disease course may derive greater mucosal benefit from JAK1 inhibition (supplementary material 2). In contrast, endoscopic remission was more likely among patients with lower baseline CDAI scores (mean: 211.6 ± 73.4 vs. 281.4 ± 88.8; $P=0.019$) (supplementary material 3), indicating that lower systemic disease burden at baseline may favor mucosal healing.

In clinical outcome analyses, distinct patterns emerged. Patients who achieved clinical response exhibited significantly higher baseline CDAI scores than non-responders (318.6 ± 85.5 vs. 245.3 ± 91.6; $P=0.001$), consistent with a greater capacity for measurable improvement (supplementary material 4). By contrast, clinical remission was more frequently observed in patients with older age (median: 34 vs. 27 years; $P=0.038$), lower baseline SES-CD scores (median: 7.0 vs. 12.5; $P=0.018$), and lower CDAI scores (233.2 ± 68.7 vs. 319.4 ± 96.5; $P<0.001$), suggesting that milder disease activity at baseline favors remission (supplementary material 5).

No significant associations were found between treatment outcomes and baseline CRP, ESR, fecal calprotectin, BMI, smoking status, or number and class of previously used biologics. The different type in disease behaviour, disease location or the presence of perianal lesions based on Montreal Classification had no association with therapeutic efficacy (Supplementary material 7). Similarly, no individual clinical or biochemical marker reliably predicted mucosal healing, underscoring the multifactorial nature of deep tissue repair in Crohn's disease.

Collectively, these findings highlight the importance of baseline disease activity in shaping treatment outcomes. Patients with high symptom burden are more likely to achieve substantial reductions in disease activity scores, while those with less active disease are more likely to achieve complete remission. These insights may support more personalized treatment strategies and help refine patient selection criteria for JAK1-targeted therapy.

Discussion

In this real-world, single-centre study, we evaluated the effectiveness and safety of 12-week upadacitinib induction therapy in biologic-experienced patients with active CD in central China. Our findings demonstrate that upadacitinib was associated with meaningful clinical and endoscopic improvements, accompanied by significant reductions in systemic and intestinal inflammatory biomarkers. The treatment was generally well tolerated, with a manageable safety profile consistent with previous clinical trials.

The observed clinical response rates of 53.2%, align closely with those reported in the pivotal U-EXCEL and U-EXCEED trials, which reported endoscopic response rates of 56.6% and 50.5% [15]. The clinical remission rate in our cohort (42.9%) was comparable, while the endoscopic response (50.0%) and endoscopic remission rate (38.9%) was slightly higher. These differences may partly reflect

the variation in baseline disease burden. Notably, two real-world studies in the UK and the United States reported higher clinical remission rates of 64% and 52.1% using the Harvey-Bradshaw Index, highlighting the impact of endpoint definition on inter-study comparisons [16, 18].

Biomarker dynamics supported the clinical and endoscopic findings, with significant reductions in CRP, ESR, and FC. While normalization rates were higher for CRP and ESR, FC remission was achieved in only 29.6% of patients, likely reflecting its heightened sensitivity to residual mucosal inflammation. These results confirm the anti-inflammatory efficacy of selective JAK1 inhibition in CD and suggest that serum markers may underestimate persistent disease activity in some patients.

The observed phenomenon in this CD trials—where treatment response (e.g., clinical/endoscopic response) is more common in patients with high baseline disease activity, while treatment remission (clinical/endoscopic remission) is more frequent in those with low baseline activity—primarily stems from the interplay between efficacy assessment criteria and disease biology: Response relies on relative improvement magnitude (≥100-score reduction in CDAI or ≥50% decrease in SES-CD). High-activity patients exhibit substantial inflammatory burden, enabling rapid JAK/STAT pathway inhibition by upadacitinib to achieve large score reductions that readily meet response thresholds. Remission requires attainment of absolute thresholds (CDAI < 150 or SES-CD ≤ 4). Low-activity patients start closer to these targets with milder tissue damage, allowing comparable anti-inflammatory effects to more easily cross remission cutoffs, whereas high-activity patients need deeper repair to reach these stringent endpoints. This pattern reflects upadacitinib's dual role in rapidly controlling high inflammatory loads (favoring response) and promoting profound mucosal healing (favoring remission), underscoring the need for individualized treatment goal-setting based on baseline activity. Julian Panés et al. found that patients achieving endoscopic response during the induction phase demonstrated a higher proportion of CDAI clinical remission at the end of maintenance therapy [19]. Remo Panaccione and colleagues analyzed that endoscopic improvement during induction therapy was independently associated with reduced disease-related hospitalizations during maintenance treatment [20]. These findings partially suggest that patients with lower disease activity are more likely to achieve better clinical outcomes, which is consistent with our hypothesis. However, the correlation between baseline disease status and induction-phase outcomes has been rarely reported, which requires further validation through larger sample sizes and more rigorous analyses.

Our safety analysis revealed that upadacitinib was well tolerated in this biologic-refractory population. Most adverse events were mild, transient, and laboratory-based, including lymphopenia and hepatic transaminase elevations. The incidence and spectrum of adverse events were comparable to those reported in global trials. Importantly, the case of pulmonary tuberculosis considered to be serious adverse event and led to treatment discontinuation marked the first such report in a CD population treated with upadacitinib. Although tuberculosis reactivation has been described in patients with psoriatic arthritis and rheumatoid arthritis receiving JAK inhibitors, this finding underscores the need for rigorous pre-treatment screening and vigilance, particularly in regions with intermediate or high TB prevalence [21, 22].

Our exploratory analyses identified several clinical predictors of treatment response. Patients with lower baseline CDAI and SES-CD scores were more likely to achieve remission, while those with higher CDAI at baseline exhibited greater absolute score reductions, reflecting a broader dynamic range for symptomatic improvement. These patterns suggest that baseline disease activity may guide patient selection and therapeutic expectations. Subgroup analyses indicated that perianal disease and the number of prior biologic failures did not significantly impact clinical or endoscopic outcomes, supporting the applicability of upadacitinib across a range of CD phenotypes.

This study addresses a critical evidence gap by providing real-world data on upadacitinib use in an Asian CD population, specifically within China, where epidemiologic and clinical patterns of IBD continue to evolve. Our findings support the incorporation of upadacitinib as a viable induction option in biologic-refractory patients and may inform individualized treatment strategies based on clinical profiling.

Several limitations should be acknowledged. First, endoscopic reassessment was performed in only 38.3% of patients, primarily due to patient preference and compliance challenges, limiting the completeness of mucosal outcome data. Second, the retrospective design precludes causal inference and may introduce selection bias. Third, the follow-up duration was limited to the induction phase, and long-term maintenance efficacy and safety remain to be determined. Future prospective, multicenter studies with extended observation periods are warranted to validate these findings and evaluate sustained treatment responses.

Conclusion

In summary, upadacitinib demonstrated favorable clinical, endoscopic, and biomarker responses with an acceptable safety profile in a real-world cohort of biologic-experienced patients with active CD. These results provide supportive evidence for the clinical utility of JAK1 inhibition in routine practice and reinforce the importance of baseline disease profiling in guiding treatment selection.

Abbreviations

JAK1	Janus kinase 1
CD	Crohn's disease
CRP	C-reactive protein
ESR	Erythrocyte sedimentation rate
FC	Fecal calprotectin
CDAI	Crohn's Disease Activity Index
SES-CD	Simple Endoscopic Score for Crohn's Disease
TNF	Tumor necrosis factor
STAT	Signal transducer and activator of transcription
AEs	Adverse events
SAEs	Serious adverse events
IQR	Interquartile range
BMI	Body mass index
CI	Confidence interval

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12876-025-04305-z.

Supplementary Material 1.

Supplementary Material 2.

Supplementary Material 3.

Supplementary Material 4.

Supplementary Material 5.

Supplementary Material 6.

Supplementary Material 7.

Acknowledgements
Not applicable.

Authors' contributions
XF collected, analyzed the data and completed the article; LT, YF, HW provided the data and helped with data collection and analysis. YidC contributed to the manuscript writing and data analysis, FL, QY, XZ, JL, QX, and YiyC contributed to data analysis and data verification; LZ and RL designed the study and provided critical review of the manuscript. All authors contributed to the article and approved the submitted version.

Funding
The research presented herein was financially supported by grants from the National Key R&D Program of China (Grant Number 2023YFC2507300), as well as the National Natural Science Foundation of China (Grant Numbers 82470562 and 82170547).

Data availability
For the protection of patients' privacy, the de-identified patient data that support the findings of this study are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate
This study was conducted in accordance with the principles of the Declaration of Helsinki. Ethical approval for the use of human subjects was obtained from the Independent Ethics Committee of Union Hospital, Tongji Medical College, Huazhong University of Science and Technology (Ethics Review Number 2024-No. 0880-01). Due to the retrospective nature of the study, patient data were obtained from the electronic medical record system, and the waiver of informed consent was also approved by the Independent Ethics Committee of Union Hospital, Tongji Medical College, Huazhong University of Science and Technology (Ethics Review Number 2024-No. 0880-01).

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Received: 4 June 2025 / Accepted: 3 September 2025
Published online: 08 October 2025

References

1. Torres J, Mehandru S, Colombel JF, Peyrin-Biroulet L. Crohn's disease. Lancet. 2017;389(10080):1741–55. https://doi.org/10.1016/S0140-6736(16)31711-1.
2. Lin D, Jin Y, Shao X, et al. Global, regional, and national burden of inflammatory bowel disease, 1990–2021: insights from the global burden of disease 2021. Int J Colorectal Dis. 2024;39(1):139. https://doi.org/10.1007/s00384-024-04711-x.
3. Kumar A, Cole A, Segal J, Smith P, Limdi JK. A review of the therapeutic management of crohn's disease. Th Adv Gastroenterol. 2022;15:17562848221078456. https://doi.org/10.1177/17562848221078456.
4. Farraj KL, Pellegrini JR, Munshi RF, et al. Chronic steroid use: an overlooked impact on patients with inflammatory bowel disease. JGH Open. 2022;6(12):910–4. https://doi.org/10.1002/jgh3.12841.
5. Chande N, Patton PH, Tsoulis DJ, Thomas BS, MacDonald JK. Azathioprine or 6-mercaptopurine for maintenance of remission in crohn's disease. Cochrane Database Syst Rev. 2015;2015(10):CD000067. https://doi.org/10.1002/14651858.CD000067.pub3.
6. Patel V, Wang Y, MacDonald JK, McDonald JWD, Chande N. Methotrexate for maintenance of remission in crohn's disease. Cochrane Database Syst Rev. 2014;2014(8):CD006884. https://doi.org/10.1002/14651858.CD006884.pub3.
7. Cai Z, Wang S, Li J. Treatment of inflammatory bowel disease: a comprehensive review. Front Med Lausanne. 2021;8:765474. https://doi.org/10.3389/fmed.2021.765474.
8. Denesh D, Carbonell J, Kane JS, Gracie D, Selinger CP. Patients with inflammatory bowel disease (IBD) prefer oral tablets over other modes of medicine administration. Expert Rev Gastroenterol Hepatol. 2021;15(9):1091–6. https://doi.org/10.1080/17474124.2021.1898944.
9. Buisson A, Serrero M, Orsat L, et al. Comparative acceptability of therapeutic maintenance regimens in patients with inflammatory bowel disease: results from the nationwide ACCEPT2 study. Inflamm Bowel Dis. 2023;29(4):579–88. https://doi.org/10.1093/ibd/izac119.
10. Herrera-deGuise C, Serra-Ruiz X, Lastiri E, Borruel N. JAK inhibitors: A new dawn for oral therapies in inflammatory bowel diseases. Front Med. 2023;10. https://doi.org/10.3389/fmed.2023.1089099.
11. Salas A, Hernandez-Rocha C, Duijvestein M, et al. Jak-STAT pathway targeting for the treatment of inflammatory bowel disease. Nat Rev Gastroenterol Hepatol. 2020;17(6):323–37. https://doi.org/10.1038/s41575-020-0273-0.
12. Haan C, Rolvering C, Raulf F, et al. Jak1 has a dominant role over Jak3 in signal transduction through γc-containing cytokine receptors. Chem Biol. 2011;18(3):314–23. https://doi.org/10.1016/j.chembiol.2011.01.012.
13. Parmentier JM, Voss J, Graff C, et al. In vitro and in vivo characterization of the JAK1 selectivity of Upadacitinib (ABT-494). BMC Rheumatol. 2018;2:23. https://doi.org/10.1186/s41927-018-0031-x.
14. Aguilar D, Revilla L, Garrido-Trigo A, et al. Randomized controlled trial substudy of cell-specific mechanisms of Janus kinase 1 inhibition with Upadacitinib in the Crohn's disease intestinal mucosa: analysis from the CELEST study. Inflamm Bowel Dis. 2021;27(12):1999–2009. https://doi.org/10.1093/ibd/izab116.
15. Loftus EVJ, Panés J, Lacerda AP, et al. Upadacitinib induction and maintenance therapy for crohn's disease. N Engl J Med. 2023. https://doi.org/10.1056/NEJMoa2212728.
16. Elford AT, Bishara M, Plevris N, et al. Real-world effectiveness of Upadacitinib in Crohn's disease: a UK multicentre retrospective cohort study. Frontline Gastroenterol. 2024;15(4):297–304. https://doi.org/10.1136/flgastro-2024-102668.
17. Friedberg S, Choi D, Hunold T, et al. Upadacitinib is effective and safe in both ulcerative colitis and crohn's disease: prospective Real-World experience. Clin Gastroenterol Hepatol. 2023;21(7):1913–e19232. https://doi.org/10.1016/j.cgh.2023.03.001.
18. Devi J, Xu A, Stone M et al. Real-World Effectiveness and Safety of Upadacitinib in Crohn's disease: A Multi-Centre Study. Clin Gastroenterol Hepatol. Published online March 7, 2025:S1542-3565(25)00154-5. https://doi.org/10.1016/j.cgh.2025.01.012

19. Panés J, Louis E, Bossuyt P, et al. Induction of endoscopic response, remission, and ulcer-free endoscopy with Upadacitinib is associated with improved clinical outcomes and quality of life in patients with Crohn's disease. Inflamm Bowel Dis. 2025;31(2):394–403. https://doi.org/10.1093/ibd/izae200.
20. Panaccione R, Ma C, Jairath V, et al. Achievement of endoscopic remission after induction reduces hospitalization burden in Crohn's disease: findings from a pooled post hoc analysis of Risankizumab and Upadacitinib phase III trials. J Crohns Colitis. 2024;19(2):jjae128. https://doi.org/10.1093/ecco-jcc/jjae128.
21. Valor-Méndez L, Manger B, Wacker J, Kleyer A, Schett G. Lymph node and pulmonary tuberculosis during Upadacitinib treatment in a psoriatic arthritis patient. Rheumatol Adv Pract. 2022;6(2):rkac032. https://doi.org/10.1093/rap/rkac032.
22. Kakehasi AM, Radominski SC, Baravalle MD, et al. Safety of upadacitinib in Latin American patients with rheumatoid arthritis: an integrated safety analysis of the SELECT phase 3 clinical program. Clin Rheumatol. 2023;42(5):1249–58. https://doi.org/10.1007/s10067-023-06513-y.

Publisher's Note