JCC Plus

WILEY

SHORT REPORT OPEN ACCESS

Combination of Upadacitinib and Risankizumab in Refractory Crohn's Disease

Clara Ramos-Belinchon[1] | Nikolas Plevris[1] | Ian Arnott[1] | Shahida Din[1,2] | Jonathan Blackwell[1] | Charlie W. Lees[1,3]

[1]Edinburgh IBD Unit, Western General Hospital, Edinburgh, UK | [2]Cancer Research UK Edinburgh Centre, Institute of Genetics and Cancer, University of Edinburgh, Edinburgh, UK | [3]Centre for Genomics and Experimental Medicine, Institute of Genetics and Cancer, University of Edinburgh, Western General Hospital, Edinburgh, UK

Correspondence: Charlie W. Lees (charlie.lees@ed.ac.uk)

Received: 12 December 2025 | **Revised:** 24 February 2026 | **Accepted:** 19 March 2026

Keywords: biologic pharmaceuticals | Crohn's disease | risankizumab | small molecule | upadacitinib

ABSTRACT

Background and Aim: Dual targeted therapies (DTT) are a promising off-label approach for the treatment of refractory Crohn's disease (CD). Upadacitinib and risankizumab are approved for the treatment of moderate to severe CD. Our aim was to evaluate the effectiveness and safety of a combination of upadacitinib and risankizumab for refractory CD.

Methods: In this retrospective, observational study we assessed $n = 15$ CD patients who received the combination upadacitinib and risankizumab at the Edinburgh IBD Unit, Scotland. All patients included had a minimum overlap of 8 weeks. The primary outcome was steroid-free clinical response (SFCR) at 12 weeks defined as a decrease in Harvey Bradshaw Index (HBI) ≥ 3 and/or HBI < 5; if not available, a reduction of Physician Global Assessment (PGA) ≥ 1 was also considered as a response. Secondary outcomes included clinical remission (HBI < 5 or considered by PGA if HBI was not available), C-reactive protein (CRP) remission (CRP$\leq$ 5 mg/L) and faecal calprotectin (FC) remission (FC < 250 μg/g) at 12 weeks. Additional secondary outcomes were persistence at 24 and 52 weeks in patients with planned long-term DTT, and successful withdrawal in patients with planned short-term DTT. Safety outcomes were also recorded.

Results: Fifteen patients were included with a median of 3 prior advanced therapies (IQR 2–5). SFCR was achieved in 53% (8/15). Steroid-free clinical remission, CRP and FC remission were achieved in 40% (6/15), 27% (4/15) and 27% (4/15) of the total patients, respectively. No treatment-related serious adverse events were observed.

Conclusions: In this case series, combination upadacitinib and risankizumab demonstrated, short-term effectiveness and safety in a highly refractory cohort of CD patients.

1 | Introduction

Novel advanced therapies (AT) targeting distinct inflammatory pathways have significantly improved disease outcomes in patients with Crohn's disease (CD) [1, 2]. Nevertheless, a therapeutic ceiling persists, leaving a subset of patients refractory to current treatments [3]. Additionally, up to 43% of CD patients will develop an extraintestinal manifestation (EIM) which may require tailored therapeutic approaches [4]. Dual targeted therapies (DTT) combining either two biologic agents or a biologic agent and a small molecule could be a promising strategy to help improve remission rates in these scenarios [5].

Upadacitinib is an oral, selective Janus Kinase (JAK)-1 inhibitor with proven post-induction effectiveness demonstrated in the U-EXCEL and U-EXCEED phase 3 trials (clinical remission rates of 49.5% and 38.9%) [6]. Risankizumab is a monoclonal antibody to interleukin (IL)-23 p19 with post-induction clinical remission rates of 45% and 42% in the phase 3 trials ADVANCE and MOTIVATE, respectively [7]. Both are approved by European

This is an open access article under the terms of the Creative Commons Attribution License, which permits use, distribution and reproduction in any medium, provided the original work is properly cited.

© 2026 The Author(s). *JCC Plus* published by John Wiley & Sons, Ltd. on behalf of European Crohn's and Colitis Organisation.

Plain Language Summary

Refractory Crohn's disease may benefit from receiving combination therapy with two advanced therapies such as Upadacitinib and risankizumab which are approved treatments for Crohn's disease. We studied a cohort of 15 patients with difficult-to-treat Crohn's disease who received this combination at the Edinburgh IBD Unit. After the first 12 weeks of treatment, more than half of the patients had an improvement in their symptoms. Forty percent achieved full control of their symptoms and one-third had normalisation of their blood and stool markers. No major safety concerns were identified. These early results show promising and safe results for refractory Crohn's disease patients.

and American regulatory agencies for the treatment of moderate to severe CD. Here we present a dedicated case series specifically focused on the effectiveness and safety of combined upadacitinib and risankizumab in patients with refractory CD.

2 | Case Report

A total of $n = 15$ consecutive patients with CD received DTT with upadacitinib and risankizumab (minimum overlap of 8 weeks) between March 2024 and April 2025 at the Edinburgh IBD Unit, National Health Service (NHS) Lothian (United Kingdom). The decision to start DTT was routinely made at the departmental IBD multidisciplinary meeting. Inclusion criteria were age $\geq$ 16 years, diagnosis of CD and active disease defined by either a Harvey Bradshaw Index (HBI) $\geq$ 5, endoscopic/radiographic assessment, C-reactive protein (CRP) $>$ 5 mg/L or faecal calprotectin (FC) $\geq$ 250 μg/g. Patients were excluded if DTT was initiated for an indication different from active CD or if the follow-up time since DTT initiation was less than 8 weeks.

The primary outcome of the present report was steroid-free clinical response (SFCR) at 12 weeks of starting DTT defined as a decrease of $\geq$ 3 in HBI and/or HBI $<$ 5. When HBI was unavailable due to missing information in the electronic records or due to the presence of stoma, the Physician Global Assessment (PGA) (scored from 0 to 3) was used instead. For consistency, clinical response was defined as a decrease of $\geq$ 1 in the PGA score and/or a PGA score of 0. The secondary outcomes were clinical, CRP and FC remission. Clinical remission was defined as HBI $<$ 5. As for SFCR, when HBI was unavailable, a PGA of 0 was also considered remission. CRP remission was defined as CRP $\leq$ 5 mg/L and FC remission as FC $<$ 250 μg/g. Missing data was imputed as a failure. Additional secondary outcomes were persistence of DTT at 24 and 52 weeks in patients for whom long-term DTT was planned and successful withdrawal in patients for whom short-term DTT was planned. Kaplan–Meier curves were used to determine DTT persistence, defining DTT discontinuation as the event of interest and censoring at last follow-up. The planned duration of DTT was decided during the IBD multidisciplinary meeting. Safety outcomes were recorded. Treatment-related serious adverse events (SAE) were defined as any event leading to drug cessation, hospitalisation or death and considered to be related to upadacitinib or risankizumab. Hospitalisations and surgeries related to worsening disease activity were recorded separately and were not classified as treatment-related SAE.

Regarding ethical considerations, the study was classified as a clinical audit; therefore, no written informed consent was required, as per departmental policy and Health Research Authority guidance. Caldicott guardian approval was obtained (NHS Lothian).

Patient demographics and clinical characteristics are described in Table 1. The median age of our cohort was 29 years (IQR 26–42) and the group was predominantly male (73%). The median disease duration was 11 years (IQR 5–20). Our cohort was previously exposed to a median of 3 AT (IQR 2–5), and 40% had been on $\geq$ 4 AT. However, two patients had failed only one AT prior to DTT: one received short-term DTT as bridging therapy; whereas the second had a complex presentation with upper

TABLE 1 | Baseline demographics and clinical characteristics.

	$N = 15$[a]
Age	29 (26–42)
Sex	
Female	4 (27%)
Male	11 (73%)
Smoking	
Ex-smoker	4 (27%)
Never smoked	10 (67%)
Missing	1 (6%)
Disease duration (years)	11 (5–20)
Age at diagnosis	
$\leq$ 16 years (A1)	5 (33%)
17–40 years (A2)	10 (67%)
$>$ 40 years (A3)	0 (0%)
Disease location	
Ileal (L1)	4 (27%)
Colon (L2)	3 (20%)
Ileocolonic (L3)	8 (53%)
Upper gastrointestinal involvement (L4)	6 (40%)
Disease behaviour	
Nonstricturing, nonpenetrating (B1)	8 (53%)
Stricturing (B2)	7 (47%)
Penetrating (B3)	0 (0%)
Perianal disease (p)	5 (33%)
Previous surgical resections for CD	6 (40%)
Number of previous advanced therapies	
1	2 (13%)
2	4 (27%)
3	3 (20%)
$\geq$ 4	6 (40%)

Abbreviation: CD, Crohn's disease.
[a]Median (Q1–Q3); *n* (%).

3066943x, 2026, 3, Downloaded from https://onlinelibrary.wiley.com/doi/10.1002/jcc5.70034 by NICE, National Institute for Health and Care Excellence, Wiley Online Library on [29/10/2026]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

gastrointestinal involvement and an inadequate response to upadacitinib, prompting early escalation to DTT. For clarity, only ATs discontinued prior to DTT initiation were considered failures.

Nine patients (60%) already received upadacitinib when DTT with risankizumab was commenced and 5 (33%) already received risankizumab when DTT with upadacitinib was started. One patient (6.7%) who was refractory to all approved AT for CD had both medications prescribed simultaneously. All patients received DTT due to luminal activity of their CD; two patients (13%) had active perianal CD and other two (13%) had active EIM. The median time from initiation of upadacitinib or risankizumab as monotherapy until DTT commencement was 245 days (112–568). Regarding the expected duration of the combination strategy, 10 patients (67%) started the combination as a long-term maintenance and five (33%) were expected to stop one of the medications following the 12-week induction period. At the start of DTT, eight patients received upadacitinib 45 mg, five received 30 mg and one, 15 mg. Patients who were already on maintenance therapy with upadacitinib continued the same dose and those who initiated upadacitinib received a 12-week induction course of 45 mg. However, two patients who were on upadacitinib when DTT with risankizumab was started, increased the dose of upadacitinib up to 45 mg for 12 weeks: one because DTT was planned as a short-term bridging therapy and the second due to poor response to the 30 mg dose. Regarding patients who were on risankizumab when DTT with upadacitinib was commenced, two patients received lower induction dose: one received 30 mg due to concomitant treatment with steroids and the second received 15 mg due to history of acne when they were treated previously with upadacitinib monotherapy. For risankizumab, patients already receiving the treatment continued their maintenance dose of 360 mg every 8 weeks whereas those that started risankizumab received an induction of three intravenous doses (600 mg at weeks 0, 4 and 8).

At baseline, the cohort had a median HBI of 6 (IQR 3–11) and a median PGA of 2 (1–3). Regarding the biochemical data, the median FC was 558 μg/g (IQR 118–745) and the median CRP was 15 mg/L (3–27). Three patients (20%) were receiving steroids when DTT was prescribed.

The median follow up time was 31 weeks (IQR 13–57) and the median time on DTT was 16 weeks (IQR 13–31). After 12 weeks of therapy, 53% had a SFCR (8/15; 3 missing), 40% were in steroid-free clinical remission (6/15; 3 missing), 27% were in CRP remission (4/15; 9 missing) and 27% in FC remission (4/15; 11 missing). Notably, 7 patients in SFCR and 6 in steroid-free clinical remission were defined by HBI. Considering only patients with a baseline HBI $\geq$ 5, 71% had a SFCR (5/7) and 57% were in steroid-free clinical remission (4/7). Figures 1 and 2 depict the clinical and biochemical parameters pre- and post-induction. The remission rates stratified by drug sequencing and by previous exposure to upadacitinib and risankizumab are shown in Tables 2 and 3 respectively.

Regarding patients with planned long-term DTT, the cumulative persistence at 24 weeks was 85.7% and at 52 weeks, 57.1% (Figure 2). Two patients with planned long-term DTT discontinued the combination therapy due to lack of response requiring resectional surgery. Three of the five patients that started the short-term combination had stopped it within 12 weeks: two stopped DTT as planned and one stopped prematurely at week 8 following an IBD-associated hospitalisation. Two patients initially planned for only short-term DTT continued on DTT long-term: the first was due to a clinical response and the second because mild symptoms developed after upadacitinib was briefly paused following a mild infection. Considering the whole cohort at the end of follow-up, 10 patients were still on DTT, three were on risankizumab monotherapy, one on upadacitinib monotherapy and one had discontinued both AT.

Four patients developed adverse events (AE) (33%) that were mild or moderate in severity, including infections (3/15) and acne (2/15). The infections were a peristomal abscess, oesophageal thrush and an upper respiratory tract infection. No treatment-related SAE were described.

During DTT, five IBD-associated hospitalisations occurred in three patients. Two patients had resectional surgeries for treatment of CD. All patients with IBD-associated hospitalisation had a stricturing phenotype. Baseline characteristics of patients with IBD-associated hospitalisation and with IBD-associated surgery are described in Supporting Information S1: Tables 1 and 2 respectively. No perianal complications occurred during follow-up. Of the two patients with active EIMs at DTT initiation, one with enteropathic arthritis remained symptomatic during follow-up, whereas the second who had arthralgia was not assessed for EIMs during follow-up. No deaths occurred during follow-up.

3 | Discussion

This study demonstrates the effectiveness of combining a JAK-1 inhibitor with an anti-IL23 p19 for the treatment of refractory CD. After 12 weeks of DTT, more than half of the cohort achieved SFCR, 40% reached clinical remission, 27% CRP remission and 27% FC remission. These results are encouraging, particularly given the characteristics of our cohort, which included patients with long-standing disease, refractoriness to multiple biologics and a history of surgical resections.

A meta-analysis by Ahmed et al., which included 30 studies and 279 patients on a wide range of DTT, the most common being the combination of anti-tumour necrosis factor (TNF) α and anti-integrins, reported an overall clinical remission rate of 52%, decreasing to 40% when patients treated for EIM were excluded [8]. Only limited case series have reported on the combination of upadacitinib, the only JAK inhibitor (JAKi) approved for the treatment of CD, and ustekinumab, an anti-IL12/23 monoclonal antibody [9–11]. A small case series by Miyatini et al., which specifically focused on this combination, showed clinical remission in 5 out of 6 patients (83.3%) [11]. The SEQUENCE trial demonstrated a noninferior clinical remission and a greater endoscopic remission with risankizumab relative to ustekinumab as monotherapy in the treatment of anti-TNFα exposed CD

30669043x, 2026, 3, Downloaded from https://onlinelibrary.wiley.com/doi/10.1002/jcc5.70034 by NICE, National Institute for Health and Care Excellence, Wiley Online Library on [29/10/2026]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

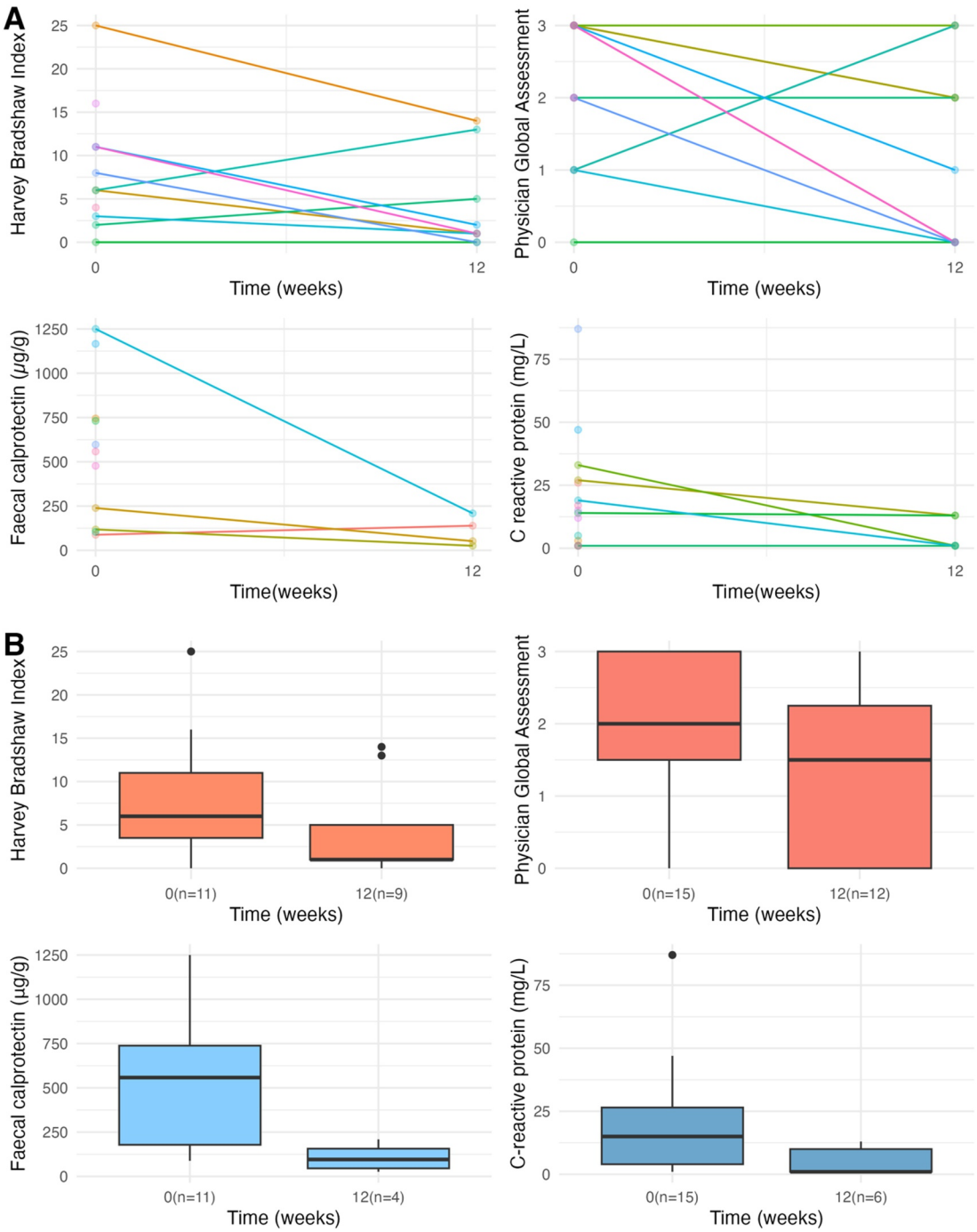

FIGURE 1 | (A) Harvey–Bradshaw Index (HBI), Physician Global Assessment (PGA), faecal calprotectin (FC), C-reactive protein (CRP) at baseline and after 12 weeks of dual targeted therapy. (B) Change in median HBI, PGA, FC and CRP during follow-up.

[12] suggesting that combining risankizumab rather than ustekinumab with a JAKi may be a promising approach. Three case series describe encouraging clinical remission rates for this combination of 71%–75% [13–15]. In contrast, our study, using a 'missing-as-failure' approach, demonstrates a lower clinical remission rate of 40%.

DTT can be implemented as short- or long-term strategy. A short-term combination is attractive for several reasons. First, the rapid onset of action of upadacitinib may allow clinicians to avoid a course of systemic steroids whereas the biologic, in this case risankizumab, gradually reaches its therapeutic effect. In this regard, it remains unclear whether a simultaneous co-induction or a sequential therapy -initiating a short-course of a small molecule followed by a biologic-is preferable [5, 15]. Second, limiting the duration of DTT may be appropriate due to the safety concerns [5]. However, in our cohort, only 40% discontinued DTT as initially programmed. This finding is consistent with a small case series by Yin et al., in which upadacitinib was used as a short-term DTT; nevertheless, 7 out of 12 patients (58.3%) required an

30669043x, 2026, 3, Downloaded from https://onlinelibrary.wiley.com/doi/10.1002/jcc5.70034 by NICE, National Institute for Health and Care Excellence, Wiley Online Library on [29/10/2026]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

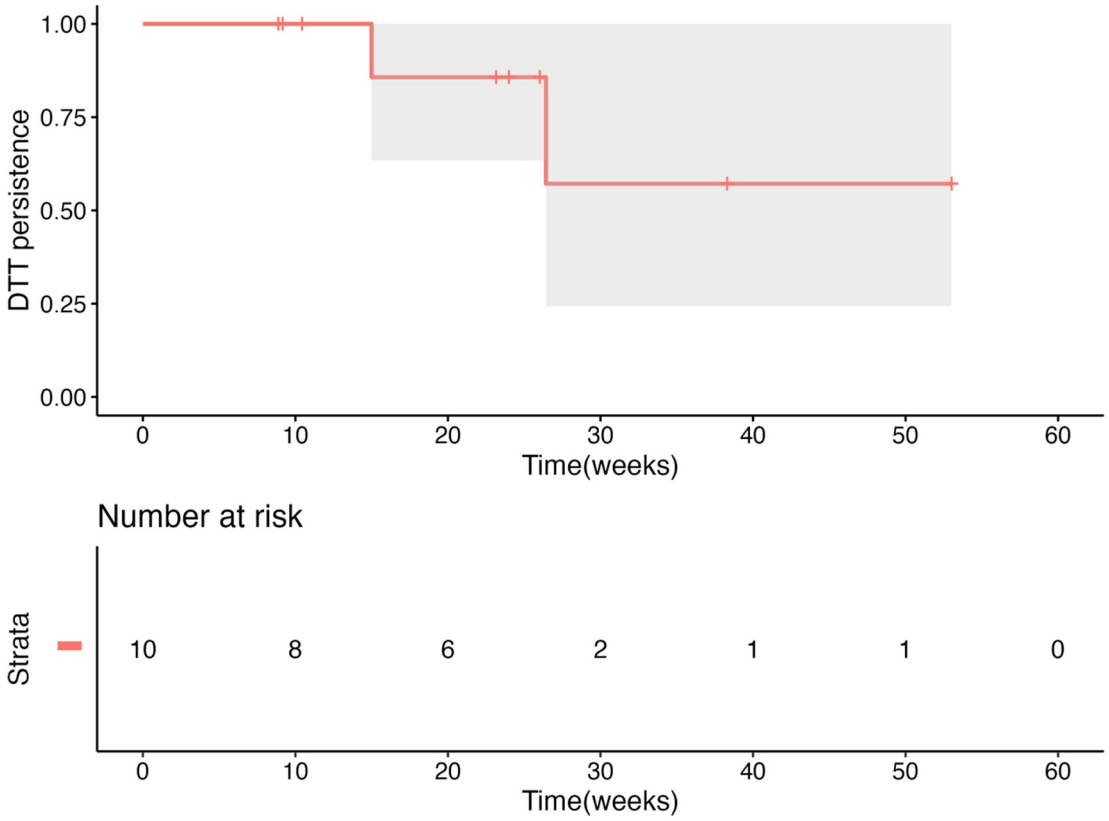

FIGURE 2 | Kaplan–Meier curve showing persistence of upadacitinib and risankizumab combination therapy for patients with planned long-term treatment. DTT, dual targeted therapy.

TABLE 2 | Remission rates stratified by drug sequencing.

	UPA > RISA $N = 9$[a]	RISA > UPA $N = 5$[a]	UPA-RISA $N = 1$[a]
Clinical response	6 (67%)	1 (20%)	0 (0%)
Clinical remission	5 (56%)	1 (20%)	0 (0%)
CRP remission	3 (33%)	1 (20%)	0 (0%)
FC remission	3 (33%)	1 (20%)	0 (0%)

Abbreviations: CRP, C-reactive protein; FC, Faecal calprotectin; RISA > UPA, risankizumab followed by upadacitinib; UPA > RISA, upadacitinib followed by risankizumab; UPA-RISA, upadacitinib and risankizumab started simultaneously.
[a]*n* (%).

TABLE 3 | Remission rates of the overall cohort and stratified by previous exposure to upadacitinib or to risankizumab.

	Overall cohort $N = 15$[a]	Previous upadacitinib $N = 4$[a]	Previous risankizumab $N = 2$[a]
Clinical response	8 (53%)	1 (25%)	2 (100%)
Clinical remission	6 (40%)	1 (25%)	0 (0%)
CRP remission	4 (27%)	0 (0%)	0 (0%)
FC remission	4 (27%)	0 (0%)	1 (50%)

Abbreviations: CRP, C-reactive protein; FC, Faecal calprotectin.
[a]*n* (%).

extended use of upadacitinib [15]. On the other hand, choosing a long-term strategy may be suitable for refractory patients with a complex disease behaviour and low risk of AE. The persistence of this subgroup at 6 months was 85.7% and 57.1% at 1 year. However, caution is required when interpreting persistence as a surrogate for effectiveness, particularly in such a refractory cohort.

3066943x, 2026, 3, Downloaded from https://onlinelibrary.wiley.com/doi/10.1002/jcc5.70034 by NICE, National Institute for Health and Care Excellence, Wiley Online Library on [29/10/2026]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Safety is undoubtedly the main concern when initiating DTT. Combining a biologic with a favourable safety profile such as risankizumab with a small molecule like upadacitinib with established AE is a rational approach [16]. In our cohort, no treatment-related SAE were described. Nevertheless, our short follow-up may hinder the detection of potential delayed AE. Reducing the dose of upadacitinib could be a mindful strategy to minimise the risk of side effects in selected patients. In our cohort, this strategy was used in 2 patients who were induced with a lower dose (30 and 15 mg). Further investigations would be warranted to explore the benefits of this strategy.

This case series has several limitations. It is a single-centre, retrospective study with a small sample size and short follow-up. These factors may lead to underestimation of safety risks and prevent conclusions regarding long-term effectiveness. Additionally, most patients had the second therapy added after persistent luminal activity with the initially prescribed AT. In this context, it is challenging to clearly distinguish whether the observed benefits reflect the effectiveness of the DTT or the effectiveness of the subsequently added AT.

In conclusion, our case series presents a novel combination therapy that appears effective and safe in the short term for patients with refractory CD.

Author Contributions

C.R.-B., N.P. and C.W.L. contributed to the design of the study. C.R.-B. collected the data. C.R.-B. analysed the data. C.R.-B., N.P., I.A., S.D., J.B. and C.W.L. drafted the first version of the manuscript and critically revised the manuscript. All authors have approved the final version of this manuscript.

Acknowledgements

The authors thank Dr Nathan Constantine-Cooke and Dr Victor Velasco-Pardo for their valuable assistance in reviewing the statistical analysis of this study.

Funding

C.W.L. is funded by a UKRI (UK Research and Innovation) Future Leaders Fellowship 'Predicting outcomes in IBD' (MR/S034919/1).

Conflicts of Interest

C.R.-B. has no disclosures. N.P. has served as a speaker for Abbvie, Janssen, Pfizer and Fresenius Kabi and served as a consultant for Abbvie and Janssen. I.A. has served as a speaker for Alphasigma/Galapagos, Bristol Myers Squibb, Takeda, Lilly, Pfizer, Vifor Pharma, Dr Falk and Ferring. S.D. is Chair of British Society of Gastroenterology Inflammatory Bowel Disease Committee and gastroenterology expert on the MHRA Gastroenterology, Rheumatology, Immunology & Dermatology Expert Advisory Group; she reports grants from Crohn's & Colitis UK, The Helmsley Charitable Trust, Edinburgh and Lothians Health Foundation, Pathological Society of Great Britain and Northern Ireland, and Lord Leonard and Lady Estelle Wolfson Foundation; consultant to Abbvie, honoraria or speaker fees from Janssen, Takeda, Ferring, and Abbvie and meeting and travel grants from Abbvie, Janssen, Takeda, Lilly, and Dr Falk. J.B. has received a research grant from Crohn's and Colitis UK. J.B. has received payment or honoraria for lectures, presentations, or educational events from Thermo Fisher Scientific, Takeda, Ferring, DrFalk, Pfizer and Johnson & Johnson. J.B. has received consultation fees from Takeda. J.B. has received support for attending meetings and travel costs from Takeda and Ferring. C.W.L. has acted as a consultant to Abbvie, Janssen, Takeda, Pfizer, Galapagos, Bristol Myers Squibb, B.I., Sandoz, Novartis, GSK, Gilead, Vifor Pharma, Dr Falk, Eli Lilly, and Iterative Health; he has received speaking fees and travel support from Pfizer, Janssen, Abbvie, Eli Lilly, Galapagos, MSD, Takeda, Shire, Ferring, Hospira and Dr Falk.

Data Availability Statement

The data that support the findings of this study are available on reasonable request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

References

1. G. Roda, Ng S. Chien, P. G. Kotze, et al., "Crohn's Disease," *Nature Reviews Disease Primers* 6, no. 1 (2020), https://www.nature.com/articles/s41572-020-0156-2.

2. M. F. Neurath, "Current and Emerging Therapeutic Targets for IBD," *Nature Reviews Gastroenterology & Hepatology* 14, no. 5 (2017): 269–278, https://doi.org/10.1038/nrgastro.2016.208.

3. S. Danese, V. Solitano, V. Jairath, and L. Peyrin-Biroulet, "The Future of Drug Development for Inflammatory Bowel Disease: The Need to ACT (Advanced Combination Treatment)," *Gut* 71, no. 12 (2022): 2380–2387, https://doi.org/10.1136/gutjnl-2022-327025.

4. S. R. Vavricka, L. Brun, P. Ballabeni, et al., "Frequency and Risk Factors for Extraintestinal Manifestations in the Swiss Inflammatory Bowel Disease Cohort," *American Journal of Gastroenterology* 106, no. 1 (2011): 110–119, https://doi.org/10.1038/ajg.2010.343.

5. V. Solitano, C. Ma, J. Hanžel, R. Panaccione, B. G. Feagan, and V. Jairath, "Advanced Combination Treatment With Biologic Agents and Novel Small Molecule Drugs for Inflammatory Bowel Disease," *Gastroenterology and Hepatology* 19, no. 5 (2023): 251–263, https://pmc.ncbi.nlm.nih.gov/articles/PMC10548249/.

6. E. V. Loftus, J. Panés, A. P. Lacerda, et al., "Upadacitinib Induction and Maintenance Therapy for Crohn's Disease," *New England Journal of Medicine* 388, no. 21 (2023): 1966–1980, https://doi.org/10.1056/nejmoa2212728.

7. G. D'Haens, R. Panaccione, F. Baert, et al., "Risankizumab as Induction Therapy for Crohn's Disease: Results from the Phase 3 ADVANCE and MOTIVATE Induction Trials," *Lancet* 399, no. 10340 (2022): 2015–2030, https://doi.org/10.1016/s0140-6736(22)00467-6.

8. W. Ahmed, J. Galati, A. Kumar, et al., "Dual Biologic or Small Molecule Therapy for Treatment of Inflammatory Bowel Disease: A Systematic Review and Meta-analysis," *Clinical Gastroenterology and Hepatology* 20, no. 3 (2022): e361–e379, https://doi.org/10.1016/j.cgh.2021.03.034.

9. M. J. Meng, M. L. Chang, C. J. Kuo, et al., "Advanced Combination Therapy With Biologics and Upadacitinib in Refractory Inflammatory Bowel Disease: A Retrospective Study From Taiwan," *Journal of Inflammation Research* 18, no. February (2025): 2733–2742, https://doi.org/10.2147/jir.s511309.

10. E. A. Spencer, S. Bergstein, M. Dolinger, et al., "Single-Center Experience With Upadacitinib for Adolescents With Refractory Inflammatory Bowel Disease," *Inflammatory Bowel Diseases* 30, no. 11 (2024): 2057–2063, https://doi.org/10.1093/ibd/izad300.

11. Y. Miyatani, D. Choi, N. K. Choi, and D. T. Rubin, "Dual-Targeted Therapy With Upadacitinib and Ustekinumab in Medically Complex Crohn's Disease," *Digestive Diseases and Sciences* 69, no. 2 (2024): 355–359, https://doi.org/10.1007/s10620-023-08182-y.

12. L. Peyrin-Biroulet, J. C. Chapman, J.-F. Colombel, et al., "Risankizumab Versus Ustekinumab for Moderate-to-Severe Crohn's Disease,"

3066943x, 2026, 3, Downloaded from https://onlinelibrary.wiley.com/doi/10.1002/jcc5.70034 by NICE, National Institute for Health and Care Excellence, Wiley Online Library on [29/10/2026]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

New England Journal of Medicine 391, no. 3 (2024): 213–223, https://doi.org/10.1056/nejmoa2314585.

13. R. S. Dalal, L. M. Clarke, H. J. Cabral, A. D. Carlin, G. B. Hardwick, and J. R. Allegretti, "Research Communication: Combination Therapy of Upadacitinib With Infliximab, Risankizumab, Ustekinumab or Vedolizumab for Refractory Crohn's disease: A Descriptive Case Series," *Alimentary Pharmacology & Therapeutics* 62, no. 10 (November 2025): 1023–1026, https://doi.org/10.1111/apt.70298.

14. E. N. Fear, B. D. McDonald, R. H. McMillan, et al., "Dual Targeted Therapy With Risankizumab and Upadacitinib Is Clinically and Biochemically Effective in Medically Complex Crohn's Disease," in *Presented at: DDW*, (May 3–6, 2025): Abstract Tu1912.

15. J. Yin, Y. El-Najjar, N. Cordova, et al., "Short-Term Use of Upadacitinib in Combination With Biologic Therapy for Inducing Clinical Remission in Patients With Active Inflammatory Bowel Disease," *Inflammatory Bowel Diseases* 30, no. 10 (2024): 1914–1916, https://doi.org/10.1093/ibd/izae105.

16. R. Battat, J. T. Chang, E. V. Loftus, and B. E. Sands, "IBD Matchmaking: Rational Combination Therapy," *Clinical Gastroenterology and Hepatology* 23, no. 3 (2025): 469–479, https://doi.org/10.1016/j.cgh.2024.05.051.

Supporting Information

Additional supporting information can be found online in the Supporting Information section.
Supporting Information S1: jcc570034-sup-0001-suppl-data.docx.

3066943x, 2026, 3, Downloaded from https://onlinelibrary.wiley.com/doi/10.1002/jcc5.70034 by NICE, National Institute for Health and Care Excellence, Wiley Online Library on [29/10/2026]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License