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Original research

Real-world effectiveness of risankizumab in Crohn's disease: a pan UK retrospective cohort study

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ABSTRACT

Objective Risankizumab is an interleukin-23 p19 subunit inhibitor which received approval for Crohn's disease (CD) by UK licensing authorities in May 2023. Our aim was to evaluate the real-world outcomes of risankizumab in the UK.

Design We conducted a retrospective, multicentre, cohort study of patients with CD treated with risankizumab across 25 health boards in the UK between 1 January 2021 and 1 November 2024. Our primary outcome was treatment persistence at 6 months. Our secondary endpoints were steroid-free clinical remission (Harvey-Bradshaw index <5), C-reactive protein (CRP) remission (CRP ≤5 mg) and faecal calprotectin (FCAL) remission (FCAL <250 µg/g).

Results We included 763 patients with a median follow-up time of 27 weeks (IQR 18–41 weeks) with a total of 432 and 110 patients having 6-month and 12-month data available. The median number of advanced therapy exposures was 3 (2–4), with 92% (704/763) having failed anti-tumour necrosis factor therapy and 72% (548/763) having failed ustekinumab. Treatment persistence at 6 and 12 months was 95.4% and 89.2%, respectively. Unadjusted persistence rates for ustekinumab-naive versus ustekinumab-exposed patients were 92.7% vs 95.3% and 89.0% vs 74.2% at 6 and 12 months, respectively (p=0.62). Rates of clinical, CRP and FCAL remission were 52% (123/236), 53% (169/319) and 44% (69/156)

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Risankizumab has been demonstrated to have efficacy for Crohn's disease (CD) in phase 3 clinical trials, but real-world data are lacking.

WHAT THIS STUDY ADDS

⇒ Our data demonstrate that risankizumab was an effective treatment option, in a highly medically refractory, real-world, CD cohort with excellent persistence and good clinical and biochemical remission rates, regardless of previous ustekinumab exposure.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Our data suggests the interleukin-23 p19 subunit inhibition is an effective mechanism of action post ustekinumab failure and other advanced therapy failures in CD.

► Additional supplemental material is published online only. To view, please visit the journal online (https://doi.org/10.1136/flgastro-2025-103449).

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at 6 months. Rates of clinical remission for ustekinumab naive versus exposed were 57% (29/51) vs 51% (94/185) (p=0.54) 6 months. Adverse events occurred in 17% (n=127) of the cohort, of which 12% (n=92) were serious.

Conclusion Risankizumab was effective in a large, real-world, medically refractory CD cohort with excellent persistence and good clinical and biochemical remission rates.

INTRODUCTION

Crohn's disease (CD) is a chronic relapsing and remitting disease of the alimentary tract, driven by numerous proinflammatory cytokines, with interleukin (IL)-23 being one of the key drivers of inflammation.[1] Risankizumab is an IL-23 p19 subunit antagonist which received approval for the treatment of CD in the UK by the UK licensing authority (National Institute for Health and Care Excellence committee) in May 2023.[2] This was based on efficacy in phase 3 clinical trials, where clinical remission rates of up to 45% were observed for induction therapy[3] and 52% for maintenance therapy.[4] Additionally, the SEQUENCE trial found risankizumab was superior to ustekinumab, an IL-12/23 p40 antagonist, for patients who previously failed an anti-tumour necrosis factor (TNF).[5]

To date, there have been limited studies assessing the real-world efficacy of risankizumab in moderate-to-severe CD,[6–8] and the majority of these studies have largely focused on induction data. There remains a gap to describe medium and long-term outcomes in real-world patients on risankizumab. Furthermore, there is a dearth of data on whether previous ustekinumab exposure affects effectiveness in the real-world setting. Our aim was to assess the treatment persistence, effectiveness and safety of risankizumab in a large multicentre study of patients with moderate to severe CD in the UK. Additionally, we sought to explore whether risankizumab effectiveness differed between ustekinumab-naive and ustekinumab-exposed patients.

METHODS

Study design

We conducted a multicentre retrospective cohort analysis involving 25 National Health Service (NHS) health boards in the UK, including tertiary and regional centres (see online supplemental table 1 for list of sites and their contributions). NHS hospitals in the UK were invited to participate through a variety of methods including invitation via established communication channels in UK inflammatory bowel disease (IBD) working groups and email invitation. Data were retrospectively collected at each hospital by review of electronic medical records.

Participants

We identified adult (≥18 years old) patients with CD at participating sites who received at least one dose of risankizumab. Inclusion criteria were (1) confirmed diagnosis of CD (based on standard clinical, radiological, endoscopic and histological criteria); (2) risankizumab started for the indication of CD; (3) minimum of 12 weeks of follow-up after initiation of risankizumab as of 1 November 2024. Patients who ceased the drug within 3 months were still analysed. Exclusion criteria were (1) commencement of risankizumab for a different indication; (2) less than 3-month follow-up data available with no evidence of treatment cessation.

Data collection

We collected baseline demographic data, disease characteristics, prior therapies and follow-up data from electronic medical records. In patients with prior ustekinumab exposure, we recorded the reason for cessation and maximum dosing frequency with dosing frequencies less than 8 weeks considered escalated dosing. Harvey-Bradshaw Index (HBI) was used to assess clinical disease activity. We recorded stool frequency score (or frequency of stoma bag emptying in patients with stomas), abdominal pain score, as well as biomarkers of disease activity including C-reactive protein (CRP), serum albumin and faecal calprotectin (FCAL). Endoscopic assessments which occurred within 3 months of commencing risankizumab and during follow-up were recorded in addition to changes to risankizumab dosage, corticosteroid prescribing including drug name, concomitant immunomodulators, biologics or small molecules and exclusive enteral nutrition. For patients with perianal disease, we recorded physician global assessment on whether the patient had active or inactive perianal disease, as well as perianal complications including development of a new perianal fistula, perianal abscess or unplanned examination under anaesthesia. We recorded adverse events including surgery, hospitalisation and mortality. Patients were followed until their most recent clinical interaction, or until risankizumab was discontinued. As an observational study, all interventions were undertaken at the discretion of the treating clinician.

Primary and secondary outcomes

Our primary outcome was treatment persistence at 6 months. Secondary outcomes included treatment persistence at 3 and 12 months, clinical remission, corticosteroid-free clinical remission and response, CRP remission and response, FCAL remission and response, combined biomarker remission and normal serum albumin, at 3 months (±4 weeks), 6 months (±8 weeks) and 12 months (±8 weeks). We also assessed corticosteroid use outside of the induction period, adverse events, hospitalisation and surgery as additional secondary outcomes. Baseline predictors for treatment persistence and clinical remission, including prior ustekinumab use and reason for ceasing ustekinumab, were assessed.

Definitions

We defined clinical remission as a HBI of <5, clinical response as a HBI of <5 and/or reduction of ≥3 point decrease from baseline and corticosteroid-free clinical remission as clinical remission in the absence of corticosteroids at the time of assessment.[9] We defined CRP remission as a CRP ≤5 mg/L and CRP response as a CRP ≤5 mg/L and/or ≥50% reduction from baseline.[10] We define FCAL remission as a FCAL <250 µg/g and FCAL response as a FCAL ≤250 µg/g and/or ≥50% reduction from baseline.[10] We defined combined biomarker remission as CRP and FCAL remission. Normal serum albumin level was defined as ≥36 g/L as per our laboratory reference range. Severity of endoscopic changes was based on the formal scoring system the clinician used (such as the Simple Endoscopic Score for CD)[11] or, if no formal scoring system was used, relied on the clinician's description such as mild, moderate or severe inflammation. We defined the induction period as the first 3 months of therapy.[3] The maintenance period was considered treatment beyond 3 months. For treatment cessation, we defined primary non-response as failure to achieve clinical and/or biomarker (CRP or FCAL) remission and subsequent cessation of the drug. We defined secondary loss of response as obtaining clinical and/or biomarker remission (minimum one parameter) and subsequently losing response and ceasing therapy. We categorised previous ustekinumab cessation under (1) primary non-response, (2) secondary loss of response, (3) adverse effects, (4) patients' decision to cease or non-compliance. We also recorded if they had ceased using ustekinumab because they were in remission. Serious adverse events were defined as those that led to hospitalisation, cessation of drug, disability or death.

Statistical analysis

We used SPSS V.25 (IBM, Chicago, Illinois, USA) and Prism V.10.0 (GraphPad Software, San Diego, California, USA) for statistical analyses and generation of graphs. We present descriptive statistics as medians with IQR for continuous variables, and frequencies with percentages for categorical variables. For comparison of non-parametric continuous variables, we used the Kruskal-Wallis test. For the comparison of categorical variables, we used the χ^2 test. We assessed primary outcomes using log-rank tests of Kaplan-Meier curves. Patients were censored at last follow-up. Our analyses were performed on a per-variable basis using available data and therefore patients with missing data for a given parameter at a given time point were excluded from that specific subanalysis. Patients who discontinued therapy for any reason were considered non-remission for all indices after the time point they ceased treatment. We used Cox proportional hazards regression analyses to identify potential baseline predictors of persistence. Variables for analysis were chosen a priori and are listed in online supplemental table 2. We considered a p value <0.05 to be significant for all statistical tests.

RESULTS

Patient population

We identified 811 patients who commenced risankizumab, of which 763, 432 and 110 patients had 3-month, 6-month and 12-month outcome data available with a median follow-up time of 27 weeks (IQR 18–41 weeks). The median age of the cohort was 39 years old (IQR 29–54) half the cohort being female (50%, 383/763) (table 1). Half of the cohort (51%, 387/763) had a history of luminal IBD surgery, and 16% (125/763) had a stoma when commencing risankizumab. The median number of advanced therapy exposures was 3 (2–4), with 92% (704/763) having failed anti-TNF therapy and 72% (548/763) having failed ustekinumab (figure 1, table 1, online supplemental table 3). The majority of patients who had ustekinumab exposure had ceased due to secondary loss of response (61%, 332/548), and almost a quarter of the ustekinumab exposed were on an escalated dosing schedule (23%, 125/548) (online supplemental table 3). We observed that 2% (17/763), 24% (179/763), 35% (269/763), 31% (238/763) and 8% (60/763) had been treated with zero, one, two, three and four different classes of advanced therapies, respectively. Median baseline disease activity indices were elevated with the HBI of 6 (IQR 3–9), CRP of 6 mg/L (IQR 2–17), FCAL of 588 µg/g (IQR 232–1171) and albumin of 39 g/L (IQR 35–42). Of 22% (166/763) of patients that had a baseline endoscopic assessment, 73% had moderate or severe inflammation (online supplemental table 4).

Risankizumab persistence

Persistence rates were 97.8%, 95.4% and 89.2% at 3, 6 and 12 months, respectively (figure 2). On multivariable Cox regression analysis, prednisolone use at initiation of risankizumab was the only significant predictor for reduced persistence (adjusted HR 3.24, 95% CI 1.74 to 5.91, p<0.001). Subanalysis of persistence rates including only patients with a minimum of 12 months follow-up (110/763) demonstrated persistence rates of 100%, 99.0% and 94.1% at 3, 6 and 12 months, respectively (online supplemental figure 1). Unadjusted persistence rates for ustekinumab naive versus ustekinumab exposed patients were 95.6% vs 95.4% and 95.6% vs 88.3% at 6 and 12 months, respectively (p=0.62) (figure 2). Reasons for risankizumab treatment cessation included primary non-response 4% (27/763), secondary loss of response 1% (9/763), adverse events 2% (12/763) and non-adherence or lost to follow-up 1% (5/763).

Effectiveness outcomes

Rates of corticosteroid-free clinical remission were 59% (310/514), 52% (123/236) and 50% (31/62) at 3, 6 and 12 months (online supplemental figure 2). CRP

Table 1 Phenotype at initiation

All patients (n=763)	
Female sex, n (%)	383 (50)
Age at baseline, years, median (IQR)	39 (29–54)
Disease duration, years, median (IQR)	11 (6–20)
Smoking status*	
Never, n (%)	486 (70)
Current, n (%)	85 (11)
Former, n (%)	128 (18)
Previous IBD related luminal surgery, n (%)	387 (51)
Current stoma, n (%)	125 (16)
Age at diagnosis†	
≤16 years (A1), n (%)	188 (25)
17–40 years (A2), n (%)	425 (56)
>40 years (A3), n (%)	146 (19)
Disease location at initiation	
Ileal (L1), n (%)	194 (25)
Colon (L2), n (%)	101 (13)
Ileocolonic (L3), n (%)	464 (61)
Upper gastrointestinal involvement (L4), n (%)	90 (12)
Disease behaviour	
Non-stricturing, non-penetrating (B1), n (%)	273 (36)
Stricturing (B2), n (%)	331 (43)
Penetrating (B3), n (%)	159 (21)
Perianal disease (p), n (%)	239 (31)
Active disease at baseline, n (%)	67 (9)
Total number of patients with EIMs, n (%)	173 (23)
Active EIM at baseline,‡ n (%)	94 (12)
Prior advanced therapy class exposure§	
Anti-TNF, n (%)	704 (92)
Ustekinumab, n (%)	548 (72)
Vedolizumab, n (%)	300 (40)
JAKI, n (%)	122 (16)
Etrasimod, n (%)	<5 (<1)
Corticosteroid use during induction, n (%)	162 (21)
Concomitant immunomodulator during induction, n (%)	42 (6)
Concomitant advanced therapy during induction, n (%)	10 (1)
Baseline disease activity	
HBI (n=542), median (IQR)	6 (3–9)
CRP, mg/L (n=745), median (IQR)	6 (2–17)
Albumin, g/L (n=706), median (IQR)	39 (35–42)
FCAL, µg/g (n=433), median (IQR)	588 (232–1171)

*Smoking status unavailable for 64 patients.
†Age of diagnosis not available for four patients.
‡Excluding PSC.
§Prior drug exposure listed in online supplemental table 3.
anti-TNF, anti-tumour necrosis factor; CRP, C-reactive protein; EIM, extraintestinal manifestation of IBD; FCAL, faecal calprotectin; HBI, Harvey-Bradshaw Index; IBD, inflammatory bowel disease; JAKI, Janus kinase inhibitor; PSC, primary sclerosing cholangitis.

remission rates were 58% (402/696), 53% (169/319) and 52% (51/98) at 3, 6 and 12 months. FCAL remission rates were 54% (174/324), 44% (69/156) and 44% (24/54) at 3, 6 and 12 months. Combined CRP and FCAL remission rates were 42% (129/310), 43% (52/120) and 51% (18/35) at 3, 6 and 12 months. Rates of normal albumin levels were 78% (514/663), 75% (238/317) and 62% (61/98) at 3, 6 and 12 months.

Of those with a raised HBI at baseline, the proportions who had achieved corticosteroid-free clinical remission and response were 46% (129/280) and 65% (183/280) at 3 months, 42% (51/121) and 65% (79/121) at 6 months, and 55% (15/27) and 67% (18/27) at 12 months. Of those with a raised CRP at baseline, the proportions who had achieved CRP remission and response were 35% (127/365) and 55% (201/365) at 3 months, 34% (58/173) and 55% (96/173) at 6 months and 39% (23/59) and 57% (34/59) at 12 months. Of those with a raised FCAL at baseline, the proportions who had achieved FCAL remission and response were 44% (77/172) and 60% (104/172) at 3 months, 35% (29/84) and 47% (40/84) at 6 months and 47% (14/30) and 60% (18/30) at 12 months. Of those with a hypoalbuminaemia at baseline, the proportions who had normalised their albumin were 36% (64/177), 47% (44/93) and 35% (12/34) at 3, 6 and 12 months. We observed significant reductions in HBI, CRP and FCAL during follow-up (figure 3). At baseline, 76% of patients reported abdominal pain; however, half of patients were pain free at 3, 6 and 12 months, with a reduction in those experiencing mild, moderate and severe pain (online supplemental figure 3). Stool frequency score decreased from 3 (IQR 1–5) at baseline to 2 (1–4) at 3, 6 and 12 months. A minority of patients had endoscopic assessment during the study period (online supplemental table 4) for outcomes.

When considering disease location, steroid-free clinical remission rates for colonic (L2) and ileal (L1) phenotypes were 60% (44/73) vs 60% (82/137) (p=1.0) and 59% (22/37) vs 45% (22/49) (p=0.26) at 3 and 6 months, respectively. CRP remission rates for colonic (L2) and ileal (L1) phenotypes were 60% (56/94) vs 63% (113/178) (p=0.62) and 50% (20/40) vs 62% (43/69) (p=0.29) at 3 and 6 months, respectively. There were insufficient FCAL records to permit statistical analysis.

Effect of previous ustekinumab use

Rates of clinical remission for ustekinumab naive versus exposed were 62% (89/143) vs 57% (212/371) (p=0.34) and 57% (29/51) vs 51% (94/185) (p=0.54) at 3 and 6 months, respectively. Rates of CRP remission for ustekinumab naive versus exposed were 59% (116/195) vs 57% (286/501) (p=0.62) and 55% (36/65) vs 52% (133/254) (p=0.77) at 3 and 6 months, respectively. Rates of FCAL remission for ustekinumab naive versus exposed were 58% (52/90) vs 52% (122/234) (0.43) and 47% (17/36) vs 46% (52/113) (p=1.0) at 3 and 6 months, respectively. There were insufficient data at 12 months to analyse ustekinumab

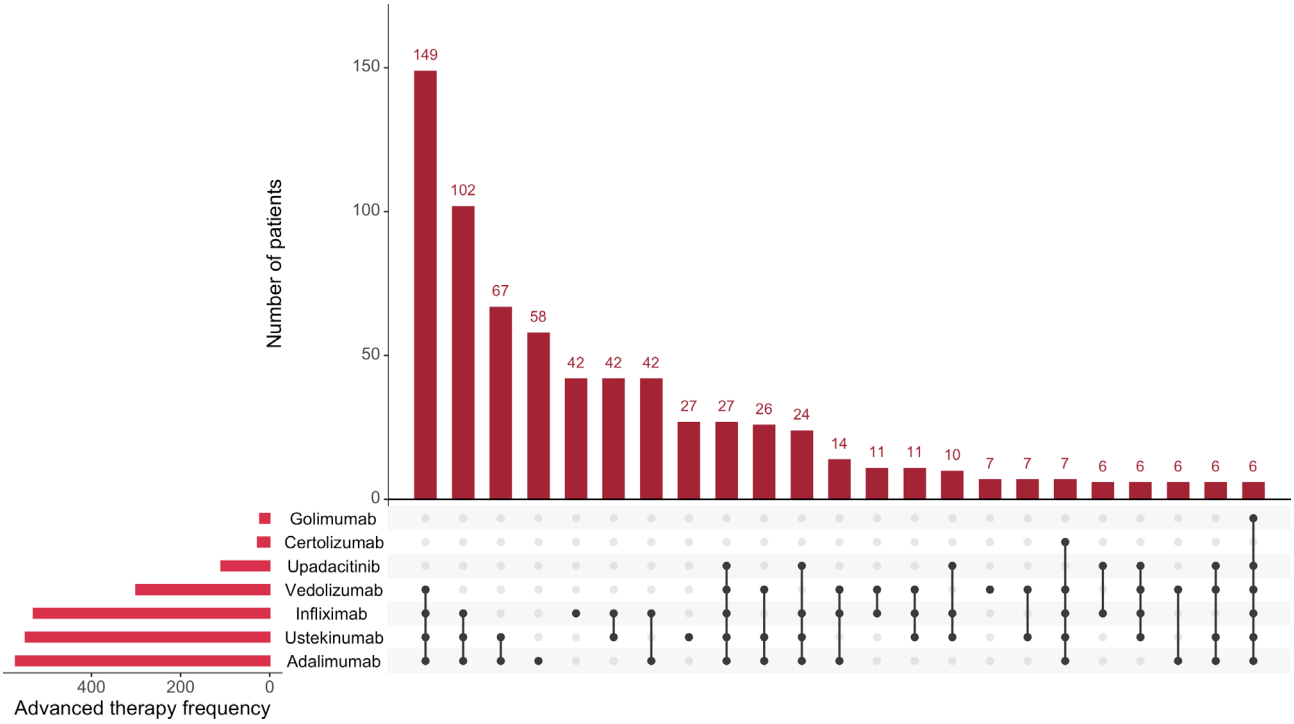

Figure 1 UpSet plot demonstrating advanced therapy exposure and combinations of advanced therapies. Combinations with fewer than five patients are not presented.

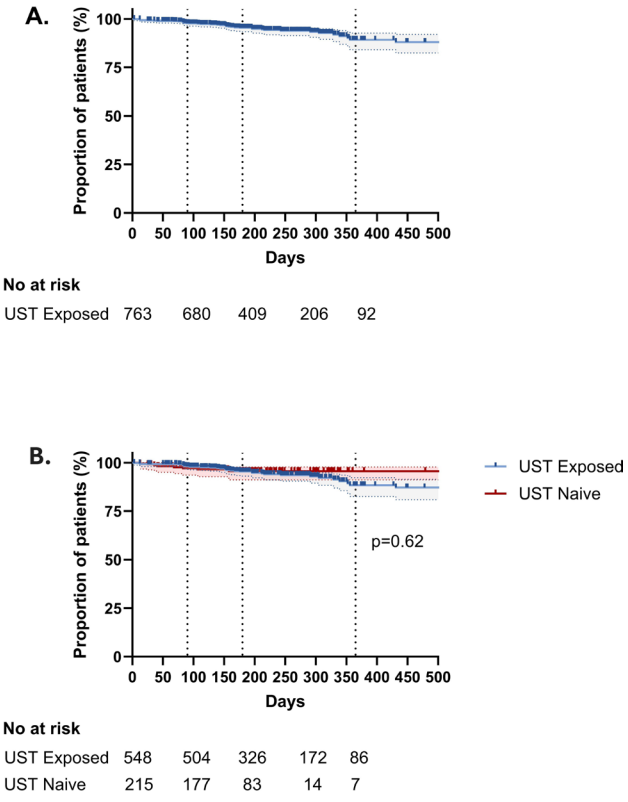

Figure 2 (A) Kaplan-Meier curve showing persistence of risankizumab therapy (dotted line depicts persistence at month 3, 6 and 12, respectively); (B) Kaplan-Meier curve showing persistence of risankizumab therapy for ustekinumab naive and exposed patients. UST, ustekinumab.

naive versus exposed patients for clinical, CRP and FCAL remission.

When considering previous advanced therapy exposure, rates of steroid-free clinical remission for those exposed to two or less advanced therapies versus more than two therapies were 66% (153/232) vs 53% (148/281) and 54% (44/81) vs 51% (79/155) at 3 and 6 months, respectively. Rates of CRP remission for those exposed to two or less advanced therapies versus more than two therapies were 64% (197/306) vs 53% (205/389) and 58% (61/105) vs 54% (108/214) at 3 and 6 months, respectively. Rates of FCAL remission for those exposed to two or less advanced therapies versus more than two therapies were 60% (95/158) vs 47% (78/165) and 47% (28/59) vs 42% (41/97) at 3 and 6 months, respectively. There were insufficient data at 12 months to analyse two or more therapy exposures for clinical, CRP and FCAL remission.

Steroid prescription, Crohn's disease-related hospitalisation and perianal outcomes

Rates of corticosteroid use were 21% (162/763, 78% prednisolone, 12% budesonide) at baseline, 9% (66/742, 79% prednisolone) at 3 months, 5% (19/392, 85% prednisolone) at 6 months and 5% (5/100, 100% prednisolone) at 12 months. Rates of exclusive enteral nutrition use were 9% (65/763), 4% (29/742), 3% (13/392) and 7% (7/100) at baseline, 3, 6 and 12 months, respectively. Concomitant immunomodulator use remained at 5–6% over follow-up. Fewer than five patients underwent dose escalation to four or six weekly dosing, of which none subsequently

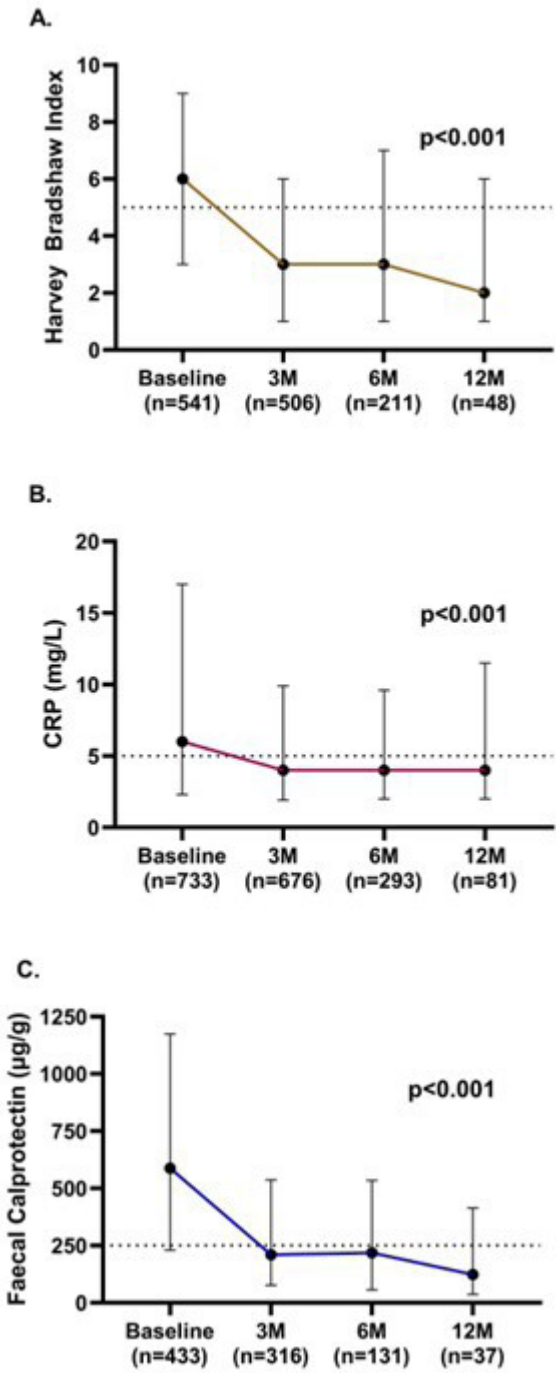

Figure 3 (A) Changes in HBI during follow-up; (B) changes in CRP during follow-up; (C) changes in FCAL during follow-up (graphs are depicted as Tukey plots). The Kruskal-Wallis test is used to determine significant differences between the three time points. CRP, C-reactive protein; FCAL, faecal calprotectin; HBI, Harvey-Bradshaw Index.

de-escalated. Concomitant advanced therapy use was used in 11 patients (1%, 11/763) and remained stable at 1% over follow-up and was largely due to those continuing therapy (<5 ceased therapy and <5 commenced a concomitant therapy during follow-up). Anti-TNF agents and Janus kinase inhibitors were the most commonly coprescribed advanced therapies (five patients each).

A total of 67 (8.8%, 67/763) patients had active perianal disease at initiation of risankizumab. Of these patients, 32.8% (22/67) had a perianal response (based on physician global assessment) to treatment and were deemed to have inactive perianal disease at week 12. At week 24, perianal response rates remained similar, with 30% (n=12/40) having inactive perianal disease. Of the 67 patients with active perianal disease at baseline, 19% (13/67) had a perianal complication which included developing a new perianal fistula (7%, 5/67), perianal abscess or unplanned examination under anaesthesia (12%, 8/67). A total of 179 (23.5%, 179 763) patients had a history of prior perianal disease that was inactive at the time of risankizumab initiation. Of these patients, 6 (3.4%) developed relapse of perianal disease based on physician global assessment during follow-up. We observed that active extraintestinal manifestations (excluding primary sclerosing cholangitis (PSC)) dropped from 12% (94/763) at baseline to 8% (56/742) and 7% (26/392) at 3 and 6 months, respectively. A total of 125 (16.4%) of patients had a stoma at initiation of risankizumab. Subanalysis including only these patients showed persistence rates of 99.2%, 96.1% and 85.4% at 3, 6 and 12 months, respectively (online supplemental figure 4).

Safety

Adverse events occurred in 17% (127/763) of the cohort, of which more than half (9%, 72/763) were due to symptomatic CD disease hospitalisations (online supplemental Table 5). Bowel resections represented more than one third of these hospitalisations (4%, 28/763). Infections occurred in 7% (50/763), of which 2% experienced a severe infection requiring hospitalisation (15/763). Serious adverse events occurred in 12% (92/763) of the cohort, of which 10% (80/763) required hospitalisations (65 symptomatic CD hospitalisations, 8 serious infections and seven experienced both symptomatic Crohn's hospitalisation and a serious infection), and 1% (11/763) were due to a side effect leading to drug cessation. There were fewer than five deaths in the cohort, of which none were considered related to the risankizumab.

DISCUSSION

In this highly medically refractory CD cohort, where 92% of the cohort had failed an anti-TNF, and 68% had failed at least two classes of advanced therapy, we observed high persistence rates of 94.5% and 87.5% at 6 and 12 months. respectively. At least 50% of patients were in clinical and CRP remission throughout follow-up, with rates of FCAL remission of 44% at 6 and 12 months. No statistically significant differences in unadjusted effectiveness outcomes were observed between ustekinumab naive and exposed patients, and ileal and colonic phenotypes. The majority of patients with active perianal disease at baseline did not experience a perianal complication during follow-up.

Our data is the largest published real world cohort to date and adds valuable information to the phase three trial data,[3 4] and the previously three published real-world cohorts.[6–8] The FORTIFY phase 3 maintenance trial observed remission rates of 52% in the 360 mg risankizumab arm at week 52, which is comparable to our remission rate of 50%, despite the potential selection bias of our study given we had no minimum Crohn's disease activity index (CDAI) requirement unlike the clinical trials.[3 4] The French real-world experience featuring 174 patients with 125 patients with 12-month follow-up data reported similar outcomes with persistence rates of 94%, 89% and 79% at weeks 12, 26 and 52 and 48% (60/125) achieved clinical remission (HBI <5) at 12 months.[7] A Belgian study reported clinical remission rates of 27.3% (15/55) at 12 months; however, this was a smaller cohort and possibly more refractory, with 85.5% exposed to ≥4 different advanced therapies.[8] While our study was not a dedicated study of perianal fistulising CD, our data suggests that risankizumab is a reasonable treatment option for patients who have failed other therapies. Together with the reported French outcomes in which approximately two thirds of patients with active perianal disease demonstrated clinical improvement, our data suggest risankizumab may be a valid treatment option for perianal CD. Dedicated clinical trials in this setting are warranted given the current paucity of options for the treatment of perianal CD and the implication of IL-23 in its pathogenesis,[12] with FUZION CD the only current clinical trial investigating an IL-23 agent, guselkumab, for the treatment of perianal fistulising CD.[13]

Approximately 30% of our cohort were ustekinumab-naive, which is unique among the limited number of published real-world cohorts, where more than 90% of patients had failed ustekinumab.[6–8] This remains an important point of difference to existing clinical trials, in which only 35 (17%) of the 205 patients in the risankizumab maintenance arm of the FORTIFY phase 3 trial had ustekinumab exposure, preventing further subanalysis.[4] We show that unadjusted persistence rates as well as clinical and CRP remission rates were similar between ustekinumab-naive and exposed patients. Our data suggest that risankizumab remains an effective treatment choice for patients with ustekinumab failure. Taken together with the SEQUENCE trial,[5] this suggests an important mechanistic difference between targeting the p40 and p19 subunit of IL-23.

Adverse events occurred in 17% of our cohort; however, half of these were due to symptomatic CD hospitalisations in a complex refractory population. Adverse events deemed to be caused by the drug were relatively low, with the majority of these not being serious. The drug was well tolerated with a small number of patients ceasing because of side effects. This safety data is in line with the reassuring safety data from registrational trials[3 4] and real-world evidence[6–8] and may have appeal across patient groups with potential clinical comorbidities.

A frequently occurring problem in clinical practice is choosing subsequent advanced therapies for patients with severe CD, particularly after anti-TNF failure, which has traditionally been the most used first-line therapy for CD in the UK. Responses to advanced therapy seem to reach 30–60%,[14] with many patients failing numerous classes of therapy as demonstrated in our cohort and the aforementioned real-world risankizumab cohorts.[6–8] Upadacitinib, a relatively new agent in CD, has been demonstrated to be an effective subsequent line advanced therapy; however, upadacitinib is not suitable for all patients given its safety profile.[15] Our data demonstrate that risankizumab is an effective option for patients with CD who have failed multiple lines of therapy. As seen in our cohort, some centres are using advanced combination treatment, as defined by combining two advanced therapies to achieve disease control in refractory cases.[16] There are theoretical benefits to this, targeting multiple immunological mechanisms driving ongoing disease activity, and while data is currently limited,[16] there are emerging clinical trials such as the VEGA trial, which suggest improved clinical efficacy with combination therapy.[17] One of the main barriers to dual therapy includes funding restrictions for multiple therapies; however, this may become less of an issue with the emergence of biosimilars for different classes of therapy,[18] which must be weighed against the medical and societal costs of refractory active IBD.[19] One of the other main barriers is safety concerns of using concurrent immunosuppressant agents; however, with the increasing number of therapies with good safety profiles such as risankizumab, this is a viable option in expert centres.

Strengths and limitations

The strength of this study is the large number of participating sites and patients, across large tertiary institutions and regional institutions within the UK NHS, describing the UK experience of risankizumab in CD. We present induction and maintenance outcomes, and an exploratory analysis of the effect of previous ustekinumab exposure.

The limitations of this study primarily relate to its retrospective nature, which limited complete assessment of response, namely endoscopic, radiological, extraintestinal manifestations and fistula data, and not all data was available at all time points. Endoscopic data were not universally scored using formal scoring systems, given they were not routinely available, with clinician's impressions used as a surrogate outcome; however, this is a common limitation of real-world studies, given formal scoring systems are not frequently used by clinicians. Our numbers at 12 months were smaller than our 3-month and 6-month outcomes, limiting subanalysis and statistical power of 12-month data. Regarding our ustekinumab naive versus exposed

outcomes, we were underpowered to perform a propensity-based analysis given most patients had been ustekinumab exposed and therefore report unadjusted comparisons of persistence of ustekinumab naive versus exposed groups. Given the majority of patients had failed multiple lines of therapy, there may be bias to higher persistence rates given the lack of other therapeutic alternatives. However, half (31/62) of the patients were in corticosteroid-free clinical remission at 12 months and 52% (51/98) were in CRP remission at 12 months supporting that risankizumab was effective.

CONCLUSION

Risankizumab was effective in a large, real-world, medically refractory CD cohort with excellent short-term persistence and good clinical and biochemical remission rates. Persistence rates were similar between ustekinumab naive and exposed patients, although clinical remission rates were higher in the ustekinumab-naive group.

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REFERENCES

1 Vuyyuru SK, Shackelton LM, Hanzel J, *et al*. Targeting IL-23 for IBD: Rationale and Progress to Date. *Drugs (Abingdon Engl)* 2023;83:873–91.
2 Risankizumab for previously treated moderately to severely active crohn's disease. NICE; 2023. Available: https://www.nice.org.uk/guidance/ta888/chapter/3-Committee-discussion#crohns-disease [Accessed 26 Feb 2025].
3 D'Haens G, Panaccione R, Baert F, *et al*. Risankizumab as induction therapy for Crohn's disease: results from the phase 3 ADVANCE and MOTIVATE induction trials. *Lancet* 2022;399:2015–30.
4 Ferrante M, Panaccione R, Baert F, *et al*. Risankizumab as maintenance therapy for moderately to severely active Crohn's disease: results from the multicentre, randomised, double-blind, placebo-controlled, withdrawal phase 3 FORTIFY maintenance trial. *Lancet* 2022;399:2031–46.
5 Peyrin-Biroulet L, Chapman JC, Colombel JF, *et al*. Risankizumab versus Ustekinumab for Moderate-to-Severe Crohn's Disease. *N Engl J Med* 2024;391:213–23.
6 Zinger A, Choi D, Choi N, *et al*. Risankizumab Effectiveness and Safety in Crohn's Disease: Real-world Data From a Large Tertiary Center. *Clin Gastroenterol Hepatol* 2024;22:1336–8.
7 Fumery M, Caron B, Hébuterne X, *et al*. Long-term Outcome of Risankizumab in Crohn's Disease: a Real-world GETAID Study. *Clin Gastroenterol Hepatol* 2024;22:2451–8.
8 Alsoud D, Sabino J, Franchimont D, *et al*. Real-world Effectiveness and Safety of Risankizumab in Patients with Moderate to Severe Multirefractory Crohn's Disease: A Belgian Multicentric Cohort Study. *Inflamm Bowel Dis* 2024;30:2289–96.
9 Harvey RF, Bradshaw JM. A simple index of Crohn's-disease activity. *Lancet* 1980;1::6102236.
10 Turner D, Ricciuto A, Lewis A, *et al*. STRIDE-II: An Update on the Selecting Therapeutic Targets in Inflammatory Bowel Disease (STRIDE) Initiative of the International Organization for the Study of IBD (IOIBD): Determining Therapeutic Goals for Treat-to-Target strategies in IBD. *Gastroenterology* 2021;160:1570–83.
11 Daperno M, D'Haens G, Van Assche G, *et al*. Development and validation of a new, simplified endoscopic activity score for Crohn's disease: the SES-CD. *Gastrointest Endosc* 2004;60:505–12.
12 Singh A, Midha V, Kochhar GS, *et al*. Management of Perianal Fistulizing Crohn's Disease. *Inflamm Bowel Dis* 2024;30:1579–603.
13 A study of guselkumab in participants with fistulizing, perianal crohn's disease (fuzion cd). EFCCA; 2025. Available: https://classic.clinicaltrials.gov/ct2/show/NCT05347095
14 Raine T, Danese S. Breaking Through the Therapeutic Ceiling: What Will It Take? *Gastroenterology* 2022;162:1507–11.
15 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;15:297–304.
16 Solitano V, Ma C, Hanžel J, *et al*. Advanced Combination Treatment With Biologic Agents and Novel Small Molecule Drugs for Inflammatory Bowel Disease. *Gastroenterol Hepatol* 2023;19:251–63.
17 Feagan BG, Sands BE, Sandborn WJ, *et al*. Guselkumab plus golimumab combination therapy versus guselkumab or golimumab monotherapy in patients with ulcerative colitis (VEGA): a randomised, double-blind, controlled, phase 2, proof-of-concept trial. *Lancet Gastroenterol Hepatol* 2023;8:307–20.
18 Angyal A, Bhat S. Biosimilars in IBD: What Every Clinician Needs to Know. *Curr Gastroenterol Rep* 2024;26:77–85.
19 Kaplan GG. The global burden of IBD: from 2015 to 2025. *Nat Rev Gastroenterol Hepatol* 2015;12:720–7.