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ORIGINAL RESEARCH

Real-world assessment of effectiveness and safety of filgotinib in 286 patients with ulcerative colitis in 9 UK centres

David Young[1,2], Sohail Rahmany[1], Deborah Taylor[1], Emma Davis[3], Michael Colwill[4], Sonia Kalyanji Mehta[4], Roisin Campbell[5], Karl Hazel[6], Karishma Sethi-Arora[7], Susan Ritchie[8], Ashley I Heinson[2], Helen Moyses[1], Keith Bodger[9], Emma Johnston[10], Lucy Hicks[11], Anjan Dhar[8,12], Jimmy Limdi[7,13], Rachel Cooney[6], John Paul Seenan[5], Kamal Patel[4], Alissa Walsh[3], Fraser Cummings[1,2]

[1]University Hospital Southampton NHS Foundation Trust, Southampton, UK; [2]University of Southampton, Southampton, UK; [3]Oxford University Hospitals NHS Foundation Trust, Oxford, UK; [4]St George's University Hospitals NHS Foundation Trust, London, UK; [5]NHS Greater Glasgow & Clyde, Glasgow, UK; [6]University Hospitals Birmingham NHS Trust, Birmingham, UK; [7]Northern Care Alliance NHS Foundation Trust, Greater Manchester, UK; [8]County Durham & Darlington NHS Foundation Trust, Darlington, UK; [9]University of Liverpool, Liverpool, UK; [10]Chelsea and Westminster Hospitals NHS Foundation Trust, London, UK; [11]Imperial College Healthcare NHS Trust, London, UK; [12]Teesside University, Middlesbrough, UK; [13]University of Manchester, Manchester, UK

Abstract

Background: Filgotinib, an oral Janus kinase 1 preferential inhibitor, has been shown to be an effective treatment for ulcerative colitis (UC) in pre-registration studies. We aimed to describe the treatment population, effectiveness and safety of filgotinib in a real-world cohort of patients with UC.

Methods: A retrospective observational cohort evaluation was conducted across nine UK inflammatory bowel disease centres. Baseline demographic and clinical data, clinical disease activity scores, endoscopic activity indices, and biomarkers (C-reactive protein and faecal calprotectin) were collected at baseline, at 8–12 weeks after initiation (post-induction) and during maintenance (the most recent review) where available. Effectiveness outcomes were assessed in patients with combined clinical disease activity and objective evidence of inflammation at filgotinib initiation.

Results: Data were analysed for a total of 286 patients with a median follow-up time of 229 (IQR 113–324) days. The median age at filgotinib initiation was 38 (IQR 27–51) years, 64% were men and median disease duration was 5.1 (IQR 1.9–10.5) years; 56% had previous exposure to advanced therapies (biologics and small molecule) and 6% previously received tofacitinib. At the post-induction review, clinical response and remission were achieved in 65% and 51% of patients, respectively. There was a reduction in biomarkers and 78% of patients using corticosteroids at baseline were steroid-free. Persistence on filgotinib at 12 months was 66%. Adverse events were recorded in 30 patients with 8 patients discontinuing filgotinib as a result of an adverse event.

Conclusions: In a large real-world cohort of patients with UC, filgotinib appears to be effective and well-tolerated.

Keywords: colitis, filgotinib, quality of life, ulcerative colitis.

Citation

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Introduction

Ulcerative colitis (UC) is a relapsing and remitting inflammatory bowel disease (IBD) primarily characterized by chronic inflammation of the colonic mucosa. Uncontrolled inflammation causes symptoms such as diarrhoea, rectal bleeding, urgency, abdominal pain and fatigue as well as increasing the risk of developing colorectal cancer and requiring a colectomy.[1] Our evolving treatment paradigms recognise the need to treat beyond symptoms and achieve biochemical and endoscopic remission where possible and to improve quality of life and reduce the risk of long-term complications.[2] Primary non-response, loss of response and intolerance to the limited number of effective treatment options are common, necessitating the introduction of new treatment options.

Inhibition of Janus kinase (JAK) uncouples signalling by multiple pro-inflammatory cytokines by interfering with the intracellular JAK–signal transducer and activators of transcription (STAT) pathway.[3] Filgotinib, an oral JAK1 preferential inhibitor, has been shown to be an effective treatment for UC in a recent phase IIb/III randomized controlled trial (SELECTION).[4] JAK inhibitors (JAKis) may have a number of advantages compared with other UC treatments, including rapid onset of action, avoidance of immunogenicity, increased convenience for patients and no requirement for infusions. Prior to the approval of filgotinib, the only JAKi licensed for the treatment of UC was a pan-JAKi (tofacitinib). In April 2023, the Medicines and Healthcare products Regulatory Agency (MHRA) extended risk minimization measures, previously introduced for tofacitinib, to all JAKis because of concerns about a possible increase in adverse effects (including malignancy, major adverse cardiovascular events and venous thromboembolism (VTE)) with these medicines.[5] It has been postulated that JAK selectivity may improve the risk–benefit profile of JAKis.[6]

Randomized controlled trials (RCTs) employ extensive inclusion and exclusion criteria to ensure a well-defined, homogeneous study population. This may, however, exclude important sub-groups of patients, select patients most likely to benefit from the treatment or exclude patients at increased risk of adverse events (such as those with multiple comorbidities or polypharmacy).[7,8] A disparity exists between patients enrolled into RCTs and the heterogeneous patient populations treated in routine clinical practice, limiting the generalizability of RCT results.[9] High-quality real-world evidence complements RCTs and supports decision-makers, including clinicians, payers and regulators. At present, our understanding of the real-world effectiveness of filgotinib in treating UC is limited, with the majority of reports being from single centres and mostly characterized by relatively small cohort sizes.[10–17] We report here the real-world experience of 286 patients with UC treated with filgotinib as part of their routine clinical care in 9 UK centres.

Materials and methods

Study design

We conducted a retrospective, observational cohort evaluation of the effectiveness and adverse effects of filgotinib in adult patients with UC at nine IBD centres in the United Kingdom as part of routine clinical practice. All centres recorded clinical disease activity scores and at least one validated IBD endoscopy scoring system as part of routine clinical care. In accordance with UK Health Research Authority guidelines, we did not require formal ethical approval for this real-world service evaluation using anonymized, routinely collected data.[18] The project was registered as a service evaluation at University Hospital Southampton NHS Foundation Trust (reference SEV/0622) and was conducted in accordance with the Declaration of Helsinki.

Patients

All adult patients with a diagnosis of UC (endoscopic and histologically confirmed) and initiated on filgotinib as part of routine clinical care at participating centres were included in the evaluation. Only patients with combined clinical (disease activity score indicating active disease) and objective disease activity at baseline were included in the assessment of clinical effectiveness (the active disease population). Objective disease activity was defined by endoscopic (Mayo Endoscopy Score (MES) ≥1 or Ulcerative Colitis Endoscopic Index of Severity (UCEIS) score ≥2) or biochemical (C-reactive protein (CRP) concentration >5 mg/L or faecal calprotectin concentration >250 µg/g) inflammation. All patients, irrespective of baseline disease activity status, were included in the safety analysis.

Study procedures

Patient demographic, clinical, laboratory, endoscopic and adverse event data were retrieved retrospectively from medical records between September and December 2023. Data were categorized according to three time points: baseline, following the induction period (8–12 weeks after starting treatment), and at the most recent maintenance review (at least 12 weeks after initiation).

Study outcomes

Data on patient characteristics collected included age, sex, ethnicity, weight, smoking status, shingles vaccination history, disease duration and extent (as per Montreal classification), presence of risk factors for serious adverse events as per the MHRA risk minimization measures[5]

(previous malignancy, major adverse cardiovascular events and VTE), and prior cytokine modulator/immunomodulator exposure. Details of filgotinib use included start and stop dates, and reason for discontinuation. Clinical data collected at each assessment time point included clinical and endoscopic activity indices, biomarkers (CRP and faecal calprotectin), and use of corticosteroids (oral or parenteral) or immunomodulators. Serum total cholesterol concentration at baseline and following induction was recorded. Two sites collected patient-reported outcome data (IBD-Control Questionnaire) directly from patients as part of routine clinical care. This tool, generic to all patients with IBD, was developed to measure disease control from the patient's perspective.[19] The IBD-Control-8 sub-score is based on questions relating to impacts of IBD on health-related quality of life (physical, social and psychological) and treatment perception, resulting in a score from 0 to 16 (0 indicating worst possible control), and the IBD-Control-VAS is a single, overall summary of disease control ranging from 0 to 100 (0 indicating worst possible control).

Clinical disease activity was assessed using the Simple Clinical Colitis Activity Index (SCCAI)[20] or Partial Mayo Score (PMS)[21] dependent on the assessment used in routine care at each site and was characterized as representing remission (SCCAI ≤2 or PMS ≤1), mild (SCCAI 3–5 or PMS 2–4), moderate (SCCAI 6–11 or PMS 5–6) or severely (SCCAI ≥12 or PMS ≥7) active disease. Clinical effectiveness outcomes were defined as: response (decrease in SCCAI ≥2 or PMS ≥3 compared with baseline or in remission) and remission (as per disease activity score in use).[21,22] Patients who discontinued filgotinib because of primary non-response, secondary loss of response, adverse events or at their own request were considered treatment failures and classified as non-responders. Endoscopic outcomes were stratified by scoring system applied: remission (MES 0 or UCEIS 0–1), mild (MES 1 or UCEIS 2–4), moderate (MES 2 or UCEIS 5–6) and severe (MES 3 or UCEIS 7–8).[23,24] Information on adverse events was gathered, including an assessment of seriousness, the probable connection to filgotinib, and whether each event led to the discontinuation of the medication. For patients continuing on filgotinib, maintenance follow-up time was defined as the time between filgotinib initiation and the date of data collection.

Statistical analysis

Quantitative data were presented as means with standard deviations (SD) or as medians with interquartile ranges (IQR) depending on the normality of the underlying distribution. Discrete data were presented as numbers and percentages. Paired continuous variables were compared using the paired *t*-test or Wilcoxon signed rank test, and categorical variables were analysed using Fisher's exact test or Pearson's χ^2 test. Ordinal data were analysed with the Friedman test and, in cases where a significant difference was observed, post hoc analysis was conducted using the Wilcoxon signed rank test for paired data to identify specific differences. Kaplan–Meier survival analysis was used to characterize treatment persistence, incorporating the log-rank test when applicable to discern group comparisons. Univariate analyses were conducted using Fisher's exact test or Pearson's χ^2 test for categorical data, and the Wilcoxon rank-sum test for continuous non-parametric data to investigate factors associated with response such as disease duration, prior advanced therapy exposure and baseline status. Multivariable analysis was conducted, incorporating all variables with a significance level below 0.2 in the univariate analysis. Statistical analyses were undertaken in R 4.2.3 (R Foundation for Statistical Computing, Vienna, Austria), with a p value <0.05 considered statistically significant.

Results

Patient characteristics

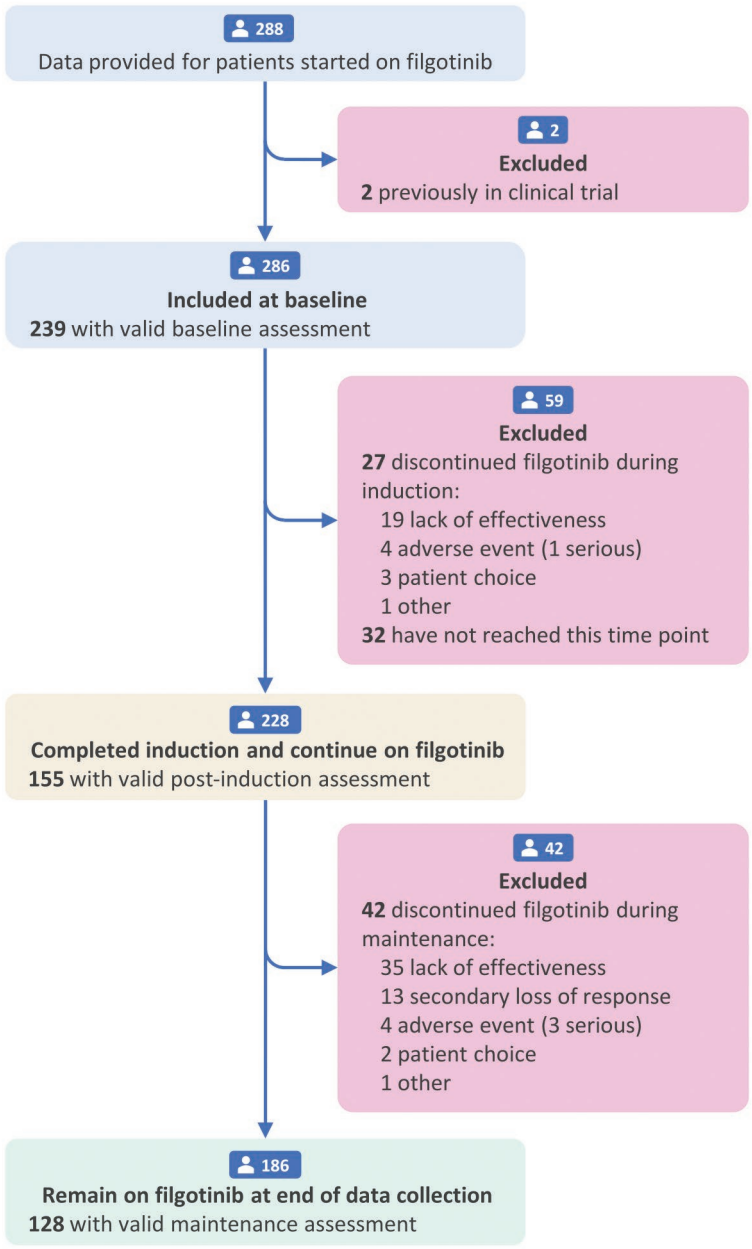
Data were analysed for a total of 286 patients with UC with disposition shown in Figure 1. Two patients were excluded as they started filgotinib as part of a clinical trial before marketing authorization was granted. The median follow-up time of those continuing on filgotinib was 229 (IQR 113–324) days. Baseline characteristics are shown in Table 1. Patients (n=215) identified as ethnically white (82%), Asian (11%) or other (7%); 44% of patients had no prior exposure to advanced therapies. The standard (200 mg OD) dose was used for initiation in 99% (282/286) of patients, with 4 patients prescribed 100 mg OD. Of the patients with a baseline disease activity score recorded, 73% (175/239) had combined clinical and objective disease activity making them eligible for analysis of clinical effectiveness outcomes. In these patients, the median baseline scores were SCCAI score 7 (IQR 5–9), PMS 6 (IQR 3–7), faecal calprotectin 871 µg/g (IQR 532–1786) and CRP 3.8 mg/L (IQR 1.1–11).

Clinical and biomarker effectiveness

Of the 175 patients meeting the definition of active disease at baseline, 65% showed a clinical response and 51% of patients achieved remission at the post-induction review (Figure 2). Considering the 104 patients using corticosteroids at baseline, 78% (67/86) and 87% (62/71) had discontinued these by the post-induction and maintenance reviews, respectively. A significant improvement in biomarkers was seen (p<0.001) (Table 2).

Univariate (Table 3) and multivariate (Table 4) analyses were conducted aiming to identify variables associated

Figure 1. Patient disposition.



with the response at the post-induction review. Shorter disease duration and prior exposure to multiple groups of advanced therapies were associated with non-response at the post-induction review.

Cumulative probabilities of filgotinib persistence were 89%, 80% and 66% at 3, 6 and 12 months, respectively (Figure 3).

Patient-reported outcomes

IBD-Control data were available for 151 patients at two sites. Both sub-scores (IBD-Control-8 and IBD-Control-VAS) and responses to the individual questions showed improvement from baseline to the post-induction review, which was maintained (Figure 4 and Figure 5, respectively). All domains of the IBD-Control-8 showed improvement (physical pain, sleep disturbance and fatigue), psychological, social and perception of treatment effectiveness; $p<0.001$ for each question at each timepoint *versus* baseline using dichotomized responses). A moderately strong negative correlation (Spearman's $\rho = -0.60$) was demonstrated between clinical disease activity score and the IBD-Control-8 sub-score (Supplementary Figure 1; available at: https://www.drugsincontext.com/wp-content/uploads/2025/01/dic.2024-11-1-Suppl.pdf).

Table 1. Baseline characteristics.

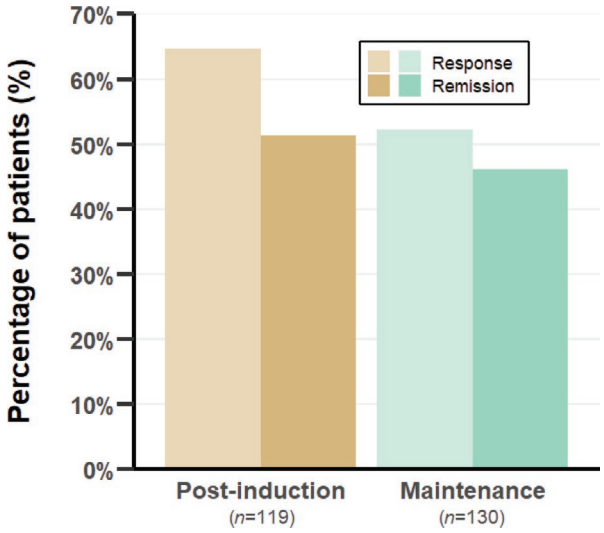
Overall (*n*=286)		
Age,[a] years	Median (IQR)	38 (27–51)
Sex, male	*n* (%)	184 (64%)
Body mass index,[a] kg/m^2	Median (IQR)	26.2 (22.8–29.4)
Disease duration,[a] years	Median (IQR)	5.1 (1.9–10.5)
Disease extent (as per Montreal classification; *n*=271)[b]	*n* (%)	
• E1 (proctitis)		35 (13%)
• E2 (left-sided)		106 (39%)
• E3 (extensive)		130 (48%)
At least one risk factor for serious adverse event (*n*=239)[c]	*n* (%)	73 (31%)
Prior advanced therapy exposure	*n* (%)	
• Anti-TNF		138 (48%)
• Vedolizumab		83 (29%)
• Ustekinumab		41 (14%)
• Tofacitinib		18 (6%)
• Upadacitinib		0
• Ozanimod		3 (1%)
Count of prior advanced therapy modes of action	*n* (%)	
• 0		126 (44%)
• 1		80 (28%)
• 2		45 (16%)
• 3		27 (9%)
• 4		8 (3%)
Active disease at baseline	*n* (%)	175 (61%)
Baseline clinical disease activity (*n*=239)	*n* (%)	
• Remission		32 (13%)
• Mild		73 (31%)
• Moderate		100 (42%)
• Severe		34 (14%)
Baseline laboratory measurements	Median (IQR)	
CRP, mg/L (*n*=224)		3.3 (1.1–8.4)
Faecal calprotectin, µg/g (*n*=126)		800 (349–1603)
Baseline endoscopic disease activity (*n*=161)	*n* (%)	
• Remission		4 (2%)
• Mild		64 (40%)
• Moderate		64 (40%)
• Severe		29 (18%)
Baseline medication use	*n* (%)	
• Corticosteroid (*n*=236)		104 (44%)
• Immunomodulator (*n*=236)		5 (2%)[d]

[a]At filgotinib initiation. [b]Maximum extent at point of filgotinib initiation. [c]As per Medicines and Healthcare products Regulatory Agency risk minimization measures.[5] [d]All five patients were using azathioprine.

Table 2. Biomarker results at the baseline, post-induction and maintenance reviews.

	Baseline		Post-induction			Maintenance		
	n	Median (IQR)	*n*	Median (IQR)	*p* value	*n*	Median (IQR)	*p* value
C-reactive protein (mg/L)	224	3.3 (1.1–8.4)	160	1.5 (1–3.9)	<0.001	133	1.2 (1–3.2)	<0.001
Faecal calprotectin (µg/g)	126	800 (349–1,603)	69	179 (38–735)	<0.001	63	108 (26–286)	<0.001

Figure 2. Proportion of patients with clinical response or in clinical remission at the post-induction and maintenance reviews.



Safety, tolerability and adherence

In total, 49 adverse events were recorded in 30 individual patients. These included gastrointestinal (*n*=20; including flare of UC (*n*=5), nausea (*n*=3), vomiting (*n*=2) and constipation (*n*=3)), surgical procedures (*n*=6; all colectomy) or neurological (*n*=5; including headache (*n*=3)). Eight patients discontinued filgotinib as a result of an adverse event. One patient (a 52-year-old man also diagnosed with primary sclerosing cholangitis) was diagnosed with adenocarcinoma in the liver of unknown primary, 4 months after starting filgotinib. One patient (a 56-year-old man with a BMI of 38 kg/m^2 but no other risk factors for VTE) developed a VTE after 12 months on filgotinib. Herpes zoster reactivation occurred in one patient (a 63-year-old woman who had not previously received the shingles vaccination). A statistically significant increase in total serum cholesterol concentration between baseline and post-induction was noted (p<0.001) but deemed unlikely to be clinically relevant (0.71 mmol/L; Figure 6).

Sub-group analysis

Patients with at least one indicator of moderate or severely active disease at baseline (considering clinical disease activity indices and endoscopic assessment) accounted for 66% (176/265) of our cohort. Effectiveness outcomes in this group were significantly worse than those with assessments indicating exclusively remission or mildly active disease and the difference in persistence at 1 year (64% *versus* 75%, respectively) approached statistical significance (Supplementary Figure 2).

Our cohort included 35 patients with proctitis who would typically be excluded from clinical trial programmes. The median IBD-Control-8 score of 4 (IQR 2–9) indicates that symptoms were having a significant impact on daily life and 93% (27/29) had a disease activity score indicating active disease. Filgotinib persistence and effectiveness at the time of the most recent review were similar in patients with proctitis to those in patients with more extensive disease (Supplementary Figure 3).

A total of 18 patients had prior exposure to tofacitinib (median treatment duration of 7.5 months); 33% (5/15) of these patients achieved remission with filgotinib at the most recent review (Supplementary Figure 4), including 36% (4/11) of the patients who previously discontinued tofacitinib because of lack of effectiveness (Supplementary Table 1). All three of the patients who had discontinued tofacitinib because of intolerance had subsequently discontinued filgotinib. When patients with prior exposure to tofacitinib were excluded, patients with prior exposure to other advanced therapies had significantly worse drug persistence and effectiveness outcomes than those who were naive to advanced therapies (Supplementary Figure 5). Drug persistence was similar regardless of whether patients had been exposed to a small number of advanced therapy groups (1 or 2) compared with those with experience of multiple (3 or 4) groups (p=0.65; Supplementary Figure 6). Drug persistence and effectiveness outcomes were similar for patients using corticosteroids at filgotinib initiation (p=0.3 and p=0.77, respectively; Supplementary Figure 7). Of the patients with primary non-response

Table 3. Univariate analysis of variables associated with response at the post-induction review.

Characteristic		Primary non-response (*n*=57)[a]	Response (*n*=123)[a]	*p* value
Age (years)		31 (26–44)	39 (28–51)	**0.07**
Sex	Female	19 (33%)	44 (36%)	0.75
	Male	38 (67%)	79 (64%)	
Disease duration (years)		2.4 (1.4–8.8)	6.6 (2.2–10.8)	**0.01**
Disease extent (*n*=174)	E1 (proctitis)	5 (9%)	13 (11%)	0.61
	E2 (left-sided)	19 (34%)	47 (40%)	
	E3 (extensive)	32 (57%)	58 (49%)	
Count of prior advanced therapy modes of action	None	18 (32%)	57 (46%)	**0.03**
	1 or 2	25 (44%)	53 (43%)	
	3 or 4	14 (25%)	13 (11%)	
Baseline CRP (mg/L; *n*=159)		2.9 (1.0–9.3)	4.0 (1.3–9.7)	0.25
Steroid use at baseline (*n*=169)		23 (45%)	55 (47%)	0.86
Presence of clinical or endoscopic marker of moderate or severe disease at baseline (*n*=171)		37 (69%)	68 (58%)	**0.19**

[a]Median (IQR) or *n* (%).
Bold values indicate significance level <0.2 and therefore included in multivariate analysis.

Table 4. Multivariate analysis of variables associated with response at the post-induction review.

Characteristic		Odds ratio	95% CI	*p* value
Age (per year)		1.01	0.98–1.04	0.45
Disease duration (per year)		1.07	1.01–1.15	0.03*
Count of prior advanced therapy modes of action (reference: none)	1 or 2	0.42	0.19–0.92	0.03*
	3 or 4	0.19	0.07–0.52	<0.01*
Presence of clinical or endoscopic marker of moderate or severe disease at baseline		0.66	0.32–1.34	0.26

*Indicates significance.

who continued filgotinib and had a subsequent maintenance review, 23% (5/22) achieved clinical remission.

Discussion

Despite an array of available treatment options, managing UC remains challenging because of modest response rates, frequent primary non-response, secondary loss of response and intolerance. We set out to describe the real-world effectiveness of filgotinib in a large cohort of patients from multiple IBD centres across the United Kingdom. This analysis suggests filgotinib is an effective and well-tolerated treatment option in patients both naive and exposed to other advanced therapies. In common with almost all evaluations of advanced therapies in IBD, effectiveness was statistically worse in patients with prior exposure to advanced therapies.

The baseline characteristics demonstrated that our cohort is a good representation of the patients treated in routine clinical care. The male predominance likely represents avoidance of this treatment option in female patients at risk of becoming pregnant. Additionally, 44% of our cohort had no previous exposure to advanced therapies as compared to 18% in the LEO

Figure 3. Persistence with filgotinib.

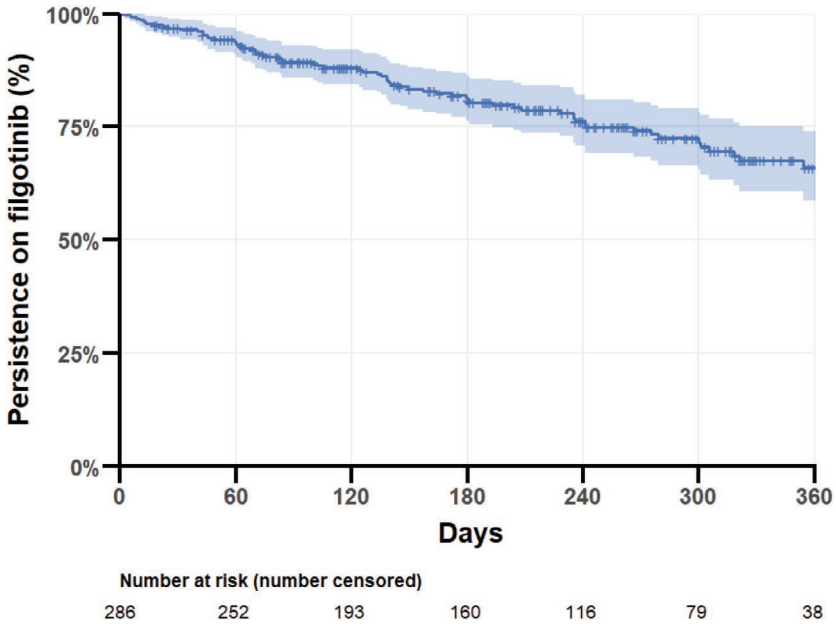
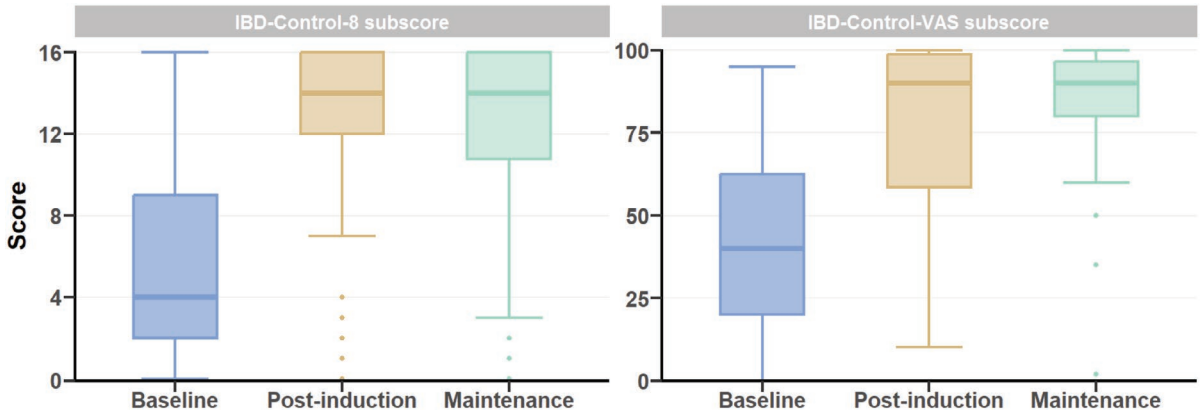


Figure 4. IBD-Control questionnaire results.



tofacitinib real-world experience cohort.[25] Further, 30% (42/140) of patients who started on filgotinib in the first half of the data collection period (before 22 February 2023) were naive to advanced therapies, compared with 57% (84/146) of those who started on or after that date, likely a reflection of increased clinician confidence with filgotinib and greater acceptance of JAKis as a first-line treatment option. It is noteworthy that filgotinib is accessible in the United Kingdom at a competitive price. There was almost no use of concomitant immunomodulator with filgotinib, in contrast to the routine use of concomitant immunosuppressants with filgotinib in rheumatological practice.[26–28] Given the challenges of using azathioprine, such as monitoring, tolerability and safety, the azathioprine-sparing effect of JAKis needs to be explored further. MHRA guidance suggests that JAKis should only be used if there are no suitable alternatives in patients aged ≥65 years, current or past long-time smokers, or in the presence of other risk factors for cardiovascular disease or malignancy.[5] In this real-world cohort, at least one of these criteria was met in 27% (65/239) of patients although 40% (26/65) had no prior advanced therapy exposure. Overall, 51%, 28% and 14% (*n*=33, 18 and 9, respectively) of patients had prior exposure to anti-TNF therapy, vedolizumab and ustekinumab, respectively, whereas 9% (6/65) of patients had been exposed to all three classes. In the real-world setting, choices about the use of these medicines require

Figure 5. Proportion of patients reporting negative (red), neutral (orange) or positive (green) responses to each of the IBD-Control-8 items.

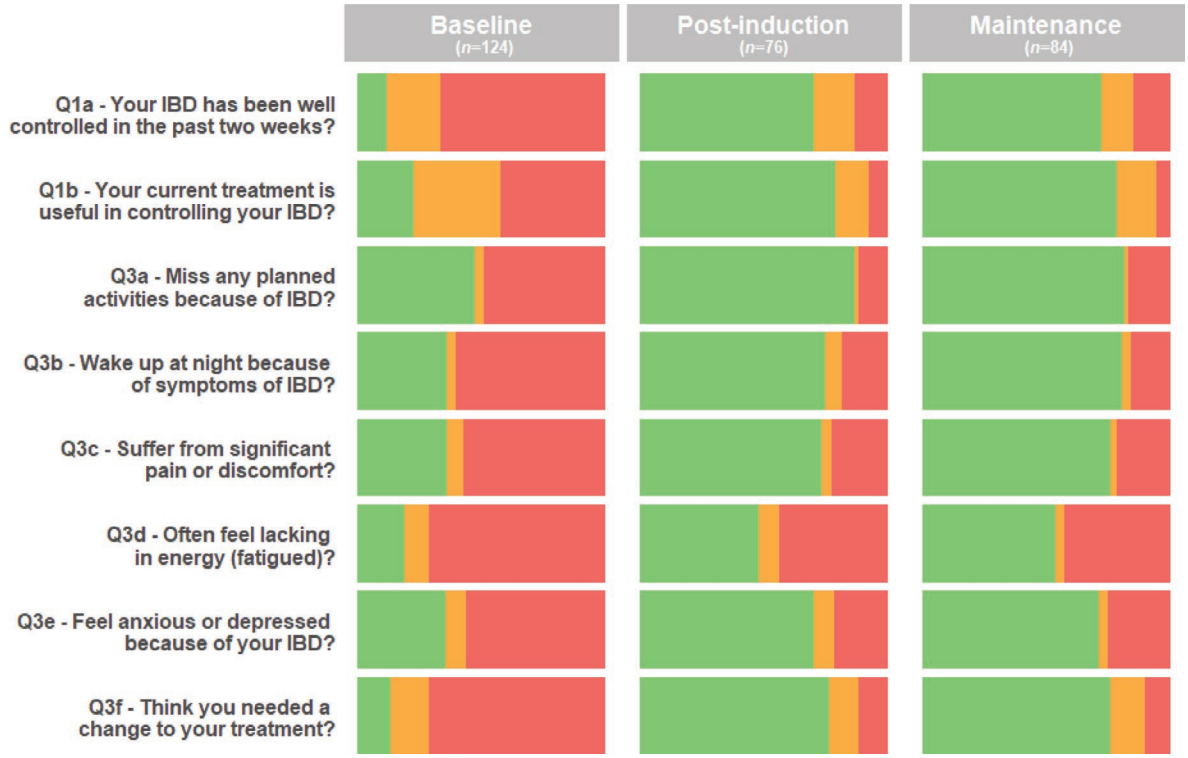
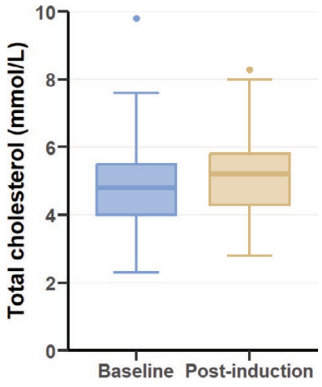


Figure 6. Change in total serum cholesterol concentration with filgotinib treatment.



clinicians to make nuanced and personalized decisions, taking multiple factors into account, balancing the risks involved and considering the potential harm associated with untreated inflammation.

Clinical effectiveness of filgotinib, assessed using validated disease activity scores, demonstrated that the majority of patients improved within the induction period. Although the product license permits extending the induction period to 22 weeks for patients without an initial response,[29] very few patients in our cohort receiving extended induction gained therapeutic benefit, which may suggest limited value to this approach. Correlation analysis demonstrated a significant improvement in quality of life associated with a reduction in disease activity score. A significantly longer median disease duration in patients with response following induction (2.4 *versus* 6.6 years) is similar to that in the LEO study,[25] although other cohorts have not demonstrated this with tofacitinib.[30,31] We postulate that patients who persist with medical therapy (over colectomy) may be experiencing a less aggressive form of the disease.

One important advantage of real-world evidence, compared with that obtained from phase III RCTs, is the opportunity to assess effectiveness of the medicine in groups commonly excluded from these trials. At the point of filgotinib initiation, 44% (105/239) of patients had a clinical disease activity score indicating remission or mildly active disease. The proportion of patients using corticosteroids at baseline was similar between this group and the patients with moderate-to-severe clinical disease activity at baseline (p=0.39). It is clear that a significant proportion of the patients treated in routine practice in the United Kingdom do not meet the symptom threshold used in RCTs and consequently by the National Health Technology Assessment Agency.[32]

Clinical disease activity assessments rely on a predefined set of 'typical' symptoms, which may not encompass the entire spectrum of symptoms that patients may experience because of active inflammation, as well as the impact on many other facets of a patient's well-being. In clinical practice, justification of the use of advanced therapies is not based solely on clinical disease activity but also on inflammatory burden and the impact of symptoms on quality of life. A novel feature of the IBD-Control questionnaire is that it contains two items asking the patient's perception of treatment effectiveness (Q1b and Q3f), enabling a broader assessment of disease control.[33] Responses to these items improved markedly with filgotinib treatment, reflecting patient perception and therefore holistic disease control. Overall, 13% of the patients included in this evaluation had proctitis and, despite an anatomically limited area of active disease, both clinical disease activity scores and the patient-reported outcome measures demonstrate a negative impact on quality of life in the majority of patients. Indeed, outcomes for these patients were similar to those with more extensive disease.

The effectiveness of JAKi cycling (use of an alternative JAKi) remains unclear with a paucity of evidence to support the use of another JAKi in patients in whom the first JAKi has failed. Each of the available JAKis displays a specific binding affinity profile for the four members of the JAK family (JAK1, JAK2, JAK3 and TYK2), which may impact therapeutic response.[34] These data showed that a proportion of patients achieved remission with filgotinib, despite previous therapeutic failure to tofacitinib, suggesting that this strategy may hold merit. A recently published UK-based retrospective cohort study of JAKi cycling in UC (n=99; predominant first and second agents were tofacitinib and upadacitinib, respectively) drew similar conclusions.[35] Upadacitinib was approved for the treatment of UC in the United Kingdom in January 2023 and, consequently, our cohort only includes those with previous exposure to tofacitinib.

The safety profile of filgotinib in our cohort appeared to be consistent with previously reported data. The role of vaccination to minimize the increased risk of herpes zoster in patients receiving JAKis warrants further discussion.[36] Notably, only 16 patients in our cohort had received at least one dose of a herpes zoster vaccine (n=86).

Real-world effectiveness data are also available from Edinburgh (n=91) in a population that was mostly (67%) naive to advanced therapies.[14] Overall clinical remission (PMS <2) was achieved by 72% of the cohort and drug persistence at the end of follow-up was 82%. This cohort included patients who did not meet our definition of active disease at initiation, although patient characteristics generally closely resembled those of our cohort. A Japanese multicentre retrospective study (n=238) showed clinical remission rates of 47% and 65% at weeks 10 and 58, respectively (available-case analysis), in patients with clinically active UC at initiation, with comparable effectiveness regardless of prior advanced therapy exposure.[17] The authors also concluded that JAKi cycling may be worthy of consideration, albeit with an expectation of reduced effectiveness.

To maximize the robustness of our effectiveness analysis results, we restricted the assessment of clinical effectiveness outcomes to patients who met a stringent definition of active disease at initiation, considering both clinical activity scores and objective markers of inflammation. In most instances, the reason patients were excluded from the active disease set was because of missing information (n=66; Supplementary Table 2). Overall, 24 patients in clinical remission had a discordant inflammatory biomarker result and 16 patients lacked objective evidence of inflammation despite clinical disease activity; 5 patients initiated filgotinib in clinical remission and with no objective evidence of inflammation. Clinical and objective markers may incorrectly suggest remission because of steroid use, dietary manipulation or ongoing effect of the previous advanced therapy (for instance, if discontinued because of intolerance). A sensitivity analysis (Supplementary Figure 8) examining the clinical effectiveness outcomes in all patients, irrespective of baseline active disease status, yielded results that were consistent with the findings presented earlier.

Important strengths of this evaluation are the inclusion of all patients initiating filgotinib at multiple centres, providing a large cohort for analysis, including sufficient patients to facilitate sub-group analysis, as well as the use of validated clinical and endoscopic outcome data. We acknowledge several limitations of our study. Although the majority of patients (70%) were from three sites, disease demographics and outcomes were broadly similar across all locations. Limited endoscopic follow-up data were available. We acknowledge that endoscopic assessment is the gold standard for measuring the effectiveness of IBD treatments; however, regular endoscopy is arguably resource intensive in the real-world setting and often unacceptable to patients. We believe that the combination of validated disease activity scores and biomarkers represents a pragmatic surrogate for a real-world evaluation. The use of calprotectin in combination with a clinical disease activity score at the end of induction has been shown to be a good prognostic marker for longer-term remission with filgotinib.[37] We also acknowledge some inherent flaws of our retrospective observational study design, notably missing data (in particular faecal calprotectin results and adverse events) and difficulty effectively controlling for potential confounding variables.

Conclusion

Filgotinib was effective and well-tolerated in this large real-world multicentre cohort of patients with UC. The ideal position of filgotinib in treatment algorithms is yet to be determined; however, our findings support its role early in treatment pathways in patients not previously exposed to advanced therapies as both an induction agent, potentially in place of steroids, and as a maintenance agent instead of azathioprine as well as later in patients with more treatment-refractory disease.

Conference presentation: Early analysis of a partial data set was presented as a poster at the European Crohn's and Colitis Organisation Congress in 2024.

Supplementary material available at: https://www.drugsincontext.com/wp-content/uploads/2025/01/dic.2024-11-1-Suppl.pdf

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Correspondence: David Young, Pharmacy Department, University Hospital Southampton NHS Foundation Trust, Tremona Road, Southampton, UK, SO16 6YD. Email: david.young@uhs.nhs.uk

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