Reasons for choice and areas for improvement in advanced therapies (biologics and JAKis) for patients with ulcerative colitis in the United Kingdom

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Introduction

- Ulcerative colitis (UC) is a chronic inflammatory bowel disease that mostly affects the colon and rectum,[1] with a reported incidence in the United Kingdom of 15.7 (95% confidence interval, 15.4–15.9) per 100,000 person-years[2]
- UC significantly impacts patients' quality of life (QOL) due to multiple symptoms such as increased bowel frequency and urgency, loose stools, bleeding, and fatigue[3]
- Patients with mild to moderate UC are usually first treated with 5-aminosalicylates and corticosteroids, and disease flares in these patients are often treated with corticosteroids[4]
- Advanced therapies (ATs) for treatment of moderate to severe UC, which include oral medications (Janus kinase inhibitors; JAKis) and injectable biologic therapies, provide enhanced disease control and clinical remission[5,6]
- Determining the reasons for treatment choice and identifying areas that require improvement for both oral JAKis and injectable biologics can help inform future treatment for UC and position these drugs in treatment algorithms

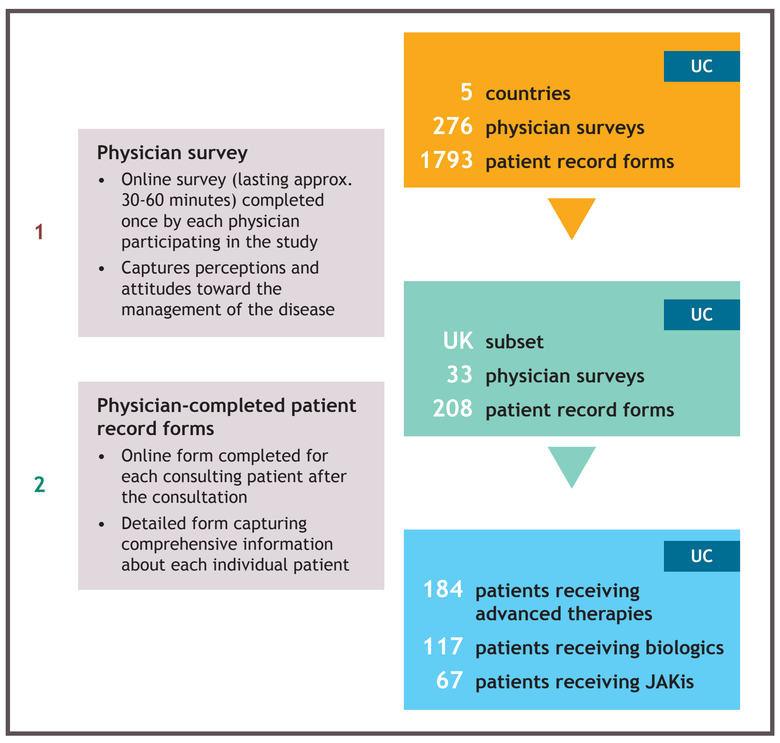
Objectives

- This study aimed to identify reasons for choice and areas for improvement for both oral JAKis and biologic ATs in UC. Considerations investigated in the survey included
  - Efficacy
  - Safety
  - Treatment administration or monitoring
  - Access or cost

Methods

- Data were derived from the Adelphi Real World Inflammatory Bowel Disease Disease Specific Programme for UC,[7] a point-in-time survey of gastroenterologists (GIs) and their 184 patients with UC in the United Kingdom who were receiving consultation (**Figure 1**)

Figure 1. Overview of study design



- The survey was conducted under the relevant guidelines, with patient consent. The data were collected from September 2020–March 2021 in the United Kingdom, and captured GI-reported patient demographics, comorbidities, reasons for choice, and areas for improvement in patient treatment for 7 consecutive consulting UC patients and an additional 2 patients receiving JAKis
  - GIs also reported patient clinical characteristics at the initiation of current treatment, and at the time of current consultation
  - In total, 117 patients receiving biologics and 67 patients receiving JAKis, at the time of consultation, were included in the analysis
  - Between-group comparisons were derived using the Mann–Whitney *U* test, *t* test, and chi-square test

Results

Demographics, clinical characteristics, and history

- Patients' mean age was 37.9 years (standard deviation [SD], 11.5), 66.3% were male, the mean body mass index (BMI) was 26.1 kg/m^2, and the mean disease duration was 3.5 years (SD, 3.2)
- Almost half (48.0%) of patients were in full-time employment
- Overall, the demographics between the biologic and JAKi groups were comparable (**Table 1**)

Table 1. GI-reported demographics of patients receiving biologics and JAKis

	Biologics (n = 117)	JAKis (n = 67)	*P* value
Age, mean (SD), years	37.6 (12.4)	38.6 (9.8)	0.58
Sex, n (%)			
Male	75 (64.1)	47 (70.1)	0.42
Female	42 (35.9)	20 (29.9)	
BMI, mean (SD), kg/m^2	26.3 (4.5)	25.9 (5.1)	0.65
Disease duration	*Biologics (n = 107)*	*JAKis (n = 63)*	
Mean (SD), years	3.7 (3.8)	3.1 (2.0)	0.24
Employment status, n (%)	*Biologics (n = 114)*	*JAKis (n = 63)*	
Working full time	56 (49.1)	29 (46.0)	< 0.05
Working part time	24 (21.1)	19 (30.2)	
On long-term sick leave	4 (3.5)	8 (12.7)	
Homemaker	8 (7.0)	5 (7.9)	
Student	10 (8.8)	2 (3.2)	
Retired	6 (5.3)	0 (0.0)	
Unemployed	6 (5.3)	0 (0.0)	

- The average duration of treatment was significantly longer among patients receiving biologics (12.6 months) versus patients who received JAKis (6.6 months); $P < 0.05$
- Patients receiving JAKis had received more previous treatment lines than patients receiving biologics ($P < 0.05$; **Table 2**). For example, patients receiving JAKis were more likely to receive a JAKi as third-line treatment (67.2%) compared with patients receiving biologics (46.2%)
- Biologics were prescribed significantly more often as a first-line AT than JAKis ($P < 0.05$). Patients receiving biologics were more likely to have received only 1 AT (72.7%) compared with patients receiving JAKis (22.4%)

Table 2. GI-reported treatment history of patients receiving biologics and JAKis

	Biologics (n = 117)	JAKis (n = 67)	*P* value
Current AT, n (%)			
Anti-TNF	79 (67.5)	0	-
Anti-integrin	36 (30.8)	0	
Anti-interleukin 12/23	2 (1.7)	0	
JAKis	0	67 (100.0)	
Current treatment, n (%)			
AT received with conventional treatment[a]	62 (53.0)	28 (41.8)	0.17
AT as monotherapy	55 (47.0)	39 (58.2)	
Time on current treatment, mean (SD), months	12.6 (12.2)	6.6 (4.8)	< 0.05
No. of treatment lines, mean (SD)	2.5 (0.9)	2.9 (0.9)	< 0.05
No. of treatment lines, n (%)			
1	11 (9.4)	3 (4.5)	< 0.05
2	52 (44.4)	19 (28.4)	
≥ 3	54 (46.2)	45 (67.2)	
No. of AT lines, mean (SD)	1.4 (0.6)	2.1 (0.9)	< 0.05
No. of AT lines, n (%)			
1	85 (72.6)	15 (22.4)	< 0.05
2	24 (20.5)	35 (52.2)	
≥ 3	8 (6.8)	17 (25.4)	

[a]Conventional treatment: aminosalicylates, corticosteroid, immunomodulator.
TNF, tumor necrosis factor.

- At treatment initiation, there was a significant ($P < 0.05$) difference in the level of disease progression between patients who received biologics versus those who received JAKis; 35.0% of patients receiving biologics deteriorated rapidly versus 11.9% of patients receiving JAKis (**Table 3**)

Table 3. GI-reported clinical characteristics at initiation in patients receiving biologics and JAKis

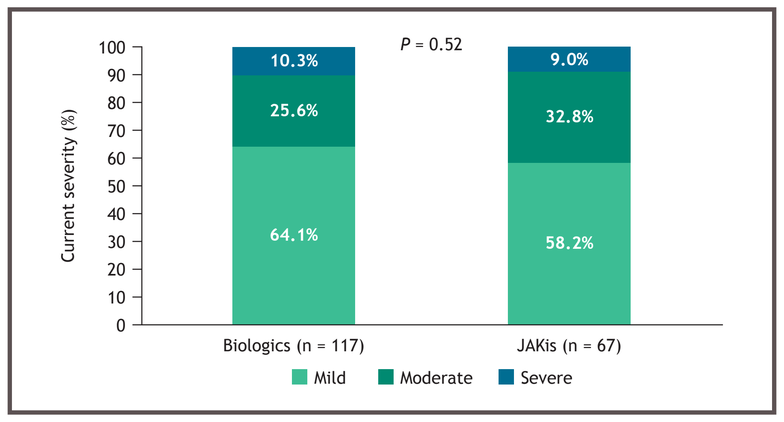
	Biologics (n = 117)	JAKis (n = 67)	*P* value
Disease severity, n (%)			
Mild	3 (2.6)	1 (1.5)	0.41
Moderate	62 (53.0)	41 (61.2)	
Severe	52 (44.4)	25 (37.3)	
Flaring at initiation, n (%)	*n = 116*	*n = 67*	
Not flaring	43 (37.1)	28 (41.8)	0.53
Flaring	73 (62.9)	39 (58.2)	
Disease progression, n (%)			
Improving	5 (4.3)	4 (6.0)	< 0.05
Stable	11 (9.4)	9 (13.4)	
Deteriorating slowly	60 (51.3)	46 (68.7)	
Deteriorating rapidly	41 (35.0)	8 (11.9)	
Symptom severity, mean (SD)	3.0 (1.1)	2.9 (1.0)	0.81
Pain severity, mean (SD)	2.5 (1.1)	2.5 (1.1)	0.88
Severity of impairment on QOL, mean (SD)	3.0 (1.0)	2.9 (1.1)	0.33

Mean scores are calculated from a scale of 0 = none to −5 = extremely severe.

GI-reported clinical outcomes

- At the time of the current consultation, there were no significant differences in overall severity (**Figure 2**) between patients who received biologics and patients who received JAKis

Figure 2. GI-reported current severity in patients receiving biologic and JAKi therapies



GI-reported comorbidities

- Anxiety (9.8%) and depression (6.0%) were reported as the most common comorbidities among the overall population, with no significant differences in comorbidities between patients receiving biologics or JAKis (**Table 4**)

Table 4. GI-reported current comorbidities of patients receiving biologics and JAKis

	Biologics (n = 117)	JAKis (n = 67)	*P* value
Anxiety	11 (9.4)	7 (10.4)	0.80
Depression	8 (6.8)	3 (4.5)	0.75
Hypertension	6 (5.1)	2 (3.0)	0.71
Axial spondyloarthritis	6 (5.1)	3 (4.5)	1.00
Psoriasis	4 (3.4)	5 (7.5)	0.29

GI-reported reasons for choice, areas of improvement, and switching of treatment

- Despite therapies being chosen for efficacy (biologics, 100%; JAKis, 94%), efficacy remained a stated key area for improvement for both biologics (58.1%) and JAKis (47.8%), along with safety (biologics, 53.0%; JAKis, 53.7%; **Table 5**)
- However, treatment administration and monitoring were regarded as greater unmet needs for patients receiving biologics (39.3%) versus JAKis (4.5%; $P < 0.05$)

Table 5. GI-reported reasons for choice and areas for improvement for patients who received biologics and JAKis

	Biologics (n = 117)	JAKis (n = 67)	*P* value
Reasons for choice of current AT, n (%)			
Efficacy	117 (100.0)	63 (94.0)	< 0.05
Safety/tolerability	54 (46.2)	18 (26.9)	< 0.05
Treatment administration and monitoring	33 (28.2)	41 (61.2)	< 0.05
COVID-19	7 (6.0)	10 (14.9)	0.06
Access/cost	40 (34.2)	13 (19.4)	< 0.05
Other	45 (38.5)	25 (37.3)	1.00
Areas for improvement for current AT, n (%)			
Efficacy	68 (58.1)	32 (47.8)	0.22
Safety/tolerability	62 (53.0)	36 (53.7)	1.00
Treatment administration and monitoring	46 (39.3)	3 (4.5)	< 0.05
Access/cost	14 (12.0)	25 (37.3)	< 0.05
Other	14 (12.0)	9 (13.4)	0.82

COVID-19, Coronavirus disease 2019.

- Treatment administration and monitoring was chosen significantly more often as a reason for patients switching to the current JAKi (42.2%) versus those receiving biologics (17.0%) ($P < 0.05$; **Table 6**)

Table 6. GI-reported reasons for switching from patients' previous treatment to current biologic or JAKi

	Biologics (n = 106)	JAKis (n = 64)	*P* value
Reasons for switch from previous treatment, n (%)			
Efficacy	101 (95.3)	57 (89.1)	0.14
Safety/tolerability	25 (23.6)	13 (20.3)	0.71
Treatment administration and monitoring	18 (17.0)	27 (42.2)	< 0.05
COVID-19	4 (3.8)	7 (10.9)	0.10
Access/cost	4 (3.8)	6 (9.4)	0.18
Other	12 (11.3)	17 (26.6)	0.02

- Only 34.3% of patients who received JAKis were perceived by GIs as suitable candidates for biologics (**Table 7**)
- Among patients receiving JAKis, the main reason reported by GIs for these patients not receiving biologics was their dislike of injections or infusions associated with biologics (56.5%)
- GIs also perceived biologics as too troublesome to administer among 21.7% of their patients

Table 7. GI-reported suitability and reasons for not receiving biologics among patients who received JAKis

	JAKis (n = 67)
Suitable candidates for biologics, n (%)	23 (34.3)
Top 5 reasons for not receiving biologics, n (%)	*JAKis (n = 23)*
The patient dislikes injections/infusions	13 (56.5)
The patient does not want to go to an infusion center	10 (43.5)
Biologics are inconvenient/too troublesome to administer	5 (21.7)
Patient reluctance due to time commitments	4 (17.4)
Concerns regarding malignancy	3 (13.0)

- Approximately half (49.6%) of patients receiving biologics were considered candidates for JAKis, but had not been prescribed a JAKi, as GIs preferred to explore other treatment options first (36.2%) and expressed concerns over the possibility of blood clots with this treatment (24.1%; **Table 8**)

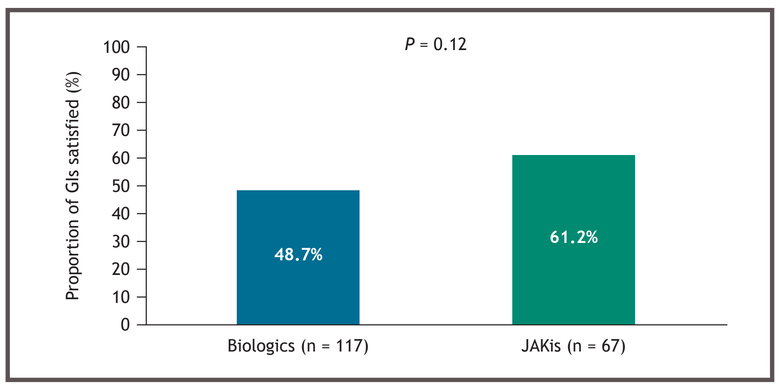
Table 8. GI-reported suitability and reasons for not receiving biologics among patients who received biologics

	Biologics (n = 117)
Suitable candidates for JAKis, n (%)	58 (49.6)
Top 5 reasons for not receiving JAKis, n (%)	*Biologics (n = 58)*
Prefer to exhaust all other treatment options first	21 (36.2)
Concerns regarding blood clots	14 (24.1)
Formulary restriction	14 (24.1)
Very recent diagnosis	8 (13.8)
Concerns regarding infection	8 (13.8)

GI-reported overall satisfaction

- The proportion of GIs who were satisfied and believed that the best possible control was achieved with patient treatment was 48.7% for biologics and 61.2% for JAKis (**Figure 3**)

Figure 3. GI satisfaction with control of patient treatment



Limitations

- This analysis does not account for potential confounders that may be associated with additional reasons of treatment choice, such as prior medications or sequencing

Conclusions

- GIs considered efficacy and safety as key areas for improvement among both biologics and JAKis, demonstrating an existing unmet need for ATs, including addressing the mental burden that patients experience
- Biologics were more commonly prescribed as a first-line AT than JAKis, and overall, were reported to be significantly safer than JAKis. Nonetheless, JAKis were reported to have significantly less unmet needs pertaining to treatment administration and monitoring
- Despite being favored for treatment administration, JAKis are still likely to be reserved until other treatment options are explored. This was true even though more than half of patients currently receiving JAKis were not given biologics due to patients' dislike of injections or infusions

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