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Filgotinib induction-study baseline characteristics of patients with ulcerative colitis who achieve sustained corticosteroid-free remission: *post hoc* analysis of the phase 2b/3 SELECTION study

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Background/Aims: Obtaining and maintaining corticosteroid-free remission are important goals of treatment for ulcerative colitis (UC). Characteristics associated with achieving corticosteroid-free remission were assessed in filgotinib-treated patients in SELECTION, a 58-week, phase 2b/3 trial in moderately to severely active UC. **Methods:** This *post hoc* analysis used data from filgotinib-treated patients receiving corticosteroids at maintenance baseline in SELECTION. Univariate logistic regression was performed to assess induction baseline characteristics associated with 6 months of corticosteroid-free remission at week 58, defined as clinical remission without using corticosteroids for at least 6 months. **Results:** At maintenance baseline, 92 and 81 patients were receiving corticosteroids in the filgotinib 200 mg and filgotinib 100 mg groups, respectively. Age, body mass index, history of pancolitis, disease duration, fecal calprotectin levels, C-reactive protein levels, Mayo Clinic Score, concomitant corticosteroids, immunomodulators, and aminosalicylates had no statistically significant effect on the likelihood of achieving corticosteroid-free remission. Baseline characteristics associated with increased odds of corticosteroid-free remission were Mayo Clinic Endoscopic Subscore of 2 (vs. 3) in the filgotinib 200 mg and filgotinib 100 mg groups, and female (vs. male) sex, current (vs. former or never) smoking, and being biologic-naive (vs. experienced) in the filgotinib 200 mg group. **Conclusions:** Steroid tapering can be achieved in patients with UC receiving filgotinib 200 mg independently of baseline characteristics such as clinical activity and duration of illness. However, the likelihood of achieving corticosteroid-free remission was higher among patients who were biologic-naive, current smokers, had low endoscopic inflammatory burden and who were female. **(Intest Res 2025;23:65-75)**

Key Words: Corticosteroids; Filgotinib; Ulcerative colitis

INTRODUCTION

Ulcerative colitis (UC) is a chronic, immune-mediated inflammatory bowel disease affecting the rectum and colon and characterized by symptoms of rectal bleeding and diarrhea. The goal of maintenance treatment for UC is to obtain and maintain corticosteroid-free remission, and guidelines recommend against the use of systemic corticosteroids for maintaining remission in patients with UC due to safety concerns.[1-3]

Filgotinib is a once daily, oral, Janus kinase 1 (JAK) preferential inhibitor approved in Europe and Japan for the treatment of adults with moderately to severely active UC. Approval of

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this indication for filgotinib is based on data from the phase 2b/3 SELECTION trial (n = 1,348; 659 biologic-naive, 689 biologic-experienced), which showed filgotinib to be well tolerated and efficacious at inducing and maintaining clinical remission compared with placebo in patients with moderately to severely active UC.[4] At week 58 of SELECTION maintenance, 25 of 92 patients treated with corticosteroids at maintenance baseline had achieved at least 6 months of corticosteroid-free remission with filgotinib 200 mg (the approved dose), compared with 3 of 47 patients in the matched placebo group (P = 0.0055).[4] Subsequent analyses suggested that the corticosteroid-sparing effects of filgotinib 200 mg seen in the SELECTION trial were rapid and sustained, including in patients whose disease was refractory to prior treatments, compared with placebo.[5] Patient characteristics at week 10 (maintenance baseline) that were correlated with corticosteroid-free remission for at least 6 months were: presence of histological remission; endoscopic improvement; lower Mayo Clinic Score; being biologic-naive; and having no previous exposure to, or failure of, tumor necrosis factor antagonists and vedolizumab.[5] Analyses were conducted for the filgotinib 200 mg and filgotinib 100 mg groups combined, and assessed the effects of patient characteristics at week 10 (not at induction baseline).[5] However, to date, patients' baseline characteristics before the initiation of treatment with filgotinib that are associated with achieving corticosteroid-free remission with filgotinib have not been assessed.

Physicians take into consideration their patients' characteristics before initiating treatment and are thus likely to value an assessment of induction baseline characteristics that are associated with achieving corticosteroid-free remission. This *post hoc* analysis of SELECTION trial data aimed to identify the characteristics at induction baseline that were associated with achieving corticosteroid-free remission for at least 6 months among filgotinib-treated patients who were receiving corticosteroids at maintenance baseline. Results in this *post hoc* analysis are presented separately for the filgotinib 200 mg and filgotinib 100 mg groups and expand on the number of characteristics evaluated previously, including those without significant association.

METHODS

1. SELECTION Study Design and Participants

SELECTION was a phase 2b/3, double-blind, randomized, placebo-controlled, multicenter trial (NCT02914522) designed to assess the efficacy and safety of filgotinib in the induction and maintenance of remission in patients with moderately to severely active UC. The trial design and inclusion and exclusion criteria have been published previously.[4] Eligible patients were aged 18–75 years and had moderately to severely active UC (total Mayo Clinic Score 6–12; Endoscopy Subscore ≥2, Rectal Bleeding Subscore ≥1, Stool Frequency Subscore ≥1, Physician's Global Assessment Subscore ≥2), with a documented diagnosis of UC for at least 6 months confirmed by endoscopic and histopathological evidence.

The trial comprised two 11-week induction studies (A and B) and a 47-week maintenance study. In the induction studies, patients were randomized in a 2:2:1 ratio to receive filgotinib 100 mg, filgotinib 200 mg, or matched placebo orally once daily for 11 weeks. Patients who were biologic-naive were enrolled in induction study A and those who were biologic-experienced were enrolled in induction study B. Patients with clinical remission or Mayo Clinic Score response at week 10 (maintenance baseline) were considered responders and could enter the maintenance study. The definition of clinical remission was a Mayo Clinic Endoscopy Subscore of 0 or 1, Rectal Bleeding Subscore of 0, and Stool Frequency Subscore of 0 or 1 with a decrease of at least 1 point from induction baseline. Mayo Clinic Score response was defined as a decrease in score of at least 3 points and at least 30% from induction baseline, and a Rectal Bleeding Subscore of 0 or 1 or decrease of at least 1 point from induction baseline. Patients who received filgotinib in induction study A or B were re-randomized in a 2:1 ratio to continue their filgotinib regimen or receive placebo-to-match orally once daily in the maintenance study. Patients who received placebo in the induction studies continued to receive placebo in the maintenance study.

The trial was conducted in accordance with the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use Good Clinical Practice Guidelines and the Declaration of Helsinki. The study protocol and amendments were reviewed and approved by the Independent Ethics Committee or Institutional Review Board at each study site (Kitasato University Shirokane Institutional Review Board and others). All patients provided written informed consent before study inclusion.

2. Corticosteroid Usage

Patients receiving oral systemic corticosteroid therapy (prednisone ≤30 mg/day or budesonide ≤9 mg/day) were eligible to enter the SELECTION trial provided that the dose was sta-

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ble for at least 2 weeks before randomization and for the first 14 weeks after randomization.[4] Corticosteroids were tapered according to a predefined schedule starting at week 14. The rate of steroid reduction was to be between 2.5 mg/wk and 5.0 mg/wk (or equivalent if not prednisone). For patients using budesonide, the budesonide dose was to be reduced by 3 mg every 3 weeks. At the discretion of the treating physician, steroid doses could be increased or restarted at doses up to the baseline dose if symptoms returned. Treatment was considered to have failed if corticosteroid doses were increased to a dose higher than a patient's baseline dose. Treatment allocation in the induction and maintenance studies was stratified according to baseline corticosteroid use to enable *post hoc* analyses.

3. Statistical Analysis

This analysis was conducted using data from patients receiving corticosteroids at maintenance baseline. The placebo group sample was too small to conduct any analysis of prognostic factors associated with corticosteroid-free remission. Univariate logistic regression was performed to analyze baseline characteristics associated with 6-month corticosteroid-free remission, defined as achieving clinical remission at week 58 without using corticosteroids to treat UC over a continuous period of at least 6 months. Associations between baseline characteristics and total corticosteroid dose exposure from maintenance baseline were assessed in the filgotinib 200 mg group using univariate linear regression with corticosteroid dose as dependent variable and baseline characteristic as independent variable. *P*-values were based on the Wald chi-square test using type 3 analysis of effects. *P*-values of less than 0.05 were considered statistically significant.

RESULTS

1. Participants

In total, 92 patients who received filgotinib 200 mg in the induction and maintenance studies and 81 patients who received filgotinib 100 mg in the induction and maintenance studies were receiving oral systemic corticosteroids at baseline in the maintenance study. All patients in the maintenance study were induction study responders. The 6-month corticosteroid-free remission rate at week 58 among patients treated with corticosteroids at maintenance baseline was 27.2% (25/92) in the filgotinib 200 mg group and 13.6% (11/81) in the filgotinib 100 mg group.[4] Among patients who received placebo during induction and maintenance, 47 were receiving oral systemic corticosteroids at maintenance baseline, of whom only 3 patients (6.4%) achieved at least 6 months of corticosteroid-free remission.

Demographic and clinical characteristics at induction baseline are shown in Table 1 for patients in the filgotinib 200 mg and filgotinib 100 mg groups who were receiving corticosteroids at maintenance baseline. Characteristics are shown overall for each of the filgotinib treatment groups and by presence or absence of corticosteroid-free remission. Of patients receiving corticosteroids at maintenance baseline, 83.7% of those in the filgotinib 200 mg group and 91.4% of those in the filgotinib 100 mg group were taking systemic corticosteroids at induction study baseline. In addition, 22.8% in the filgotinib 200 mg group and 19.8% in the filgotinib 100 mg group were taking concomitant immunomodulators, and 79.3% in the filgotinib 200 mg group and 71.6% in the filgotinib 100 mg group were taking concomitant aminosalicylates.

2. Effects of Baseline Characteristics on Corticosteroid-Free Remission

Among patients who were receiving oral systemic corticosteroids at maintenance baseline, none of the following induction baseline characteristics had statistically significant effects on the likelihood of achieving corticosteroid-free remission for 6 months with filgotinib 200 mg or filgotinib 100 mg: age, body mass index, history of pancolitis, disease duration, fecal calprotectin levels, C-reactive protein levels, Mayo Clinic Score, concomitant corticosteroids, concomitant immunomodulators, and concomitant aminosalicylates (Table 2). A baseline Mayo Clinic Endoscopic Subscore of 2 (vs. 3) was associated with significantly increased odds of corticosteroid-free remission for 6 months in the filgotinib 200 mg and filgotinib 100 mg groups. In the filgotinib 200 mg group only, the odds of achieving corticosteroid-free remission for 6 months were significantly increased in patients who were female, current (vs. former or never) smokers or biologic-naive.

3. Effects of Baseline Characteristics on Corticosteroid Dose Exposure

Table 3 shows the effects of induction baseline characteristics on the mean total corticosteroid dose exposure from maintenance baseline in the filgotinib 200 mg group. Mean (95% confidence interval) and median (interquartile range) total corticosteroid dose exposure from maintenance baseline in the filgotinib 200 mg group by baseline characteristic are listed in

Table 1. Induction Baseline Characteristics of Patients Treated with CS at Maintenance Baseline in the Filgotinib 200 mg and Filgotinib 100 mg Groups, Overall and by Presence or Absence of CS-Free Remission

Induction baseline characteristic	Filgotinib 200 mg			Filgotinib 100 mg		
	Total (n = 92)	CS-free remission[a] (n = 25)	No CS-free remission[b] (n = 67)	Total (n = 81)	CS-free remission[a] (n = 11)	No CS-free remission[b] (n = 70)
Age (yr), mean ± SD	43.2 ± 14.4	42.0 ± 16.1	43.6 ± 13.8	41.9 ± 12.8	39.2 ± 9.7	42.4 ± 13.2
Sex						
Female	53 (57.6)	19 (76.0)	34 (50.7)	38 (46.9)	6 (54.5)	32 (45.7)
Male	39 (42.4)	6 (24.0)	33 (49.3)	43 (53.1)	5 (45.5)	38 (54.3)
BMI						
< 18.5 kg/m^2	10 (10.9)	1 (4.0)	9 (13.4)	7 (8.6)	2 (18.2)	5 (7.1)
18.5 to < 25.0 kg/m^2	45 (48.9)	14 (56.0)	31 (46.3)	44 (54.3)	5 (45.5)	39 (55.7)
25.0 to < 30.0 kg/m^2	25 (27.2)	6 (24.0)	19 (28.4)	19 (23.5)	4 (36.4)	15 (21.4)
≥ 30.0 kg/m^2	12 (13.0)	4 (16.0)	8 (11.9)	11 (13.6)	0	11 (15.7)
Smoking status						
Current	8 (8.7)	5 (20.0)	3 (4.5)	5 (6.2)	1 (9.1)	4 (5.7)
Former	26 (28.3)	3 (12.0)	23 (34.3)	24 (29.6)	3 (27.3)	21 (30.0)
Never	58 (63.0)	17 (68.0)	41 (61.2)	52 (64.2)	7 (63.6)	45 (64.3)
History of pancolitis	47 (51.1)	13 (52.0)	34 (50.7)	46 (56.8)	7 (63.6)	39 (55.7)
Duration of UC						
< 1 yr	5 (5.4)	3 (12.0)	2 (3.0)	9 (11.1)	3 (27.3)	6 (8.6)
1 to < 3 yr	23 (25.0)	5 (20.0)	18 (26.9)	14 (17.3)	2 (18.2)	12 (17.1)
3 to < 7 yr	27 (29.3)	6 (24.0)	21 (31.3)	21 (25.9)	3 (27.3)	18 (25.7)
≥ 7 yr	37 (40.2)	11 (44.0)	26 (38.8)	37 (45.7)	3 (27.3)	34 (48.6)
Fecal calprotectin level[c]						
≤ 500.0 μg/g	19 (20.7)	6 (24.0)	13 (19.4)	22 (27.2)	4 (36.4)	18 (25.7)
> 500.0 to 1,320.5 μg/g	16 (17.4)	2 (8.0)	14 (20.9)	14 (17.3)	2 (18.2)	12 (17.1)
> 1,320.5 to 2,658.0 μg/g	23 (25.0)	4 (16.0)	19 (28.4)	24 (29.6)	1 (9.1)	23 (32.9)
> 2,658.0 μg/g	33 (35.9)	12 (48.0)	21 (31.3)	21 (25.9)	4 (36.4)	17 (24.3)
Missing	1 (1.1)	1 (4.0)	0	0	0	0
CRP level[c]						
≤ 1.690 mg/L	29 (31.5)	4 (16.0)	25 (37.3)	23 (28.4)	4 (36.4)	19 (27.1)
> 1.690 to 4.415 mg/L	20 (21.7)	9 (36.0)	11 (16.4)	22 (27.2)	4 (36.4)	18 (25.7)
> 4.415 to 11.550 mg/L	25 (27.2)	6 (24.0)	19 (28.4)	21 (25.9)	1 (9.1)	20 (28.6)
> 11.550 mg/L	18 (19.6)	6 (24.0)	12 (17.9)	15 (18.5)	2 (18.2)	13 (18.6)
MCS						
≤ 8	26 (28.3)	9 (36.0)	17 (25.4)	24 (29.6)	4 (36.4)	20 (28.6)
≥ 9	66 (71.7)	16 (64.0)	50 (74.6)	57 (70.4)	7 (63.6)	50 (71.4)
MES						
2	33 (35.9)	16 (64.0)	17 (25.4)	23 (28.4)	6 (54.5)	17 (24.3)
3	59 (64.1)	9 (36.0)	50 (74.6)	58 (71.6)	5 (45.5)	53 (75.7)
Prior use of biologics	49 (53.3)	7 (28.0)	42 (62.7)	40 (49.4)	3 (27.3)	37 (52.9)

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Table 1. Continued

Induction baseline characteristic	Filgotinib 200 mg			Filgotinib 100 mg		
	Total (n = 92)	CS-free remission[a] (n = 25)	No CS-free remission[b] (n = 67)	Total (n = 81)	CS-free remission[a] (n = 11)	No CS-free remission[b] (n = 70)
Concomitant oral, systemically absorbed CS						
Yes	77 (83.7)	21 (84.0)	56 (83.6)	74 (91.4)	10 (90.9)	64 (91.4)
Oral, systemically absorbed CS dose						
> 0 to 10 mg/day	28 (30.4)	8 (32.0)	20 (29.9)	27 (33.3)	4 (36.4)	23 (32.9)
> 10 to 20 mg/day	35 (38.0)	7 (28.0)	28 (41.8)	25 (30.9)	2 (18.2)	23 (32.9)
> 20 mg/day	14 (15.2)	6 (24.0)	8 (11.9)	22 (27.2)	4 (36.4)	18 (25.7)
No	15 (16.3)	4 (16.0)	11 (16.4)	7 (8.6)	1 (9.1)	6 (8.6)
Concomitant immunomodulators	21 (22.8)	7 (28.0)	14 (20.9)	16 (19.8)	1 (9.1)	15 (21.4)
Concomitant aminosalicylates	73 (79.3)	22 (88.0)	51 (76.1)	58 (71.6)	9 (81.8)	49 (70.0)

Values are presented as number (%) unless otherwise indicated.
[a]Patients who achieved clinical remission at week 58 without using CS to treat UC over a continuous period of at least 6 months.
[b]Patients who did not achieve clinical remission at week 58 without using CS to treat UC over a continuous period of at least 6 months.
[c]Ranges represent division of the data set by the 3 quartiles.
CS, corticosteroid; SD, standard deviation; BMI, body mass index; UC, ulcerative colitis; CRP, C-reactive protein; MCS, Mayo Clinic Score; MES, Mayo Clinic Endoscopic Subscore.

Supplementary Table 1. Total mean (95% confidence interval) prednisone-equivalent corticosteroid dose exposure from maintenance baseline to week 58 was 213.7 (161.37 to 266.04) mg in the filgotinib 200 mg group; it was 145.7 (95.09 to 196.31) mg among patients with corticosteroid-free remission and 239.1 (170.01 to 308.15) mg among those with no corticosteroid-free remission.

Most baseline characteristics had no statistically significant effect on corticosteroid dose exposure from maintenance baseline in the filgotinib 200 mg group (Table 3). However, corticosteroid dose exposure from maintenance baseline to week 58 was significantly higher among patients who had never smoked (vs. former or current smokers). Concomitant use of aminosalicylates (vs. nonuse) at baseline was associated with a lower corticosteroid dose exposure from maintenance baseline.

DISCUSSION

An important aim of treatment for UC is to obtain and maintain steroid-free remission.[1-3] Discontinuation of corticosteroids is a core component of comprehensive disease control in UC according to international consensus.[6] In addition, guidelines recommend that courses of oral systemic corticosteroids are used not more than once per year.[1-3] Knowing which baseline characteristics in patients with UC are associated with corticosteroid-free remission is relevant for clinical trial design and disease management in everyday clinical practice. In the SELECTION trial, filgotinib 200 mg (the approved dose) induced clinical remission at week 10 in 26.1% of biologic-naive patients (vs. 15.3% with placebo, $P = 0.0157$) and 11.5% of biologic-experienced patients (vs. 4.2% with placebo, $P = 0.0103$), and maintained clinical remission at week 58 in 37.2% of patients (vs. 11.2% with placebo, $P < 0.0001$).[4] Among patients receiving filgotinib 100 mg, 23.8% achieved clinical remission at week 58 (vs. 13.5% with placebo, $P = 0.0420$); clinical remission at week 10 was not significantly different between filgotinib 100 mg and placebo.[4] Symptom improvement in the SELECTION trial was rapid, with UC symptoms of rectal bleeding and stool frequency improving within 7 days after treatment initiation with filgotinib 200 mg in both biologic-naive and biologic-experienced patients.[7]

At SELECTION trial baseline, 30.7% of biologic-naive patients and 45.7% of biologic-experienced patients were receiving systemic corticosteroids.[4] The current *post hoc* analysis found that patients with UC who have a Mayo Clinic Endoscopic Subscore of 2 (vs. 3), are female, are current (vs. former or never) smokers, or are biologic-naive may have a higher likelihood of sustained corticosteroid-free remission with filgotinib 200 mg treatment. In addition, corticosteroid dose exposure from maintenance baseline in the filgotinib 200 mg group was lower among those with concomitant use of ami-

Table 2. Associations Between CS-Free Clinical Remission (Dependent Variable) and Induction Baseline Characteristics by Treatment Group in Patients Treated with CS at Maintenance Baseline

Induction baseline characteristic	Filgotinib 200 mg (n = 92)		Filgotinib 100 mg (n = 81)	
	OR (95% CI)	*P*-value	OR (95% CI)	*P*-value
Age	0.993 (0.960 to 1.025)	0.649	0.980 (0.928 to 1.031)	0.442
Male sex (ref: female)	0.325 (0.116 to 0.916)	0.034[a]	0.702 (0.196 to 2.515)	0.587
BMI (ref: 18.5 to < 25.0 kg/m^2)		0.574		0.610
< 18.5 kg/m^2	0.246 (0.028 to 2.134)		3.120 (0.473 to 20.564)	
25.0 to < 30.0 kg/m^2	0.699 (0.230 to 2.130)		2.080 (0.491 to 8.808)	
≥ 30.0 kg/m^2	1.107 (0.285 to 4.297)		0.000 (0.000 to NA)[b]	
Smoking status (ref: current)		0.028[a]		0.906
Former	0.078 (0.012 to 0.508)		0.571 (0.047 to 6.983)	
Never	0.249 (0.053 to 1.159)		0.622 (0.060 to 6.405)	
History of pancolitis (ref: no history)	1.078 (0.421 to 2.756)	0.876	1.346 (0.361 to 5.026)	0.658
Duration of UC (ref: < 1 yr)		0.374		0.320
1 to < 3 yr	0.185 (0.024 to 1.432)		0.333 (0.043 to 2.564)	
3 to < 7 yr	0.190 (0.026 to 1.416)		0.333 (0.053 to 2.115)	
≥ 7 yr	0.282 (0.041 to 1.930)		0.176 (0.029 to 1.090)	
Fecal calprotectin level (ref: ≤ 500.0 μg/g)[c]		0.236		0.508
> 500.0 to 1,320.5 μg/g	0.310 (0.053 to 1.816)		0.750 (0.118 to 4.760)	
> 1,320.5 to 2,658.0 μg/g	0.456 (0.107 to 1.942)		0.196 (0.020 to 1.905)	
> 2,658.0 μg/g	1.238 (0.373 to 4.109)		1.059 (0.228 to 4.921)	
CRP level (ref: ≤ 1.690 mg/L)[c]		0.118		0.610
> 1.690 to 4.415 mg/L	5.114 (1.293 to 20.221)		1.056 (0.229 to 4.867)	
> 4.415 to 11.550 mg/L	1.974 (0.487 to 7.994)		0.238 (0.024 to 2.320)	
> 11.550 mg/L	3.125 (0.740 to 13.193)		0.731 (0.116 to 4.593)	
MCS ≤ 8 (ref: ≥ 9)	1.654 (0.618 to 4.429)	0.316	1.429 (0.377 to 5.420)	0.600
MES of 2 (ref: 3)	5.229 (1.953 to 13.997)	0.001[a]	3.741 (1.013 to 13.817)	0.048[a]
Biologic-experienced (ref: biologic-naive)	0.231 (0.085 to 0.632)	0.004[a]	0.334 (0.082 to 1.366)	0.127
Concomitant oral, systemically absorbed CS use (ref: nonuse)	1.031 (0.296 to 3.597)	0.962	0.938 (0.102 to 8.627)	0.955
Oral, systemically absorbed CS dose (ref: > 0 to 10 mg/day)		0.276		0.590
> 10 to 20 mg/day	0.625 (0.195 to 2.005)		0.500 (0.083 to 3.004)	
> 20 mg/day	1.875 (0.491 to 7.153)		1.278 (0.280 to 5.825)	
Concomitant immunomodulators (ref: nonuse)	1.472 (0.514 to 4.220)	0.472	0.367 (0.043 to 3.096)	0.357
Concomitant aminosalicylates (ref: nonuse)	2.301 (0.608 to 8.704)	0.220	1.929 (0.383 to 9.699)	0.425

P-values are based on the Wald chi-square test using the type 3 analysis of effects in logistic regression.
[a]Statistical significance, $P < 0.05$.
[b]OR of 0 results from 0 counts owing to small sample size.
[c]Ranges represent division of the data set by the 3 quartiles.
CS, corticosteroid; OR, odds ratio; CI, confidence interval; ref, reference; BMI, body mass index; NA, not applicable; UC, ulcerative colitis; CRP, C-reactive protein; MCS, Mayo Clinic Score; MES, Mayo Clinic Endoscopic Subscore.

nosalicylates (vs. nonuse) and was higher among those who had never smoked (vs. former or current smokers).

The higher likelihood of sustained corticosteroid-free remission in patients with UC who had an induction baseline Mayo Clinic Endoscopic Subscore of 2 (vs. 3) indicates that remission is easier to maintain in patients with less severe disease.

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Table 3. Univariate Analysis of Associations Between Induction Baseline Characteristics and Total CS Dose Exposure from Maintenance Baseline in Patients in the Filgotinib 200 mg Group Treated with CS at Maintenance Baseline (n = 92)

Induction baseline characteristic	No.	Total CS dose exposure (mg), mean (95% CI)	Difference in mean (95% CI)	*P*-value	Type 3 overall *P*-value
Overall	92	213.7 (161.37 to 266.04)			
Sex					
Female (ref)	53	178.1 (127.45 to 228.72)	84.0 (−19.61 to 187.65)	0.116	
Male	39	262.1 (158.29 to 365.93)			
BMI					
< 18.5 kg/m^2	10	319.9 (95.99 to 543.91)	105.5 (−68.11 to 279.18)	0.237	0.447
18.5 to < 25.0 kg/m^2 (ref)	45	214.4 (125.49 to 303.35)			
25.0 to < 30.0 kg/m^2	25	197.9 (125.47 to 270.33)	−16.5 (−140.42 to 107.38)	0.794	
≥ 30.0 kg/m^2	12	155.4 (75.17 to 235.66)	−59.0 (−220.37 to 102.37)	0.476	
Smoking status					
Current	8	108.1 (23.46 to 192.79)	−156.3 (−338.47 to 25.80)	0.096	0.035[a]
Former	26	133.0 (74.55 to 191.37)	−131.5 (−245.48 to −17.52)	0.026[a]	
Never (ref)	58	264.5 (188.09 to 340.83)			
History of pancolitis					
Yes	47	184.4 (121.65 to 247.16)	−66.5 (−171.76 to 38.72)	0.219	
No (ref)	42	250.9 (160.37 to 341.48)			
Unknown	3	151.7 (−500.90 to 804.24)			
Duration of UC					
< 3 yr (ref)	28	180.8 (108.97 to 252.53)			
3 to < 7 yr	27	238.7 (128.86 to 348.62)	58.0 (−76.53 to 192.51)	0.400	0.685
≥ 7 yr	37	220.4 (126.87 to 313.88)	39.6 (−85.30 to 164.54)	0.536	
Fecal calprotectin level[b]					
≤ 500.0 μg/g (ref)	19	280.5 (141.45 to 419.60)			
> 500.0 to 1,320.5 μg/g	16	195.5 (−10.42 to 401.52)	−85.0 (−254.13 to 84.17)	0.328	0.538
> 1,320.5 to 2,658.0 μg/g	23	167.8 (114.83 to 220.82)	−112.7 (−267.24 to 41.84)	0.157	
> 2,658.0 μg/g	33	222.3 (144.02 to 300.49)	−58.3 (−201.83 to 85.29)	0.428	
Missing	1	7.5 (NA to NA)			
CRP level[b]					
≤ 1.690 mg/L (ref)	29	283.4 (151.74 to 415.07)			
> 1.690 to 4.415 mg/L	20	221.1 (107.29 to 334.96)	−62.3 (−205.32 to 80.76)	0.396	0.243
> 4.415 to 11.550 mg/L	25	149.1 (87.29 to 210.87)	−134.3 (−268.63 to −0.02)	0.053	
> 11.550 mg/L	18	182.9 (95.01 to 270.82)	−100.5 (−248.16 to 47.18)	0.186	
MCS					
≤ 8	26	202.8 (81.19 to 324.37)	−15.2 (−130.51 to 100.05)	0.796	
≥ 9 (ref)	66	218.0 (160.62 to 275.39)			
MES					
2	33	246.3 (141.53 to 351.12)	50.9 (−56.88 to 158.62)	0.357	
3 (ref)	59	195.5 (136.57 to 254.35)			

(Continued to the next page)

Table 3. Continued

Induction baseline characteristic	No.	Total CS dose exposure (mg), mean (95% CI)	Difference in mean (95% CI)	*P*-value	Type 3 overall *P*-value
Rectal Bleeding Subscore < 2					
Yes	33	274.4 (154.39 to 394.47)	94.7 (−11.79 to 201.18)	0.085	
No (ref)	59	179.7 (131.90 to 227.58)			
Stool Frequency Subscore ≤ 2					
Yes	40	190.7 (103.75 to 277.74)	−40.6 (−145.03 to 63.79)	0.448	
No (ref)	52	231.4 (165.11 to 297.62)			
Biologic-naive					
Yes	44	176.0 (117.78 to 234.31)	−72.2 (−175.05 to 30.70)	0.172	
No (ref)	48	248.2 (162.33 to 334.12)			
Prior use of TNF-α antagonist, induction study B					
Yes	45	261.1 (170.65 to 351.56)	174.9 (−123.65 to 473.36)	0.257	
No (ref)	4	86.2 (−31.29 to 203.79)			
Prior failure of TNF-α antagonist, induction study B					
Yes	43	268.0 (174.03 to 362.00)	173.0 (−74.90 to 420.94)	0.178	
No (ref)	6	95.0 (−1.87 to 191.87)			
Prior use of vedolizumab, induction study B					
Yes	29	255.5 (130.44 to 380.51)	21.2 (−147.33 to 189.68)	0.807	
No (ref)	20	234.3 (122.39 to 346.21)			
Prior failure of vedolizumab, induction study B					
Yes	24	288.1 (139.50 to 436.64)	80.8 (−83.32 to 244.99)	0.339	
No (ref)	25	207.2 (115.33 to 299.15)			
Prior use of TNF-α antagonist and vedolizumab, induction study B					
Yes	26	278.6 (141.36 to 415.85)	67.7 (−97.23 to 232.61)	0.425	
No (ref)	23	210.9 (110.98 to 310.84)			
Concomitant aminosalicylates					
Yes	73	186.2 (141.87 to 230.58)	−133.1 (−258.34 to −7.76)	0.040[a]	
No (ref)	19	319.3 (124.39 to 514.16)			

P-values are based on the Wald chi-square test using the type 3 analysis of effects in linear regression.
[a]Statistical significance, $P<0.05$.
[b]Ranges represent division of the data set by the 3 quartiles.
CS, corticosteroid; CI, confidence interval; BMI, body mass index; UC, ulcerative colitis; NA, not applicable; CRP, C-reactive protein; MCS, Mayo Clinic Score; MES, Mayo Clinic Endoscopic Subscore; ref, reference; TNF, tumor necrosis factor.

In patients treated with infliximab, decreasing week-8 Mayo Clinic Endoscopic Subscores (from 3 to 0) were associated with higher rates of long-term corticosteroid-free symptomatic remission.[8] A previous study showed that long-term maintenance therapy with the JAK inhibitor tofacitinib was more effective in patients who had a baseline Mayo Clinic Endoscopic Subscore of 0 compared with 1.[9] In addition, a prospective longitudinal cohort study found that the risk of clinical relapse was higher in patients who achieved mucosal healing with a Mayo Clinic Endoscopic Subscore of 1 compared with 0.[10] Our findings are thus broadly consistent with previous studies indicating poorer long-term treatment outcomes in patients with more severe UC.

Patients in the SELECTION study who were biologic-naive tended to have less severe disease (based on induction baseline Mayo Clinic Score) than patients who were biologic-experienced.[11] The association of biologic-naive (vs. biologic-experienced) status at induction baseline with a higher likelihood

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of sustained corticosteroid-free remission in our study may thus be driven by lower disease severity in these patients. With regard to the association of female sex with an increased likelihood of maintaining corticosteroid-free remission, numerous sex-based differences in the pathogenesis, epidemiology, clinical course and outcomes of inflammatory bowel disease have been reported previously.[12] Unfortunately, however, our sample size was too small to perform a robust multivariate analysis, and as such we were unable to determine conclusively which of the associations identified in our study were independent.

The lower corticosteroid dose exposure during the maintenance study in current and former (vs. never) smokers and higher likelihood of sustained corticosteroid-free remission in current (vs. former or never) smokers adds to previous studies showing a positive impact of cigarette smoking on disease activity and corticosteroid use in patients with UC (this is in contrast to Crohn's disease, for which smoking increases the risk of disease and adverse outcomes[13,14]).[15-18] In patients with UC, smoking dose-dependently reduced the need for corticosteroids and smoking cessation after a UC diagnosis increased the need for corticosteroid treatment.[17] Among patients diagnosed with UC, current smokers were less likely than nonsmokers to be prescribed corticosteroids during a median 9-year follow-up.[18] However, no difference in corticosteroid prescribing rate between smokers and nonsmokers or between persistent smokers and quitters was found in a large cohort study in UC.[19] Transdermal nicotine patches assessed in randomized controlled trials were beneficial for active disease but ineffective as maintenance therapy for UC.[20,21] Smoking cessation is encouraged for general health in patients with UC.[3]

The current analysis has important strengths, including using data from a double-blind, randomized, placebo-controlled trial. In total, 173 patients (92 in the filgotinib 200 mg group and 81 in the filgotinib 100 mg group) were receiving corticosteroids at baseline in the maintenance study. A limitation of the current analysis is that it was not prespecified. The small size of the subgroup analysis and the small number of patients who achieved corticosteroid-free remission were also limitations. As a result, we could not perform a robust multivariate analysis to determine independent associations. Patients who did not achieve clinical remission or Mayo Clinic Score response at week 10 in SELECTION were not re-randomized to continue the study. Steroid tapering was protocol specified as of week 14 but was not mandatory. The observed effects on corticosteroid exposure may be a consequence of the study design and should thus be interpreted with caution.

In conclusion, filgotinib treatment enabled achievement of corticosteroid-free remission in patients with UC independently of baseline characteristics or previous therapies. However, the likelihood of achieving corticosteroid-free remission in the filgotinib 200 mg group was higher among patients who were biologic-naive, were current (vs. former or never) smokers, had a lower endoscopic inflammatory burden (Mayo Clinic Endoscopic Subscore of 2 vs. 3) and those who were female. These results could help physicians in clinical practice to develop a treatment strategy for their patients with UC.

ADDITIONAL INFORMATION

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Conflict of Interest

Kobayashi T has served as an advisory board member, consultant, or speaker for AbbVie, Activaid, Ajinomoto Bio-Pharma, Alfresa Pharma, Alimentiv, Astellas Pharma, Bristol Myers Squibb, Celltrion, Covidien, EA Pharma, Eisai, Eli Lilly, Ferring Pharmaceuticals, Gilead Sciences, Janssen Pharmaceuticals, JIMRO, JMDC, Kissei Pharmaceutical, Kyorin Pharmaceutical, Mitsubishi Tanabe Pharma, Mochida Pharmaceutical, Nippon Kayaku, Pfizer, Takeda, Thermo Fisher Scientific and Zeria Pharmaceutical, and has received research funding from AbbVie, Alfresa Pharma, EA Pharma, Kyorin Pharmaceutical, Mochida Pharmaceutical, Nippon Kayaku, Otsuka Holdings, Sekisui Medical, Takeda, Thermo Fisher Scientific, and Zeria Pharmaceutical. Dignass A reports fees for participation in clinical trials, review activities such as data monitoring boards, statistical analysis, and endpoint committees from AbbVie, Abivax, Arena Pharmaceuticals, the Falk Foundation, Gilead/Galapagos, Janssen Pharmaceuticals, and Pfizer; consultancy fees from AbbVie, Amgen, Arena Pharmaceuticals, Biogen, Boehringer Ingelheim, Bristol Myers Squibb/Celgene, Celltrion,

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Data Availability Statement

Gilead Sciences shares anonymized individual patient data upon request or as required by law or regulation with qualified external researchers based on submitted curriculum vitae and reflecting non conflict of interest. The request proposal must also include a statistician. Approval of such requests is at Gilead Science's discretion and is dependent on the nature of the request, the merit of the research proposed, the availability of the data, and the intended use of the data. Data requests should be sent to datarequest@gilead.com.

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Supplementary Material

Supplementary materials are available at the Intestinal Research website (https://www.irjournal.org).

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