Supplementary materials

Unmet Needs in Real-World Advanced Therapy-Naïve and -Experienced Patients with Moderately to Severely Active Ulcerative Colitis in the United States

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Supplementary Table 1 Symptom groups used in the responder cluster analysis

General symptom groups	Symptoms collected from survey
Directly gastrointestinal-related	Abdominal cramps
	Abdominal pain
	Colic
	Diarrhea–bloody
	Rectal bleeding
	Bowel movement urgency
	Nighttime bowel movement urgency
	Tenesmus
Extra-intestinal	Vomiting/nausea
	Loss of appetite
	Weight loss
	Anorexia
	Night sweats
	Fever
Anorectal	Anal discharge/passing of mucus
	Rapid postprandial bowel movements
Rheumatic	Arthralgia
	Joint swelling
	Back pain
Bloating-related	Abdominal distension; bloating
	Flatulence
Diarrhea; non-bloody	Diarrhea–non-bloody
Fatigue-related	Anemia
	Fatigue/tiredness

Supplementary Table 2 AT status, responder status, and current treatment according to patients' sex in the 2017–2018 cohort (*n* = 539) and 2020–2021 cohort (*n* = 448)

	2017–2018 cohort			2020–2021 cohort		
***n* (%)**	**Overall (*n* = 539)**	**Male (*n* = 264)**	**Female (*n* = 275)**	**Overall (*n* = 448)**	**Male (*n* = 259)**	**Female (*n* = 189)**
AT status						
Naïve	331 (61.4)	171 (64.8)	160 (58.2)	99 (22.1)	63 (24.3)	36 (19.0)
Experienced	208 (38.6)	93 (35.2)	115 (41.8)	349 (77.9)	196 (75.7)	153 (81.0)
p value (male vs. female)		0.133[a]			0.205[a]	
Derived responder cluster status						
Responders	231 (42.9)	117 (44.3)	114 (41.5)	209 (46.7)	126 (48.6)	83 (43.9)
Non-responders	308 (57.1)	147 (55.7)	161 (58.5)	239 (53.3)	133 (51.4)	106 (56.1)
p value (male vs. female)		0.542[a]			0.339[a]	
Current treatment (hierarchical)						
None of the following	15 (2.8)	5 (1.9)	10 (3.6)	2 (0.4)	2 (0.8)	0
5-ASA	167 (31.0)	91 (34.5)	76 (27.6)	50 (11.2)	32 (12.4)	18 (9.5)
Corticosteroid (± 5-ASA)	34 (6.3)	22 (8.3)	12 (4.4)	22 (4.9)	16 (6.2)	6 (3.2)
IM (± corticosteroid ± 5-ASA)	115 (21.3)	53 (20.1)	62 (22.5)	25 (5.6)	13 (5.0)	12 (6.3)
AT (biologic/biosimilar/JAKi)	208 (38.6)	93 (35.2)	115 (41.8)	349 (77.9)	196 (75.7)	153 (81.0)
p value (male vs. female)		0.067[b]			0.289[b]	

[a]Calculated using Fisher exact test. [b]Calculated using chi-square test

5-ASA 5-aminosalicylic acid, *AT* advanced therapy, *JAKi* Janus kinase inhibitor, *IM* immunomodulator

Supplementary Table 3 AT status, responder status, and current treatment according to patient age in the 2017–2018 cohort (*n* = 539) and 2020–2021 cohort (*n* = 448)

	2017–2018 cohort				2020–2021 cohort			
n (%)	**Overall (*n* = 539)**	**Age 18–34 years (*n* = 184)**	**Age 35–49 years (*n* = 176)**	**Age ≥50 years (*n* = 179)**	**Overall (*n* = 448)**	**Age 18–34 years (*n* = 178)**	**Age 35–49 years (*n* = 165)**	**Age ≥50 years (*n* = 105)**
AT status								
Naïve	331 (61.4)	118 (64.1)	109 (61.9)	104 (58.1)	99 (22.1)	37 (20.8)	36 (21.8)	26 (24.8)
Experienced	208 (38.6)	66 (35.9)	67 (38.1)	75 (41.9)	349 (77.9)	141 (79.2)	129 (78.2)	79 (75.2)
p value (18–34 vs. 35–49 vs. ≥50 years)			0.491[a]				0.734[a]	
Derived responder cluster status								
Responders	231 (42.9)	78 (42.4)	61 (34.7)	92 (51.4)	209 (46.7)	88 (49.4)	72 (43.6)	49 (46.7)
Non-responders	308 (57.1)	106 (57.6)	115 (65.3)	87 (48.6)	239 (53.3)	90 (50.6)	93 (56.4)	56 (53.3)
p value (18–34 vs. 35–49 vs. ≥50 years)			0.006[a]				0.560[a]	
Current treatment (hierarchical)								
None of the following	15 (2.8)	4 (2.2)	1 (0.6)	10 (5.6)	2 (0.4)	0 (0.0)	1 (0.6)	1 (1.0)
5-ASA	167 (31.0)	76 (41.3)	42 (23.9)	49 (27.4)	50 (11.2)	19 (10.7)	19 (11.5)	12 (11.4)
Corticosteroid (± 5-ASA)	34 (6.3)	16 (8.7)	11 (6.3)	7 (3.9)	22 (4.9)	10 (5.6)	6 (3.6)	6 (5.7)
IM (± corticosteroid ± 5-ASA)	115 (21.3)	22 (12.0)	55 (31.3)	38 (21.2)	25 (5.6)	8 (4.5)	10 (6.1)	7 (6.7)
AT (biologic/biosimilar/JAKi)	208 (38.6)	66 (35.9)	67 (38.1)	75 (41.9)	349 (77.9)	141 (79.2)	129 (78.2)	79 (75.2)
p value (18–34 vs. 35–49 vs. ≥50 years)			<0.001[a]				0.920[a]	

[a]Calculated using chi-square test

5-ASA 5-aminosalicylic acid, *AT* advanced therapy, *JAKi* Janus kinase inhibitor, *IM* immunomodulator

Supplementary Table 4 Physician-reported reasons for switching treatment to current treatment in AT-naïve patients in the 2017–2018 cohort (*n* = 187) who had received a previous treatment

***n* (%)**	**Responders (*n* = 51)**	**Non-responders (*n* = 136)**
Lack of alleviation of pain	3 (5.9)	84 (61.8)
Secondary lack of efficacy (loss of response over time)/condition worsened	8 (15.7)	66 (48.5)
Treatment did not clear the patient's diarrheal symptoms specifically	2 (3.9)	69 (50.7)
I wanted to use an AT that can be used as a monotherapy	3 (5.9)	62 (45.6)
Remission not induced	10 (19.6)	48 (35.3)
Remission not maintained	6 (11.8)	44 (32.4)
Condition improved	25 (49.0)	8 (5.9)
Side effects	11 (21.6)	8 (5.9)
Primary lack of efficacy (initial non-response)	9 (17.6)	6 (4.4)
Lack of tolerability	2 (3.9)	5 (3.7)
Patient request to change drug	3 (5.9)	2 (1.5)
Comorbidities	3 (5.9)	1 (0.7)
Fewer administrative hurdles	0	3 (2.2)
Patient out-of-pocket expense	1 (2.0)	1 (0.7)
Formulary-driven switch	1 (2.0)	1 (0.7)
Lack of compliance by patient	0	2 (1.5)
Test/laboratory results required switch	1 (2.0)	0
Administration reaction	1 (2.0)	0
I wanted to use an AT that can be used in combination with biologics	0	1 (0.7)
The patient required an AT with a different mode of action	1 (2.0)	0
Insurance restrictions	1 (2.0)	0
Other (specify)	1 (2.0)	3 (2.2)

Ordered according to frequency of occurrence in overall population with the exception of "Other (specify)"

AT advanced therapy

Supplementary Table 5 Physician-reported reasons for switching treatment to current treatment in AT-experienced patients in the 2017–2018 cohort (*n* = 154)

***n* (%)**	**Responders (*n* = 61)**	**Non-responders (*n* = 93)**
Remission not induced	17 (27.9)	47 (50.5)
Secondary lack of efficacy (loss of response over time)/condition worsened	20 (32.8)	40 (43.0)
Remission not maintained	17 (27.9)	19 (20.4)
I wanted to use an AT that can be used as a monotherapy	9 (14.8)	25 (26.9)
Primary lack of efficacy (initial non-response)	14 (23.0)	15 (16.1)
Lack of alleviation of pain	6 (9.8)	21 (22.6)
Treatment did not clear the patient's diarrheal symptoms specifically	11 (18.0)	15 (16.1)
Side effects	7 (11.5)	11 (11.8)
Condition improved	8 (13.1)	4 (4.3)
Lack of tolerability	5 (8.2)	7 (7.5)
The patient required an AT with a different mode of action	5 (8.2)	6 (6.5)
Patient request to change drug	4 (6.6)	6 (6.5)
I wanted to use an AT that can be used in combination with biologic	2 (3.3)	3 (3.2)
Insurance restrictions	3 (4.9)	1 (1.1)
Formulary-driven switch	2 (3.3)	2 (2.2)
Administration reaction	2 (3.3)	1 (1.1)
Patient developed anti-drug antibodies/immunogenic response	1 (1.6)	1 (1.1)
Test/laboratory results required switch	2 (3.3)	0
Frequency of injections	1 (1.6)	1 (1.1)
Antibodies to biologic/biosimilar detected	2 (3.3)	0
Comorbidities	0	2 (2.2)
Patient dissatisfied with mode of administration	1 (1.6)	0
Patient out-of-pocket expense	1 (1.6)	0
Lack of compliance by patient	1 (1.6)	0
Fewer administrative hurdles	1 (1.6)	0
Efficacy of treatment	1 (1.6)	0
Formulary/listing	1 (1.6)	0
Other (specify)	0	1 (1.1)

Ordered according to frequency of occurrence in overall population with the exception of "Other (specify)"

AT advanced therapy

Supplementary Table 6 Physician-reported reasons for switching treatment to current treatment in AT-naïve patients in the 2020–2021 cohort (n = 36) who had received a previous treatment

***n* (%)**	**Responders (*n* = 16)**	**Non-responders (*n* = 20)**
Disease progression	6 (37.5)	7 (35.0)
Lack of secondary efficacy of previous treatment (loss of response over time)	4 (25.0)	5 (25.0)
Lack of tolerability of previous regimen	3 (18.8)	6 (30.0)
Remission not induced with previous treatment	3 (18.8)	4 (20.0)
Patient poor compliance with previous regimen	2 (12.5)	4 (20.0)
Patient request to switch from previous regimen	3 (18.8)	3 (15.0)
Lack of primary efficacy of previous treatment (initial non-response)	2 (12.5)	3 (15.0)
Remission not maintained with previous treatment	4 (25.0)	1 (5.0)
Side effects of previous regimen	3 (18.8)	2 (10.0)
Current treatment is more cost-effective for patient	3 (18.8)	1 (5.0)
The patient required an AT with a different mode of action	2 (12.5)	2 (10.0)
Flexibility of current dosing regimen	1 (6.3)	2 (10.0)
Lack of flare control with previous treatment	0	3 (15.0)
Lack of alleviation of pain	0	2 (10.0)
Symptomatic control not achieved with previous regimen	1 (6.3)	1 (5.0)
Current treatment is more cost-effective for healthcare system	1 (6.3)	0
Fewer administrative hurdles with current treatment	1 (6.3)	0
Insurance coverage of current treatment	0	1 (5.0)
Other (specify)	1 (6.3)	1 (5.0)

Ordered according to frequency of occurrence in overall population with the exception of "Other (specify)"

AT advanced therapy

Supplementary Table 7 Physician-reported reasons for switching treatment to current treatment in AT-experienced patients in the 2020–2021 cohort (*n* = 224)

***n* (%)**	**Responders (*n* = 106)**	**Non-responders (*n* = 118)**
Lack of secondary efficacy of previous treatment (loss of response over time)	37 (34.9)	59 (50.0)
Lack of flare control with previous treatment	35 (33.0)	42 (35.6)
Disease progression	40 (37.7)	35 (29.7)
Remission not induced with previous treatment	41 (38.7)	30 (25.4)
Remission not maintained with previous treatment	34 (32.1)	31 (26.3)
The patient required an AT with a different mode of action	24 (22.6)	25 (21.2)
Lack of primary efficacy of previous treatment (initial non-response)	27 (25.5)	20 (16.9)
Symptomatic control not achieved with previous regimen	22 (20.8)	14 (11.9)
Lack of alleviation of pain	9 (8.5)	18 (15.3)
Side effects of previous regimen	11 (10.4)	6 (5.1)
Lack of tolerability of previous regimen	8 (7.5)	6 (5.1)
Patient request to switch from previous regimen	7 (6.6)	7 (5.9)
Antibodies to biologic/biosimilar detected	10 (9.4)	3 (2.5)
Mode of administration of current regimen is preferred	8 (7.5)	4 (3.4)
Current treatment is more cost-effective for patient	4 (3.8)	5 (4.2)
Insurance coverage of current treatment	4 (3.8)	4 (3.4)
Patient request to switch to the current regimen	7 (6.6)	0
Administration reaction of previous treatment	3 (2.8)	2 (1.7)
Patient poor compliance with previous regimen	1 (0.9)	4 (3.4)
Current treatment is more cost-effective for healthcare system	1 (0.9)	2 (1.7)
Comorbidities required change of treatment	0	1 (0.8)
Frequency of injections of previous treatment	0	1 (0.8)
Other (specify)	1 (0.9)	5 (4.2)

Ordered according to frequency of occurrence in overall population with the exception of "Other (specify)"

AT advanced therapy