

Supplemental online content for:

Association of Chronic Immune-Mediated Diarrhea and Colitis With Favorable Cancer Response

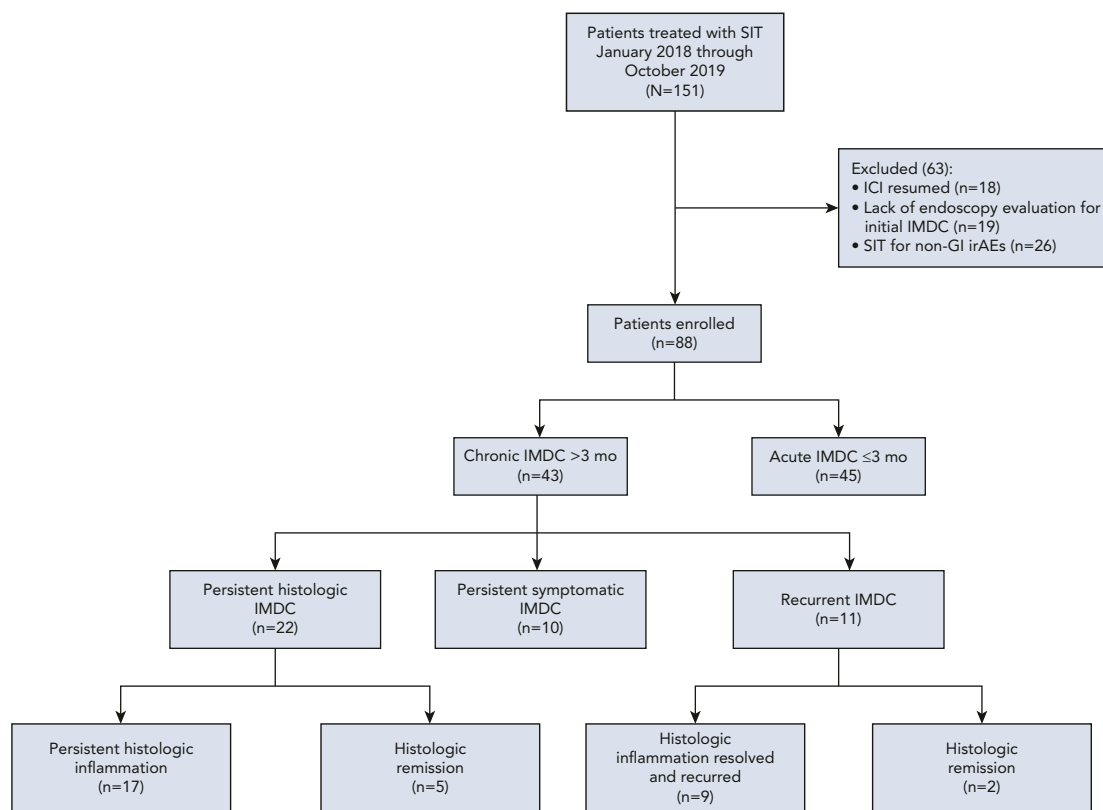
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eFigure 1: Flow Diagram of Patient Selection

eTable 1: Baseline Immune-Mediated Diarrhea and Colitis Characteristics Stratified by Disease Duration

eTable 2: Characteristics of Patient Subgroups With Chronic Immune-Mediated Diarrhea and Colitis



eFigure 1. Flow diagram of patient selection.

Abbreviations: GI, gastrointestinal; ICI, immune checkpoint inhibitor; IMDC, immune-mediated diarrhea and colitis; irAEs, immune-related adverse effects; SIT, selective immunosuppressive therapy.

eTable 1. Baseline IMDC Characteristics Stratified by Disease Duration

Characteristic	Chronic IMDC (>3 mo) n (%)	Acute IMDC (≤3 mo) n (%)	P Value
Patients, n	43	45	
Median days from ICI to IMDC onset (IQR), n=88	104 (46–220)	68 (46–116.5)	.099
Median days of IMDC (IQR), n=88	64 (30–105)	31 (20.5–43)	<.001
Colitis grade			.927
1–2	29 (67)	28 (62)	
3–4	14 (33)	17 (38)	
Diarrhea grade			.746
1–2	13 (30)	16 (36)	
3–4	30 (70)	29 (64)	
Endoscopic presentation			.100
Mucosal ulceration	12 (28)	10 (22)	
Nonulcerative inflammation	21 (49)	31 (69)	
Normal	10 (23)	4 (9)	
Disease location on endoscopy			.384
Colon	30 (70)	36 (80)	
Small bowel	1 (2)	0 (0)	
Both locations	12 (28)	9 (20)	
Histologic features			.049
Acute active colitis	3 (7)	12 (27)	
Chronic active colitis	30 (70)	25 (56)	
Microscopic colitis	10 (23)	8 (18)	
Median days of steroids (IQR), n=83	80 (57–125)	35 (25–54.5)	<.001
Median number of steroid tapering attempts (IQR)	2 (1–2)	1 (0–1)	<.001
Type of SIT			<.001
Vedolizumab	26 (60)	19 (42)	
Infliximab	2 (2)	24 (53)	
Combination	15 (35)	2 (4)	

(continued)

eTable 1. Baseline IMDC Characteristics Stratified by Disease Duration (cont.)

Characteristic	Chronic IMDC (>3 mo) n (%)	Acute IMDC (≤3 mo) n (%)	P Value
Median days from IMDC to first dose of SIT (IQR), n=88	13 (7–38)	12 (6.5–24.5)	.231
Infliximab, n=42	14.5 (9–41)	17.5 (12–35)	
Vedolizumab, n=46	13 (3–42.5)	9 (4.5–20)	
Number of doses of SIT			<.001
1–2	2 (5)	31 (69)	
≥3	41 (95)	14 (31)	
Repeat endoscopy after medical treatment, n=55	38 (88)	17 (38)	<.001
Change in IMDC treatment			<.001
Change of SIT ^a	16 (37)	2 (5)	
FMT	9 (21)	0 (0)	
IMDC outcome			
Hospitalization	32 (74)	35 (78)	.804
Median days of hospitalization (IQR), n=69	9 (6–13)	7 (4–10)	.177
Clinical remission	32 (74)	45 (100)	<.001
Endoscopic remission ^b	18 (47)	15 (88)	.006
Histologic remission ^c	8 (21)	12 (71)	.001
All-cause death	9 (21)	17 (38)	.104

Abbreviations: FMT, fecal microbiota transplantation; ICI, immune checkpoint inhibitor; IMDC, immune-mediated diarrhea and colitis; IQR, interquartile range; SIT, selective immunosuppressive therapy.

^aChange of nonsteroid immunosuppressant includes infliximab change to vedolizumab, vedolizumab change to infliximab, or infliximab or vedolizumab change to ustekinumab.

^bThe denominator of endoscopic remission was patients with repeat endoscopy.

^cThe denominator of histologic remission was patients with repeat endoscopy.

eTable 2. Characteristics of Patient Subgroups With Chronic IMDC (n=43)

Characteristic	Persistent Symptomatic IMDC n (%)	Recurrent IMDC n (%)	Persistent Histologic IMDC n (%)	P Value
Patients, n	10	11	22	
Cancer type				.253
Genitourinary	5 (50)	4 (36)	9 (41)	
Melanoma	3 (30)	3 (27)	6 (27)	
Lung	0 (0)	1 (9)	2 (9)	
Head and neck	1 (10)	1 (9)	2 (9)	
Gastrointestinal	0 (0)	1 (9)	1 (5)	
Hematologic	1 (10)	0 (0)	0 (0)	
Other	0 (0)	1 (9)	2 (9)	
Cancer stage				.255
III	4 (40)	2 (18)	3 (14)	
IV	6 (60)	9 (82)	19 (87)	
ICI type				.637
CTLA-4	2 (20)	1 (9)	5 (23)	
PD-1/L1	4 (40)	8 (73)	11 (50)	
Combination	4 (40)	2 (18)	6 (27)	
Median dose of ICI (IQR)	3.5 (1–6)	8 (6–26)	3.5 (2–15)	.564
Diarrhea grade				.455
1–2	4 (40)	8 (73)	17 (77)	
3–4	6 (60)	3 (27)	5 (23)	
Colitis grade				.200
1–2	1 (10)	3 (27)	9 (41)	
3–4	9 (90)	8 (73)	13 (59)	
Endoscopic presentation				.383
Mucosal ulceration	4 (40)	2 (18)	6 (27)	
Nonulcerative inflammation	5 (50)	4 (36)	12 (55)	
Normal	1 (10)	5 (46)	4 (18)	
Histologic features				.521
Acute active colitis	0 (0)	1 (9.09)	2 (9)	
Chronic active colitis	9 (90)	6 (55)	15 (68)	
Microscopic colitis	1 (10)	4 (36)	5 (23)	
Median overall days of steroids (IQR), n=83	160 (113–205)	80 (59–98)	64 (43–81)	<.001
Median number of steroid tapering attempts before SIT use (IQR)	3 (2–3)	2 (1–2)	1 (0–2)	.001

Abbreviations: ICI, immune checkpoint inhibitor; IMDC, immune-mediated diarrhea and colitis; IQR, interquartile range; SIT, selective immunosuppressive therapy.