

Supplemental Table 1. Patient selection in MDACC and MSKCC (N=184)

Center	Vedolizumab alone	Infliximab alone	Combined sequentially
MDACC	61	71	18
MSKCC	1	23	10

MDACC: The University of Texas MD Anderson Cancer Center

MSKCC: Memorial Sloan Kettering Cancer Center

At MSKCC, all patients treated with vedolizumab for biopsy-proven IMDC, who met inclusion criteria, were enrolled. A 2:1 matched cohort of biopsy-proven IMDC patients treated with infliximab was also included.

Supplemental Table 2. Patients' baseline demographic and clinical characteristics (N=184).

Characteristic	No. of patients (%)
Median age at IMDC— years (IQR), n=184	64 (51-73)
Male sex	118 (64)
White race	169 (92)
Median Charlson Comorbidity Index at IMDC, points. (IQR), n=184	8 (6-9)
Cancer type	
Melanoma	63 (34)
Genitourinary cancer (GU)	61 (33)
Lung cancer	31 (17)
Others*	29 (16)
Cancer Stage	
Stage III	33 (18)
Stage IV	151 (82)
Checkpoint inhibitor type	
CTLA-4	28 (15)
PD-(L)1	92 (50.00)
Combination	64 (35)
Cancer progression at IMDC	54 (29)
Median follow-up duration, mo. (IQR), n=184	14 (8-27)
Cancer progression at last follow up	84(46)
Non-GI organs involving adverse events†— no. (%)	
Skin	48 (26)
Endocrine	35 (19)
Pancreas	24 (13)
Liver	23 (12)
Musculoskeletal	18 (10)
Hematological	13 (7)
Lungs	11 (7)
Other‡	15 (8)
All-cause mortality	68 (37)

IQR denotes interquartile range, NSAID non-steroidal anti-inflammatory drug, PPI, proton pump inhibitor, GI gastrointestinal, GU genitourinary, CTLA-4 cytotoxic T lymphocyte antigen-4, and PD-(L) 1 programmed death-1/programmed death ligand 1. IMDC, immune-mediated diarrhea and colitis.

*Other cancer types included GI/hepatobiliary cancer, head and neck/endocrine cancer, hematologic cancer, breast cancer, cervical cancer, sarcoma cancer. †GI adverse events were defined according-to

Common Terminology Criteria for Adverse Events version 5.0. ‡Other non-GI adverse events consisted of mucositis, fatigue, and eye toxicity.

Supplemental Table 3. IMDC characteristics of patients received different treatment regimen (N=184).

Characteristic	Vedolizumab n=62	Infliximab n=94	Combined sequentially n=28	P
Median time from ICI initiation to IMDC onset, days (IQR), n=184	104 (53-212)	96 (33-188)	108.5 (51-215)	0.068
Diarrhea grade, no. (%)				0.134
1-2	20 (32)	33 (35)	6 (21)	
3-4	42 (68)	61 (65)	22 (79)	
Colitis grade– no. (%)				0.086
1-2	30 (48)	57 (62)	15 (55)	
3-4	32 (52)	37 (39)	13 (46)	
Median duration of initial IMDC symptoms, days (IQR), n=184	56 (27-80)	50 (31-69)	63 (49-104)	0.056
Median duration of steroids for initial IMDC, days (IQR), n=184	35 (27-43)	50 (41-68)	44 (35-100)	<0.001
IV steroids, no. (%)	36 (58)	58 (62)	23 (83)	0.032
Number of steroid tapering attempts prior to SIT use, median (IQR), n=184	1 (1-3)	2 (2-3)	2 (1-3)	0.035
Number dose of SIT, no. (%)				<0.001
1-2	21 (34)	77 (82)	0 (0.00)	
≥3	41 (66)	17 (18)	28 (100.00)	
Doses of SIT, mean (SD)	3 (2)	2 (1)	6 (4)	<0.001
Median duration from IMDC onset to first dose of SIT, days (IQR), n=184	11 (9-48)	23 (19-37)	33 (22-62)	0.003
Hospitalization, no. (%)	40 (65)	67 (71)	21 (75)	0.284
Multiple hospitalizations, no. (%)	10 (16)	26 (28)	14 (50)	0.011
Median duration of hospitalization, days (IQR), n=104	11 (6-16)	14 (8-20)	16 (10-27)	0.013
Clinical remission, no. (%)	55 (89)	83 (88)	19 (68)	0.296
Recurrent IMDC, no. (%)	8 (14)	27 (29)	7 (25)	0.008
Steroid/IFX/VDZ associated Infection*, no. (%)	12 (19)	23 (25)	8 (29)	0.281

*Infections included: urinary tract infection, intestinal infection (E Coli), periodontitis, pneumonia, bacteremia, candida esophagitis.

IFX: infliximab; IMDC: immune mediated diarrhea and colitis; IQR: interquartile range; IV: intravenous; SIT: selective immunosuppressive therapy; VDZ: vedolizumab; SD: standard deviation;

Supplemental Table 4. Cancer progression among subgroups of patients treated with IFX and VDZ within the same time window (2017-2020). N=163

Characteristic	Vedolizumab n=62	Infliximab n=94	Combined sequentially n=28	P
Cancer progression rate at IMDC onset, n=50	15 (24)	30(41)	5(18)	0.092
Cancer progression rate at last follow up, n=76	21 (34)	42(58)	12(43)	0.022
p	0.323	0.034	0.080	

IMDC: immune mediated diarrhea and colitis

Supplemental Table 5. Univariate and multivariate logistic regression analysis for risk factors of cancer progression.

Variable	Univariate analysis			Multivariate analysis		
	Odds ratio	95% CI	P	Odds ratio	95% CI	P
Charlson Comorbidity Index	1.20	1.04-1.39	0.012	1.21	1.03-1.42	0.020
Cancer type						
Genitourinary cancer	0.47	0.19-1.14	0.095	0.37	0.13-1.02	0.667
Melanoma	0.79	0.31-1.91	0.595	0.18	0.06-0.53	0.005
Lung cancer	0.76	0.28-2.10	0.599	0.43	0.13-1.41	0.875
Other		Reference				
Cancer stage IV vs. III	1.87	0.58-4.13	0.120			
Duration of ICI treatment	0.99	0.98-1.00	0.067			
ICIs doses	0.96	0.92-1.01	0.069			
ICIs type						
anti-CTLA-4		Reference				
anti-PD-(L)-1	1.58	0.66-3.79	0.306			
Combination	1.69	0.68-4.22	0.261			
Duration from ICI to colitis onset	0.99	0.97-1.00	0.078			
Duration of colitis symptoms	0.99	0.98-1.01	0.102			
Diarrhea grade 3-4 vs. 1-2	1.37	0.77-2.46	0.289			
Colitis grade 3-4 vs. 1-2	1.66	0.88-3.12	0.119			
Overall duration of steroids	1.01	1.00-1.02	0.007			
IV steroids	1.41	0.77-2.59	0.271			
Number of steroid tapering attempts prior to SIT use	1.17	0.86-1.60	0.322			
Type of SIT						
Vedolizumab		Reference			Reference	
Infliximab	2.32	1.19-4.49	0.013	5.24	2.33-11.77	<0.001
Combined sequentially	1.46	0.59-3.65	0.414	2.07	0.76-5.58	0.817
No. of SIT doses	0.80	0.68-0.94	0.070			
Duration of IMDC to last follow-up	0.89	0.86-0.93	0.332			

CTLA-4: cytotoxic T-lymphocyte-associated protein 4; ICI: immune checkpoint inhibitor, IMDC: immune mediated diarrhea and colitis; IV: intravenous; PD-(L)-1: programmed cell death 1 protein/ligand; SIT, selective immunosuppressive therapy

Supplemental Table 6. Multivariate Cox regression analysis for overall survival.

Characteristic	Hazard Ratio	95% CI	<i>P</i>
Charlson Comorbidity Index	1.18	1.04-1.34	0.009
ICI type			
PD-(L)1		Reference	
CTLA-4	0.28	0.12-0.67	0.004
Combination	0.92	0.54-1.56	0.745
SIT type			
Vedolizumab	Reference		
Infliximab	2.04	1.15-3.62	0.014
Combined Sequentially	1.17	0.48-2.82	0.734

CTLA-4: cytotoxic T-lymphocyte-associated protein 4; ICI: immune checkpoint inhibitor; IMDC: immune mediated diarrhea and colitis; PD-(L)-1: programmed cell death 1 protein/ligand; SIT: selective immunosuppressive therapy.