

Supplemental Table 1. ICD-9 and ICD-10 Codes Used in Initial Database Search.

Code	Description
555-558.89	Noninfectious enteritis and colitis
558	Noninfectious gastroenteritis and colitis
558.2	Chemical colitis
K51.5	Left sided colitis
K51.50	Left sided colitis without complications
K51.51	Left sided colitis with complications
K51.511	Left sided colitis with rectal bleeding
K51.518	Left sided colitis with other complication
K51.519	Left sided colitis with unspecified complication
K52	Other and unspecified noninfective gastroenteritis and colitis
K52.1	Toxic gastroenteritis and colitis
K52.3	Indeterminate colitis
K52.8	Other specified noninfective gastroenteritis and colitis
K52.89	Other specified noninfective gastroenteritis and colitis
K52.9	Noninfective gastroenteritis and colitis, unspecified

Supplemental Table 2. Additional Clinical Data.

Medical history	
Prior non-liver, non-upper GI disease	
	Ulcerative colitis
	Microscopic colitis
	Diverticulosis
	Diverticulitis
	Colorectal cancer
	Small bowel malignancy
	History of <i>Clostridioides difficile</i> infection
	Irritable bowel syndrome
Autoimmune disease	
	ICI hypophysitis ^a
	ICI hypothyroidism ^a
	ICI thyrotoxicosis ^a
	ICI hepatitis ^a
	ICI arthritis ^a
	Hypothyroidism
	Type 1 diabetes mellitus
	Sarcoidosis
	Inflammatory bowel disease
	Microscopic colitis
	Rheumatoid arthritis
	Polymyalgia rheumatica
	Seronegative inflammatory arthritis
	Psoriasis
	Vitiligo
Family history of autoimmune disease	

	Ulcerative colitis
	Crohn's disease
	Multiple sclerosis
	Thyroid disease
	Inflammatory arthritis
Cancer history	
Type of malignancy	
	Melanoma
	Renal cell carcinoma
	Non-small cell lung cancer
	Sarcoma
	Head and neck squamous cell carcinoma
	Urothelial carcinoma
	Basal cell carcinoma
	Colorectal cancer
	Sezary syndrome
	Mesothelioma
	Gastrointestinal stromal tumor
	Acinic cell carcinoma of the parotid gland
	Mucinous adenocarcinoma of likely colonic origin
Type of ICI	
	Combination ipilimumab plus nivolumab
	Ipilimumab
	Nivolumab
	Pembrolizumab
	Atezolizumab
Immune-enhancing medications	

	Interleukin [IL]-2
	Interferon [IFN]- γ
	Toll-like receptor [TLR]-9 agonist
	Tebentafusp
	Anti-CD47 antibody

GI, gastroenterological. ICI, immune checkpoint inhibitor. ^aImmune-related adverse events (irAE).

Supplemental Table 3. Diagnostics and Treatment of Patients with Immune Checkpoint Inhibitor Colitis (N= 64).

Severe IMC, no. (%)	38 (59.4%)
Fecal lactoferrin, no. (%)	7 (10.9%)
Calprotectin, no. (%)	20 (31.3%)
Calprotectin (mg/k), mean (range)	824 (44-2500)
Endoscopy, no. (%)	24 (37.5%)
Normal endoscopic appearance, no (%)	7 (29.2%)
Imaging findings ^a suggestive of IMC in patients without endoscopy, no. (%)	14 (21.9%)
Calprotectin or fecal lactoferrin elevated in patients without endoscopy or imaging, no. (%)	3 (4.69%)
Anti-diarrheals ^b , no. (%)	55 (85.9%)
Mesalamine, no. (%)	3 (4.69%)
Steroid treatment, no. (%)	57 (89.1%)
Steroid duration, days (mean, SD)	111 (161)
Prednisone, no. (%)	48 (75%)
Budesonide, no. (%)	7 (10.9%)
Dexamethasone, no. (%)	4 (6.25%)
Maximum prednisone equivalents, mg/kg/ day (mean, SD)	0.95 (0.60)
Infliximab use, no. (%)	10 (15.6%)
Average number of infliximab infusions, median (IQR)	1 (1-1.75)
Average days on steroids prior to infliximab (mean, SD)	36.6 (29.6)
Vedolizumab use, no. (%)	1 (1.56%)

^aAbdominal x-ray, computed tomography of the abdomen/pelvis, or positron emission tomography. ^bLoperamide, diphenoxylate-atropine, tincture of opium, octreotide, bismuth subsalicylate.

Supplemental Table 4. Univariate and Multivariate Predictors of Progression-Free Survival > 6 Months Among Patients Using ICI (N=128).

	Univariate Predictors			Multivariate Predictors		
Clinical Variables						
	Odds Ratios (OR)	95% CI	P- Value	Odds Ratios (OR)	95% CI	P-Value
Demographics						
Age (years)	0.99	0.96 - 1.02	0.568			
Male	1.08	0.53 - 2.17	0.836			
Female	0.93	0.46 -1.87	0.836			
Race						
White	1.42	0.59 - 3.38	0.431			
Black	3.20	0.32 - 31.61	0.320			
Asian	0.49	0.12 - 2.06	0.331			
Other	0.61	0.19 - 2.00	0.416			
Type of Malignancy						
Melanoma	1.83	0.41 - 1.66	0.600			
RCC	1.21	0.41 - 3.55	0.735			
NSCLC	3.44	0.89 - 13.37	0.074	1.07	0.17 - 6.75	0.941
Sarcoma	0.36	0.09 - 1.41	0.141			
Head and Neck	0.76	0.16 - 3.55	0.730			

SCC						
Other	1.19	0.43 - 3.30	0.742			
Presence of IMC	1.55	0.77 - 3.12	0.217			
Presence of High Grade IMC	0.81	0.30 - 2.23	0.690			
Stage IV malignancy	0.52	0.16 - 1.64	0.263			
Type of Immune Checkpoint Inhibitor						
Ipilimumab plus nivolumab	0.35	0.17 - 0.74	0.006	0.40	0.05 - 2.98	0.373
Ipilimumab	0.53	0.21 - 1.37	0.189	0.52	0.06 - 4.18	0.537
Nivolumab	1.50	0.45 - 5.00	0.509	0.65	0.06 - 7.00	0.723
Pembrolizumab	3.10	1.39 - 6.93	0.006	0.70	0.09 - 5.42	0.732
Atezolizumab	3.32	0.64 - 17.09	0.152			
Number of Infusions ^a	1.38	1.18 - 1.61	<0.001	1.34	1.14 - 1.57	<0.001
Dose of ICI (mg/kg)	1.24	0.83 - 1.85	0.295			
Medical History						

Non-liver, non-upper GI ^b	0.87	0.37 - 2.01	0.738			
Personal history of autoimmune disease ^b	1.77	0.77 - 4.06	0.180			
Prior irAE	3.32	0.64 - 17.09	0.152			
Family history of autoimmune disease ^b	1.03	0.28 - 3.76	0.959			
Prior immune-enhancing therapy ^b	0.56	0.16 - 2.02	0.378			
Prior interferon- γ therapy	0.76	0.16 - 3.55	0.730			
Vitamin D use	1.05	0.49 - 2.23	0.909			
Smoking (current or prior)	1.28	0.64 - 2.57	0.484			
NSAID use	1.46	0.57 - 3.76	0.429			
Any vaccine	0.77	0.32 - 1.86	0.561			
Flu vaccine	0.55	0.20 - 1.51	0.247			
Pneumonia vaccine	0.56	0.16 - 2.02	0.378			
Other vaccine	1.00	0.99 - 1.01	1.000			
Weight at start of ICI (kg)	0.99	0.97 - 1.01	0.207			
Medications						

Steroid at start of ICI	1.04	0.40 - 2.69	0.939			
Steroid Duration (days)	1.00	1.00 - 1.01	0.259			
Infliximab Use	0.42	0.10 - 1.71	0.226			
Vedolizumab Use	1.00	0.99 - 1.01	1.000			

ICI, immune checkpoint inhibitor. IMC, immune checkpoint inhibitor-mediated colitis.

RCC, renal cell carcinoma. NSCLC, non-small cell lung cancer. SCC, squamous cell carcinoma. irAE, immune related adverse event. ^aNumber of infusions of ICI prior to IMC diagnosis (cases) or total (controls). ^bSee Supplemental Table 2.

Supplemental Table 5. Univariate and Multivariate Predictors of Progression-Free Survival > 6 Months Among Patients with Immune Checkpoint Inhibitor Colitis (N= 64).

	Univariate Predictors			Multivariate Predictors		
Clinical Variables						
	Odds Ratios (OR)	95% CI	P-Value	Odds Ratios (OR)	95% CI	P-Value
Demographics						
Age (years)	0.99	0.95 - 1.04	0.806			
Male	0.56	0.20 - 1.53	0.258			
Female	1.79	0.65 - 4.94	0.258			
Race						
White	1.26	0.36 - 4.43	0.718			
Black	1.00	0.99 - 1.01	1.000			
Asian	0.25	0.03 - 2.59	0.248			
Other	0.81	0.15 - 4.37	0.809			
Type of Malignancy						
Melanoma	0.46	0.17 - 1.25	0.128			
RCC	7.00	0.81 - 60.68	0.077	7.02	0.57 - 87.0	0.129
NSCLC	4.67	0.51 - 42.45	0.171			

Sarcoma	0.18	0.02 - 1.75	0.140			
Head and Neck SCC	1.70	0.15 - 19.72	0.673			
Other	1.04	0.25 - 4.30	0.955			
Stage IV malignancy	0.74	0.16 - 3.42	0.704			
Presence of High-Grade IMC	0.81	0.30 - 2.23	0.690			
Type of Immune Checkpoint Inhibitor						
Ipilimumab plus nivolumab	0.43	0.15 - 1.20	0.108	0.64	0.03 - 13.3	0.771
Ipilimumab	0.25	0.059 - 1.04	0.056	0.32	0.026 - 3.86	0.369
Nivolumab	1.74	0.30 - 10.3	0.540			
Pembrolizumab	3.20	0.99 - 10.38	0.053	0.93	0.08 - 10.4	0.952
Atezolizumab	1.00	0.99 - 1.01	1.000			
Number of Infusions ^a	1.54	1.12 - 2.10	0.007	1.49	1.03 - 2.17	0.034
Dose of ICI (mg/kg)	1.09	0.71 - 1.69	0.684			
Medical History						
Non-liver, non-upper GI ^b	0.77	0.26 - 2.29	0.638			
Personal history of autoimmune disease ^b	1.37	0.47 - 4.00	0.565			
Prior irAE	2.25	0.40 -	0.356			

		12.57				
Family history of autoimmune disease ^b	1.03	0.31 - 6.64	0.636			
Prior immune-enhancing therapy ^b	1.00	0.99 - 1.01	1.000			
Prior interferon- γ therapy	0.82	0.05 - 13.77	0.893			
Vitamin D use	1.87	0.67 - 5.24	0.233			
Smoking (current or prior)	1.27	0.47 - 3.41	0.632			
NSAID use	0.80	0.21 - 3.09	0.746			
Any vaccine	0.77	0.32 - 1.86	0.561			
Flu vaccine	0.59	0.12 - 2.86	0.509			
Pneumonia vaccine	0.82	0.11 - 6.20	0.846			
Other vaccine	1.00	0.99 - 1.01	1.000			
Weight at start of ICI (kg)	0.98	0.95 - 1.01	0.159			
Medications						
Steroid at start of ICI	0.64	0.17 - 2.36	0.501			
Steroid Duration (days)	1.00	1.00 - 1.01	0.259			
Infliximab Use	0.29	0.07 - 1.27	0.100	0.97	0.18 - 5.31	0.970
Vedolizumab Use	1.00	0.99 - 1.01	1.000			

ICI, immune checkpoint inhibitor. IMC, immune checkpoint inhibitor-mediated colitis.

RCC, renal cell carcinoma. NSCLC, non-small cell lung cancer. SCC, squamous cell carcinoma. irAE, immune related adverse event. ^aNumber of infusions of ICI prior to IMC diagnosis (cases) or total (controls). ^bSee Supplemental Table 2.

Supplemental Table 6. Univariate and Multivariate Predictors of Severe Immune Checkpoint Inhibitor Colitis (N= 64).

	Univariate Predictors			Multivariate Predictors		
Clinical Variables						
	Odds Ratios (OR)	95% CI	P-Value	Odds Ratios (OR)	95% CI	P-Value
Demographics						
Age (years)	0.97	0.93 - 1.02	0.195			
Male	0.77	0.28 - 2.13	0.618			
Female	1.30	0.47 - 3.58	0.618			
Race						
White	2.43	0.68 - 8.74	0.173			
Black	0.68	0.04 - 11.31	0.785			
Asian	0.21	0.02 - 2.11	0.184			
Other	0.66	0.12 - 3.54	0.625			
Type of Malignancy						
Melanoma	1.44	0.53 - 3.92	0.475			
RCC	0.65	0.15 - 2.86	0.566			
NSCLC	1.41	0.24 - 8.34	0.704			
Sarcoma	1.00	0.99 - 1.01	1.000			
Head and Neck SCC	0.32	0.03 - 3.78	0.369			
Other	0.29	0.06 - 1.27	0.100			

Stage IV malignancy	0.86	0.19- 3.96	0.848			
Type of Immune Checkpoint Inhibitor						
Ipilimumab plus nivolumab	3.00	0.99 - 9.13	0.053	5.74	0.94 - 35.0	0.058
Ipilimumab	8.93	1.07 - 74.8	0.043	12.80	0.89 - 183.2	0.060
Nivolumab	0.31	0.05 - 1.81	0.191			
Pembrolizumab	0.26	0.09 - 0.81	0.020	1.05	0.18 - 6.15	0.960
Atezolizumab	0.21	0.02 - 2.11	0.184			
Number of Infusions ^a	0.94	0.87 - 1.01	0.099	0.99	0.91 - 1.08	0.825
Dose of ICI (mg/kg)	1.13	0.60 - 2.13	0.705			
Medical History						
Non-liver, non-upper GI disease ^b	0.59	0.19 - 1.76	0.342			
Personal history of autoimmune disease ^b	0.57	0.20 - 1.67	0.305			
Prior irAE	0.47	0.10 - 2.31	0.354			
Family history of autoimmune disease ^b	0.36	0.08 - 1.66	0.191			
Prior immune-enhancing therapy ^b	0.68	0.04 - 11.31	0.785			
Prior interferon- γ therapy	0.77	0.05 - 12.9	0.857			
Vitamin D use	3.33	1.10 - 10.14	0.034	2.65	0.72 - 9.78	0.144
Smoking (current or prior)	1.44	0.53 - 3.92	0.475			

NSAID use	0.64	0.16 - 2.47	0.513			
Any vaccine	0.83	0.20 - 3.45	0.801			
Flu vaccine	0.90	0.18 - 4.41	0.899			
Pneumonia vaccine	0.67	0.09 - 5.06	0.695			
Other vaccine	1.00	0.99 - 1.01	1.000			
Weight at start of ICI (kg)	1.01	0.98 - 1.04	0.504			
Medications						
Steroid at start of ICI	0.32	0.08 - 1.23	0.098	0.74	0.15 - 3.72	0.719
Steroid Duration (days)	1.00	1.00 - 1.01	0.537			
Infliximab Use	3.20	0.62 - 16.49	0.164			
Vedolizumab Use	1.00	0.99 - 1.01	1.000			

ICI, immune checkpoint inhibitor. IMC, immune checkpoint inhibitor-mediated colitis.

RCC, renal cell carcinoma. NSCLC, non-small cell lung cancer. SCC, squamous cell carcinoma. irAE, immune related adverse event. ^aNumber of infusions of ICI prior to IMC diagnosis (cases) or total (controls). ^bSee Supplemental Table 2.