Characteristics and outcomes of cancer patients with pre-existing microscopic colitis after exposure to immune checkpoint inhibitors

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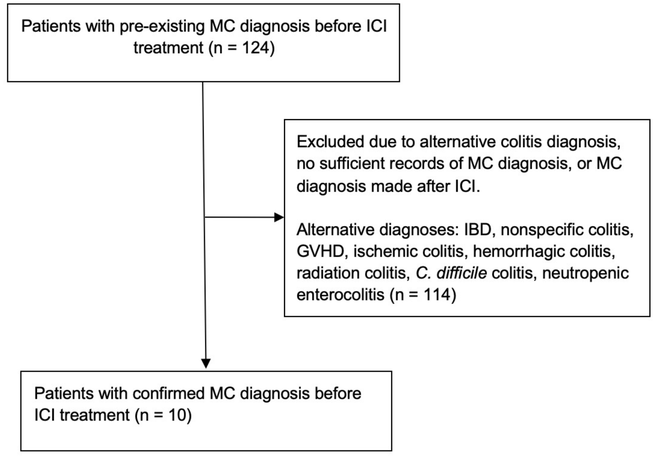
Background

Immune checkpoint inhibitors (ICIs) are frequently associated with adverse events, often affecting the gastrointestinal tract. We conducted this study to determine the characteristics and outcomes of cancer patients with pre-existing microscopic colitis (MC) who underwent ICI treatment.

Methods

In this retrospective study, we identified 10 patients with pre-existing MC who received ICIs at our center 01/2010-06/2020. Clinical characteristics and disease outcomes were recorded.

Figure 1. Patient selection flow chart.



Results

Of 124 screened patients with MC before ICI exposure, 10 had sufficient data to be included in the study. Melanoma (40%) and lung cancer (30%) were the most prevalent cancer types, with 70% of stage IV cancer. Most patients (90%) received anti–programmed death ligand 1 monotherapy. Six patients (60%) had collagenous colitis, and 4 (40%) had lymphocytic colitis. The median time from MC diagnosis to ICI initiation was 4 years, with 1 patient on budesonide within 2 months of ICI initiation. Eight patients (80%) developed colitis exacerbations after ICI requiring selective immunosuppression. One patient received a compassionate-use fecal transplantation. The median time from ICI to colitis exacerbation was 14 days, with 40% and 50% of patients experiencing grade 3 diarrhea and grade 2 colitis, respectively leading to hospitalization in 3 patients.

Six patients received steroids and vedolizumab with no colitis recurrence. Of 8 patients who had colitis exacerbation, 6 resumed ICI therapy afterwards; with 5 receiving concomitant vedolizumab for secondary prophylaxis.

Patients' Characteristics (N=10)	Value
-Median age at ICI initiation, years (IQR)	67 (65-72)
-Men, no. (%)	5 (50)
-Pre-existing autoimmune diseases, no. (%)	2 (20)
-Type of MC, no. (%)	
Lymphocytic colitis	4 (40)
Collagenous colitis	6 (60)
-Median time from MC diagnosis to ICI initiation, years (IQR) (N = 9)	4 (2-12)
-Median time from last active MC episode prior to ICI initiation, years (IQR)	3 (4-9)
Melanoma	4 (40)
Lung	3 (30)
Endocrine[3]	2 (20)
Rectal adenocarcinoma	1 (10)
Renal cell carcinoma	1 (10)
-Cancer stage, no. (%)	
III	3 (30)
IV	7 (70)
-ICI type before MC flare, no. (%)	
CTLA-4	1 (10)
PD-L1	9 (90)
-Median duration of ICI treatment, months (IQR)	12 (1-28)
-Reason for ICI cessation, no. (%) (N = 9)	
GI adverse event	6 (67)
Cancer progression	2 (22)
Death	1 (11)
-ICI resumed after management of MC flare up, no. (%)	6 (75)
-All-cause mortality, no. (%)	4 (40)

Figure 2.

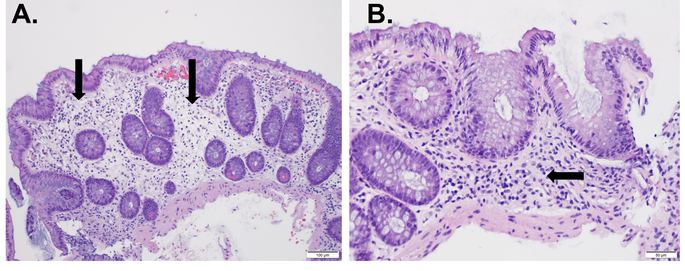


Figure 2. Pathology images after ICI. **A.** Colitis with epithelial architectural distortion, edema, focal glandular dropout and mild increase in mononuclear inflammation in lamina propria (10x); **B.** Colitis with basal lymphoplasmacytosis. (20x)

Colitis Characteristics after ICI (N=10)	Value
-MC status after ICI initiation, no. (%)	
Persistent symptoms	2 (20)
Exacerbation of colitis	8 (80)
-Median time from ICI initiation to colitis exacerbation, days (IQR) (N = 8)	14 (8-128)
-Highest grade of diarrhea after ICI initiation, no. (%)	
1	4 (40)
2	2 (20)
3	4 (40)
-Highest grade of colitis after ICI initiation, no. (%)	
0	2 (20)
1	3 (30)
2	5 (50)
-Median duration of initial colitis exacerbation symptoms, months (IQR) (N = 8)	4 (2-6)
-Hospitalization, no. (%)	3 (30)
-Median duration of hospitalization, days (IQR) (N = 3)	5 (4.5-7)
-Median peak fecal calprotectin, mcg/gm (IQR) (N = 8)	368 (119-591)
-Treatment of colitis exacerbation, no. (%) (N = 8)	
Mesalamine	1 (12.5)
Systemic corticosteroids	8 (100)
Vedolizumab/ustekinumab (in addition to systemic corticosteroids)	8 (100)
Fecal microbiota transplantation	1 (12.5)
-Subsequent recurrent colitis – no. (%)	2 (25)
-Mortality due to MC, no. (%)	0 (0)

Conclusion

Our findings suggest that ICI exposure increases the risk of exacerbation of underlying colitis necessitating and responding to potent immunosuppression therapy.