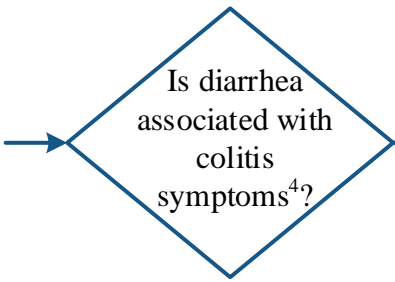


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## GENERAL EVALUATION

### PRESENTATION

Patient presents with new onset of diarrhea<sup>1</sup> one week after immunotherapy initiation and up to 6 months<sup>2</sup> after last dose of immunotherapy<sup>3</sup>



Yes  
 Moderate/severe colitis (Grade 2 and above)<sup>5</sup>

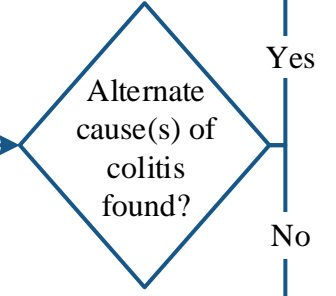
No  
 Diarrhea alone

### ASSESSMENT

- Hold immunotherapy and order the following:
- GI consult
  - GI Multiplex PCR panel and fecal CMV PCR<sup>6</sup>
  - Consider infectious workup for non-GI organs if there is fever or symptoms suggesting individual organ involvement
  - CT abdomen/pelvis with oral and IV contrast
  - Laboratory evaluation: CBC, complete metabolic panel (CMP), amylase, lipase, and ANA
  - Inflammatory blood markers: ESR and CRP
  - Inflammatory stool markers: lactoferrin and calprotectin
  - Fecal pancreatic elastase to rule out exocrine pancreatic insufficiency
  - Total IgA and tissue transglutaminase (tTG) IgA to rule out celiac disease
  - Screening tests<sup>7</sup>, if not drawn within the past 6-12 months

For assessment and treatment of diarrhea, see [Page 4](#)

### TREATMENT



- Initiate appropriate therapy
- Consider Infectious Diseases consult

For further assessment/management, see [Page 2](#)

For recurrent colitis/diarrhea assessment and treatment, see [Page 5](#)

<sup>1</sup> Diarrhea is defined as the presence of 3 or more unformed stools a day  
<sup>2</sup> On rare occasions, GI toxicities may develop beyond the typical 6 month window  
<sup>3</sup> PD-1 inhibitors (pembrolizumab, nivolumab), PD-L1 inhibitors (atezolizumab, avelumab, durvalumab), CTLA-4 inhibitor (ipilimumab)  
<sup>4</sup> Colitis symptoms include abdominal pain, rectal bleeding, and blood or mucus in stools  
<sup>5</sup> Refer to [Appendix A](#) for Modified Common Terminology Criteria for Adverse Events (CTCAE)  
<sup>6</sup> Fecal CMV PCR has low sensitivity and poor negative predictive value for the diagnosis of CMV colitis. Consider early colonoscopy in immunosuppressed patients to exclude CMV colitis and perform colonoscopy in patient with positive fecal CMV by PCR.  
<sup>7</sup> Screening tests include HIV antibody; T-spot tuberculosis; hepatitis A, B and C panel; and urine *Histoplasma* antigen

CMV = cytomegalovirus  
 ANA = antinuclear antibodies

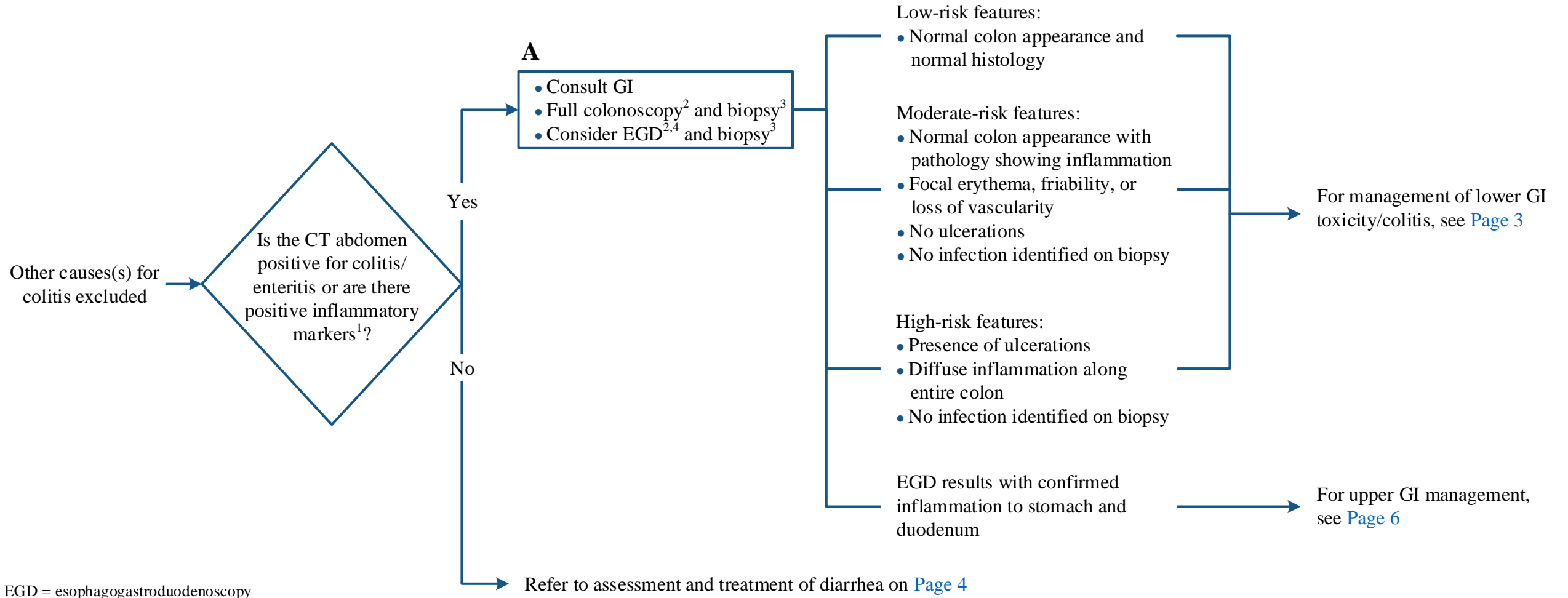
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## GENERAL EVALUATION - continued

### PRESENTATION

### ASSESSMENT

### ENDOSCOPY FINDINGS



EGD = esophagogastroduodenoscopy

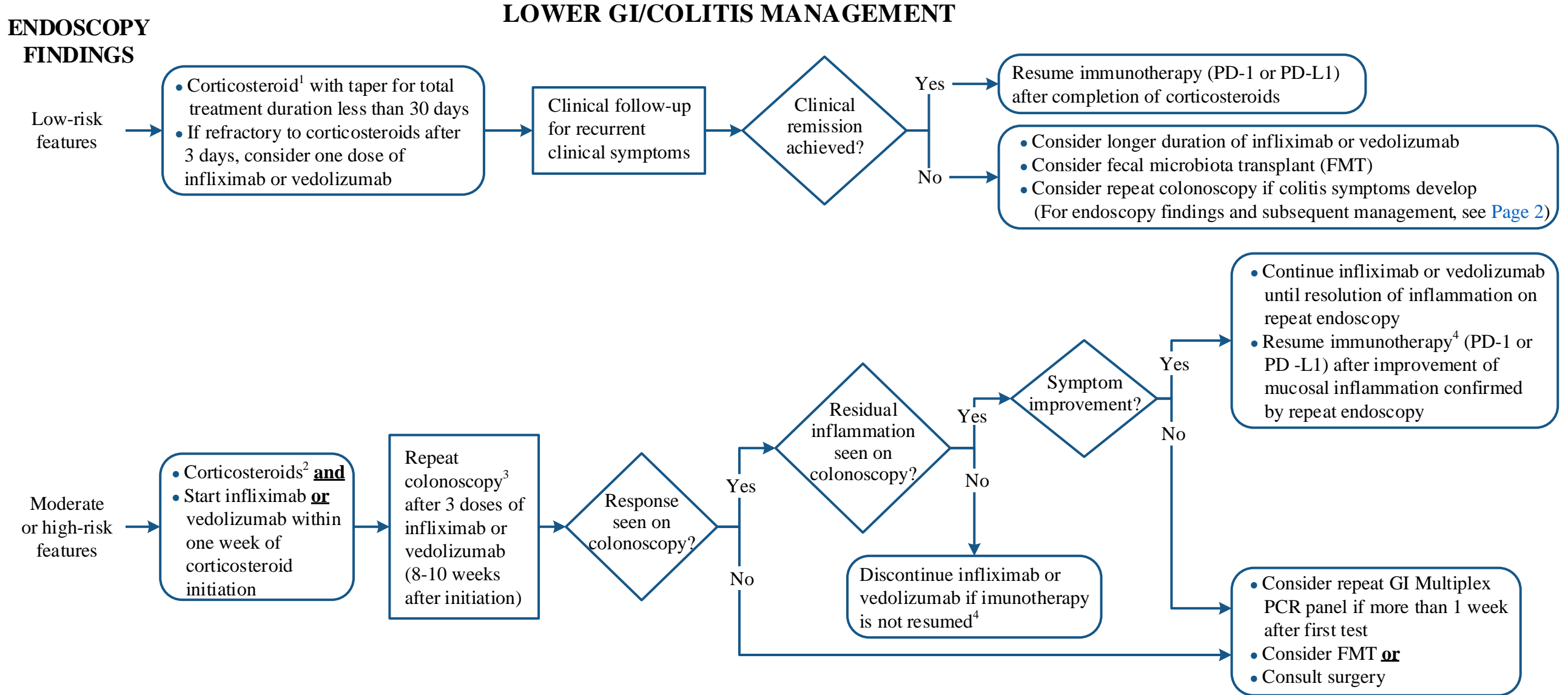
<sup>1</sup> Stool: lactoferrin and calprotectin; blood: ESR and CRP

<sup>2</sup> Perform colonoscopy and EGD only if ANC greater than 0.5 K/microliter

<sup>3</sup> Examine biopsies for the presence of CMV and other opportunistic infections in immunosuppressed patients

<sup>4</sup> Order EGD if there are signs and symptoms of concurrent nausea/vomiting and/or epigastric pain

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<sup>1</sup> May consider budesonide as an additional option

<sup>2</sup> Start steroid taper over 2 weeks after starting infliximab or vedolizumab (total corticosteroid treatment duration should be less than 30 days)

<sup>3</sup> Consider early repeat colonoscopy after 2 doses of infliximab or vedolizumab if symptoms persist

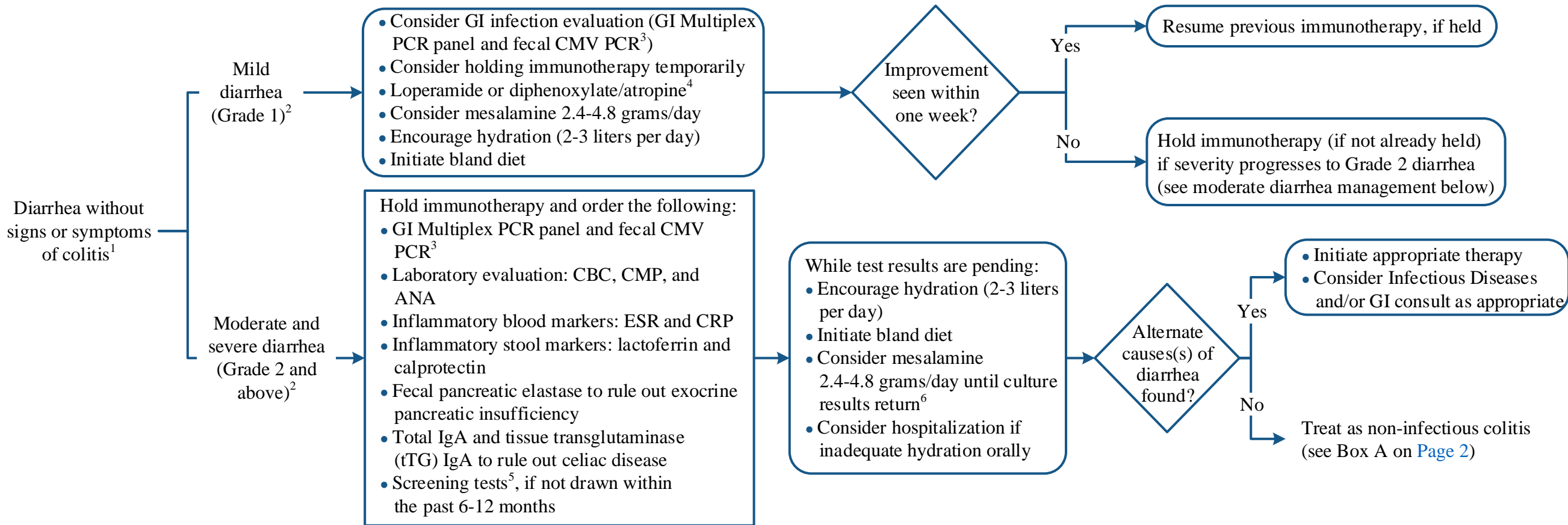
<sup>4</sup> If resuming immunotherapy, continue long-term vedolizumab concurrently

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## DIARRHEA MANAGEMENT

### PRESENTATION

### ASSESSMENT/TREATMENT



<sup>1</sup> Colitis symptoms include abdominal pain, rectal bleeding, and blood or mucus in stools

<sup>2</sup> Refer to [Appendix A](#) for Modified Common Terminology Criteria for Adverse Events (CTCAE)

<sup>3</sup> Fecal CMV PCR has low sensitivity and poor negative predictive value for the diagnosis of CMV colitis. Consider early colonoscopy in immunosuppressed patients to exclude CMV colitis and perform colonoscopy in patients with positive fecal CMV by PCR.

<sup>4</sup> Consider anti-motility agents only if non-invasive pathogens have been excluded

<sup>5</sup> Screening tests include HIV antibody; T-spot tuberculosis; hepatitis A, B and C panel; and urine *Histoplasma* antigen

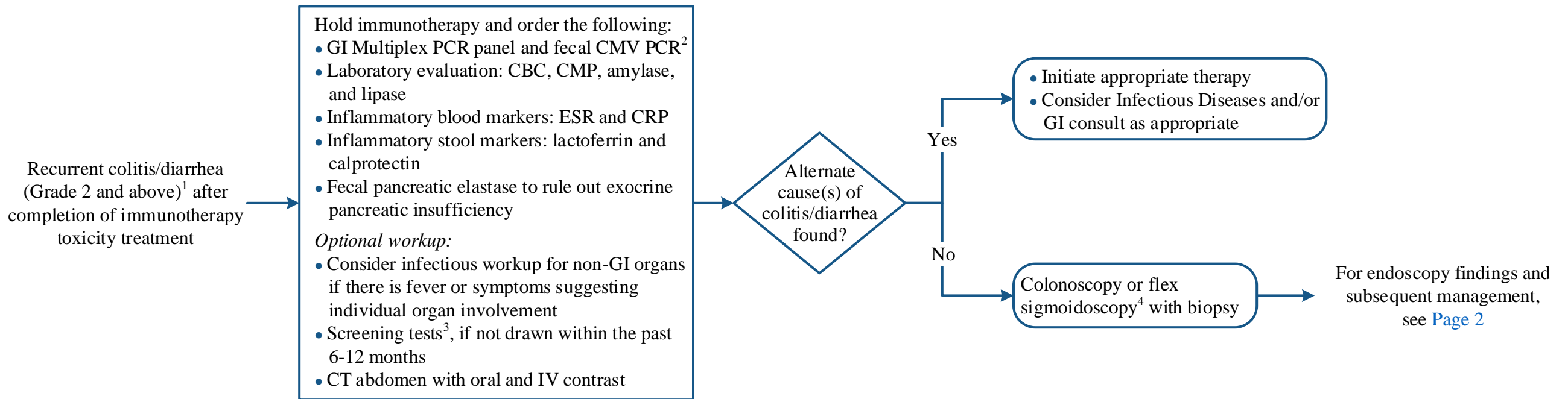
<sup>6</sup> If cultures return negative and/or no improvement is seen after 2 days of treatment, discontinue mesalamine and consider starting corticosteroids. If patient has symptom improvement with mesalamine, continue treatment regardless of culture results.

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## RECURRENCE MANAGEMENT

### ASSESSMENT

### TREATMENT



<sup>1</sup> Refer to [Appendix A](#) for Modified Common Terminology Criteria for Adverse Events (CTCAE)

<sup>2</sup> Fecal CMV PCR has low sensitivity and poor negative predictive value for the diagnosis of CMV colitis. Consider early Colonoscopy in immunosuppressed patients to exclude CMV colitis and perform colonoscopy in patients with positive fecal CMV by PCR.

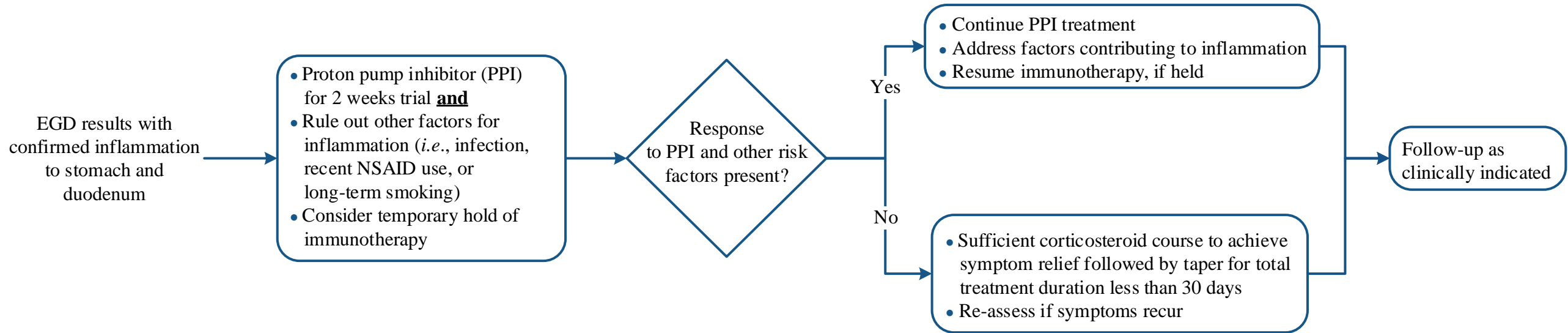
<sup>3</sup> Screening tests include HIV antibody; T-spot tuberculosis; hepatitis A, B and C panel; and urine *Histoplasma* antigen

<sup>4</sup> If initial colonoscopy confirmed left colon involvement, then consider flex sigmoidoscopy on follow-up

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## UPPER GI MANAGEMENT

### ASSESSMENT/TREATMENT





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## APPENDIX A: Modified<sup>1</sup> Common Terminology Criteria for Adverse Events (CTCAE)

Gastrointestinal Disorders					
Adverse Effect	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
Diarrhea	Increase of less than 4 stools per day over baseline; mild increase in ostomy output compared to baseline	Increase of 4-6 stools per day over baseline; moderate increase in ostomy output compared to baseline; limiting instrumental ADL	Increase of greater than 7 stools per day over baseline; hospitalization indicated; severe increase in ostomy output compared to baseline; limiting self-care ADL	Life-threatening consequences; urgent intervention indicated	Death
Colitis	Asymptomatic; clinical or diagnostic observations only; intervention not indicated	Abdominal pain; mucus or blood in stool	Severe abdominal pain; peritoneal signs	Life-threatening consequences; urgent intervention indicated	Death

<sup>1</sup> Modified version includes elements of version 4 and version 5

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## SUGGESTED READINGS

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- Wang, Y., Abu-Sbeih, H., Mao, E., Ali, N., Ali, F. S., Qiao, W., ... Diab, A. (2018). Immune-checkpoint inhibitor-induced diarrhea and colitis in patients with advanced malignancies: retrospective review at MD Anderson. *Journal for Immunotherapy of Cancer*, 6(1), 37.



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## DEVELOPMENT CREDITS

This practice consensus statement is based on majority opinion of the Immune Colitis experts at the University of Texas MD Anderson Cancer Center for the patient population. These experts included:

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