

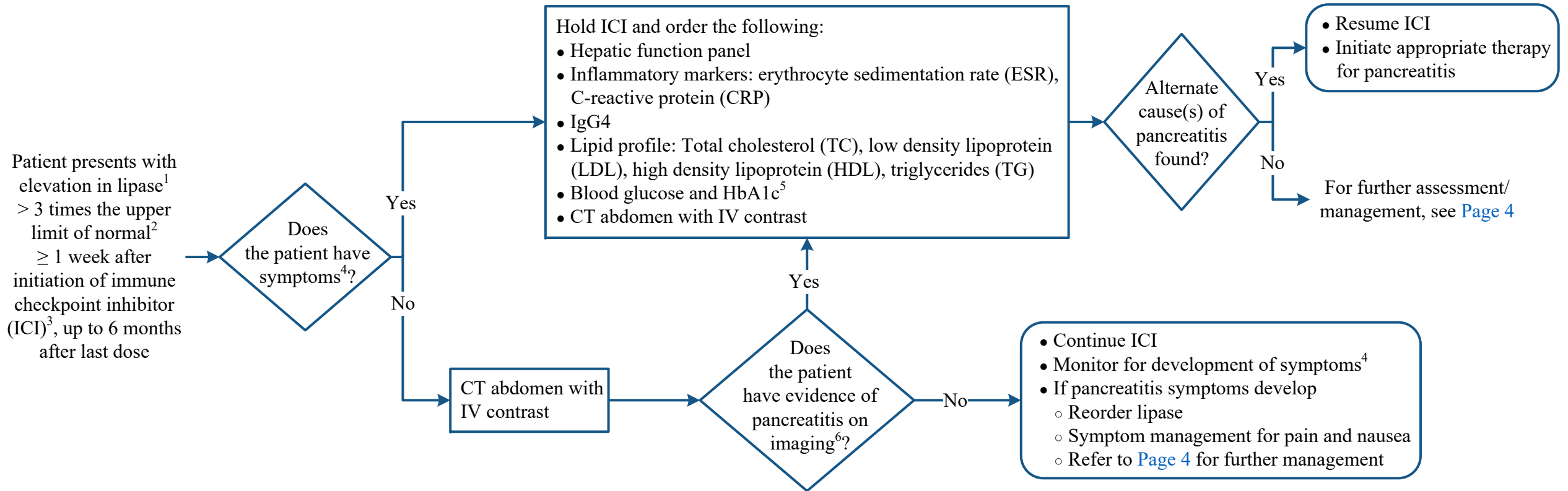
Disclaimer: This algorithm has been developed for UT MD Anderson using a multidisciplinary approach considering circumstances particular to UT MD Anderson's specific patient population, services and structure, and clinical information. This is not intended to replace the independent medical or professional judgment of physicians or other health care providers in the context of individual clinical circumstances to determine a patient's care. This algorithm should not be used to treat pregnant women.

## GENERAL EVALUATION – Elevation in Lipase

### PRESENTATION

### ASSESSMENT

### TREATMENT



<sup>1</sup> There is no available evidence to order amylase for evaluation of ICI-mediated pancreatitis and pancreatic injury. Do not check amylase/lipase without an appropriate indication.

<sup>2</sup> Upper limit of normal at UT MD Anderson is 60 U/L for lipase and 100 U/L for amylase

<sup>3</sup> PD-1 inhibitors (pembrolizumab, nivolumab, cemiplimab, dostarlimab, tislelizumab, toriplaimab), PD-L1 inhibitors (atezolizumab, avelumab, durvalumab), CTLA-4 inhibitor (ipilimumab, tremelimumab)

<sup>4</sup> Epigastric pain radiating to the back, nausea/vomiting, inability to tolerate oral feeding, bloating, diarrhea

<sup>5</sup> Imaging evidence of pancreatitis includes peripancreatic fat stranding, enhancement of pancreas, pancreatic enlargement. If glucose or HA1c are elevated, refer to [Evaluation and Management of Suspected Immune-Mediated Endocrine Toxicities algorithm](#).

<sup>6</sup> Imaging evidence of pancreatitis includes peripancreatic fat stranding, enhancement of pancreas, pancreatic enlargement

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## GENERAL EVALUATION – Epigastric Pain

### PRESENTATION

Patient presents with new onset epigastric pain  $\geq 1$  week after initiation of ICI<sup>1</sup>, up to 6 months after last dose

**A**

- Hold ICI and order the following:
- Lipase
  - Hepatic function panel
  - Inflammatory markers: ESR, CRP
  - IgG4
  - Lipid profile: TC, LDL, HDL, TG
  - Blood glucose and HbA1c<sup>2</sup>
  - CT abdomen with IV contrast

### ASSESSMENT

Is  
lipase > 3 times  
the upper limit of  
normal (ULN) and/or  
CT abdomen has  
evidence of  
pancreatitis<sup>3</sup>?

Yes

Obtain  
Gastroenterology  
(GI) consult

No

- Resume ICI
- Monitor for development of symptoms<sup>4</sup>

### TREATMENT

Alternate  
cause(s) of  
pancreatitis  
found?

Yes

- Resume ICI
- Initiate appropriate therapy for pancreatitis

No

For further assessment/  
management, see [Page 4](#)

- If pancreatitis symptoms<sup>4</sup> develop:
- Refer to Box A
  - Symptom management for pain and nausea

<sup>1</sup> PD-1 inhibitors (pembrolizumab, nivolumab, cemiplimab, dostarlimab, tislelizumab, toriplaimab), PD-L1 inhibitors (atezolizumab, avelumab, durvalumab), CTLA-4 inhibitor (ipilimumab, tremelimumab)

<sup>2</sup> Imaging evidence of pancreatitis includes peripancreatic fat stranding, enhancement of pancreas, pancreatic enlargement. If glucose or HA1c are elevated, refer to [Evaluation and Management of Suspected Immune-Mediated Endocrine Toxicities algorithm](#).

<sup>3</sup> Imaging evidence of pancreatitis includes peripancreatic fat stranding, enhancement of pancreas, pancreatic enlargement

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## GENERAL EVALUATION – CT Evidence of Pancreatitis (Asymptomatic)

### PRESENTATION

Patient has incidental finding of pancreatitis on staging CT abdomen  $\geq 1$  week after ICI<sup>1</sup>, up to 6 months after last dose

Hold ICI and order the following:

- Lipase
- Hepatic function panel
- Inflammatory markers: ESR, CRP
- IgG4
- Lipid profile: TC, LDL, HDL, TG
- Blood glucose and HbA1c<sup>2</sup>
- Right upper quadrant ultrasound

### ASSESSMENT

Is lipase  $> 3$  times the ULN and/or patient develops symptoms of pancreatitis<sup>2</sup>?

Yes

Obtain Gastroenterology (GI) consult

Alternate cause(s) of pancreatitis found?

Yes

- Resume ICI
- Initiate appropriate therapy for pancreatitis

No

For further assessment/management, see [Page 4](#)

No

- Resume ICI
- Monitor for development of symptoms<sup>3</sup> if no symptoms initially
- If pancreatitis symptoms<sup>2</sup> develop
  - Reorder lipase
  - Symptom management for pain and nausea
  - Consider IV fluids
  - Refer to [Page 4](#) for further management

### TREATMENT

<sup>1</sup> PD-1 inhibitors (pembrolizumab, nivolumab, cemiplimab, dostarlimab, tislelizumab, toriplaimab), PD-L1 inhibitors (atezolizumab, avelumab, durvalumab), CTLA-4 inhibitor (ipilimumab, tremelimumab)

<sup>2</sup> Imaging evidence of pancreatitis includes peripancreatic fat stranding, enhancement of pancreas, pancreatic enlargement. If glucose or HA1c are elevated, refer to [Evaluation and Management of Suspected Immune-Mediated Endocrine Toxicities algorithm](#).

<sup>3</sup> Epigastric pain radiating to the back, nausea/vomiting, inability to tolerate oral feeding, bloating, diarrhea

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## DIAGNOSIS, GRADING, AND TREATMENT

### GRADING

#### Grade 1 (Mild)<sup>2</sup>:

- Temporarily hold ICI
- Consider GI consult/referral
- IV hydration
- Pain and nausea control
- Advance diet as tolerated

#### Grade 2 (Moderately severe)<sup>2</sup>:

- Temporarily hold ICI
- Place GI consult/referral
- IV hydration
- Pain and nausea control
- Advance diet as tolerated

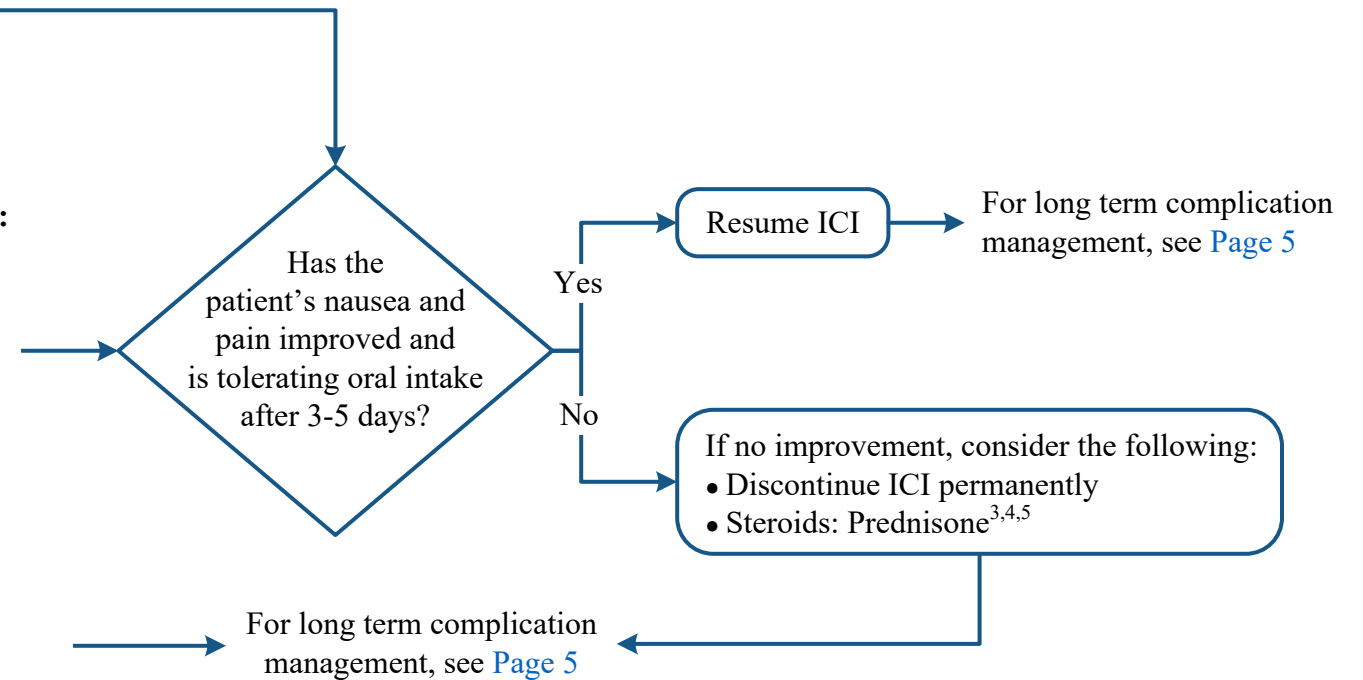
#### Grade 3 (Severe)<sup>2</sup>:

- Stop ICI permanently
- Place GI consult/referral
- IV hydration
- Pain and nausea control
- Advance diet as tolerated
- Consider steroids: Prednisone<sup>3,4,5</sup>

### TREATMENT

ICI-mediated pancreatitis and pancreatic injury  $\geq$  1 week after initiation of ICI<sup>1</sup>, up to 6 months after last dose and no alternate cause of pancreatitis

Inpatient management of ICI-related pancreatitis



PJP = *pneumocystis jiroveci* pneumonia  
TMP/SMX = trimethoprim/sulfamethoxazole

<sup>1</sup> PD-1 inhibitors (pembrolizumab, nivolumab, cemiplimab, dostarlimab, tislelizumab, toriplaimab), PD-L1 inhibitors (atezolizumab, avelumab, durvalumab), CTLA-4 inhibitor (ipilimumab, tremelimumab)

<sup>2</sup> Per the Revised Atlanta Criteria for Pancreatitis Grading (refer to [Appendix A](#))

<sup>3</sup> 0.5-1 mg/kg/day until Grade 1. If improvement seen with supportive care (IV hydration, pain/nausea control, and advancing diet as tolerated) in 3-5 days, then taper off over 4 weeks.

<sup>4</sup> If hospitalized with poor oral intake, use equivalent doses of IV prednisolone until able to resume oral prednisone. Patient may be discharged once able to tolerate adequately by mouth and symptoms of pain and nausea are well controlled.

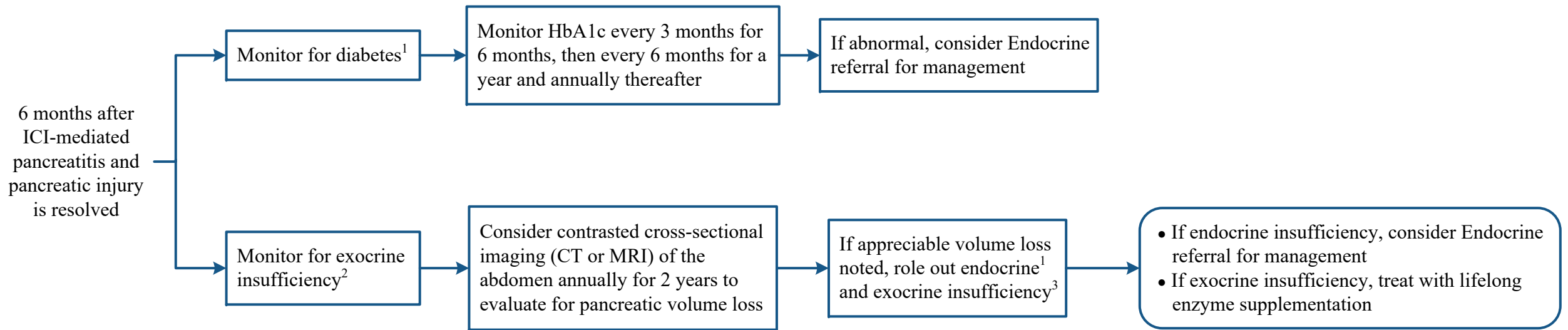
<sup>5</sup> Initiate PJP prophylaxis with TMP/SMX. Continue PJP prophylaxis for 2 weeks after completion of prednisone.

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## LONG TERM COMPLICATIONS

### MONITORING

### TREATMENT



Recurrence of pancreatitis → Refer to General Evaluation assessments on [Pages 1-3](#)

<sup>1</sup> Abrupt onset of diabetes should raise suspicion of type 1 diabetes and prompt referral to Endocrinology

<sup>2</sup> Monitor for symptoms of diarrhea and weight loss every 3 months for 6 months, then every 6 months for a year and annually thereafter for 2 years

<sup>3</sup> Evaluation for steatorrhea with fecal elastase and fecal fat testing. Evaluate for diabetes with HbA1c.

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APPENDIX A: Revised Atlanta Criteria for Pancreatitis Grading

|                    | Grade 0                             | Grade 1 (mild)                                                          | Grade 2 (moderate)                                                     | Grade 3 (severe)                                    |
|--------------------|-------------------------------------|-------------------------------------------------------------------------|------------------------------------------------------------------------|-----------------------------------------------------|
| Enzymes            | < 3 times the upper limit of normal | ≥ 3 times the upper limit of normal                                     | ≥ 3 times the upper limit of normal                                    | ≥ 3 times the upper limit of normal                 |
| Pain               | Absent                              | Upper abdominal, radiating to back; nausea/vomiting                     | Upper abdominal, radiating to back; nausea/vomiting                    | Upper abdominal, radiating to back; nausea/vomiting |
| CT Findings        | Normal                              | Interstitial pancreatitis                                               | Necrosis: Pancreatic and/or peri-pancreatic                            | Necrosis: Pancreatic and/or peri-pancreatic         |
| Organ Failure (OF) | None                                | None                                                                    | None or transient (< 48 hours)                                         | Persistent OF: One or more organs                   |
| Criteria           | No pancreatitis                     | Presence of 2 or more features or definite computed tomography findings | Grade 1 criteria plus computed tomography findings and/or transient OF | Grade 1 criteria plus persistent OF                 |

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## SUGGESTED READINGS

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## DEVELOPMENT CREDITS

This practice consensus statement is based on majority opinion of the IOTOX-Mediated Pancreatitis experts at The University of Texas MD Anderson Cancer Center for the patient population. These experts included:

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