Evaluation and Management of Suspected Immune-Mediated Pneumonitis

Disclaimer: This algorithm has been developed for MD Anderson using a multidisciplinary approach considering circumstances particular to 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

PRESENTATION

Patient presents with new onset symptoms or new infiltrates 1 week after immune checkpoint inhibitor (ICI) initiation and up to 6 months after discontinuation.

ASSESSMENT

Hold ICI and order the following:

- CT chest without contrast (if not already performed)
- Consider non-invasive infectious workup
  - Nasal swab for potential viral pathogens
  - Sputum cultures, blood cultures, urine antigen (pneumococcus and legionella)
- Urgent Pulmonary consult and evaluation for bronchoscopy with BAL
  - Absolute cell count
  - CD4 and CD8 cell counts
  - Aerobic and anaerobic cultures
  - Respiratory viral panel PCR
  - Pneumocystis jiroveci PCR
  - CMV PCR
  - Fungal cultures
- Screening tests

If BAL = bronchioalveolar lavage
CMV = cytomegalovirus

TREATMENT

Is there shortness of breath, cough, chest pain, fever, or increased oxygen requirements?

Alternate cause(s) of pulmonary process found?

Yes

- For pneumonia, consult Infectious Diseases
- For disease progression, defer to oncology service

No

For further assessment/management, see Page 2

1 PD-1 inhibitors (pembrolizumab, nivolumab, cemiplimab, dostarlimab), PD-L1 inhibitors (atezolizumab, avelumab, durvalumab), CTLA-4 inhibitor (ipilimumab, tremelimumab)
2 On rare occasions, pulmonary toxicities may develop beyond the 6-month window
3 Refer to Appendix A for Common Terminology Criteria for Adverse Events (CTCAE) Version 5.0
4 Includes HIV, T-spot tuberculosis, and hepatitis B and C. Consider screening for fungal infections, if indicated. Preemptive in case of refractory pneumonitis necessitating infliximab therapy.
5 CT chest (preferred) or chest x-ray
6 Infiltrates are confined to one lobe or < 25% of the entire lung. Radiological criteria for pneumonitis grading are based on National Comprehensive Cancer Network (NCCN) expert guidelines and require validation in independent cohorts.
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PNEUMONITIS MANAGEMENT

PRESENTATION

ASSESSMENT/TREATMENT

TREATMENT

Consider holding ICI for one cycle on a case-by-case basis. Monitor regularly with PFTs and imaging.
- Reassess for symptoms in 1-2 weeks
- Repeat CT chest without contrast in 4 weeks or as clinically indicated for worsening symptoms
- Treatment is not required

Radiological improvement seen within 4 weeks?

- Resume previous ICI
- Reimage with CT chest without contrast within 4 weeks

No

Yes

- Continue monitoring with PFTs and imaging every 1-3 months
- If severity progresses to Grade 2 or higher, see moderate pneumonitis on Page 3

PFT = pulmonary function tests

1 Radiographic patterns include organizing pneumonia, interstitial pneumonitis, or other non-specific patterns of lung injury

2 Confined to one lobe of the lung or < 25% of lung parenchyma. Radiological criteria for pneumonitis grading are based on NCCN expert guidelines and require validation in independent cohorts.

3 Refer to Appendix A for Common Terminology Criteria for Adverse Events (CTCAE) Version 5.0
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**PNEUMONITIS MANAGEMENT**

**PRESENTATION**

- Symptomatic pneumonitis

**ASSESSMENT/TREATMENT**

1. **Does patient have Grade 3/4 symptoms and imaging findings?**
   - Yes: **Severe/life-threatening pneumonitis (Grade 3/4)**
     - Hold ICI:
       - Consider empiric antibiotics if infection is not yet fully excluded
       - Initiate prednisone 1-2 mg/kg/day
       - Initiate PJP prophylaxis with TMP/SMX
     - Repeat CT chest without contrast in 3-4 weeks
   - No: **Moderate/severe pneumonitis (Grade 2)**
     - Permanently discontinue ICI
     - Inpatient care due to need for intensive respiratory support and close monitoring
     - Initiate methylprednisolone 1-2 mg/kg/day IV
     - Initiate PJP prophylaxis with TMP/SMX
     - If no response seen to steroid, convert to oral prednisone and taper ≥ 6 weeks
     - If response seen to infliximab, consider converting to oral prednisone and taper ≥ 6 weeks
     - If no response to infliximab after 1-2 weeks, consider additional infliximab dose or tocilizumab 4 mg/kg IV for one dose
     - Discuss Goal Concordant Care (GCC) with patient or if clinically indicated, with Patient Representative
   - If radiographic or physiologic evidence of recurrence present, see Page 4 for management of recurrence

**TREATMENT**

- Continue steroid taper
  - Improvement seen?
    - Yes: Resume ICI if symptoms resolve completely and improvement seen on imaging
    - No: For inpatient, reassess daily
      - For outpatient, reassess with clinical evaluation, PFT, and CT chest without contrast in 2-4 weeks

**Monitoring:**
- For inpatient, reassess daily
- For outpatient, reassess with clinical evaluation, PFT, and CT chest without contrast in 2-4 weeks

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

1 Refer to *Appendix A* for Common Terminology Criteria for Adverse Events (CTCAE) Version 5.0
2 Involvement of all lung lobes or > 50% of lung parenchyma
3 Use falls outside MDACC formulary restriction criteria for tocilizumab; formulary management review required prior to use
4 GCC should be initiated by the Primary Oncologist. If Primary Oncologist is unavailable, Primary Team/Attending Physician to initiate GCC discussion and notify Primary Oncologist. Patients, or if clinically indicated, the Patient Representative should be informed of therapeutic and/or palliative options. GCC discussion should be consistent, timely, and re-evaluated as clinically indicated. The Advance Care Planning (ACP) note should be used to document GCC discussion. Refer to GCC home page (for internal use only).
5 Moderate/severe pneumonitis to Grade 1 then taper over 4-6 weeks

Department of Clinical Effectiveness V1 Approved by the Executive Committee of the Medical Staff on 10/17/2023
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**Evaluation and Management of Suspected Immune-Mediated Pneumonitis**

**PRESENTATION**

Recurrence of pneumonitis after ICI toxicity treatment

**ASSESSMENT**

Hold ICI and order the following:
- PFTs
- CT chest without contrast (if not already performed)
- Repeat initial workup per Page 1 for General Evaluation

**TREATMENT**

Alternate cause(s) of pulmonary process found?

Yes

- For pneumonia, consult Infectious Diseases
- For disease progression, defer to oncology service

No

Treat based on grading appearance and symptoms, see Page 2
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APPENDIX A: Common Terminology Criteria for Adverse Events (CTCAE) Version 5.0

<table>
<thead>
<tr>
<th>CTCAE Term</th>
<th>Grade 1</th>
<th>Grade 2</th>
<th>Grade 3</th>
<th>Grade 4</th>
<th>Grade 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pneumonitis</td>
<td>Asymptomatic; clinical or diagnostic observations only; intervention not indicated</td>
<td>Symptomatic; medical intervention indicated; limiting instrumental ADL</td>
<td>Severe symptoms; limiting self care ADL; oxygen indicated</td>
<td>Life-threatening respiratory compromise; urgent intervention indicated (e.g., tracheostomy or intubation)</td>
<td>Death</td>
</tr>
</tbody>
</table>

ADL = activities of daily living
SUGGESTED READINGS


MD Anderson Institutional Policy #CLN1202 - Advance Care Planning Policy
Advance Care Planning (ACP) Conversation Workflow (ATT1925)


Continued on next page
SUGGESTED READINGS - continued


DEVELOPMENT CREDITS

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

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