Pulmonary Immune-Related Adverse Event Management Algorithm

Grading of Pulmonary toxicity	Action	Follow-up
Grade 1 Clinically asymptomatic and radiographic changes < 25% of lung parenchyma or changes confined to one lobe	**Investigations** • Clinical assessment incl. SpO2 • Bloods: FBC, U&E, LFT, Ca, TFT, ESR, CRP • CT Chest with Contrast • Consider screening for viral, opportunistic or specific bacterial infections* **Management** • Consider holding I-O • Consider non-urgent communicate to: Respiratory interstitial lung disease (OP)	**If remains stable / resolves:** • Single check-in and safety-netting **If worsens / persists:** • If becomes symptomatic treat as grade 2 • If sarcoid node type reaction, consider early EBUS to ensure not progressive malignancy
Grade 2 New onset or worsening of symptoms ie dyspnea, cough, fever, chest pain, new oxygen requirement	**Investigations** • As per G1 • Additional bloods: beta-d-glucan, BNP • Additional infection screening: Sputum MCS + AFB • Consider CTPA to exclude PE • Consider bronchoscopy with BAL to rule out infection **Management** • Hold I-O therapy, consider admission • Consult Respiratory (urgent referral if sats <94% on RA) • Start Prednisolone** 1mg/kg/day (max 60mg per day) + PPI • Start abx as per local protocol if suspicion of infection • Optimise underlying respiratory disease ie COPD	**If improves:** • Repeat CXR, baseline bloods and lung function tests incl TLCO weekly • Once symptoms return to baseline wean steroids over 4-6 weeks, titrating to symptoms **If worsens or persists:** • If no improvement in 48 hours treat as grade 3 • Discuss use of second-line agents (Tacrolimus, or MMF or Infliximab) early in cases of patients with multiple toxicities- Guided by respiratory team. • If recurrent G2 pneumonitis discontinue IO therapy
Grade 3 – 4 Severe new symptoms, including: new or worsening hypoxia, life-threatening difficulty in breathing, ARDS	**Investigations** • As per G2 • Additional bloods: ILD bloods (ANA and ANCA) **Management** • Admission • Urgent Respiratory Consult • Discontinue I-O therapy • Discuss escalation, ceiling of care and ventilation • Start IV methylprednisolone 1-2mg/kg/day **(250mg max for 3 doses only and step down to oral) • Cover with empirical abx +/- PCP treatment depending on clinical risk. Consider ID consult	**If symptoms resolving:** • Step down to oral prednisolone 60mg once daily, then wean by 10mg every 7 days until at 10mg. At this point consider clinically re-assessment and re-imagine at 8-12 weeks before considering cessation of steroid treatment. **If symptoms worsen or persist:** • Depending on clinical performance; CXR every 1-3 days • If not improving after 48 hours: re-discuss with urgently with respiratory and acute oncology, re-review all results, with advice of respiratory team can add alternative immunosupressants

* Atypical infection screening; Beta-D-Glucan, a-typical viral screen, covid swab, resp biofire, Urine legionella and pneumococcal antigen, mycoplasma serology, sputum for PJP

**steroid considerations: gastric protection, calcium and vit D supplementation, consider pneumocystistis prophylaxis and blood sugar monitoring

Additional information:

- Advice prior to starting immunotherapy:
    - If pre-existing respiratory disease: ILD increases risk of pulmonary immune-related toxicity. If you suspect patient has underlying condition please consider discussing with respiratory but do not delay starting treatment.
    - Patient may require additional screening such as baseline respiratory function.
- Who best to contact in respiratory team:
    - If non-urgent (specialist): respiratory interstitial lung disease (OP)
    - If urgent then resp consult or contact resp SpR on-call

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