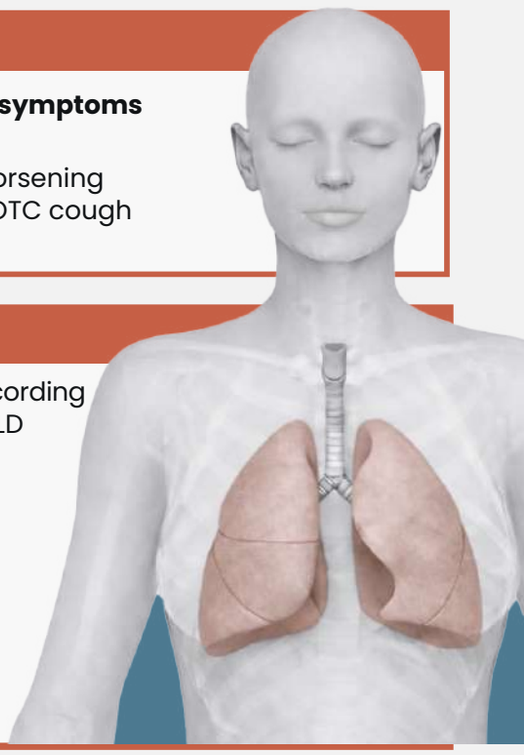
Prophylaxis, Monitoring & Management of Dato-DXd associated Adverse Events

Interstitial Lung Disease (ILD)

MONITOR

- Patients should be **monitored for new or worsening signs and symptoms of ILD/pneumonitis** during treatment with Dato-DXd
- **Educate patients to report immediately** if they have new or worsening shortness of breath, chest pain or cough (don't self-treat with OTC cough medications)



CONFIRM

- **Perform contrast-enhanced chest CT scan every 6-8 weeks** or according to institutional guidelines, and thoroughly review for any signs of ILD
- **Evaluations should include:**
  - High-resolution CT • Pulmonologist consultation (infectious disease consultation as clinically indicated)
  - Bronchoscopy and BAL if clinically indicated and feasible
  - Pulmonary function tests (including FVC and CO diffusing capacity) and pulse oximetry (SpO2)
  - Clinical laboratory tests (arterial blood gases if clinically indicated, blood culture, blood cell count, differential WBC, CRP, COVID-19 test)

MANAGE[a]

GRADE 1:

- Consider a consultation with a **pulmonologist**
- Monitor and closely **follow-up in 2-7 days** for onset of clinical symptoms and SpO2
- Consider follow-up **imaging in 1-2 weeks** (or as clinically indicated)
- Consider starting **systemic corticosteroids** (e.g., at least 0.5 mg/kg/day prednisone or equivalent) until improvement, followed by gradual taper over at least 4 weeks
- **Pause Dato-DXd** until resolved to grade 0, then:
  - **If resolved in ≤28 days** from day of onset, maintain dose
  - **If resolved in >28 days** from day of onset, reduce dose by one level

GRADE 2:

- Permanently **discontinue Dato-DXd**
- Consider a consultation with a **pulmonologist**
- Promptly start **systemic corticosteroids** (e.g., at least 1 mg/kg/day prednisone or equivalent) for at least 14 days or until complete resolution
- **Monitor symptoms** closely
- **Re-image** as clinically indicated
- If clinical or diagnostic observations worsen or do not improve in 5 days:
  - Consider **increasing corticosteroid dose** (e.g., 2 mg/kg/day prednisone or equivalent) and switching to IV administration (e.g., methylprednisolone)
  - Reconsider **additional workup** for alternative etiologies
  - **Escalate care** as clinically indicated

GRADE 3-4:

- Permanently **discontinue treatment**
- Consider a consultation with a **pulmonologist**
- **Hospitalisation** required
- Promptly initiate **intensive corticosteroid treatment** empiric high-dose methylprednisolone IV treatment (eg, 500-1000 mg/day for 3 days), followed by prednisone ≥1.0 mg/kg/day (or equivalent) for ≥14 days or until complete resolution of clinical symptoms and chest CT findings, followed by gradual taper over ≥4 weeks
- **Re-image** as clinically indicated
- If still no improvement within 3-5 days:
  - Reconsider **additional workup** for alternative etiologies
  - Consider other **immunosuppressants** and/or treat per local practice

Dato-DXd dose reduction schedule: starting dose = 6.0 mg/kg; 1st reduction = 4.0 mg/kg; 2nd reduction = 3.0 mg/kg; 3rd reduction (for patients with lung cancer only) = 2.0 mg/kg; if further dose reduction required = discontinue treatment

[a]NCI CTCAE version 5.0 grading;

BAL, bronchoalveolar lavage; CO, carbon monoxide; CRP, C-reactive protein; CT, computed tomography; Dato-DXd, datopotamab deruxtecan; FVC, forced vital capacity; ILD, interstitial lung disease; IV, intravenous; NCI CTCAE, National Cancer Institute Common Terminology Criteria for Adverse Events; OTC, over the counter; SpO2, pulse oximetry; WBC, white blood cell

References: Lisberg A, et al. Oncologist 2025; 30:oyaf225. doi: 10.1093/oncolo/oyaf225; Meric-Bernstam F, et al. Oncologist 2025; 30:oyaf031. doi: 10.1093/oncolo/oyaf031

Supported by an Independent Educational grant from AstraZeneca
March 2026