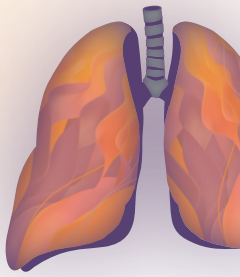
Identification and management of interstitial lung disease (ILD)/pneumonitis in patients receiving ENHERTU (trastuzumab deruxtecan) within licensed indications*

ENHERTU® trastuzumab deruxtecan



***Please refer to SmPC for more information on licensed indications[1]**

These guidelines have been developed by the UKBCG in collaboration with national ILD experts. The funding and facilitation of these guidelines was provided by Daichii Sankyo and AstraZeneca. Management decisions should be directed by the SmPC and clinical discretion. Please refer to the ENHERTU SmPC for the full list of adverse events.

ENHERTU has a conditional marketing authorisation. This means that further evidence on this medicinal product is awaited[1]

Prescribing information and adverse event reporting details can be accessed from the bottom of the next page

Why is awareness of ILD important when using ENHERTU?

- **ILD/pneumonitis can occur in patients treated with ENHERTU. However, most cases are Grade 1 or 2.[1] ILD can be managed following the guidance below**
  - In a pooled safety analysis of patients treated with ENHERTU 5.4 mg/kg (n≈2000), confirmed ILD/pneumonitis occurred in ~12% of patients. Most ILD cases were Grade 1 (~3%) or Grade 2 (~7%). Grade 3 or 4 cases occurred in ~1% of patients. Grade 5 (fatal) events occurred in ~1% of patients[1]

ENHERTU initiation and monitoring for ILD

Before ENHERTU use[2]

- Perform baseline HRCT
- Resting SpO_2
- Consider baseline PFTs (higher-risk patients*)

Patients should be advised to immediately report cough, dyspnoea, fever, and/or any new or worsening respiratory symptoms

Start ENHERTU prior to HRCT (and PFT) results

During ENHERTU use[2]

- Monitor patients via HRCT scans (every 6–9 weeks or as frequently as centres are able) and resting SpO_2
- Consider PFT monitoring in consultation with respiratory team (higher-risk patients*)

No single clinical factor definitively confirms ILD, but any of the following observations should trigger suspicion[2]

New onset or deterioration of respiratory symptoms

- Dry cough, shortness of breath (dyspnoea) particularly on exertion (exclude seasonal infections and COVID-19), other new or worsening breathing problems
- Changes in PFTs compared with baseline and recent patient measurements, reflecting decreased lung volume
- **Abnormal PFTs (such as a drop of 2% from baseline resting SpO_2) should prompt referral to an oncology nurse**

Radiological findings

- Chest radiographic abnormalities on HRCT (or equivalent), specifically the COP pattern

Biopsy findings

- Microscopic patterns of inflammation and fibrosis (on lung biopsies)

Fever

Unexplained fatigue

Identification and diagnosis of ILD in patients receiving ENHERTU

Any evidence of ILD/pneumonitis should be investigated immediately[1]

SUSPECTED ILD (any grade) due to symptoms, abnormal PFT or HRCT[2] → **Suspend ENHERTU[2]** → **Scan** using non-contrast volumetric HRCT followed by CTPA with narrow slices (1.0–1.5 mm)[2] → **Support from the MDT** including referral to a respiratory specialist[2]

***Patients are deemed high-risk if any of the following apply: Age ≥65 years, history of lung comorbidities (includes asthma, chronic obstructive pulmonary disease, prior ILD/pneumonitis, pulmonary fibrosis, pulmonary emphysema, and radiation pneumonitis), Japanese heritage, baseline SpO_2 <95%, decreased baseline renal function, history of smoking.**

COP, cryptogenic organising pneumonia; CTPA, computed tomography pulmonary angiogram; HRCT, high-resolution computed tomography; ILD, interstitial lung disease; mBC, metastatic breast cancer; MDT, multidisciplinary team; PFT, pulmonary function test; SpO_2, peripheral oxygen saturation; UKBCG, UK Breast Cancer Group.

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Management of ILD in patients receiving ENHERTU

If ILD is confirmed, act immediately and follow the management plan below[2]

	Grade 1	Grade 2	Grade 3	Grade 4
SEVERITY	**Asymptomatic[3]**	**Symptomatic[3]**		
DIAGNOSIS	Typically identified as an incidental finding of **radiographic** changes[4]	Acute onset of **new or worsening pulmonary** or other **related signs/ symptoms** such as **dyspnoea, cough** or **fever**[4]	**Severe** pulmonary symptoms limiting self-care activities of daily living; oxygen indicated[3]	**Life-threatening** respiratory compromise[3]
TREATMENT MODIFICATIONS	**WITHHOLD ENHERTU UNTIL RECOVERY (RESOLVED TO GRADE 0)*** ➤ If resolved in ≤28 days from date of onset, maintain dose ➤ If resolved in >28 days from date of onset, reduce dose one level* ➤ If ILD/pneumonitis occurs beyond day 22 and has not resolved within 49 days from the last infusion, discontinue ENHERTU	**PERMANENTLY DISCONTINUE ENHERTU IN PATIENTS WHO ARE DIAGNOSED WITH ANY SYMPTOMATIC (≥GRADE 2) ILD/PNEUMONITIS[2]**		
TOXICITY MANAGEMENT	**Consider initiating systemic steroids** (e.g. **≥0.5 mg/kg/day** prednisone or equivalent)[2]	**Initiate systemic steroids** (e.g. **≥1.0 mg/kg/day** prednisone or equivalent)[2]	**Initiate empiric high-dose methylprednisolone IV treatment** (e.g. 500–1,000 mg/day for 3 days), followed by **≥1.0 mg/kg/day** of prednisone (or equivalent)[2]	
	Until complete resolution of clinical symptoms and chest HRCT findings, followed by gradual taper over at least 4 weeks[2]			
	Monitor and closely **follow up in 2–7 days** for onset of clinical symptoms and pulse oximetry[2]	**Monitor symptoms** closely[2]	**Hospitalisation required[2]**	
	Consider **follow-up imaging in 1–2 weeks** (or as clinically indicated)[2]	**Re-image as clinically indicated[2]**	**Re-image as clinically indicated[2]**	
	If **diagnostic observations continue to worsen** despite initiation of corticosteroids, then **follow Grade 2 guidelines[2]**	If **worsening or no improvement** in clinical or diagnostic observations in 5 days:[2] ➤ **Consider increasing dose of steroids** (e.g. 2.0 mg/kg/day prednisone or equivalent) and administration may be switched to IV (e.g. methylprednisolone) followed by a **gradual taper over at least 4 weeks** ➤ **Re-consider additional work-up for alternative aetiologies** as described above ➤ **Escalate care** as clinically indicated	If still no improvement within 3 to 5 days:[2] ➤ **Re-consider additional work-up for alternative aetiologies** as described above ➤ **Consider other immuno-suppressants** and/or treat as per local practice	

*If patient is currently receiving 5.4 mg/kg dose, reduce to 4.4 mg/kg; if patient is currently receiving 4.4 mg/kg, reduce to 3.2 mg/kg[1]

Based on UKBCG guidelines, Common Terminology Criteria for Adverse Events (CTCAE) v5.0 and a review article containing expert perspectives on the management of ILD[2–4]

www.ENHERTU.co.uk

Scan this QR code (if viewing hardcopy) or click the URL above (if viewing digitally) for more information on ENHERTU (trastuzumab deruxtecan) clinical trials, expert opinions, helpful resources and more! This is a promotional website developed and funded by DS and AZ intended for UK HCPs only

ENHERTU UK PI

Scan this QR code (if viewing hard copy) or click this link (if viewing digitally) to access Prescribing Information and Adverse Event Reporting details

References

1. ENHERTU (trastuzumab deruxtecan). Summary of Product Characteristics; 2. UK Breast Cancer Group. Interstitial lung disease (ILD) guidance 2024; 3. US Department of Health and Human Services. Common Terminology Criteria for Adverse Events (CTCAE) Version 5.0. 2017; 4. Swain SM, et al. Cancer Treat Rev. 2022;106:102378.

HRCT, high-resolution computed tomography; IV, intravenous; ILD, interstitial lung disease; UKBCG, UK Breast Cancer Group.

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