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HRCT and MRI in Drug-Induced Interstitial Lung Disease: A Comprehensive Independent Systematic Review and Network Meta-Analysis of Imaging Pattern Distribution, Agent-Specific Incidence, and Reversibility Outcomes from January 2000 Through May 2026

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ADMINISTRATIVE INFORMATION

Support - Self-funded. University of Hail College of Pharmacy academic resources. No pharmaceutical industry or commercial funding received.

Review Stage at time of this submission - The review has not yet started.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY202660023

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 5 June 2026 and was last updated on 5 June 2026.

INTRODUCTION

Review question / Objective What are the HRCT pattern distributions and agent-specific ILD incidence estimates across ICI, TKI, ADC, and cytotoxic drug classes, and what is the network meta-analysis estimate of ICI pneumonitis risk by agent?

Rationale This systematic review addresses a critical evidence gap in radiological pharmacovigilance. No comprehensive synthesis with pre-specified pattern analyses exists for this topic. Prospective registration ensures transparency and minimises reporting bias.

Condition being studied Drug-induced interstitial lung disease (DIILD) including ICI pneumonitis, TKI-associated ILD, ADC-induced ILD, cytotoxic drug ILD, and amiodarone pulmonary toxicity.

METHODS

Search strategy PubMed/MEDLINE, Embase, Cochrane CENTRAL, Web of Science, and Scopus from January 1, 2000 to May 31, 2026. ClinicalTrials.gov and WHO-ICTRP on May 31, 2026. Key terms: drug-induced interstitial lung disease, DIILD, ICI pneumonitis, checkpoint inhibitor ILD, T-DXd ILD, trastuzumab deruxtecan, EGFR-TKI ILD, HRCT, organising pneumonia, NSIP, DAD, bleomycin, amiodarone pulmonary toxicity, radiological reversibility.

Participant or population Adults aged 18 years or above with confirmed DIILD from immune checkpoint inhibitors, tyrosine kinase inhibitors, antibody-drug conjugates (including T-DXd), cytotoxic chemotherapy, amiodarone, or other pharmacological agents, with HRCT or MRI data available.

Intervention High-resolution computed tomography (HRCT) or MRI for characterisation, pattern classification, severity grading, and monitoring of drug-induced interstitial lung disease.

Comparator Clinical diagnosis, bronchoalveolar lavage cytology, or surgical lung biopsy as

reference standard; pre-treatment baseline HRCT for reversibility assessment; cross-agent comparison in network meta-analysis.

Study designs to be included RCT imaging substudies; prospective cohort studies (n≥20 DIILD cases); retrospective cohort studies (n≥20); adequately sized case series (n≥10 with extractable HRCT pattern data).

Eligibility criteria Inclusion: Adults with confirmed DIILD (clinical consensus, BAL, or biopsy); any pharmacological causative agent; HRCT or MRI data with extractable pattern frequencies.Exclusion: Studies without imaging data; non-drug-induced ILD; paediatric populations; case reports (n<10); studies without extractable outcome data.

Information sources PubMed/MEDLINE, Embase, Cochrane CENTRAL, Web of Science, Scopus, ClinicalTrials.gov, WHO-ICTRP.

Main outcome(s) HRCT pattern distribution (organising pneumonia, NSIP, hypersensitivity pneumonitis-like, UIP-like, DAD) by drug class; agent-specific ICI pneumonitis odds ratio from NMA; T-DXd ILD pooled incidence; pattern-specific complete radiological reversibility rates.

Additional outcome(s) EGFR-TKI ILD incidence by ethnicity; CRT plus ICI combined pneumonitis rate; HRCT severity grade correlation with clinical outcomes; SWI/imaging features predicting irreversible injury.

Data management Data will be managed using Covidence for screening and Rayyan for deduplication. Extracted data stored in pre-piloted Excel forms. Two reviewers screen and extract independently; disagreements resolved by consensus.

Quality assessment / Risk of bias analysis Diagnostic accuracy studies: QUADAS-2 (four domains: patient selection, index test, reference standard, flow and timing). Cohort studies: Newcastle-Ottawa Scale (threshold ≥5 stars). Overall certainty of evidence rated using GRADE per primary outcome.

Strategy of data synthesis Frequentist random-effects NMA using netmeta R package for ICI pneumonitis agent comparisons. Freeman-Tukey double arcsine transformation for proportions under DerSimonian-Laird random effects. SUCRA rankings for agent-level ICI pneumonitis risk. Pattern-specific reversibility pooled as proportions.

Subgroup analysis Drug class (ICI vs TKI vs ADC vs cytotoxic vs amiodarone); ICI combination vs monotherapy; EGFR-TKI by ethnicity (Asian vs non-Asian); CRT plus ICI vs ICI alone; baseline HRCT pattern vs reversibility outcome.

Sensitivity analysis Restriction to prospective cohort studies only; exclusion of case series; restriction to HRCT studies with standardised acquisition protocols; exclusion of studies using non-HRCT chest CT.

Language restriction No language restriction.

Country(ies) involved Saudi Arabia.

Other relevant information Thoracic Radiology; Oncological Imaging; Clinical Pharmacy; Pulmonology; Pharmacovigilance.

Keywords drug-induced interstitial lung disease; DIILD; HRCT; MRI; ICI pneumonitis; trastuzumab deruxtecan; EGFR-TKI; organising pneumonia; network meta-analysis; systematic.

Dissemination plans Peer-reviewed publication in a high-impact radiology, nuclear medicine, or clinical pharmacology journal; open-access preferred.

Contributions of each author

Author 1 - Abdulrahman Alanazi - Conceived and designed the study, drafted the protocol, will lead data extraction and synthesis, and drafted the manuscript.
Email: aas2@hotmail.com
Author 2 - Basmah Alanazi - Contributed to the development of the selection criteria, will assist with data extraction and risk of bias assessment, and validity.
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