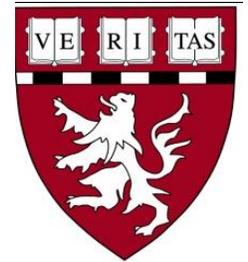


Lung Cancer in Patients with ILD: Diagnostic and Management Considerations



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Disclosures

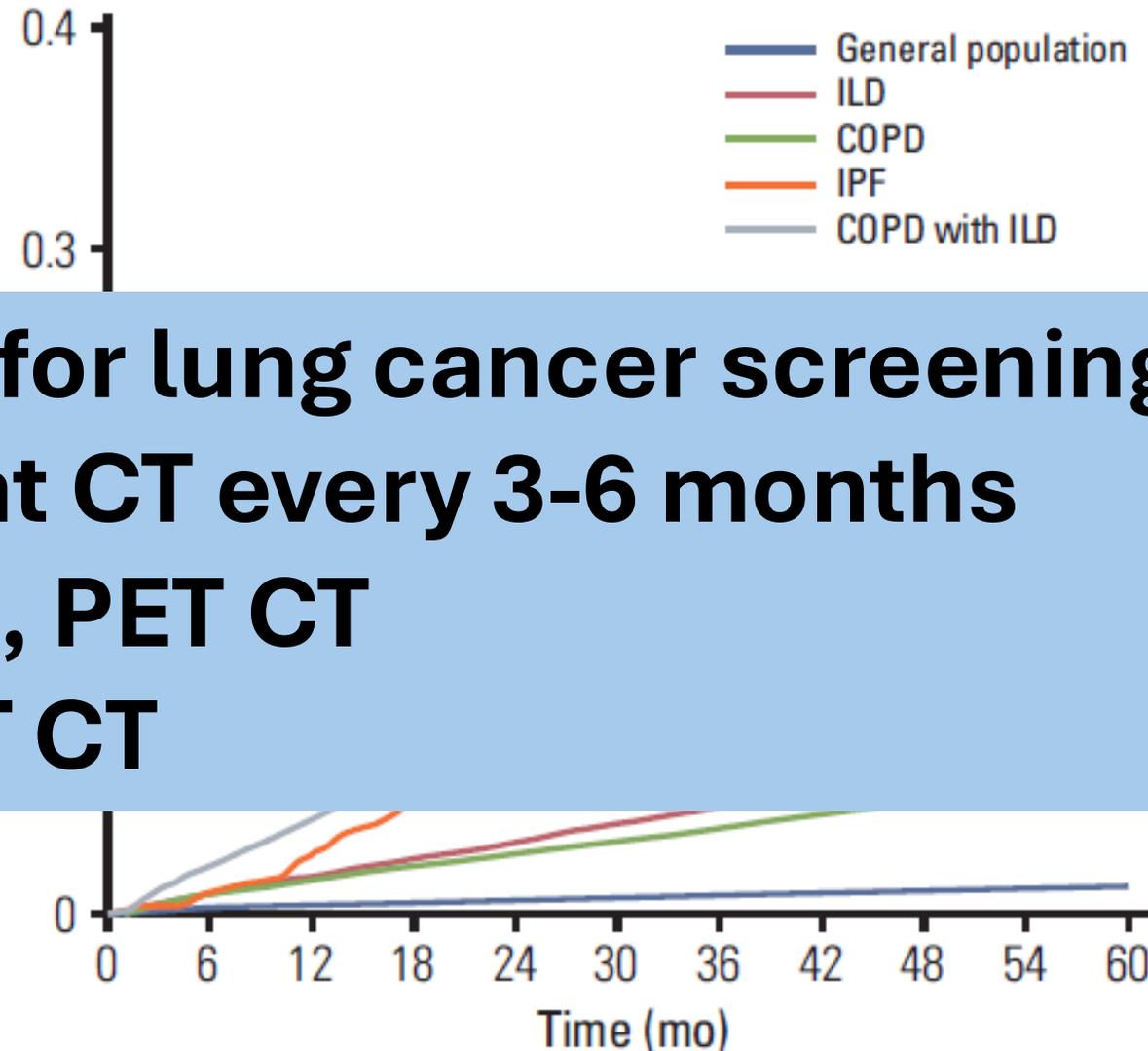
- None

Epidemiology

- Estimated up to 22% of patients with ILD will eventually develop lung

- **Mandatory annual CT for lung cancer screening**
- **Nodules <8mm, repeat CT every 3-6 months**
- **Progression of nodule, PET CT**
- **Nodules $\geq 8\text{mm}$, PET CT**

pack-year smoker cohort



Original Investigation | Oncology

Interstitial Lung Disease and Risk of Lung Cancer

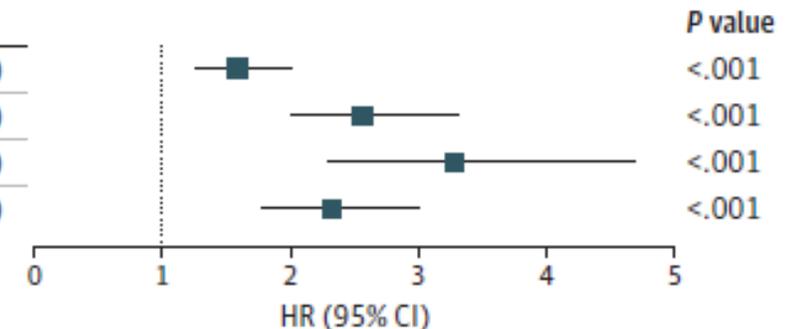
Hui Xu, MD; Li Yin, PhD; Weiwei Bian, MPH; Mingqiang Kang, MD, PhD; Hans-Olov Adami, MD, PhD; Weimin Ye, MD, PhD

Table 2. IR and HR for Association of Lung Cancer With ILD (1-Year Lag Time)

Diagnosis with ILD	Population comparison		Sibling comparison	
	No. of cases with lung cancer/IR per 100 000 person-years	HR (95% CI) ^a	No. of cases with lung cancer /IR per 100 000 person-years	HR (95% CI) ^b
No	40 592/26.2	1 [Reference]	682/82.4	1 [Reference]
Yes	227/355.4	2.16 (1.89-2.46)	145/343.1	2.91 (1.98-4.27)

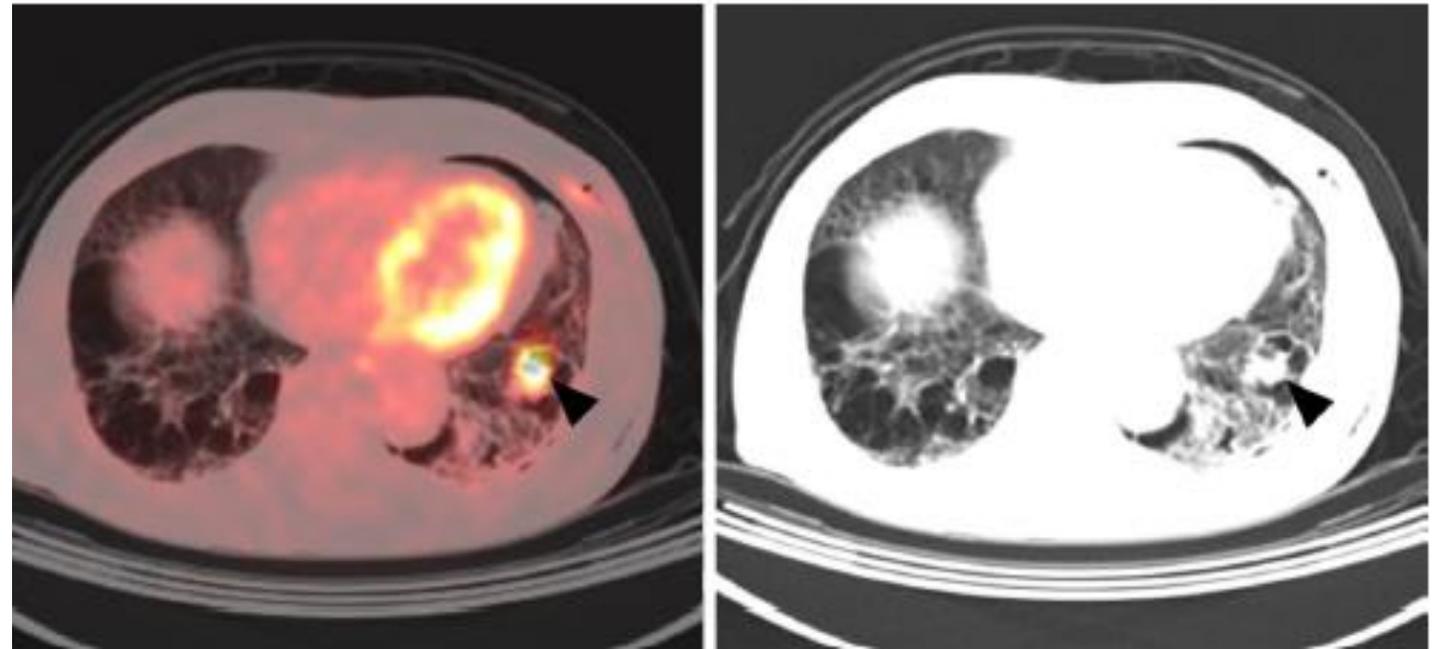
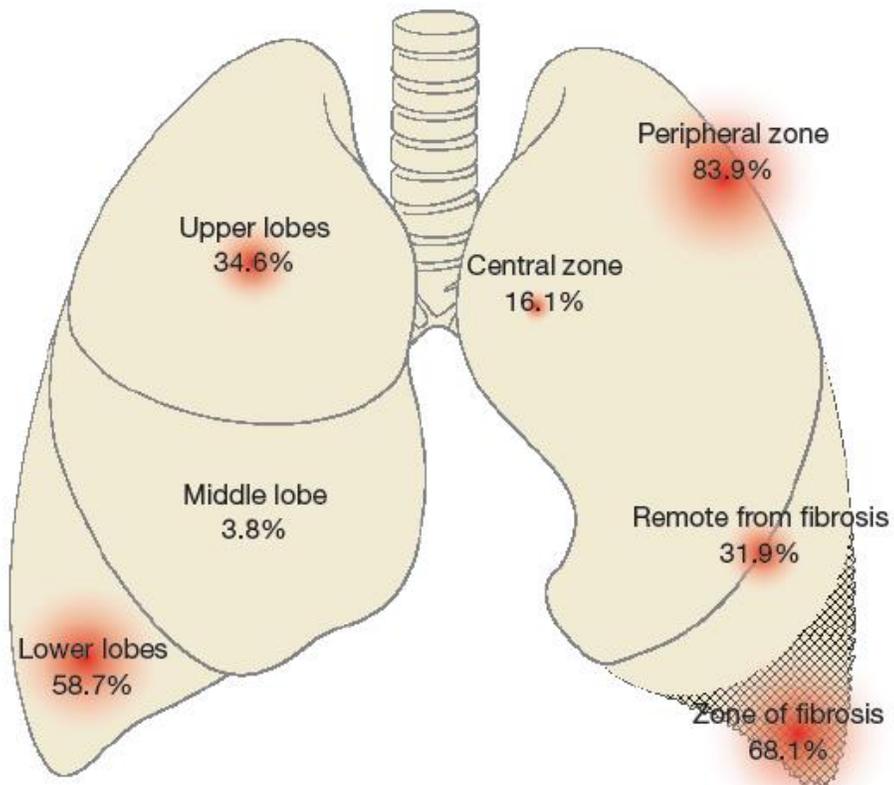
A Population comparison

Histological subtype	No. of lung cancer cases/IR	HR (95% CI)
Adenocarcinoma	75/116.7	1.60 (1.28-2.01)
Squamous cell carcinoma	63/97.8	2.56 (1.99-3.29)
Small cell carcinoma	32/49.6	3.29 (2.32-4.68)
Other ^a	57/88.6	2.32 (1.78-3.01)



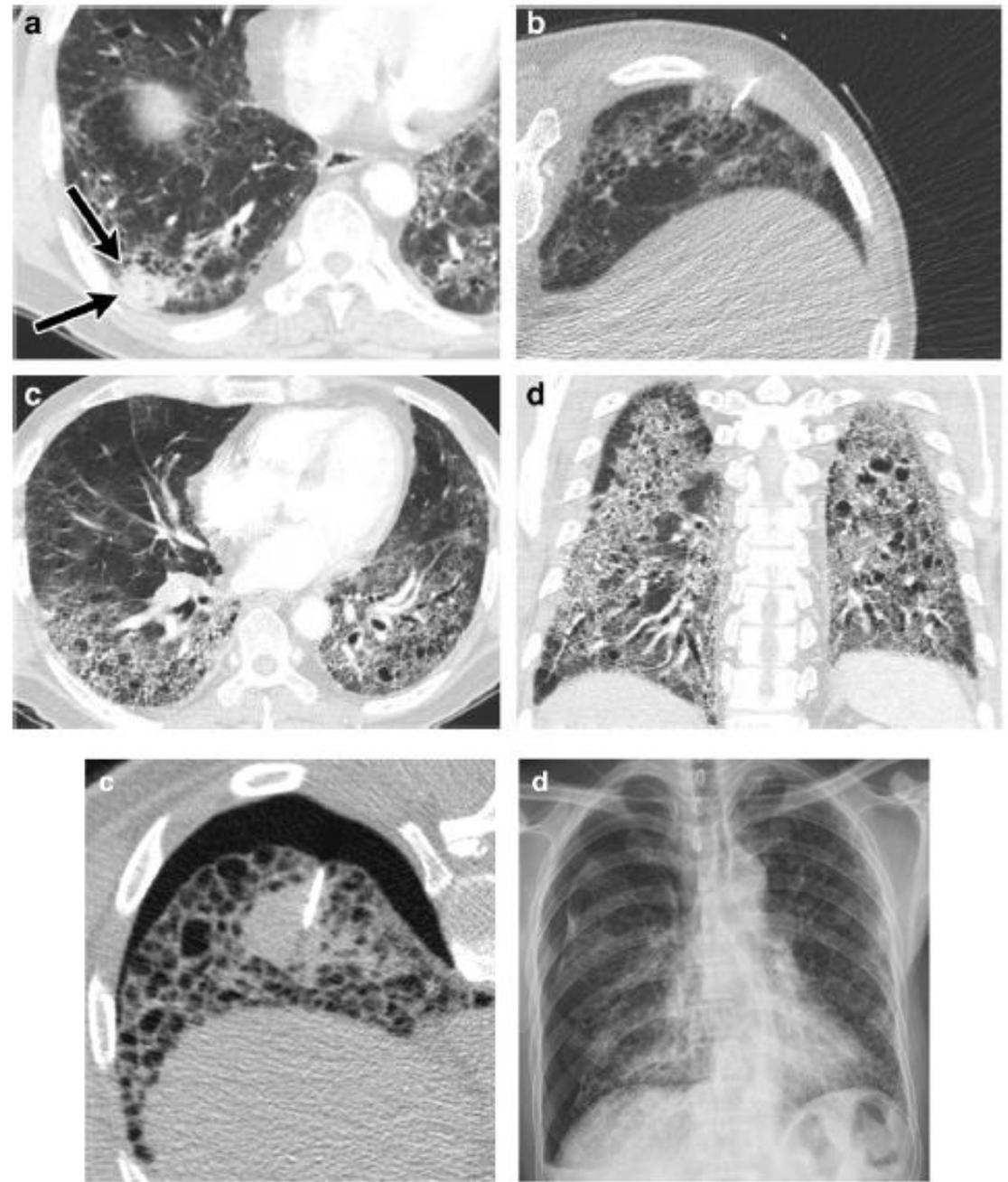
Diagnostic Considerations

- Early detection is important but challenging
- PET/CT demonstrates high sensitivity/specificity (98/86%) in IPF



Diagnostic Considerations

- CT-guided transthoracic needle biopsy demonstrates high diagnostic accuracy
 - Need to consider relatively high complication rate
 - Acute-exacerbation
 - Pneumothorax requiring chest tube
- Increasing use of advanced bronchoscopic techniques for diagnosis of peripheral lesions



Management Considerations

- Surgical Resection
- Radiation Therapy
- Percutaneous Ablation
- Systemic Therapy
- Immunotherapy

Surgical Resection: Short-term complications

- Increased short-term morbidity and mortality
 - AE-ILD: Incidence 9-23%, onset 2-10 days post-op, high mortality (up to 60%)

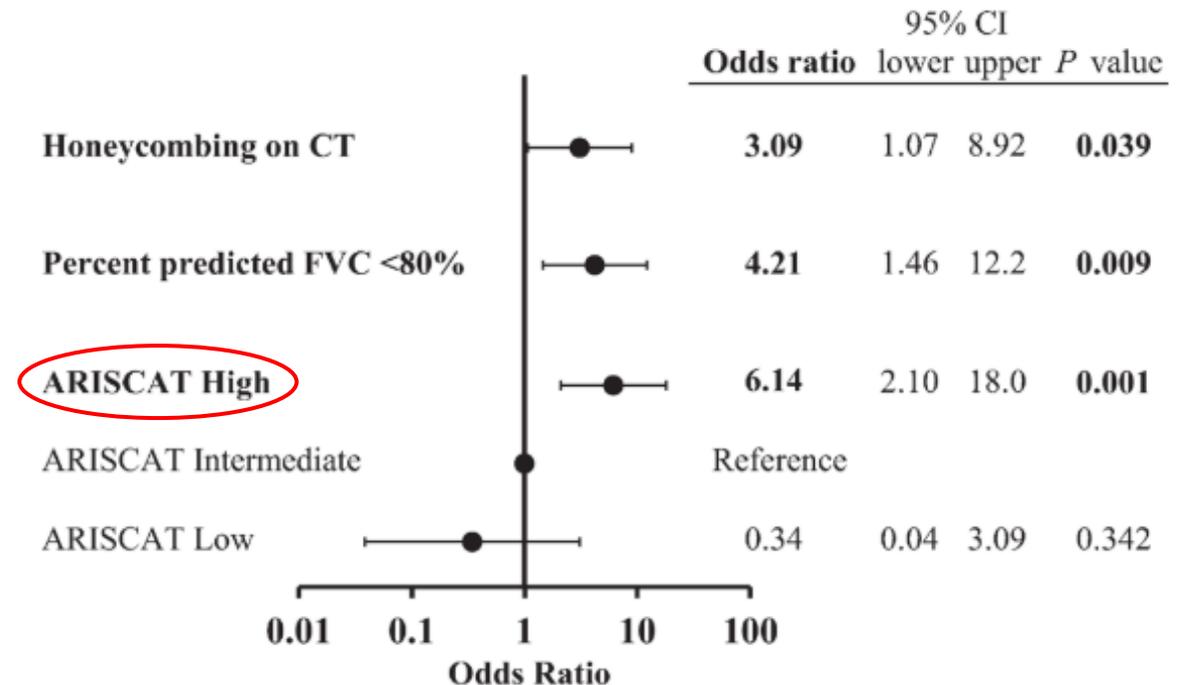
- Risk factors:

- Patient factors

- Severity of ILD (FVC, DLCO)
 - Pattern of ILD (UIP)
 - ARISCAT score (>45)

- Procedural-based factors

- Sublobar vs lobar resection



Hosoki et al. BMJ. 2020.

Sato et al. J Thorac Cardiovasc Surg. 2015;149:64-70.

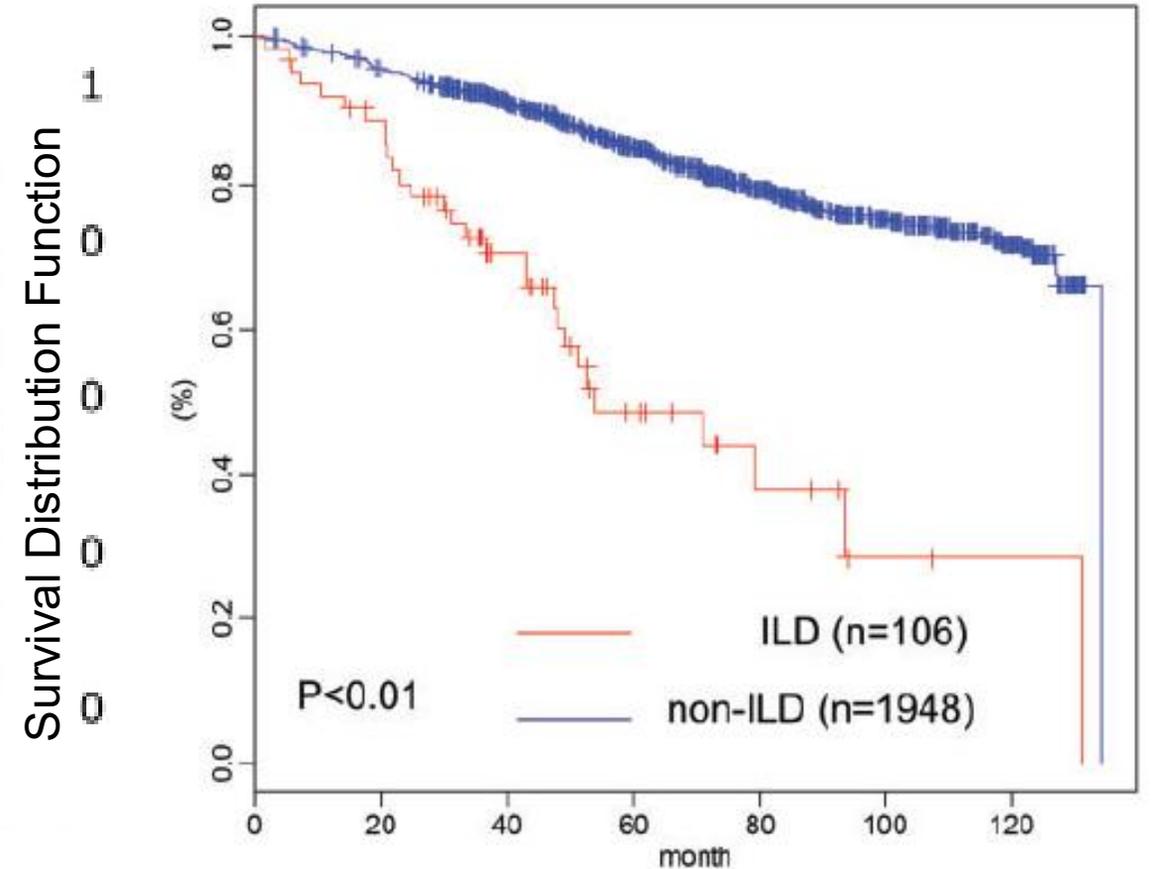
Sato et al. BMC Pulm Med. 2018;18(1):134.

Surgical Resection: Long-term survival

Patients with ILD:

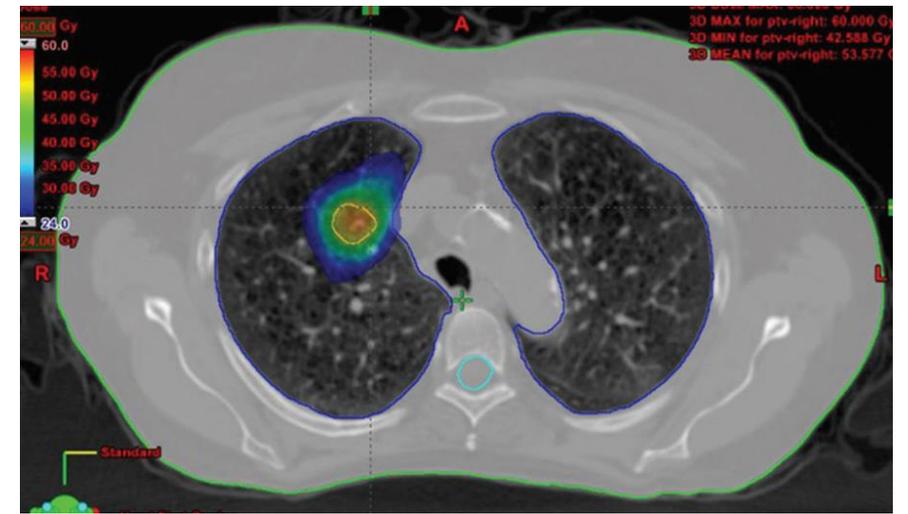
- More likely to undergo limited resection
 - Higher frequency of recurrence
 - Limited use of systemic therapy w/ recurrence
-
- Main cause of death was lung cancer
 - 5 year OS stage I: 44% vs 85%

OS in patients with Stage I disease

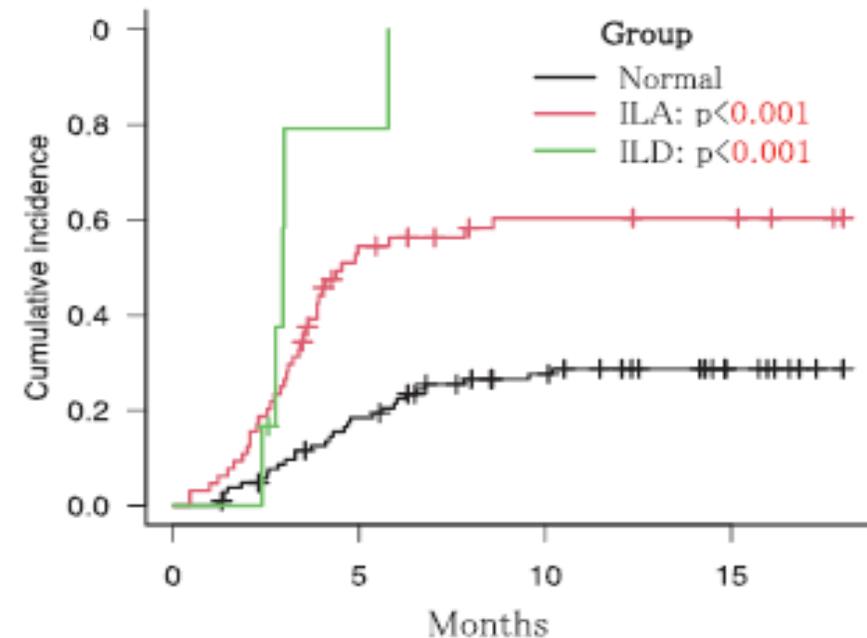


Radiation Therapy

- Standard of care for patients with early-stage NSCLC considered medically inoperable
- Data w/ ILD limited to retrospective studies, significant heterogeneity
- Even in pts with subclinical, asymptomatic ILD (ILA), thought to carry significant toxicity



Cumulative incidence of grade ≥ 2 radiation pneumonitis



Radiation Therapy

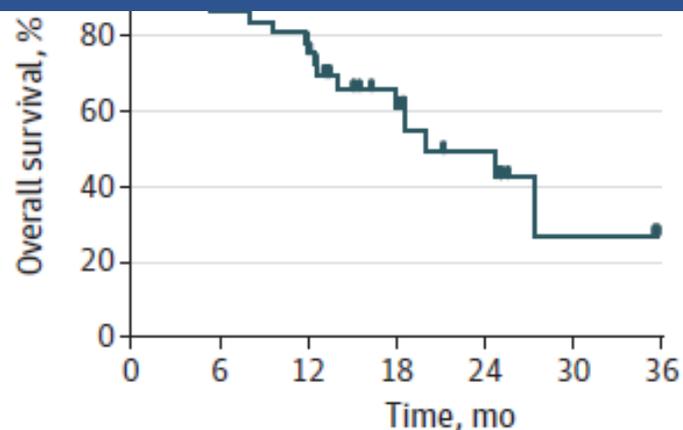
ASPIRE-ILD

- 39 pts with pre-existing ILD treated w/ stereotactic ablative radiotherapy (SABR)
- OS at 1 year 79%; Median OS 25 months; 2 year local control 92%
 - Median survival more than double the expected median survival in untreated patients
- Risk of grade 3-5 toxicity half previously reported in prior systemic reviews



National Library of Medicine
National Center for Biotechnology Information

Reducing Respiratory Symptoms of Pulmonary Irradiation in Interstitial Lung Disease (RESPIRE-ILD)



Large/Central Tumors

Poor performance status

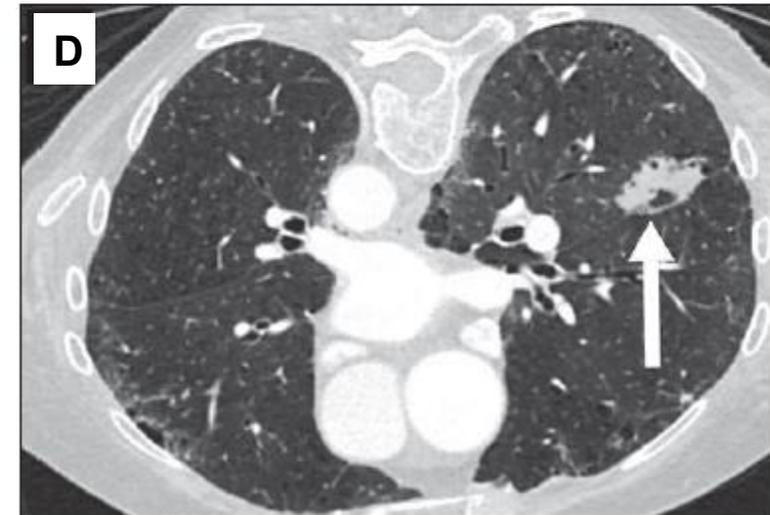
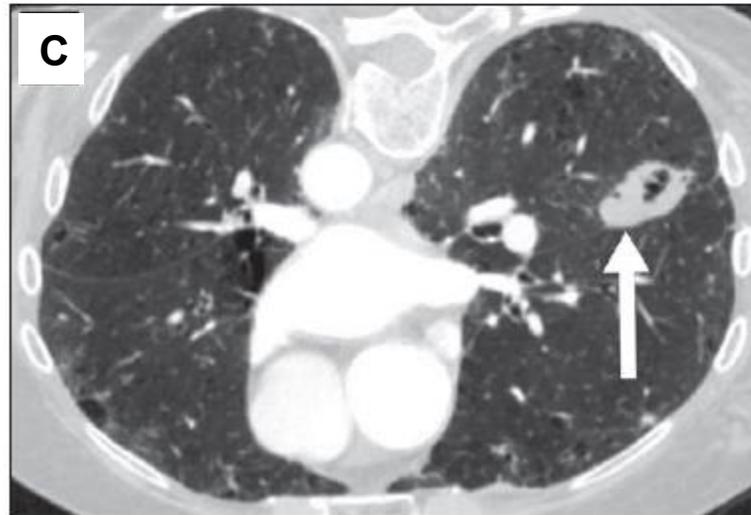
IPF vs CTD-ILD diagnosis

High ILD-GAP Score

High lung density adjacent to tumor

Percutaneous ablation

- Safety considerations:
 - Rate of major AE 14%
 - Bronchopleural fistula, pneumothorax, hemothorax, hemoptysis
 - No AE-ILD or death within 90 days
- Outcomes:
 - Local control 78% at 1 year
 - OS 77% at 1 year



Systemic Therapy

Limited data in this patient population, but first-line platinum doublet therapy for advanced NSCLC shown to be relatively safe and effective

- Pooled ORR 43%, 1 year OS 33%
- Pooled AE-ILD rate 8%; significant correlation with 1 yr survival

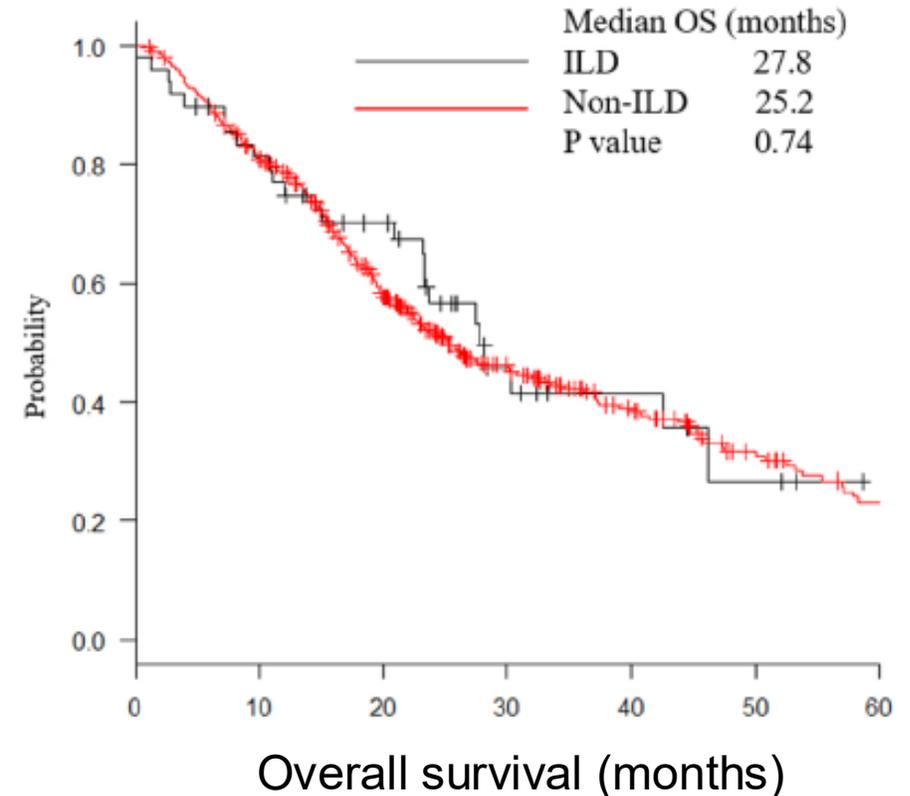
Combination chemo- and radiotherapy increase the risk of pneumonitis in patients with ILD

Rates of AE-ILD shown to be considerably higher with certain second-line agents

	UIP Pattern	
	No. of Patients Administered	Exacerbation of ILD (%)
Cisplatin	21	2 (10)
Carboplatin	40	5 (13)
Paclitaxel	31	1 (3)
Docetaxel	25	7 (28)
Etoposide	21	5 (24)
Vinorelbine	13	0
Gemcitabine	7	3 (43)
S-1	7	2 (29)
Irinotecan	6	2 (33)
Amrubicin	4	0
Pemetrexed	2	1 (50)

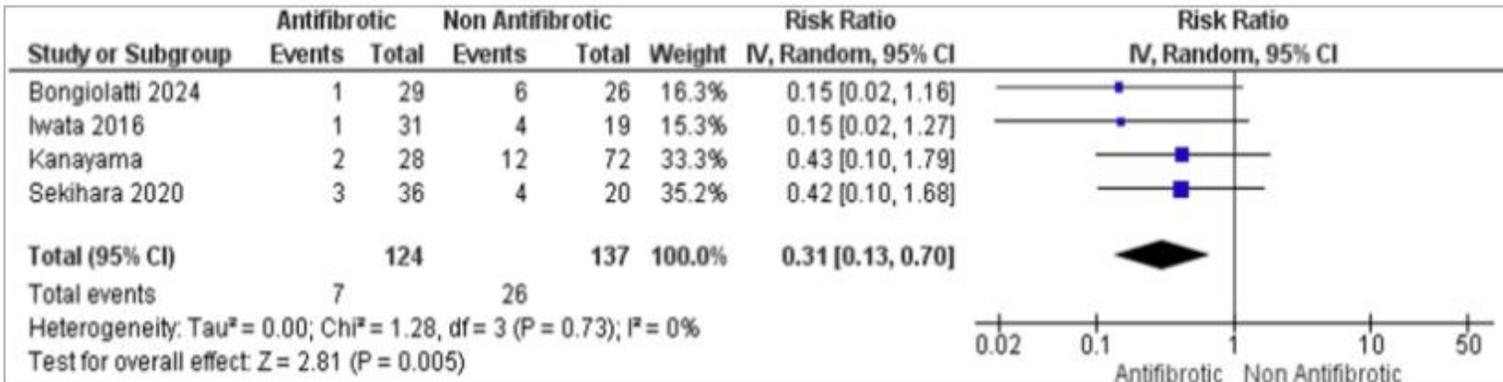
Immunotherapy

- Increased risk of pneumonitis
 - Incidence of all grade pneumonitis 27% vs 10%
 - Incidence of >grade 3 pneumonitis 15% vs 4%
- Non-inferior outcomes
 - Majority improve upon ICI discontinuation +/- corticosteroid administration
 - Similar disease control rates, progression free survival, overall survival
- Patients need to be informed and closely monitored
 - Can we better risk stratify these patients?
 - Radiographic pattern, severity of ILD

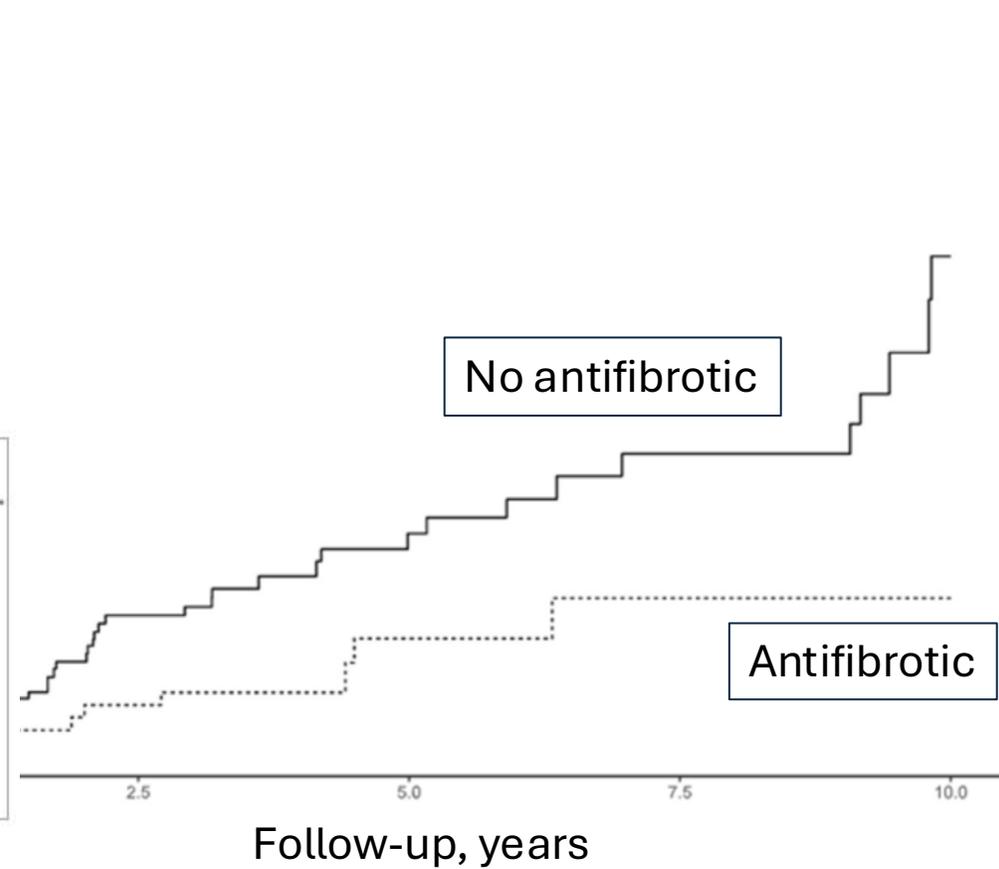


Role of antifibrotics

- Lower lung cancer incidence
- Combination with chemotherapy
- Reduction in post-operative AE-IPF



Incidence of Lung Cancer



Iwata et al. *Resp Res.* 2016;17:90
 Jo et al. *J Thorac Dis.* 2024;16(12):8528-8537.
 Rimner et al. *Int J Radiat Oncol.* 2023;116:1091-1099.
 Kijlertsuphasri et al. *BMJ Thorax.* 2026.

Summary

- Patients with ILD are at increased risk for lung cancer
- Diagnosis is complex due to underlying parenchymal abnormalities
- Regardless of treatment, patients with ILD experience higher treatment-related morbidity and mortality
 - Major concern AE-ILD
- Patients with ILD require multidisciplinary evaluation to determine a personalized treatment plan tailored to their goals of care