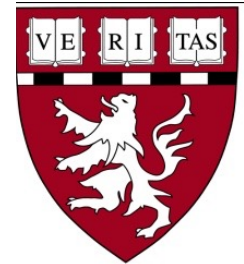


Lung Cancer in Patients with ILD: Diagnostic and Management Considerations



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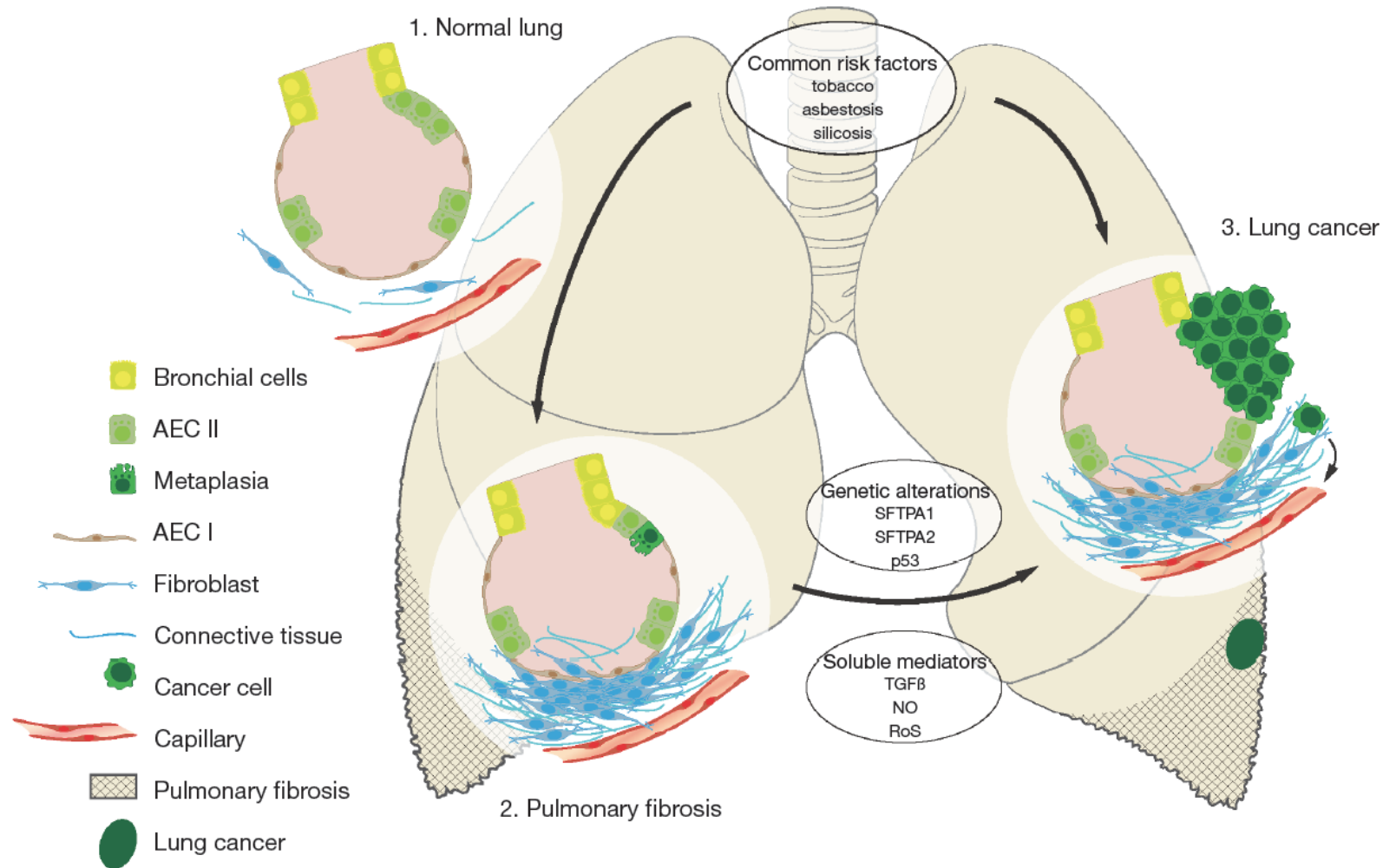
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Disclosures

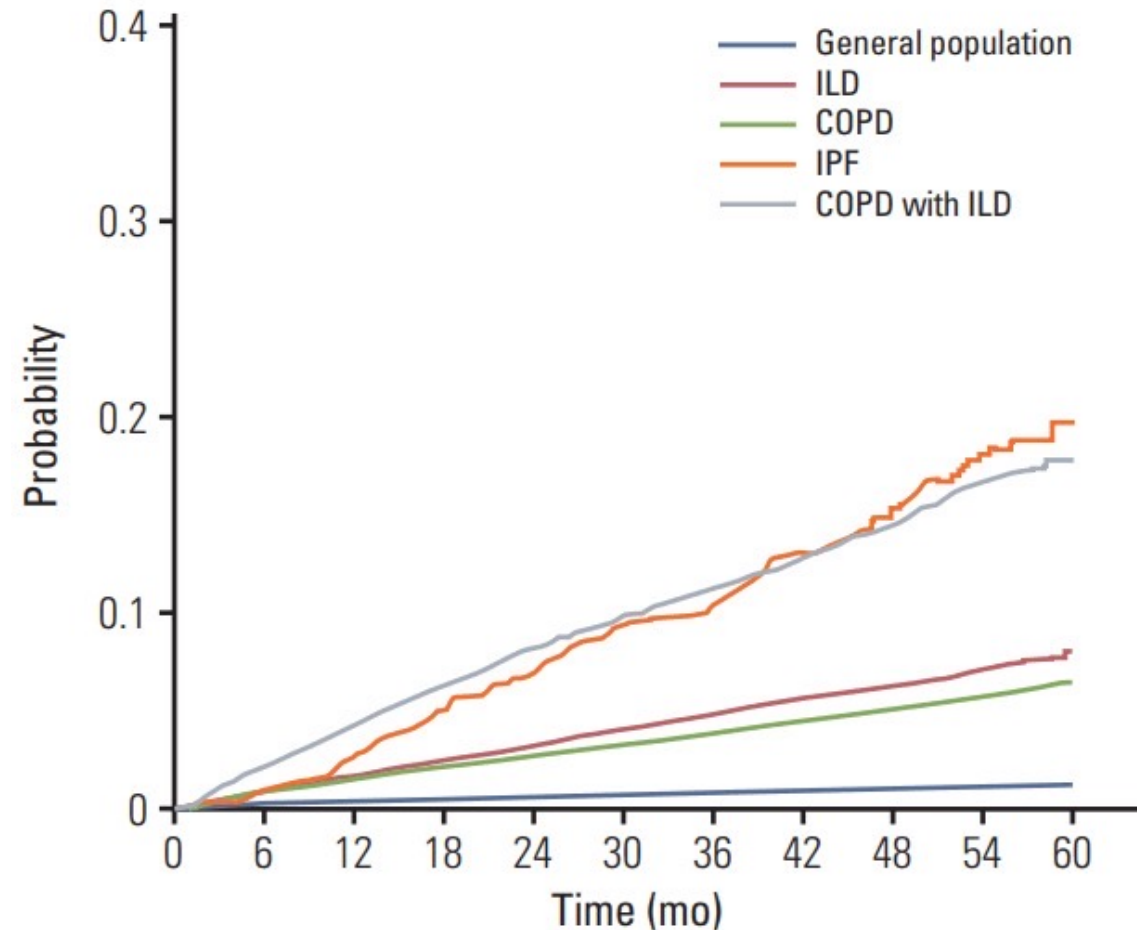
- None

Increased risk of lung cancer in ILD



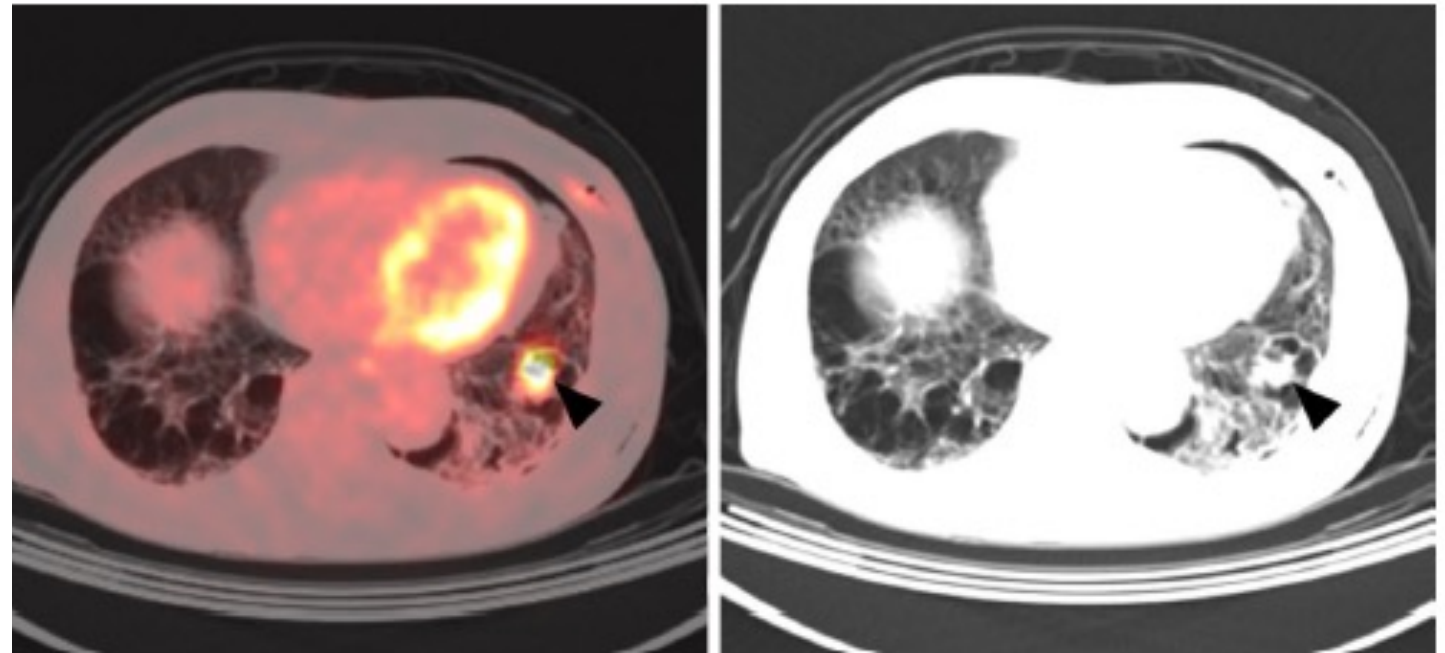
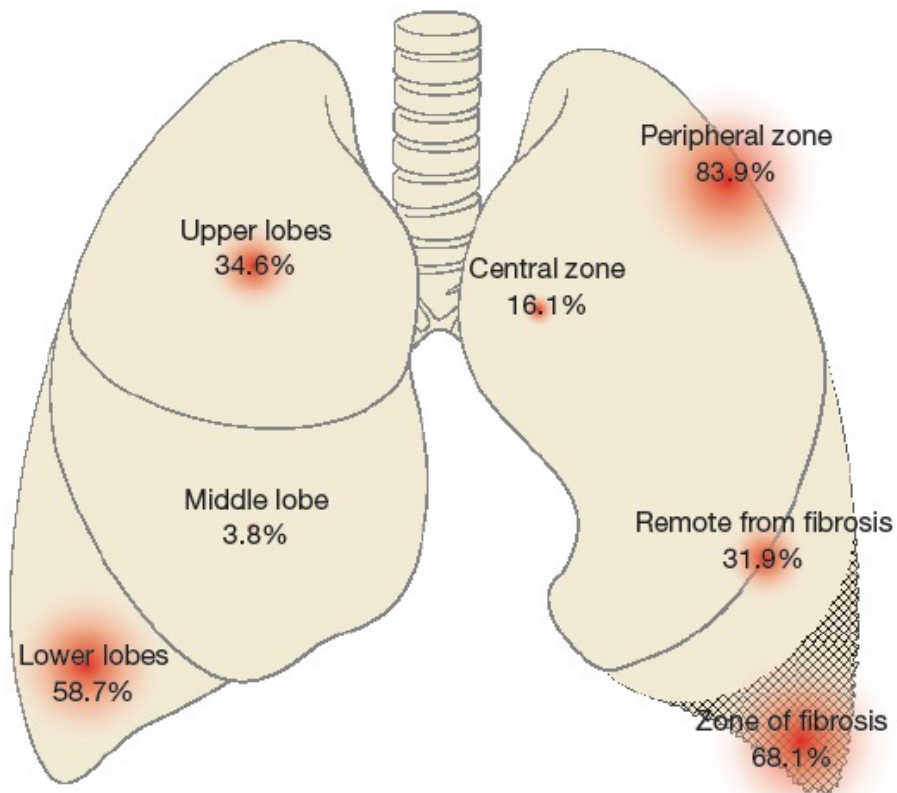
Epidemiology

- Estimated 22% of patients with ILD will eventually develop lung cancer
- Estimated prevalence in IPF 13.5%, higher rates in men and smokers
 - Cumulative incidence increases over time from diagnosis
- Higher rates in CTD-ILD vs non-CTD ILD (excluding IPF), ILA
- Most common subtypes:
 - Squamous cell carcinoma (37.8%), adenocarcinoma (30.8%)



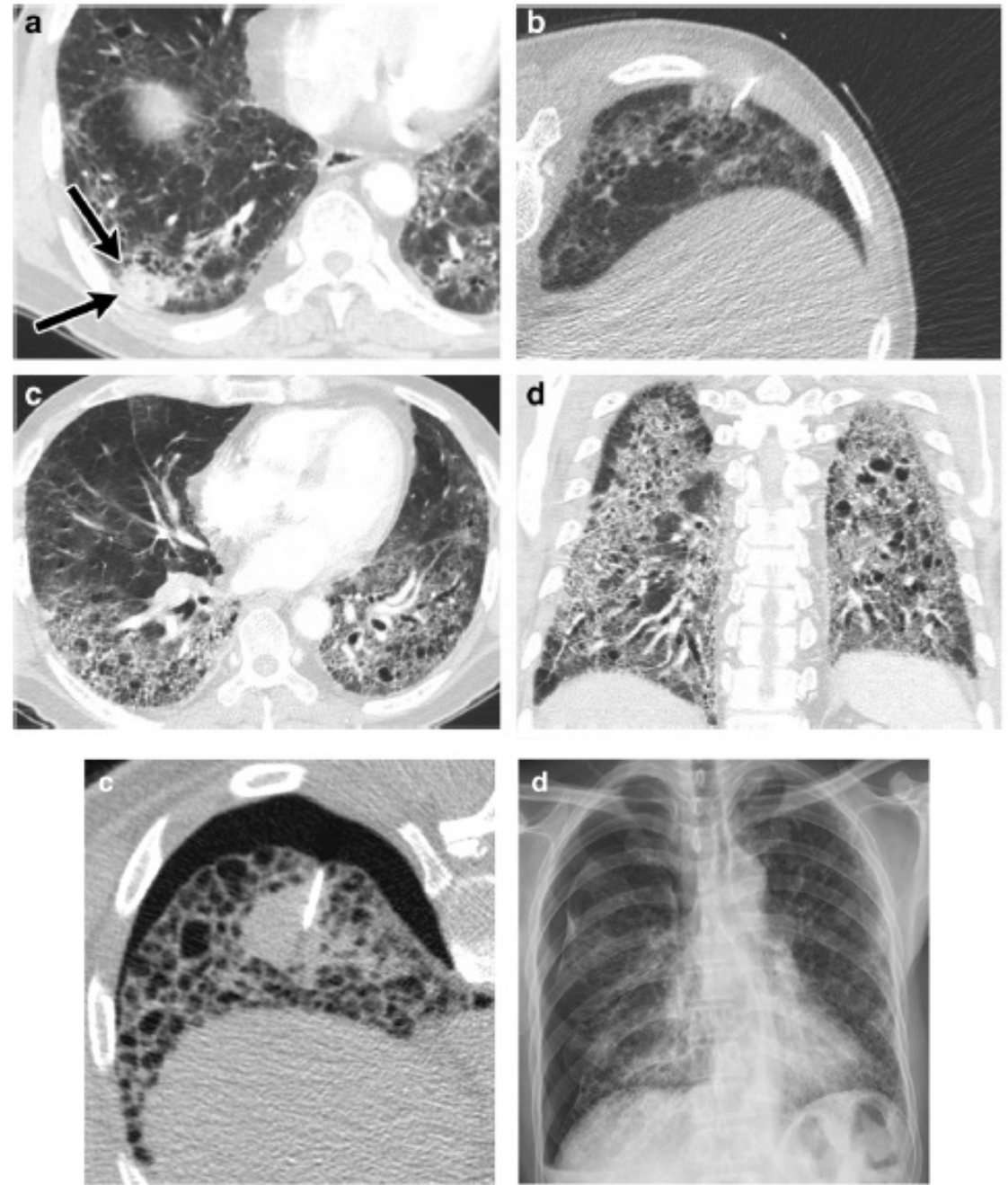
Diagnostic Considerations

- Early detection is important but challenging
- PET/CT demonstrates high sensitivity/specificity in IPF



Diagnostic Considerations

- CT-guided transthoracic needle biopsy demonstrates 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

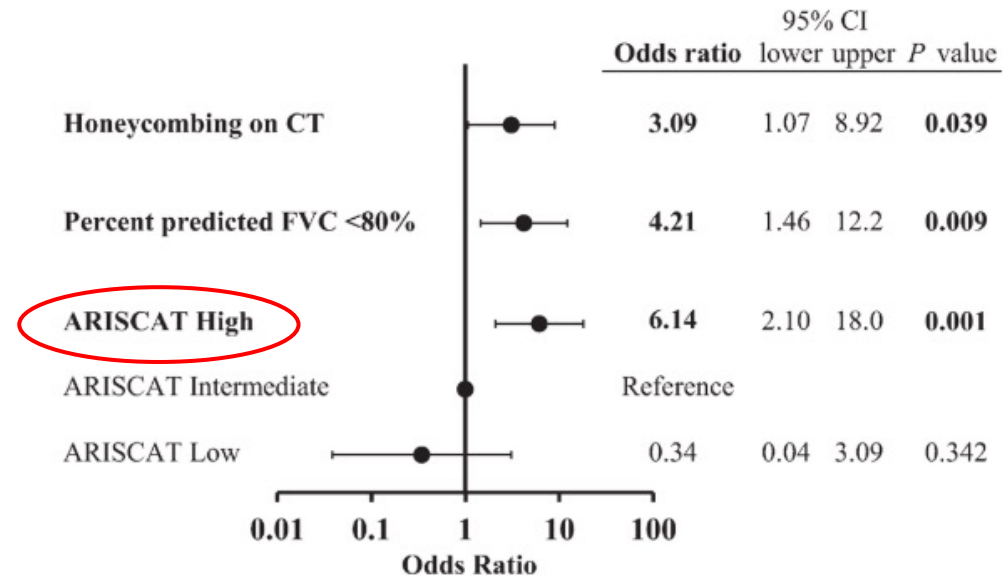
- Surgical Resection
- Radiation Therapy
- Percutaneous Ablation
- Systemic Therapy
- Immunotherapy

Surgical Resection: Short-term complications

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

- Risk factors:

- Pulmonary factors
 - Severity of ILD (FVC, DLCO)
 - Pattern of ILD (UIP)
 - Use of supplemental oxygen
- Procedural-based factors
 - Sublobar vs lobar resection



Surgical Resection: Long-term survival

Patients with ILD:

- More likely to undergo limited resection
- Less likely to receive neoadjuvant therapy



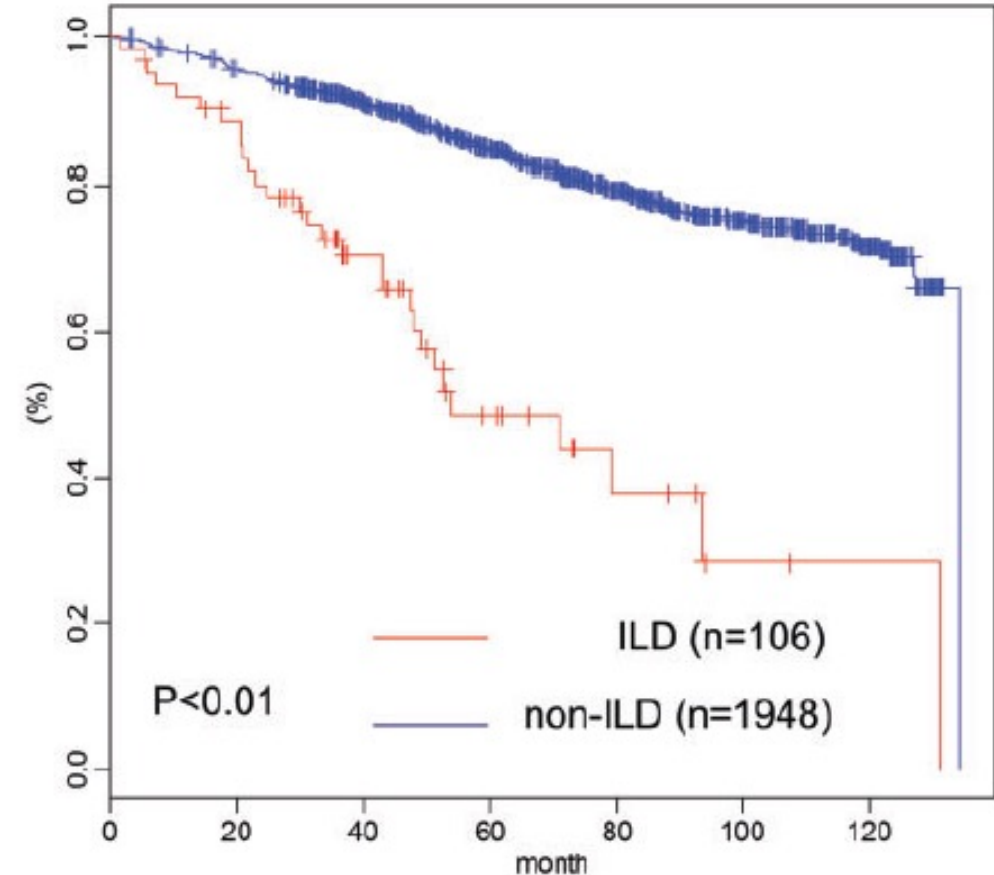
- Higher frequency of recurrence
- Limited use of systemic therapy w/ recurrence



- Main cause of death was lung cancer
 - 5 year OS: 40% vs 72%
 - 5 year OS stage I: 44% vs 85%

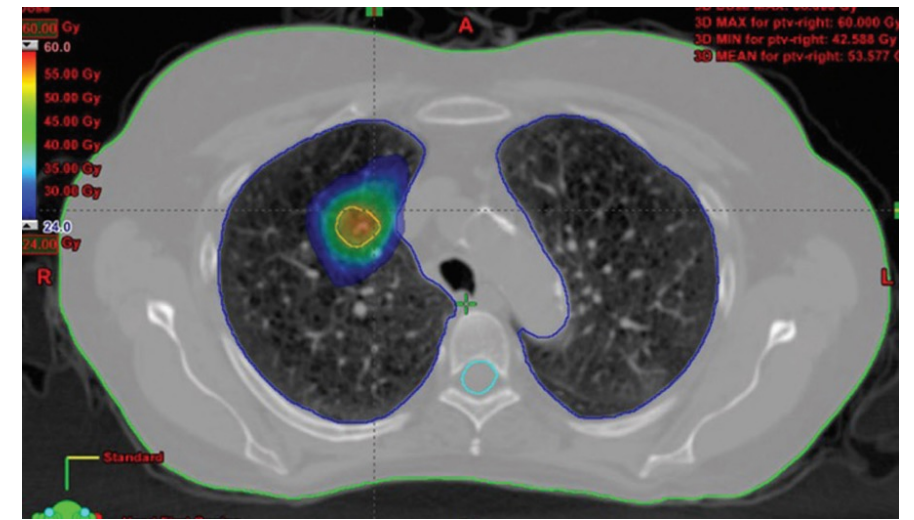
- Use of antifibrotics?

OS in patients with Stage I disease

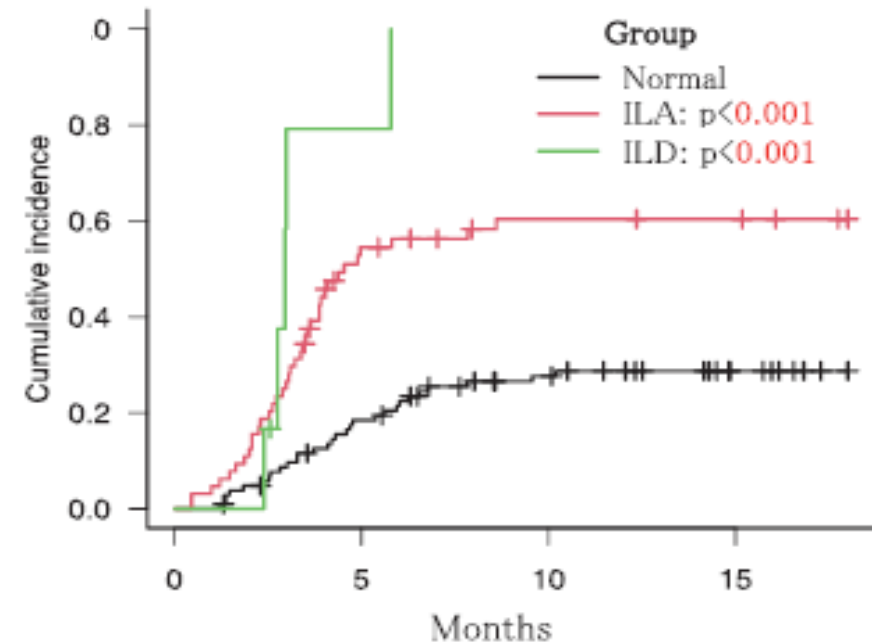


Radiation Therapy

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



Cumulative incidence of grade ≥ 2 radiation pneumonitis



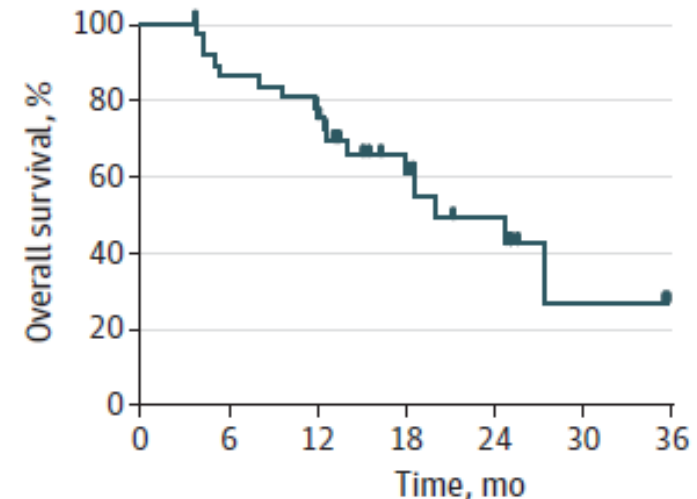
Radiation Therapy

ASPIRE-ILD

- 39 pts with pre-existing ILD treated with SABR
- OS at 1 year: 79%; Median OS 25 months
 - 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

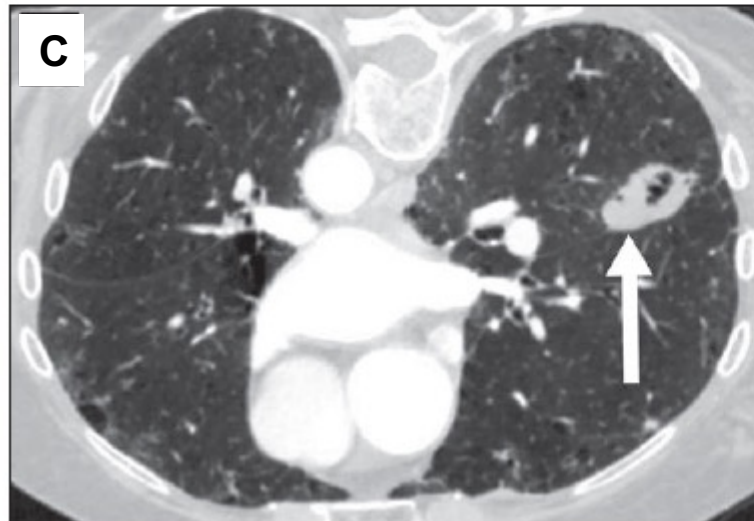
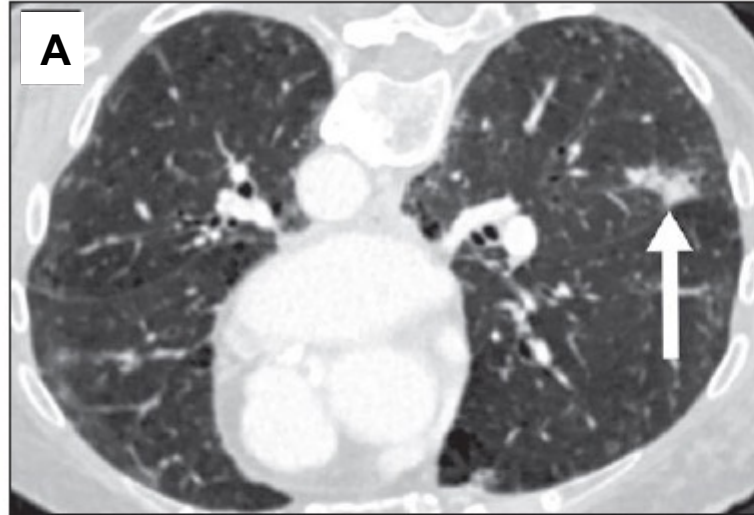
ILD type (multidisciplinary consensus diagnosis), No. (%)	
IPF	8 (21)
NSIP	0
CT-ILD	8 (21)
Chronic HP	2 (5)
Unclassifiable/other	21 (54)
ILD-GAP Index, No. (%)	
≤2	14 (36)
3-5	23 (59)
≥6	2 (5)
Baseline primary tumor size, median (IQR), cm	2.2 (1.6-2.7)
Baseline FEV ₁ [% predicted], median (IQR)	80 (66-90)
Baseline FVC [% predicted], median (IQR)	84 (69-94)
Baseline DLCO [% predicted], median (IQR)	49 (38-61)

A Overall survival



Percutaneous ablation

- Safety considerations:
 - Rate of major AE 14%
 - AE: 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%

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

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

Use of antifibrotics paired with chemotherapy may protect against development of AE-ILD

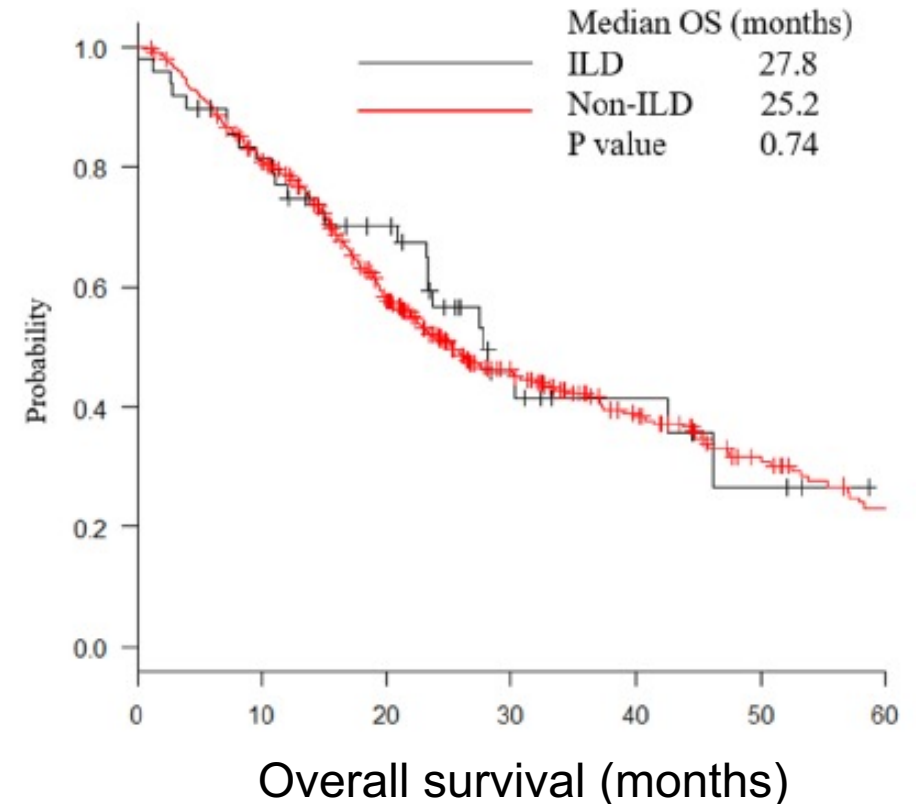
	UIP Pattern	
	No. of Patients Administered	Exacerbation of ILD (%)
Cisplatin	21	2 (10)
Carboplatin	40	5 (13)
Paclitaxel	31	1 (3)
Docetaxel	25	7 (28)
Etoposide	21	5 (24)
Vinorelbine	13	0
Gemcitabine	7	3 (43)
S-1	7	2 (29)
Irinotecan	6	2 (33)
Amrubicin	4	0
Pemetrexed	2	1 (50)

Immunotherapy: Pneumonitis

- Incidence depends on type of treatment:
 - PD-1 inhibitors have ~4-5% reported incidence (maybe higher), PD-L1 inhibitors 2%
 - CTLA-4 inhibitors have ~1% incidence
 - Combination PD-1/CTLA-4 treatment associated with 10% incidence
- Median time to onset is ~3 months, however wide range (2-24 months) and can occur months after discontinuation
- 1/3 of patients present as \geq grade 3, fatal in up to 12% of patients
- Up to 14% may develop steroid-dependent pneumonitis, 19% steroid-refractory pneumonitis
- Recurrent pneumonitis is frequent – both spontaneous and with rechallenge

Immunotherapy: Pre-existing ILD

- 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



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