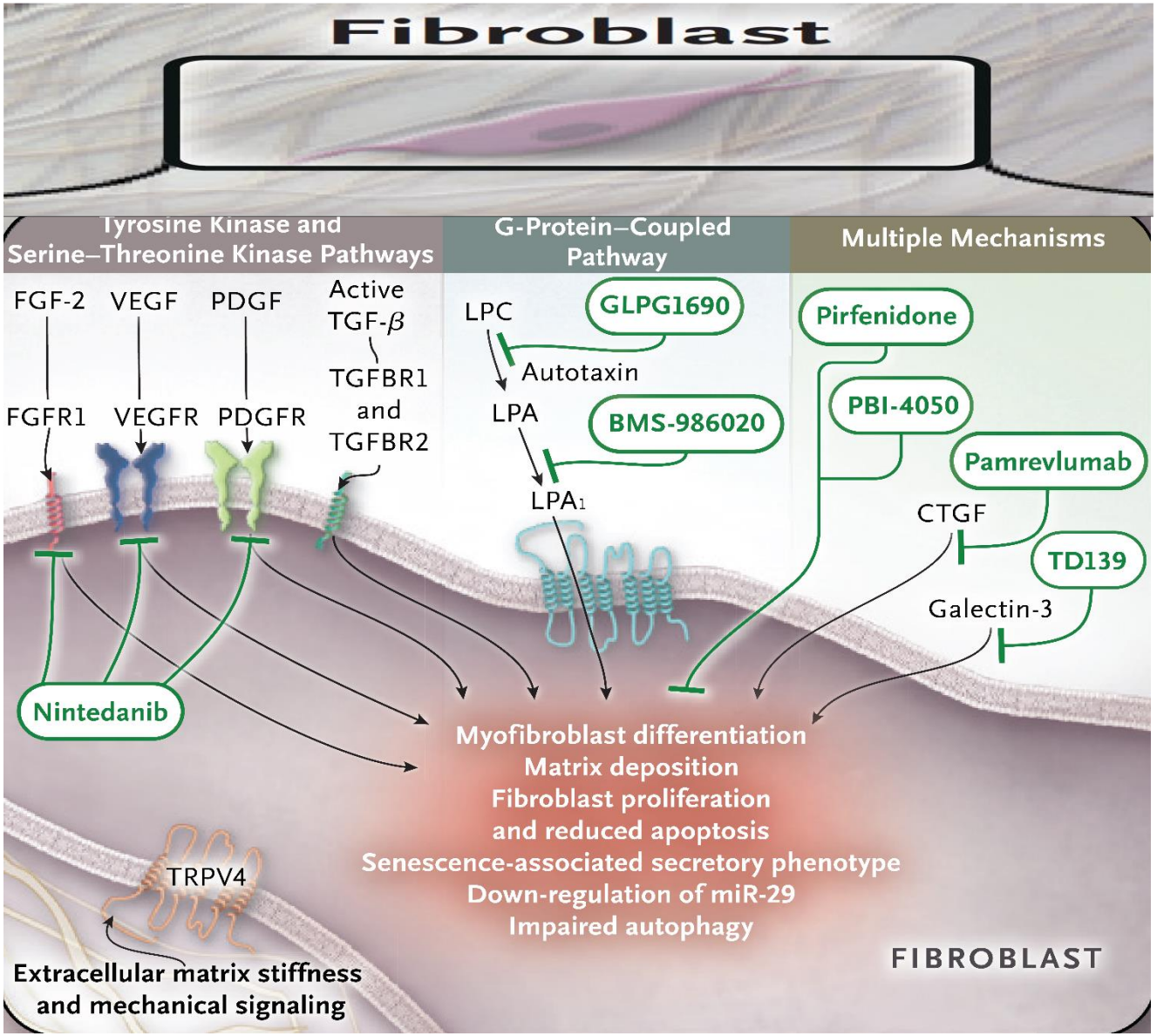
DILD Year in Review 2020

Joo Hun Park, M.D.
Pulmonary and Critical Care Medicine
Ajou University School of Medicine

Outline

- Therapeutic Interventions
- Prognosis
- Measurements & Biomarkers
- Etiology

Therapeutic Interventions



Lederer D et al. NEJM 2018; 378: 19

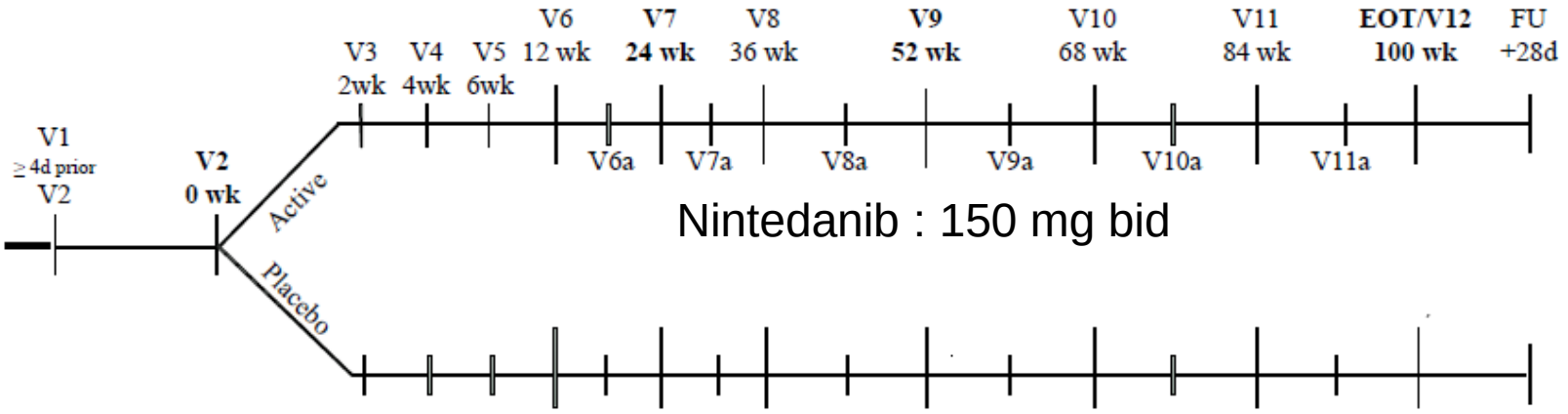
Pharmacologic Management of IPF

Variable	Nintedanib	Pirfenidone
Mechanism of action	Tyrosine kinase inhibition	Inhibition of TGF-β production and downstream signaling, collagen synthesis, and fibroblast proliferation (selected list)
Efficacy	Slows FVC decline by 50%	Slows FVC decline by 50%
FDA-approved dose	150 mg by mouth twice daily	801 mg by mouth thrice daily
Common side effects	Diarrhea	Anorexia, nausea, photosensitivity
Enzyme metabolism	Ester cleavage (major), CYP 3A4 (minor)	CYP 1A2 (major), other CYP enzymes (minor)
Cautions	Risks of both bleeding and arterial thrombosis; risk of gastrointestinal perforation (rare); anticoagulant and prothrombotic drugs should be avoided	CYP 1A2 inhibitors (e.g., fluvoxamine and ciprofloxacin) can raise pirfenidone levels; CYP 1A2 inducers (e.g., omeprazole and smoking) can lower pirfenidone levels
Need for liver-function monitoring	Yes†	Yes‡
Clinical strategies to minimize side effects	Use of antidiarrheal agents, temporary dose reduction to 100 mg twice daily	Slow dose increase over 14-day period, medication to be taken with food, use of antacids, use of antiemetic agents, sun avoidance

Lederer D et al. NEJM 2018; 378: 19

Nintedanib for Systemic Sclerosis Ass. ILD (SENSCIS)

- A total of 576 patients in 32 countries from 2015 Nov to 2017 Oct
- RCT over 52 weeks
- Inclusion : ≥18 years; fibrotic lung in CT ≥10%; FVC ≥40%; DLCO 30% to 89%
- 48.4 % on mycophenolate

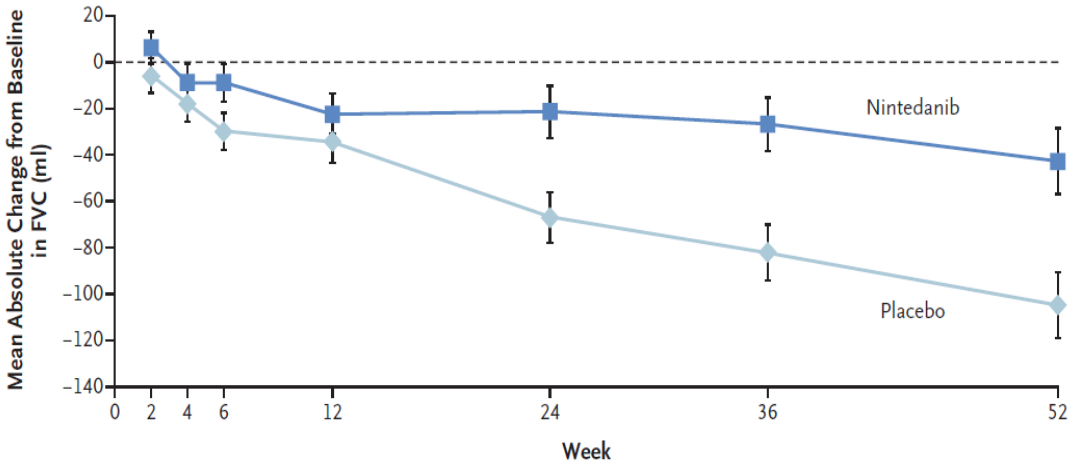


Distler O et al. NEJM 2019; 380: 2518 -2528

Nintedanib for Systemic Sclerosis Ass. ILD (SENSCIS)

- Primary endpoint: Annual decline in FVC over 52 weeks.
- Key secondary endpoints

1) Modified Rodnan Skin Score (mRSS)
2) SGRQ total score



Distler O et al. NEJM 2019; 380: 2518 -2528

Nintedanib for Systemic Sclerosis Ass. ILD (SENSCIS)

- Primary end point analysis (annual rate of change in FVC)

→ – 52.4 ml /year in the nintedanib group

→ –93.3 ml / year in the placebo group

→ Difference of FVC : 41.0 ml per year; p=0.04

- No significant difference in secondary outcomes (mRSS and SGRQ)

- Diarrhea

→ 75.7% in the nintedanib group & 31.6% in the placebo

Distler O et al. NEJM 2019; 380: 2518 -2528

Nintedanib for Systemic Sclerosis Ass. ILD (SENSCIS)

- Primary end point analysis (annual rate of change in FVC)

→ – 52.4 ml /year in the nintedanib group

→ –93.3 ml / year in the placebo group

→ Difference of FVC : 41.0 ml per year; p=0.04

- No significant difference in secondary outcomes (MRSS and SGRQ)

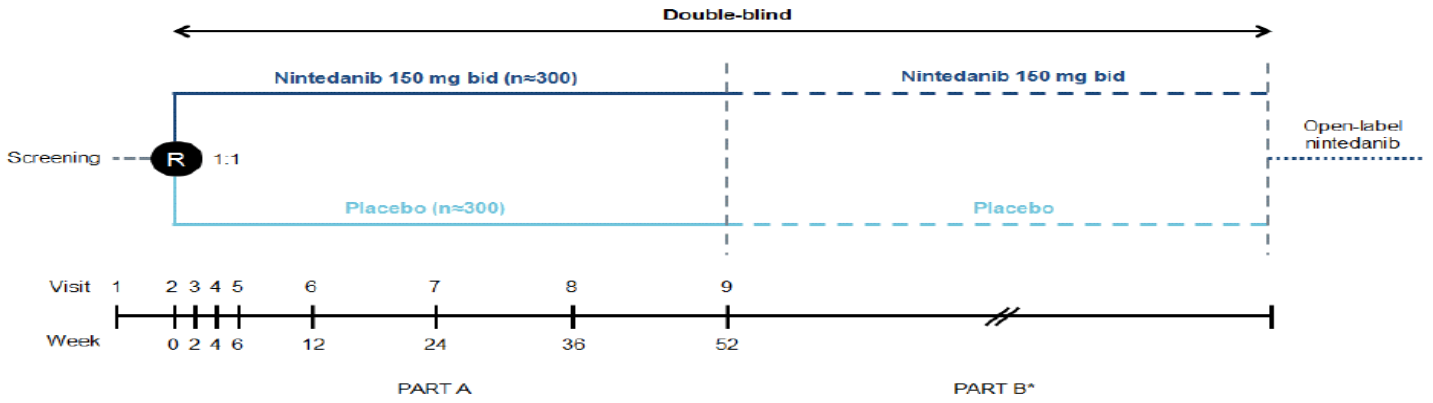
- Diarrhea

→ 75.7% in the nintedanib group & 31.6% in the placebo

Distler O et al. NEJM 2019; 380: 2518 -2528

Nintedanib in Progressive Fibrosing ILD (INBUILD Trial)

- A total of 663 patients in 15 countries from 2017 Feb to 2018 Apr
- RCT over 52 weeks
- Inclusion : age ≥ 18 years, fibrotic lung in CT ≥10%, FVC ≥45%, DLCO 30% to 80%
- Exclusion : azathioprine, cyclosporine, mycophenolate, tacrolimus, rituximab, cyclophosphamide, or oral glucocorticoids (≥20 mg / day)



Flaherty KR et al. NEJM 2019; 380: 2518 -2528

Nintedanib in Progressive Fibrosing ILD (INBUILD Trial)

- UIP pattern : 62.0% in nintedanib vs 62.2% in placebo
- Chronic HP : 26.1%,
- Autoimmune ILD : 25.6%

Flaherty KR et al. NEJM 2019; 380: 2518 -2528

Nintedanib in Progressive Fibrosing ILD (INBUILD Trial)

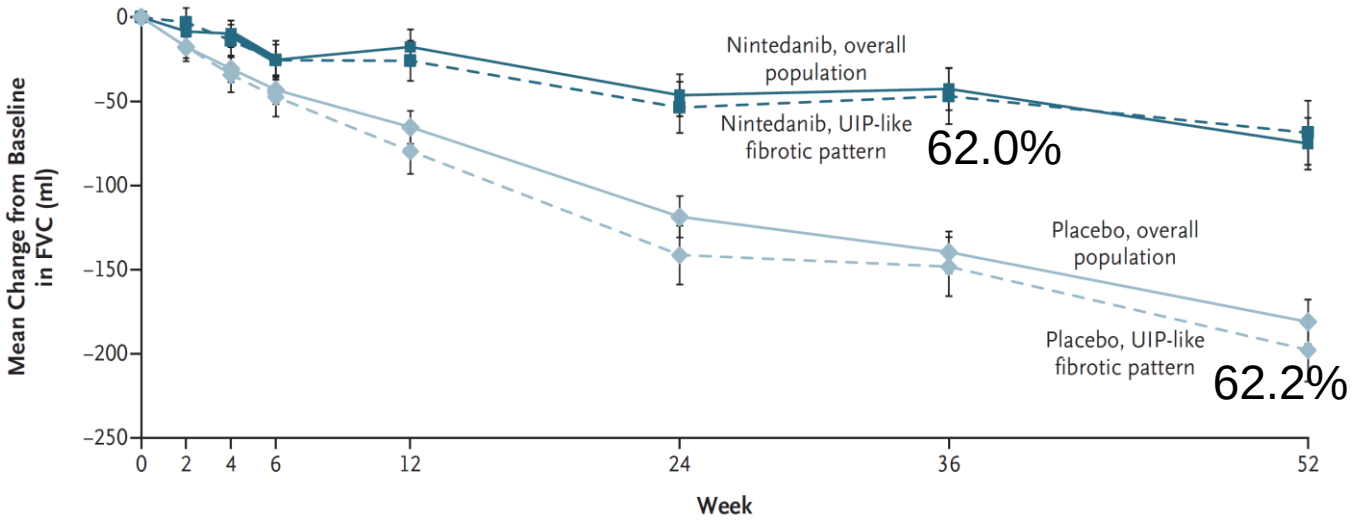
- Primary endpoint: FVC decline over 52 weeks
- Key secondary endpoints

1) King's Brief Interstitial Lung Disease (K-BILD) questionnaire : breathlessness and activities, psychological factors, and chest symptoms
2) Time until first acute exacerbation or death

Flaherty KR et al. NEJM 2019; 380: 2518 -2528

Nintedanib in Progressive Fibrosing ILD (INBUILD Trial)

End Point	Nintedanib (N=332)	Placebo (N=331)	Difference (95% CI)
Primary end point			
Rate of decline in the FVC at 52 wk — ml/yr†			
Overall population	−80.8±15.1	−187.8±14.8	107.0 (65.4 to 148.5)‡
Patients with a UIP-like fibrotic pattern	−82.9±20.8	−211.1±20.5	128.2 (70.8 to 185.6)‡
Patients with other fibrotic patterns	−79.0±21.6	−154.2±21.2	75.3 (15.5 to 135.0)§



Flaherty KR et al. NEJM 2019; 380: 2518 -2528

Nintedanib in Progressive Fibrosing ILD (INBUILD Trial)

Event	Nintedanib (N=332)	Placebo (N=331)
	no. of patients (%)	
Adverse event		
Any	317 (95.5)	296 (89.4)
Any except for progression of interstitial lung disease†	317 (95.5)	295 (89.1)
Most frequent adverse events‡		
Diarrhea	222 (66.9)	79 (23.9)
Nausea	96 (28.9)	31 (9.4)
Bronchitis	41 (12.3)	47 (14.2)
Nasopharyngitis	44 (13.3)	40 (12.1)
Dyspnea	36 (10.8)	44 (13.3)
Vomiting	61 (18.4)	17 (5.1)
Cough	33 (9.9)	44 (13.3)
Decreased appetite	48 (14.5)	17 (5.1)
Headache	35 (10.5)	23 (6.9)
Alanine aminotransferase increased	43 (13.0)	12 (3.6)
Progression of interstitial lung disease†	16 (4.8)	39 (11.8)
Weight loss	41 (12.3)	11 (3.3)

Flaherty KR et al. NEJM 2019; 380: 2518 -2528

Nintedanib in Progressive Fibrosing ILD

- Annual rate of decline in the FVC

→ Significantly lower among nintedanib group than placebo
→ Diarrhea : a common adverse event

Flaherty KR et al. NEJM 2019; 381: 1718 -1727

Pirfenidone in patients with unclassifiable progressive fibrosing ILD: RCT, phase 2 trial

- A total of 253 patients in 70 countries from 2017 May to 2018 Jun
- RCT over 24 weeks
- Inclusion : ≥18 - 85 years; fibrotic lung in CT ≥10%; FVC ≥45%; DLCO ≥ 30% to 89%

	Pirfenidone (n=127)	Placebo (n=126)
Unclassifiable ILD diagnosis		
Low-confidence rheumatoid arthritis-ILD	0	0
Low-confidence systemic sclerosis-ILD	0	1 (1%)
Low-confidence undifferentiated connective tissue disease-ILD	3 (2%)	2 (2%)
Low-confidence chronic hypersensitivity pneumonitis-ILD	10 (8%)	9 (7%)
Low-confidence idiopathic non-specific interstitial pneumonia-ILD	4 (3%)	3 (2%)
Low-confidence sarcoidosis-ILD	0	0
Low-confidence myositis-ILD	0	0
Low-confidence other defined ILD	1 (1%)	0
Unclassifiable ILD	93 (73%)	93 (74%)

Maher et al. Lancet Resp Med 2019; S2213

Pirfenidone in patients with unclassifiable progressive fibrosing ILD : RCT, phase 2 trial

- Primary endpoint : Mean change of FVC by home spirometry

- Secondary endpoints

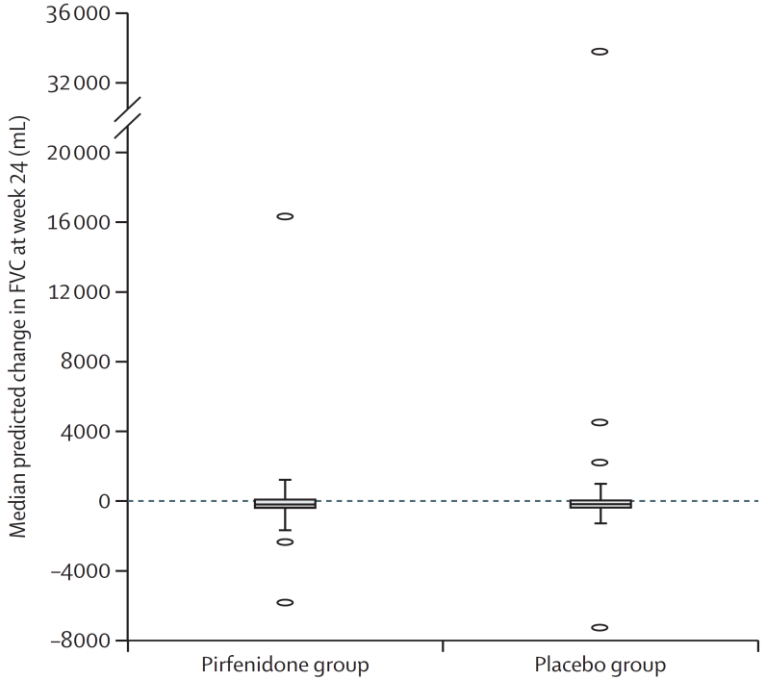
5% or 10 % of FVC decline by site spirometry;

SGRQ; DLCO; 6 MWD, etc

Maher et al. Lancet Resp Med 2019; S2213

Pirfenidone in patients with unclassifiable progressive fibrosing ILD : RCT, phase 2 trial

- FVC mean change by home spirometry (primary endpoint)
  - 87.7 mL in the pirfenidone
  - 157.1 mL in the placebo



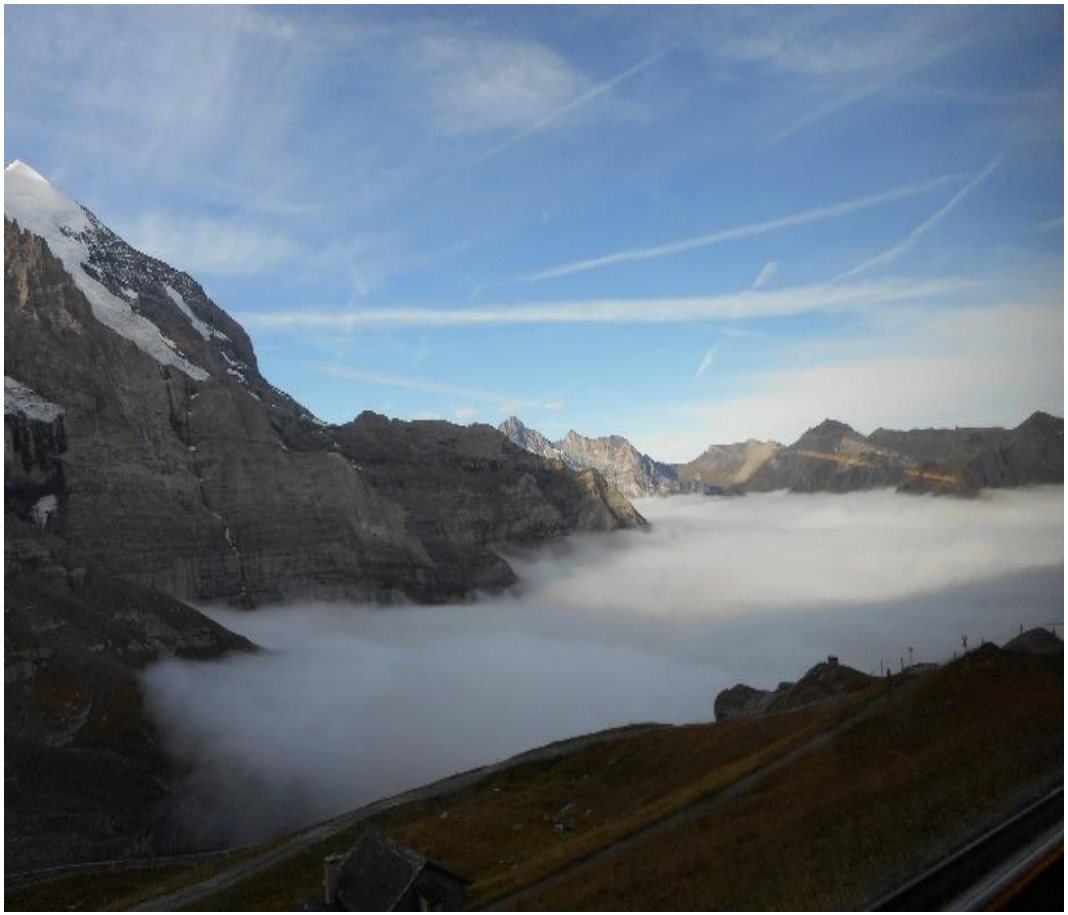
Maher et al. Lancet Resp Med 2019; S2213

Pirfenidone in patients with unclassifiable progressive fibrosing ILD : RCT, phase 2 trial

	Pirfenidone (n=127)	Placebo (n=126)
Change in FVC from baseline measured by site spirometry		
Mean, mL	20·0* (7·6)	−80·0† (7·6)
Median, mL	0·0 (−160·0 to 120·0)	−90·0 (−210·0 to 30·0)
Mean, % predicted	−0·4%* (6·9)	−2·5%† (9·2)
Median, % predicted	0·0% (−4·8 to 4·0)	−2·0% (−7·0 to 1·5)
Change in percent predicted DLco from baseline		
Mean	−0·7%‡ (7·1)	−2·5%§ (8·8)
Median	−1·0% (−4·1 to 3·2)	−2·0% (−6·0 to 1·7)
Change in 6MWD from baseline		
Mean, m	−2·0¶ (68·1)	−26·7‖ (79·3)
Median, m	0·0 (−39·0 to 40·0)	−12·0 (−53·5 to 10·5)

Maher et al. Lancet Resp Med 2019; S2213

Prognosis



Association of Angiotensin Modulators With the Course of IPF

- All patients randomized to placebo (n = 624) in the CAPACITY and ASCEND studies

→ 111 pts : angiotensin-converting enzyme inhibitor (ACEi)

→ 121 pts : angiotensin II receptor blocker (ARB)

→ 392 pts : receiving neither

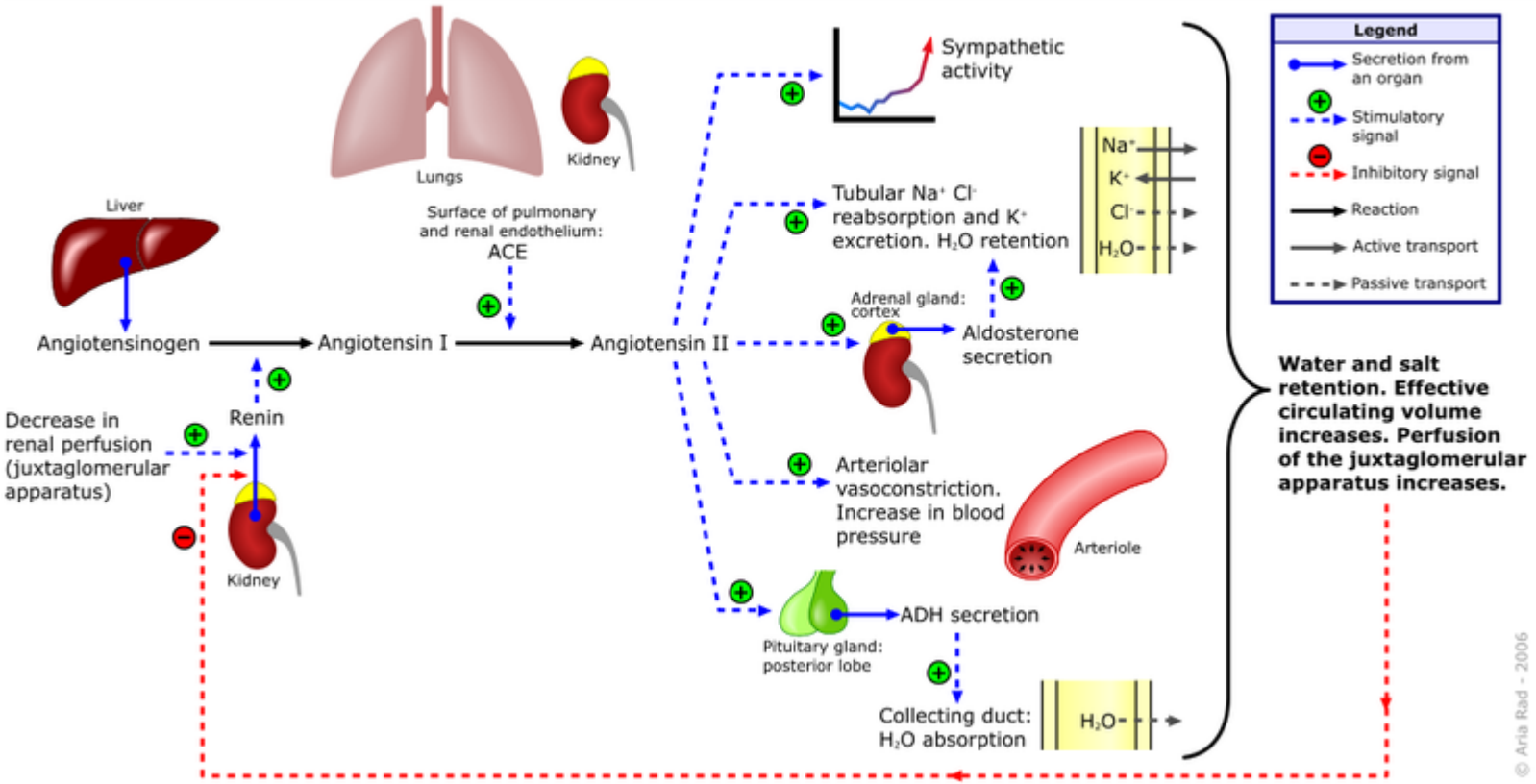
- Outcomes of disease progression

→ 10% absolute decline in % predicted FVC,
50-m decline in 6 MWD, or death

- All-cause mortality : assessed over 52 weeks.

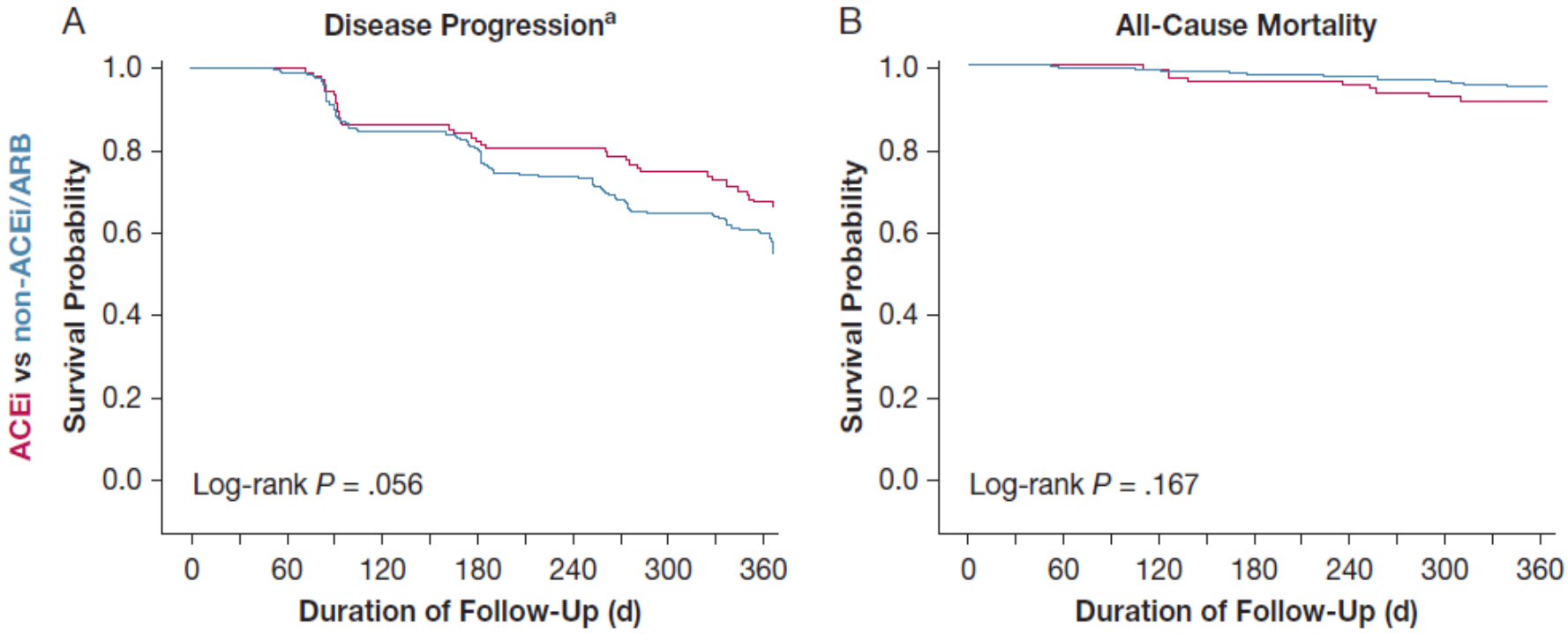
Kim J et al. Chest 2020; 157: 580 -589

Renin-angiotensin-aldosterone system



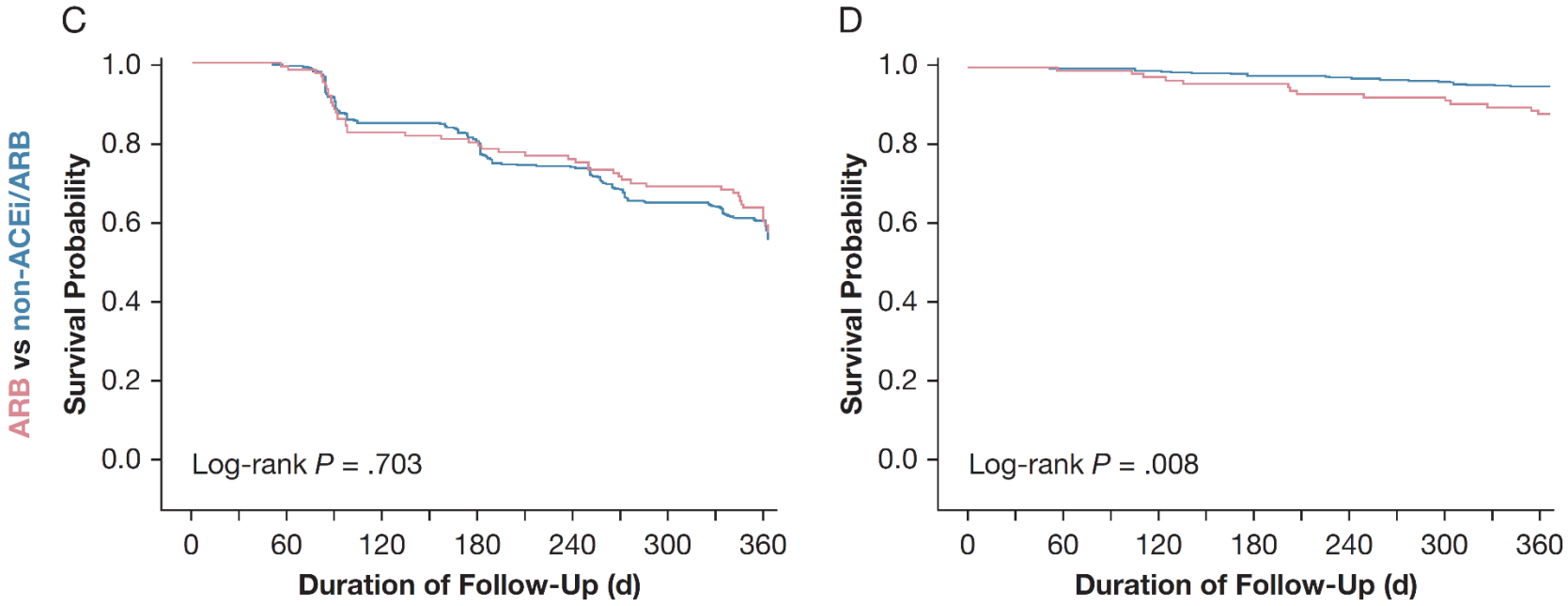
Wilkipedia

Association of Angiotensin Modulators With the Course of IPF



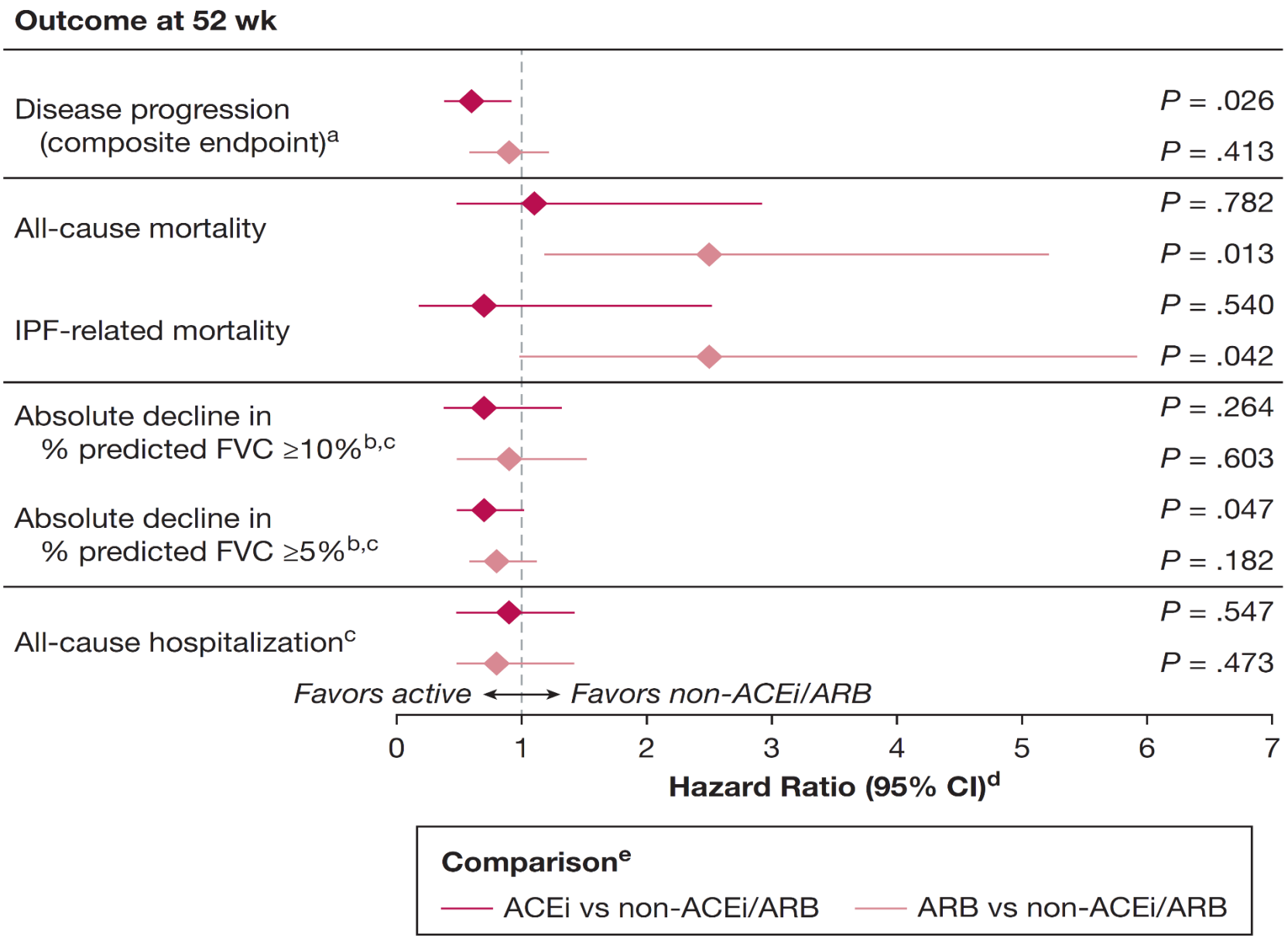
Kim J et al. Chest 2020; 157: 580 -589

Association of Angiotensin Modulators With the Course of IPF



Kim J et al. Chest 2020; 157: 580 -589

Multivariable analyses



Nintedanib plus Sildenafil in Patients with Idiopathic Pulmonary Fibrosis

Martin Kolb, M.D., Ganesh Raghu, M.D., Athol U. Wells, M.D., Jürgen Behr, M.D., Luca Richeldi, M.D., Birgit Schinzel, Dipl.Stat., Manuel Quaresma, Lic., Susanne Stowasser, M.D., and Fernando J. Martinez, M.D., for the INSTAGE Investigators*

CONCLUSIONS

In patients with IPF and a $D_{L_{CO}}$ of 35% or less of the predicted value, nintedanib plus sildenafil did not provide a significant benefit as compared with nintedanib alone. No new safety signals were identified with either treatment regimen in this population of patients. (Funded by Boehringer Ingelheim; INSTAGE ClinicalTrials.gov number, NCT02802345.)

N Engl J Med 2018;379:1722-31.
DOI: 10.1056/NEJMoa1811737

Nintedanib and Sildenafil in Patients with IPF and Right Heart Dysfunction (INSTAGE)

- Subgroup analyses

→ 117 patients with echocardiographic RHD

→ 156 patients without echocardiographic RHD

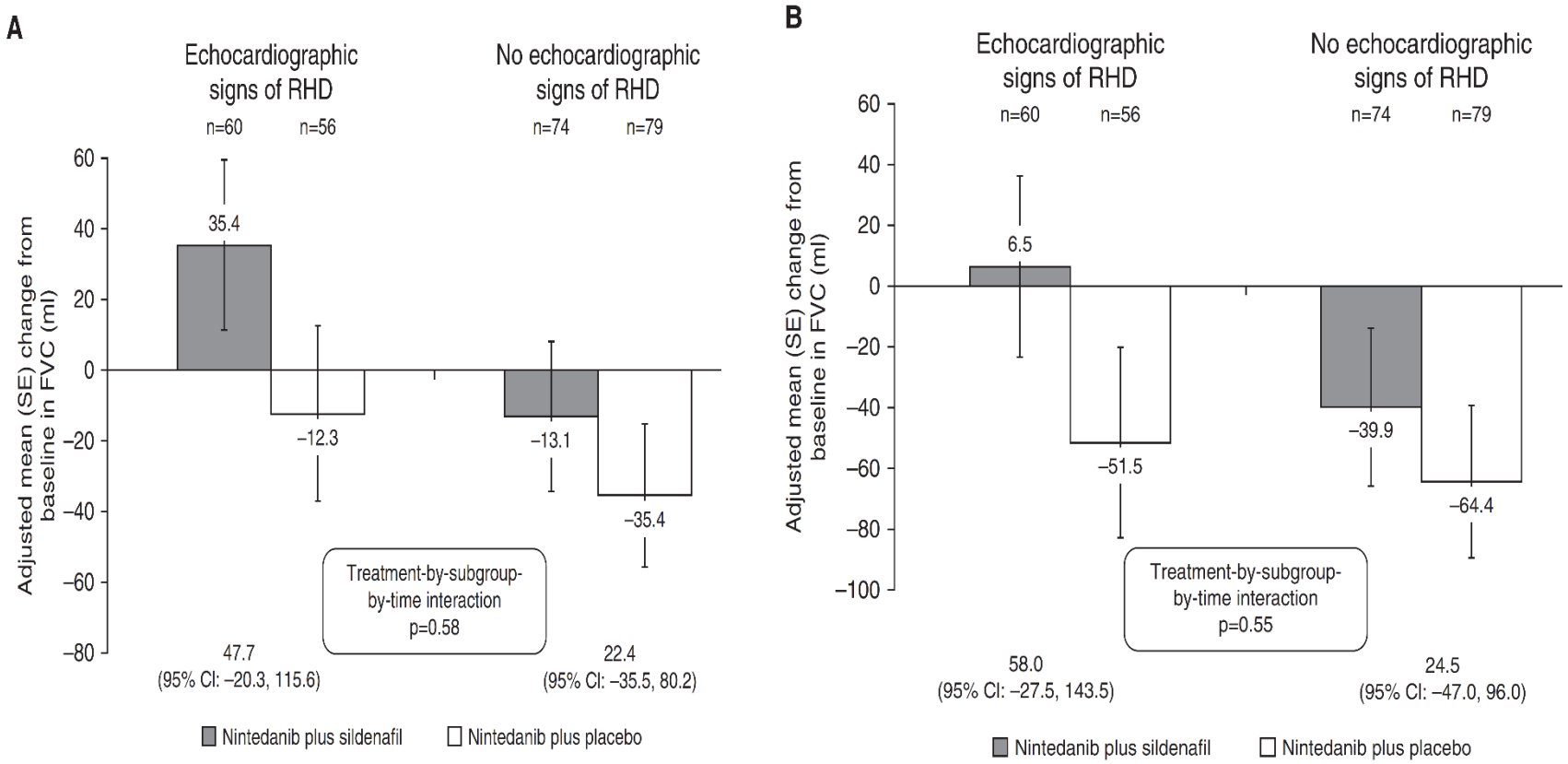
- Measured outcomes

→ change from baseline in SGRQ and FVC at weeks 12 & 24

→ changes from baseline in BNP at weeks 24

Behr J et al. AJRCCM 2019; 200: 1505 -1512

FVC (INSTAGE)



12 weeks

24 weeks

Behr J et al. AJRCCM 2019; 200: 1505 -1512

Nintedanib and Sildenafil in Patients with IPF and Right Heart Dysfunction (INSTAGE)

- Nintedanib plus sildenafil versus nintedanib alone

→ a numerically greater effect on reducing FVC decline

→ no significant differences on changes in SGRQ and FVC between patients with or without echocardiographic RHD

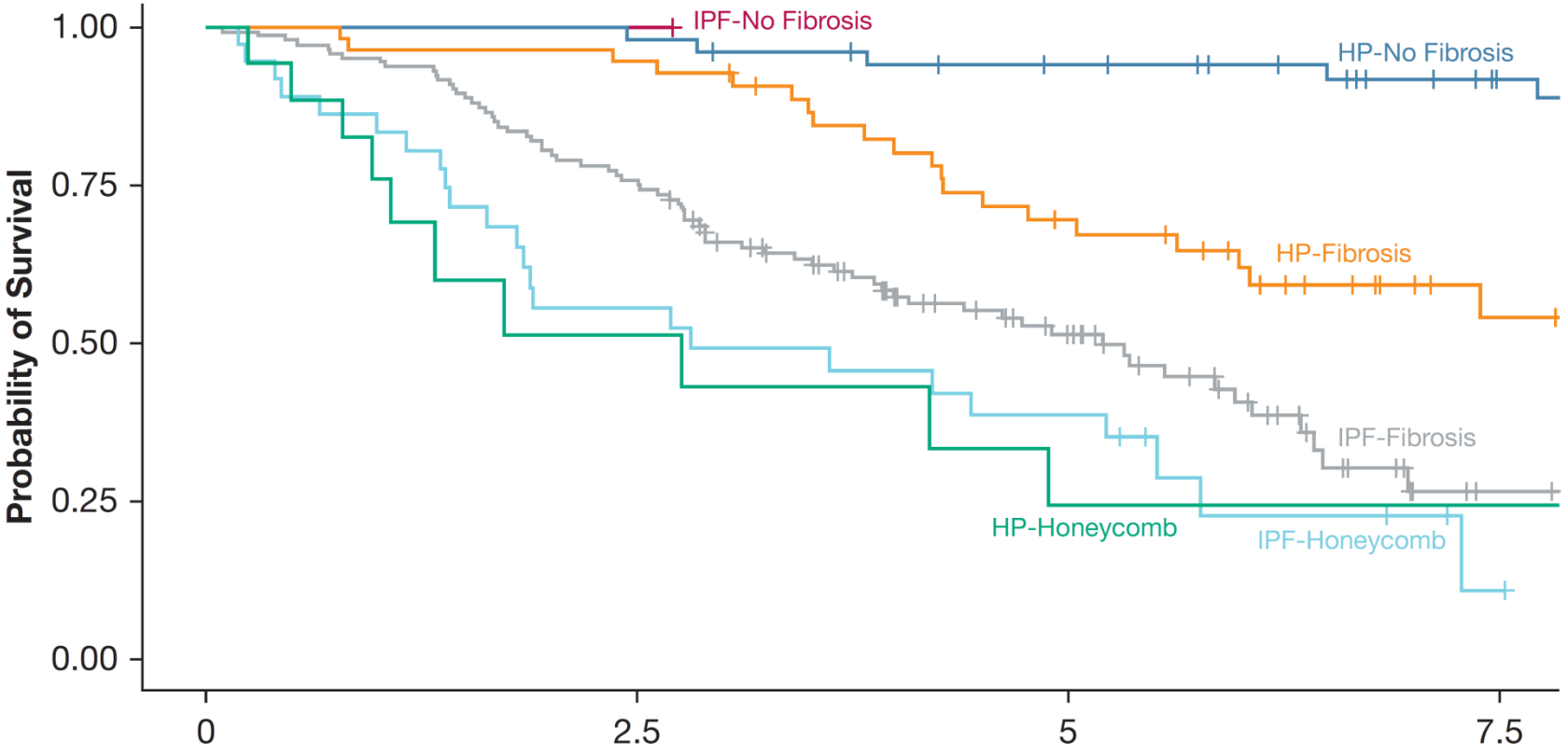
Behr J et al. AJRCCM 2019; 200: 1505 -1512

Hypersensitivity Pneumonitis Radiologic Phenotypes Are Associated With Distinct Survival Time and Pulmonary Function Trajectory

- Review of the University of Michigan's multidisciplinary ILD conference
- HP (n = 117) : diagnosis with surgical/transbronchial lung biopsy, BAL, and exposure history results
- IPF (n = 152) : clinical and histopathological diagnosis
- HRCT & FVC
- Survival time from HRCT to death or lung transplant
- Cox proportional hazards models

Salisbury M et al CHEST 2019; 155(4):699-711

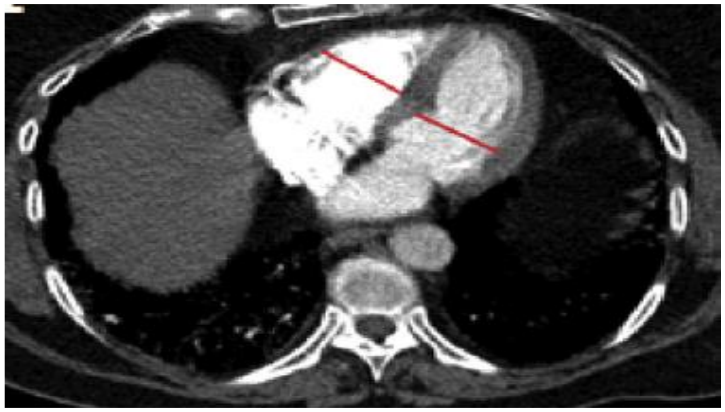
Hypersensitivity Pneumonitis Radiologic Phenotypes Are Associated With Distinct Survival Time and Pulmonary Function Trajectory



Salisbury M et al CHEST 2019; 155(4):699-711

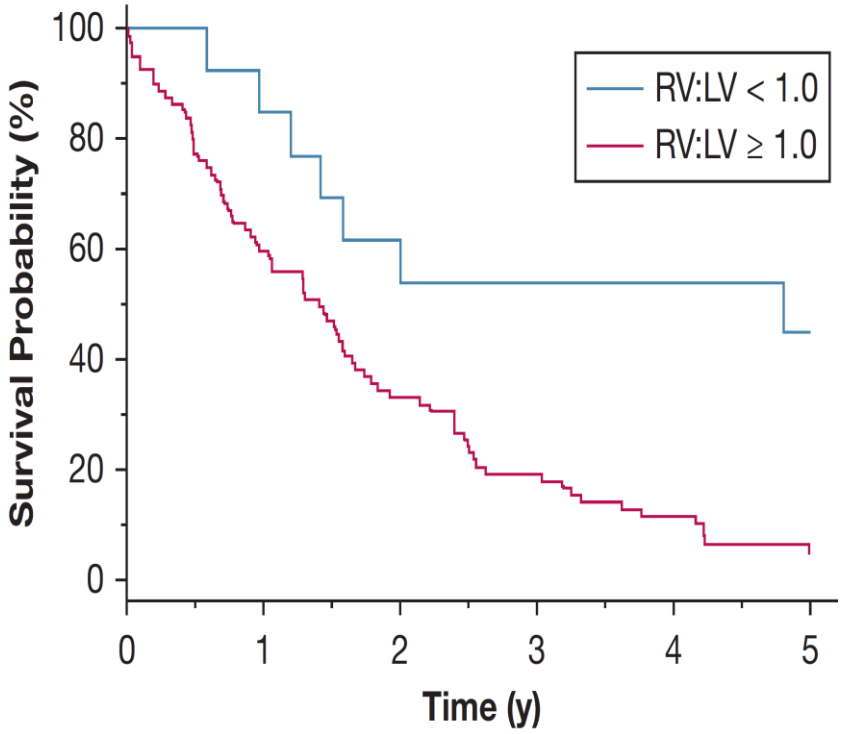
Right Ventricular to Left Ventricular Ratio at CT Pulmonary Angiogram Predicts Mortality in ILD

- METHODS: ILD patients undergoing both CTPA and right heart catheterization at the Royal Brompton Hospital between 2005 and 2015



ILD Diagnosis	CTPA Cohort (N = 92)
Idiopathic pulmonary fibrosis	58
Chronic hypersensitivity pneumonitis	13
Idiopathic nonspecific interstitial pneumonitis	13
Smoking-related ILD	3
Unclassifiable ILD	3
Fibrotic cryptogenic organizing pneumonia	1
Pleuroparenchymal fibroelastosis	1

Bax S et al CHEST 2020; 157(1):89-98



Multivariate Adjustment of the RV:LV Ratio

Variable	Hazard Ratio	95% CI	*P* Value
Fibrosis score at CT imaging (per 10% increase)	1.32	1.11-1.56	.004[a]
IPF diagnosis	1.91	1.17-3.14	.001[a]
RV:LV*largest* ratio > 1.0	3.19	1.44-7.10	.004[a]

Bax S et al CHEST 2020; 157(1):89-98

Efficacy of Pirfenidone in the Context of Multiple Disease Progression Events in IPF

- Pirfenidone 2,403 mg/d (n = 623) or placebo (n = 624) in the post hoc analysis of ASCEND and CAPACITY

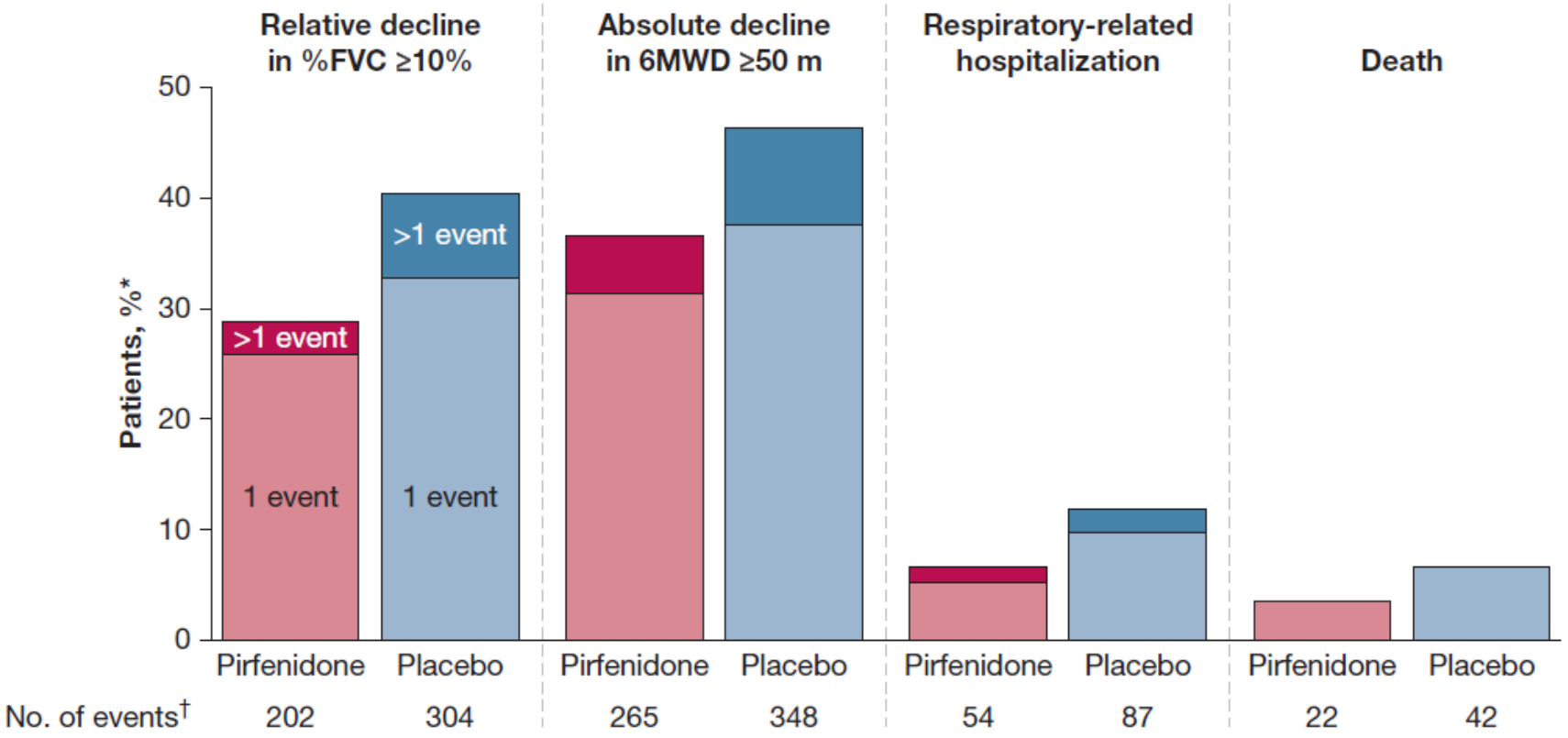
- Disease progression

→ relative decline in 10% of FVC
→ absolute decline in 50 m of 6MWD
→ respiratory hospitalization
→ death from any cause.

- Assessment of disease progression events over 12 months

Nathan S et al CHEST 2019; 155(4):712-719

Efficacy of Pirfenidone in the Context of Multiple Disease Progression Events in IPF



Nathan S et al CHEST 2019; 155(4):712-719

Biomarkers & Measurements

Diagnosis of Idiopathic Pulmonary Fibrosis

An Official ATS/ERS/JRS/ALAT Clinical Practice Guideline

UIP	Probable UIP	Indeterminate for UIP	Alternative Diagnosis
Subpleural and basal predominant; distribution is often heterogeneous*	Subpleural and basal predominant; distribution is often heterogeneous	Subpleural and basal predominant	Findings suggestive of another diagnosis, including: • CT features: ° Cysts ° Marked mosaic attenuation ° Predominant GGO ° Profuse micronodules ° Centrilobular nodules ° Nodules ° Consolidation • Predominant distribution: ° Peribronchovascular ° Perilymphatic ° Upper or mid-lung • Other: ° Pleural plaques (consider asbestosis) ° Dilated esophagus (consider CTD) ° Distal clavicular erosions (consider RA) ° Extensive lymph node enlargement (consider other etiologies) ° Pleural effusions, pleural thickening (consider CTD/drugs)
Honeycombing with or without peripheral traction bronchiectasis or bronchiolectasis†	Reticular pattern with peripheral traction bronchiectasis or bronchiolectasis May have mild GGO	Subtle reticulation; may have mild GGO or distortion ("early UIP pattern") CT features and/or distribution of lung fibrosis that do not suggest any specific etiology ("truly indeterminate for UIP")	

Possible UIP Pattern (All Three Features)

- Subpleural, basal predominance
- Reticular abnormality
- Absence of features listed as inconsistent with UIP pattern (*see* third column)

2011 ATS

Raghu G et al, AJRCCM 2018 Sep 1;198(5):e44-e68

Imaging Patterns Are Associated with Interstitial Lung Abnormality Progression and Mortality

- ILA (interstitial lung abnormality) assessed in 5,320 participants from the AGES-Reykjavik (Iceland) Study
- Chest CT follow up after 5 years : 3,167 participants
- Multivariable logistic regression to assess factors associated with ILA progression
- Cox proportional hazards models to assess mortality

Putman RK et al AJRCCM 2019 ; 200: 175-183

Imaging Patterns Are Associated with Interstitial Lung Abnormality Progression and Mortality

- Associated with imaging progression

→ age, fibrosis pattern, and MUC5B genotype

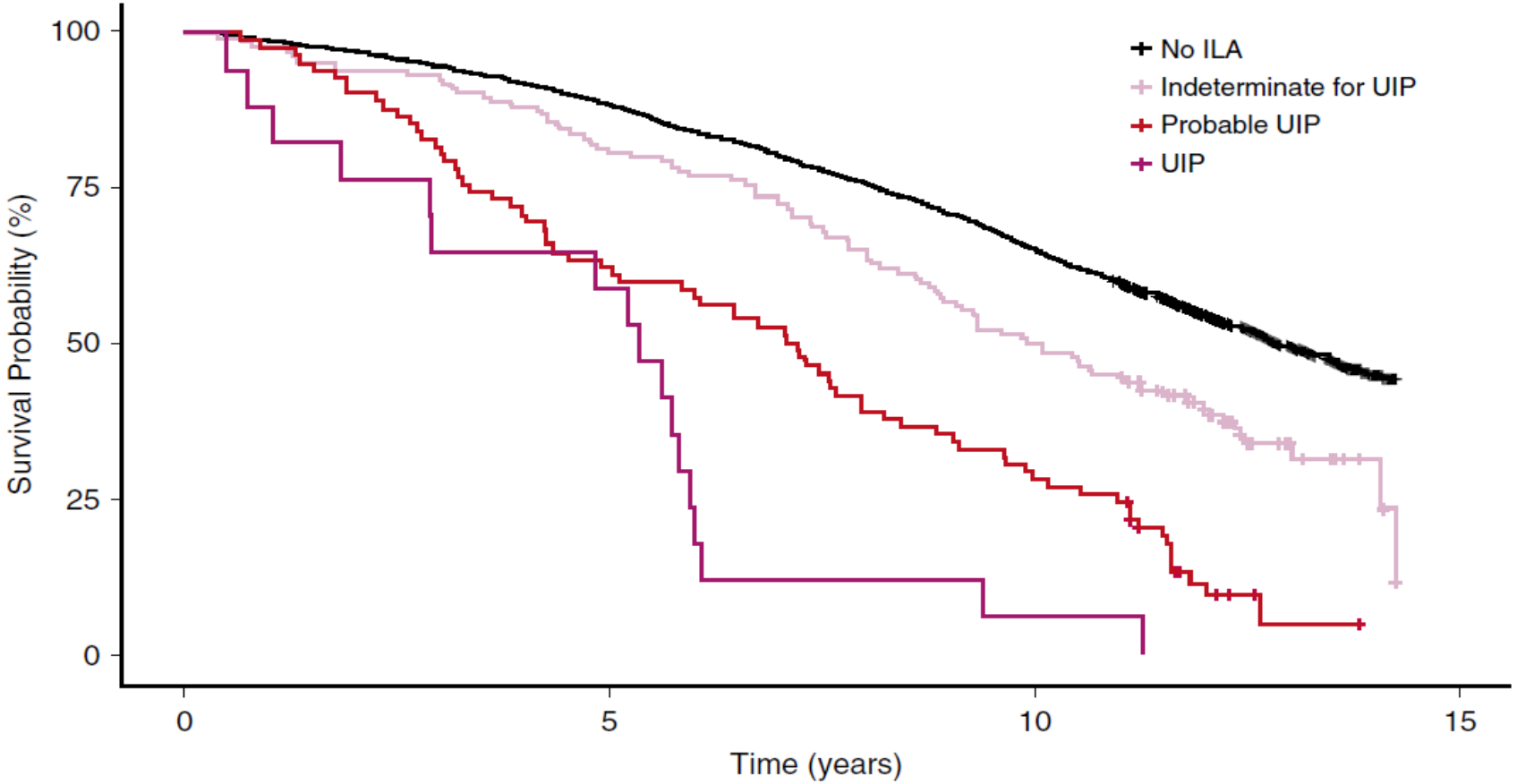
- Associated with an increased mortality compared with indeterminate UIP after adjustment

→ Probable UIP (HR, 1.7; 95% CI, 1.2–2.4)

→ UIP pattern (HR, 3.9; 95% CI, 2.3–6.8)

Putman RK et al AJRCCM 2019 ; 200: 175-183

Imaging Patterns Are Associated with Interstitial Lung Abnormality Progression and Mortality



Putman RK et al AJRCCM 2019 ; 200: 175-183

Probable UIP pattern on chest CT: Is it sufficient for a diagnosis of IPF?

- INPLUSS trial (Richeldi L et al : Efficacy and safety of nintedanib in idiopathic pulmonary fibrosis. NEJM 2014; 370: 2071–2082) → fibrosing interstitial pneumonia with a combination of traction bronchiectasis and a possible UIP pattern on CT

- Retrospective comparison of the prognosis and time to first AE in IIP patients on initial chest CT

→ 160 patients with a UIP pattern

→ 242 with a probable UIP pattern

Fukihara J et al. ERJ 2020; 55: 1802465

Conclusion

Probable UIP pattern on chest CT: Is it sufficient for a diagnosis of IPF?

- The prevalence of a histopathological UIP pattern

→ 82% (27 out of 32) for a UIP pattern on chest CT

→ 83% (90 out of 109) for a probable UIP pattern

- The probability of an MDD diagnosis of IPF

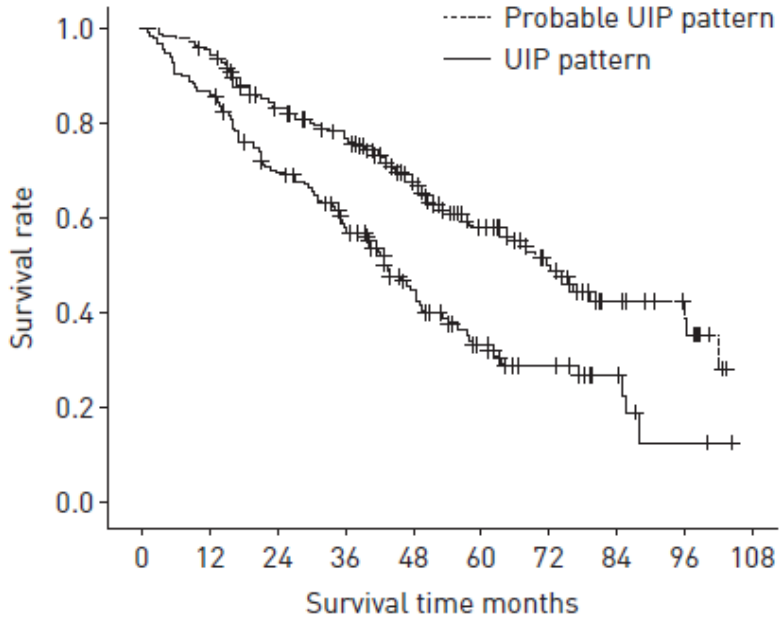
→ 83% (90 out of 109) for a probable UIP pattern

declined to 66% (72 out of 109)

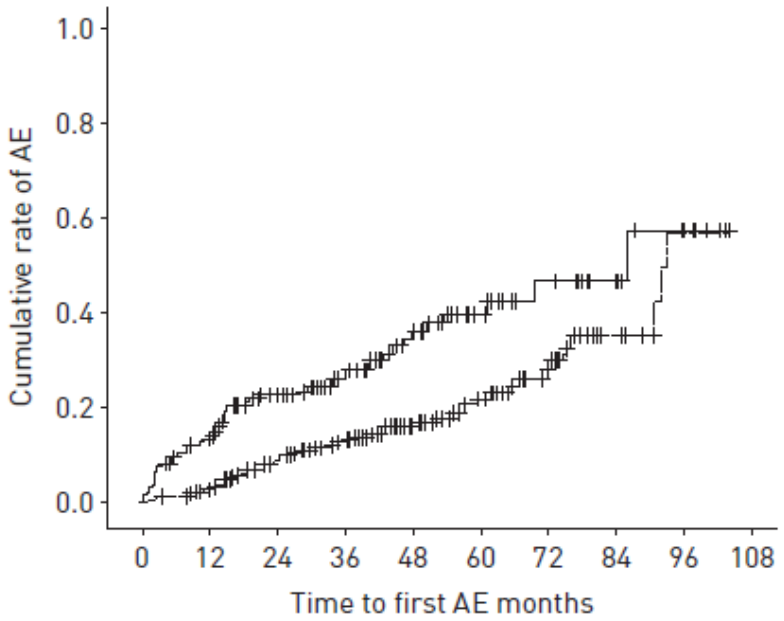
Fukihara J et al. ERJ 2020; 55: 1802465

Probable UIP pattern on chest CT: Is it sufficient for a diagnosis of IPF?

a)



b)



Longer survival time
(HR 0.713, 95% CI 0.536–0.950; p=0.021)

Longer time to first AE
(HR 0.580, 95% CI 0.389– 0.866; p=0.008)

Fukihara J et al. ERJ 2020; 55: 1802465

Probable UIP pattern on chest CT: Is it sufficient for a diagnosis of IPF?

TABLE 2 Mortality rate and Cox proportional hazard analysis for survival time

Parameters	Patients n	Deaths n	Mortality rate[#] (95% CI)	Adjusted hazard ratio (95% CI)	p-value[¶]
All patients					
UIP pattern on CT	160	99	19.8 (16.2–24.1)	Reference	0.028
Probable UIP pattern on CT	242	103	10.6 (8.8–12.9)	0.722 (0.540–0.965)	
IPF only					
UIP pattern on CT	154	96	20.5 (16.8–25.0)	Reference	0.447
Probable UIP pattern on CT	157	77	12.1 (9.7–15.2)	0.883 (0.640–1.218)	
Probable UIP pattern only					
Final diagnosis of non-IPF	85	26	7.8 (5.3–11.4)	Reference	0.014
Final diagnosis of IPF	157	77	12.1 (9.7–15.2)	1.879 (1.138–3.103)	

Fukihara J et al. ERJ 2020; 55: 1802465

Probable UIP pattern on chest CT: Is it sufficient for a diagnosis of IPF?

- Probable UIP vs. UIP among IIP patients on initial chest CT → a better prognosis and longer time to first AE
- When a final diagnosis of IPF was provided, CT pattern was not associated with these outcomes.
- This suggests diagnostic heterogeneity among patients with a probable UIP pattern.

Fukihara J et al. ERJ 2020; 55: 1802465

Telomere Length and Use of Immunosuppressive Medications in IPF

- LTL (Leukocyte telomere length) from DNA samples

→ PANTHER-IPF (n = 118)

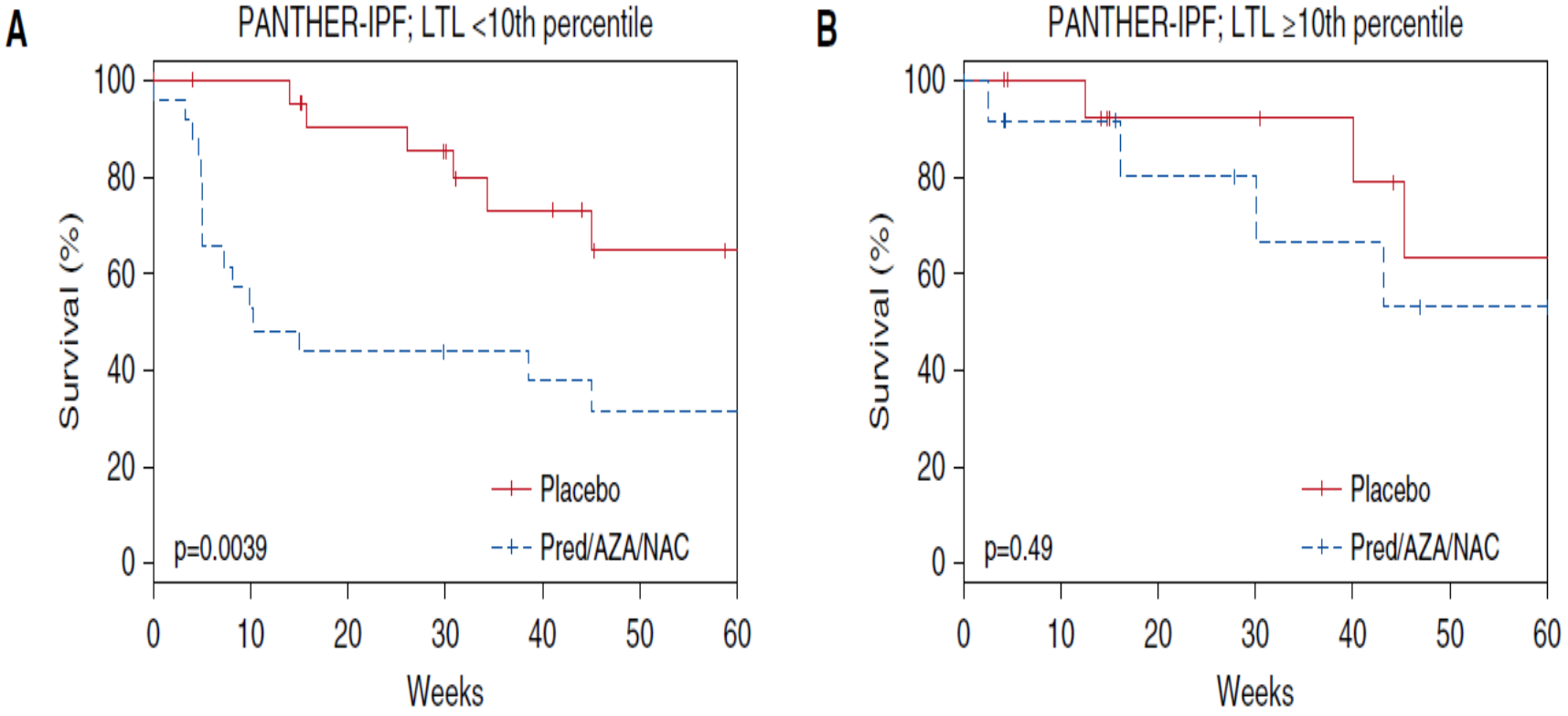
→ ACE-IPF (Anticoagulant Effectiveness in IPF) (n = 101)

→ Independent observational cohort

(Texas Southwestern Medical Center-IPF, n = 170)

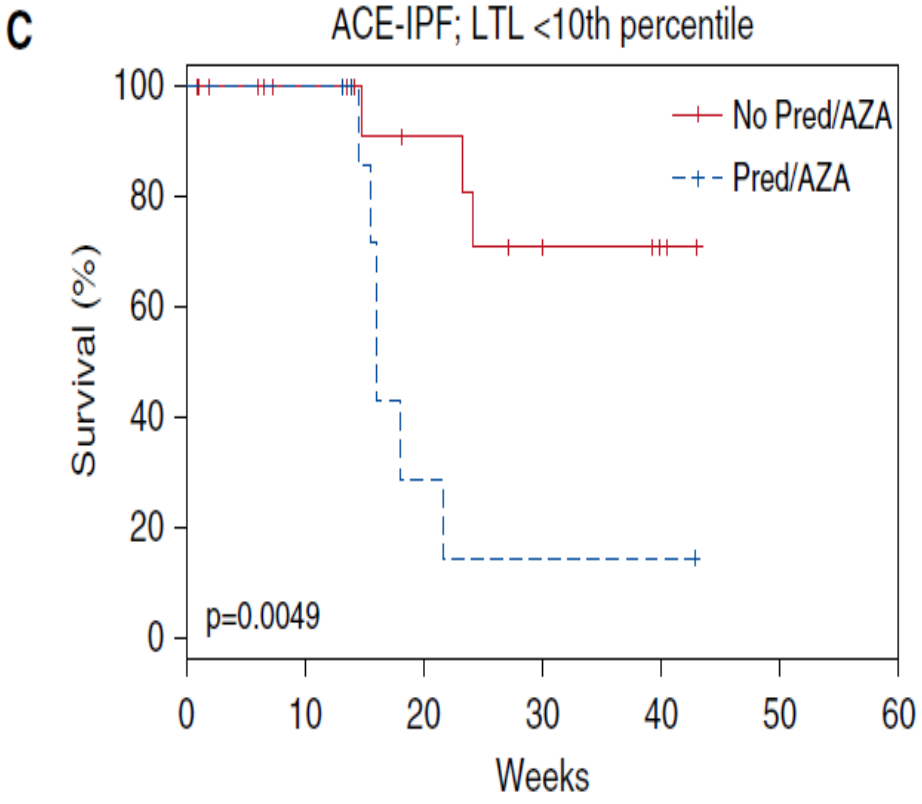
Newton et al AJRCCM 2019 ; 200: 336 - 347

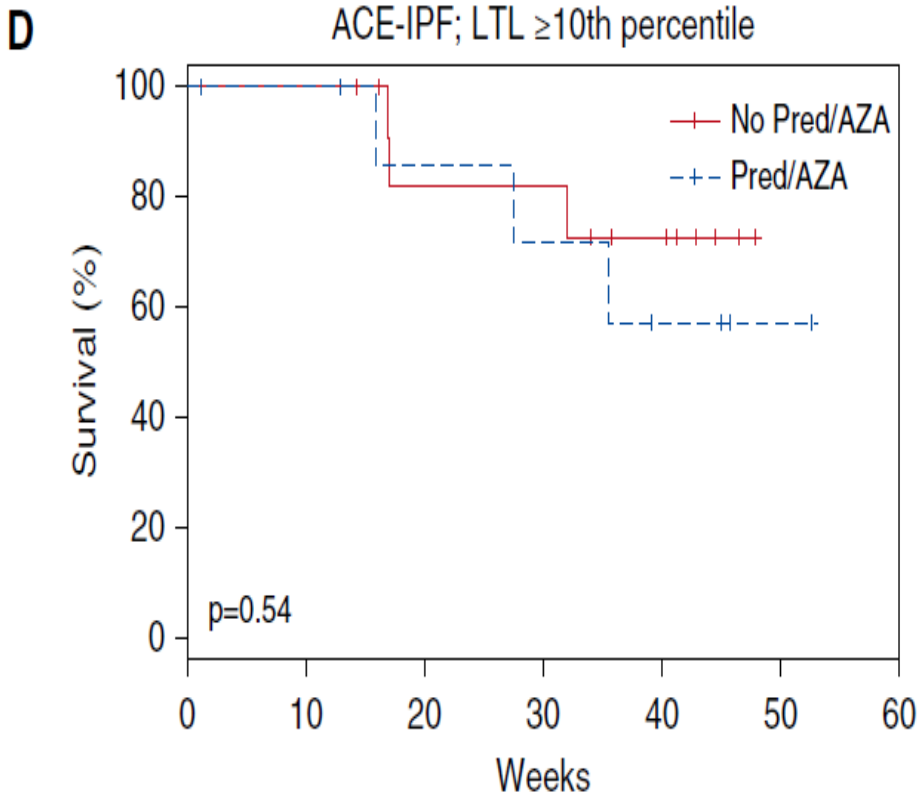
Telomere Length and Use of Immunosuppressive Medications in IPF



Newton et al AJRCCM 2019 ; 200: 336 - 347

Telomere Length and Use of Immunosuppressive Medications in IPF





Newton et al AJRCCM 2019 ; 200: 336 - 347

Telomere Length and Use of Immunosuppressive Medications in IPF

- Immunosuppression : part of the medical armamentarium for many progressive non-IPF forms of ILD (HP and CTD–ass. ILD).

- Short telomere length can be a biomarker?

→ interaction between telomere and immunosuppression

Newton et al AJRCCM 2019 ; 200: 336 - 347

Functional ageing in fibrotic ILD : Impact of frailty on adverse health outcomes

- 540 Patients prospectively recruited from ILD clinic.
- Frailty index ; self-reported frailty index of 42 deficits

→ 19 comorbidities

→ 23 deficits related to independence and self-care

- Functional ageing determined by

→ Frailty index

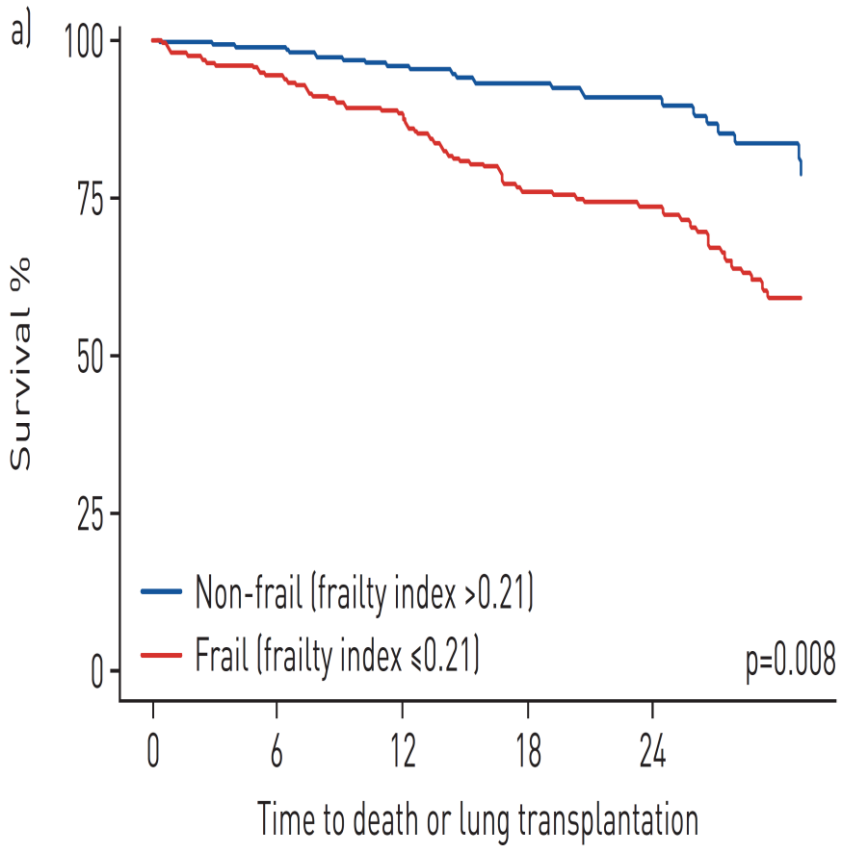
→ biological age by absolute telomere length (aTL) of blood leukocytes

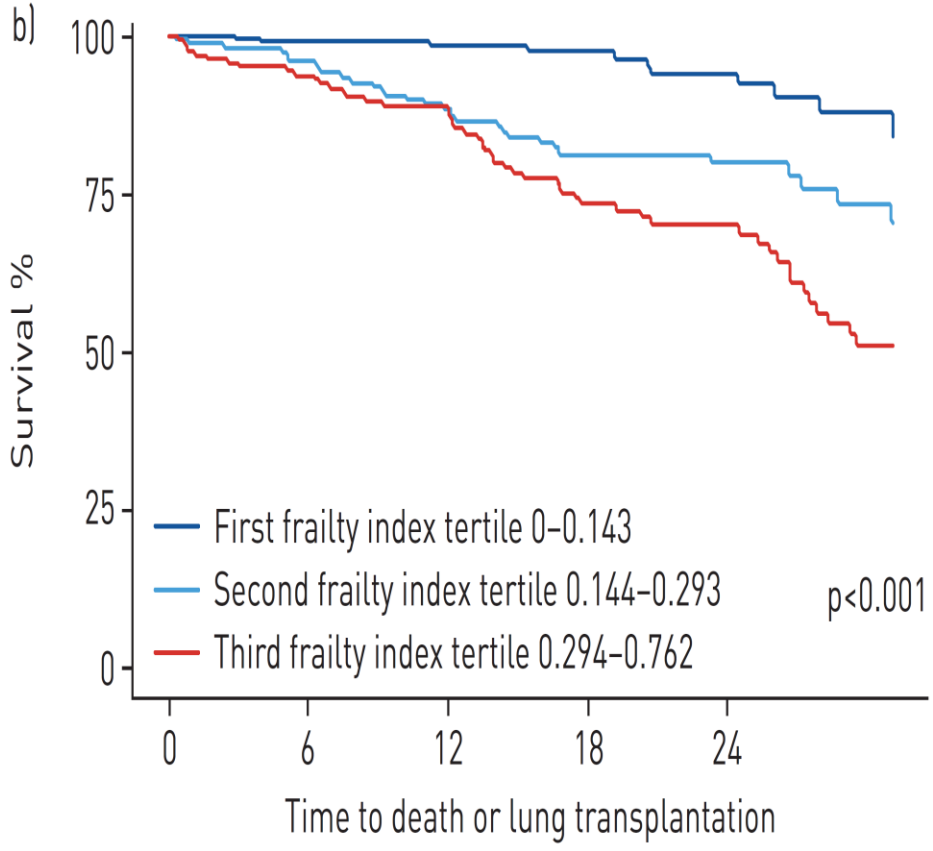
- Adverse health outcomes

→ SGRQ, hospitalisation, medication tolerability, time to death, lung transplantation

Gular SA et al. ERJ 2020; 55: 1900647

Functional ageing in fibrotic ILD : Impact of frailty on adverse health outcomes





Gular SA et al. ERJ 2020; 55: 1900647

Conclusions

Functional ageing

→ associated with adverse health outcomes in patients with fibrotic ILD, indicating the need for consideration of the individual functional age into clinical decision-making

Gular SA et al. ERJ 2020; 55: 1900647

Associations of Serum Adipokines with Subclinical ILD : Multi-Ethnic Study of Atherosclerosis (MESA)

- Adipokines → adiponectin, leptin, and resistin,
- Adiponectin

→ Inhibits the proinflammatory NF-kB

→ Increases the anti-inflammatory cytokine IL-10

- Leptin and resistin

→ Proinflammatory

→ Increases production of IL-1b, and stimulate monocyte and CD4 T-lymphocyte proliferation.

Kim S, CHEST 2020; 157(3):580-589

Associations of Serum Adipokines with Subclinical ILD : Multi-Ethnic Study of Atherosclerosis (MESA)

- A subset of MESA (n = 1,968)
- Measurements during follow-up visits (2002-2005)

→ adiponectin, leptin, and resistin

→ CT measures (markers of subclinical ILD)

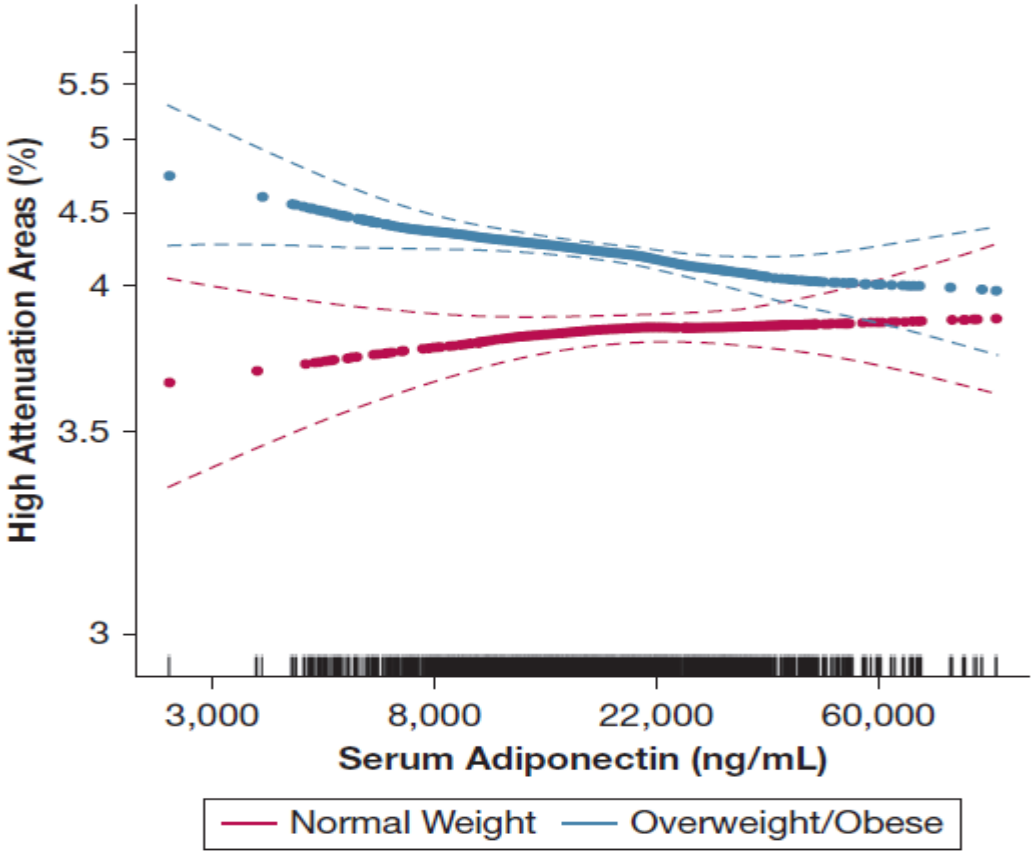
high-attenuation areas (HAAs)

interstitial lung abnormalities (ILAs)

→ FVC

Kim S, CHEST 2020; 157(3):580-589

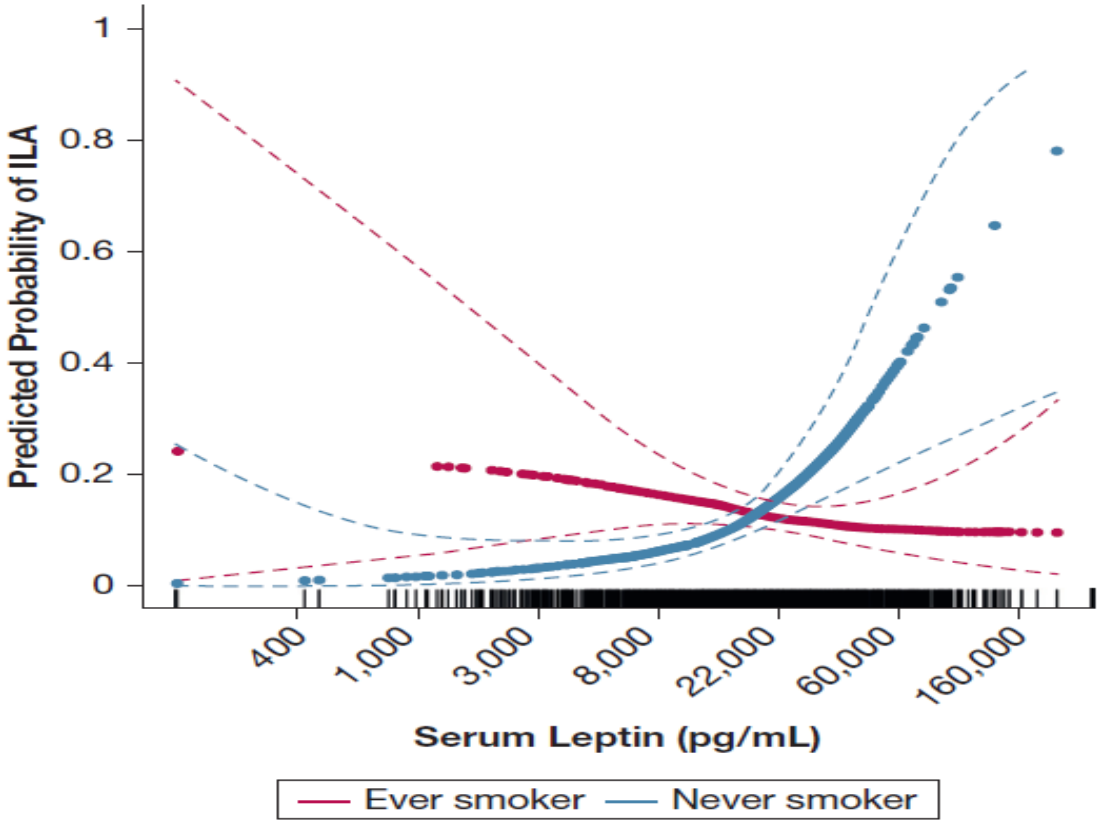
Associations of Serum Adipokines with Subclinical ILD : Multi-Ethnic Study of Atherosclerosis (MESA)



Higher adiponectin : associated with lower HAA among adults with a BMI ≥ 25 kg/m^2

Kim S, CHEST 2020; 157(3):580-589

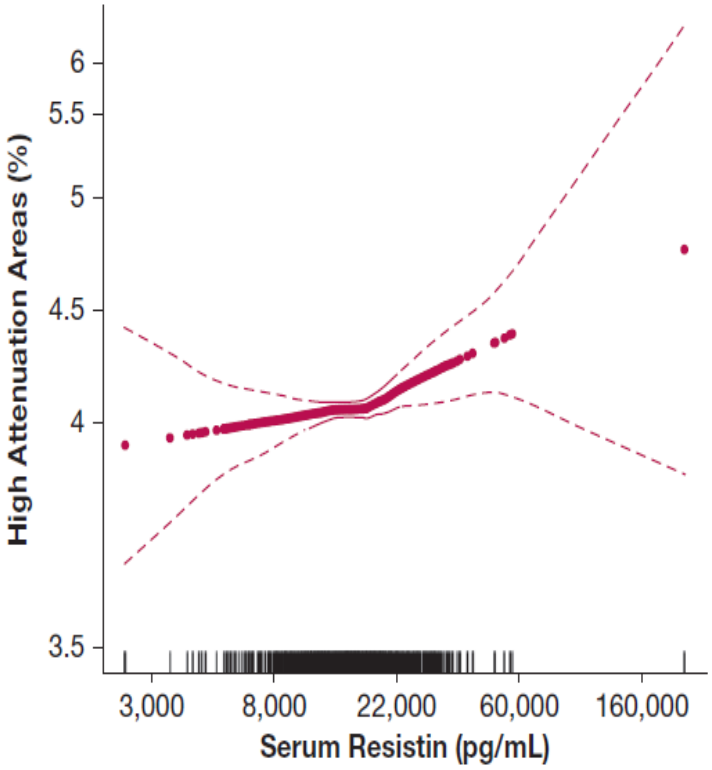
Associations of Serum Adipokines with Subclinical ILD : Multi-Ethnic Study of Atherosclerosis (MESA)

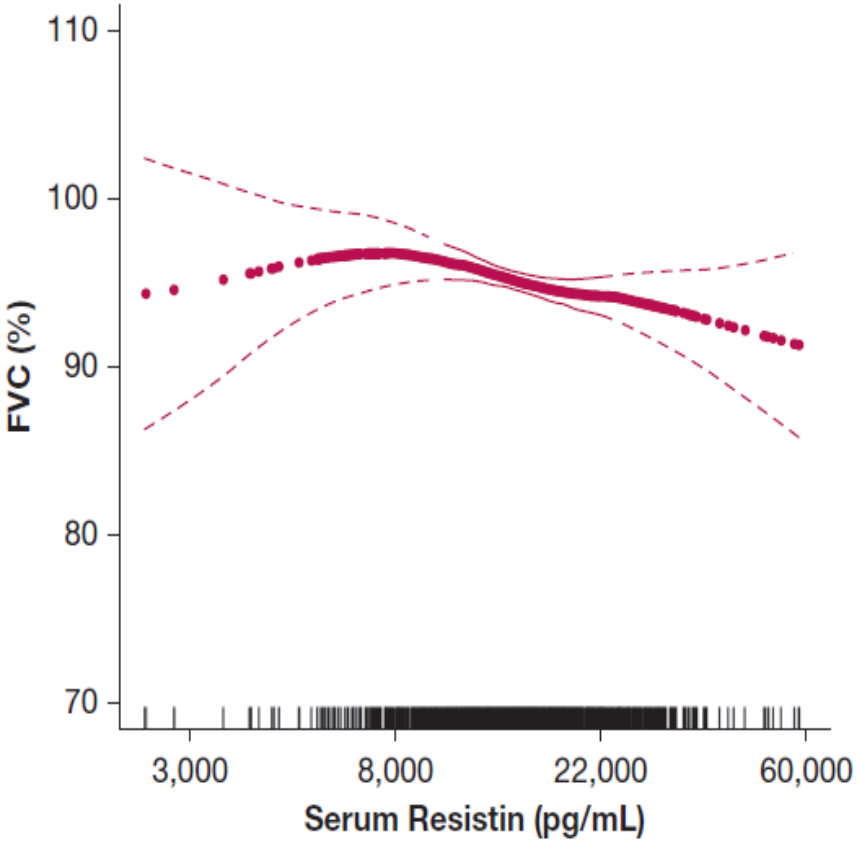


Leptin : more strongly associated
with ILA among never smokers p =0.004

Kim S, CHEST 2020; 157(3):580-589

Associations of Serum Adipokines with Subclinical ILD : Multi-Ethnic Study of Atherosclerosis (MESA)

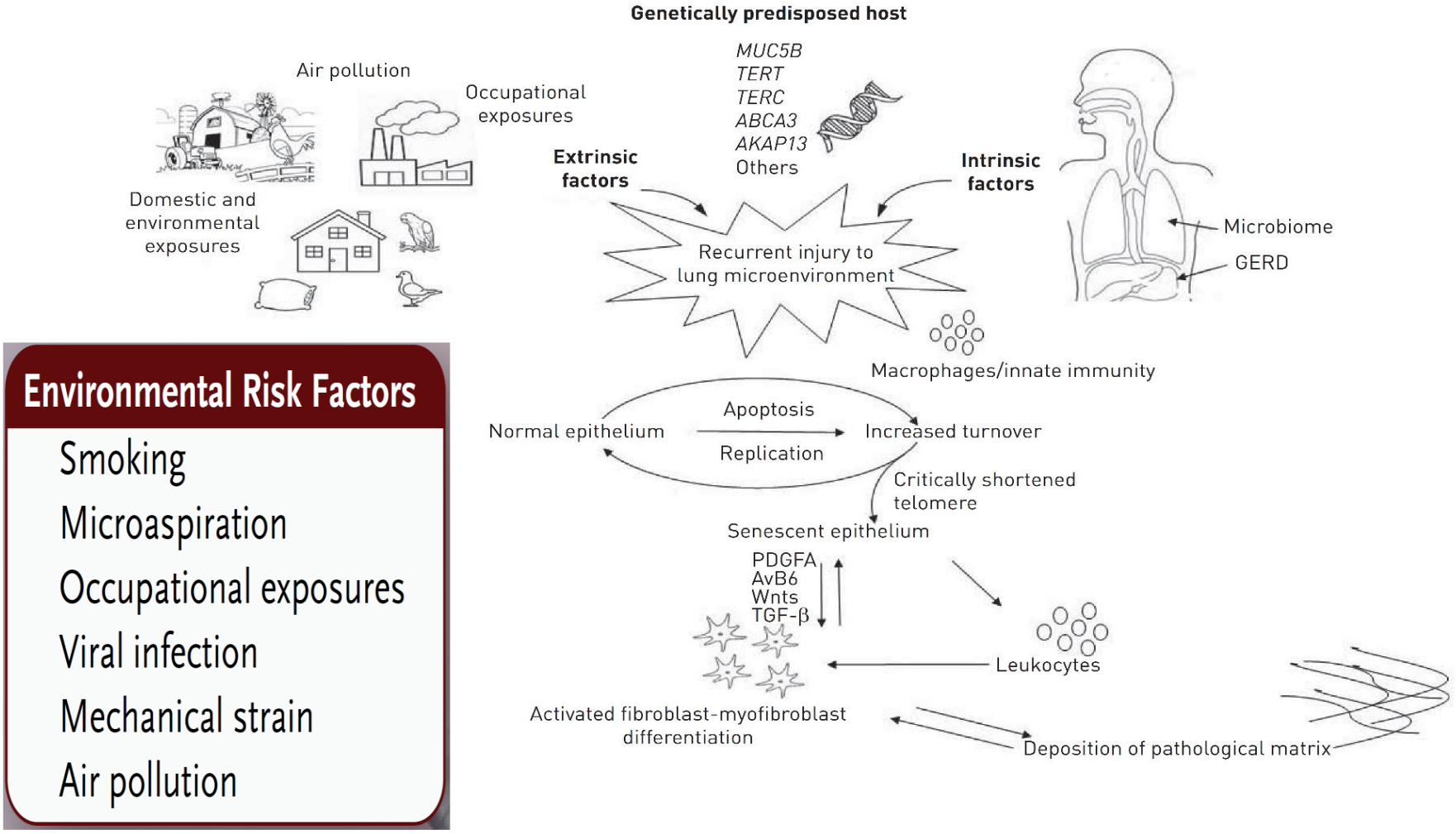




Higher serum resistin levels : associated with greater HAA

Kim S, CHEST 2020; 157(3):580-589

Etiology



Sack C et al. ERJ 2019; 53 : 1801699

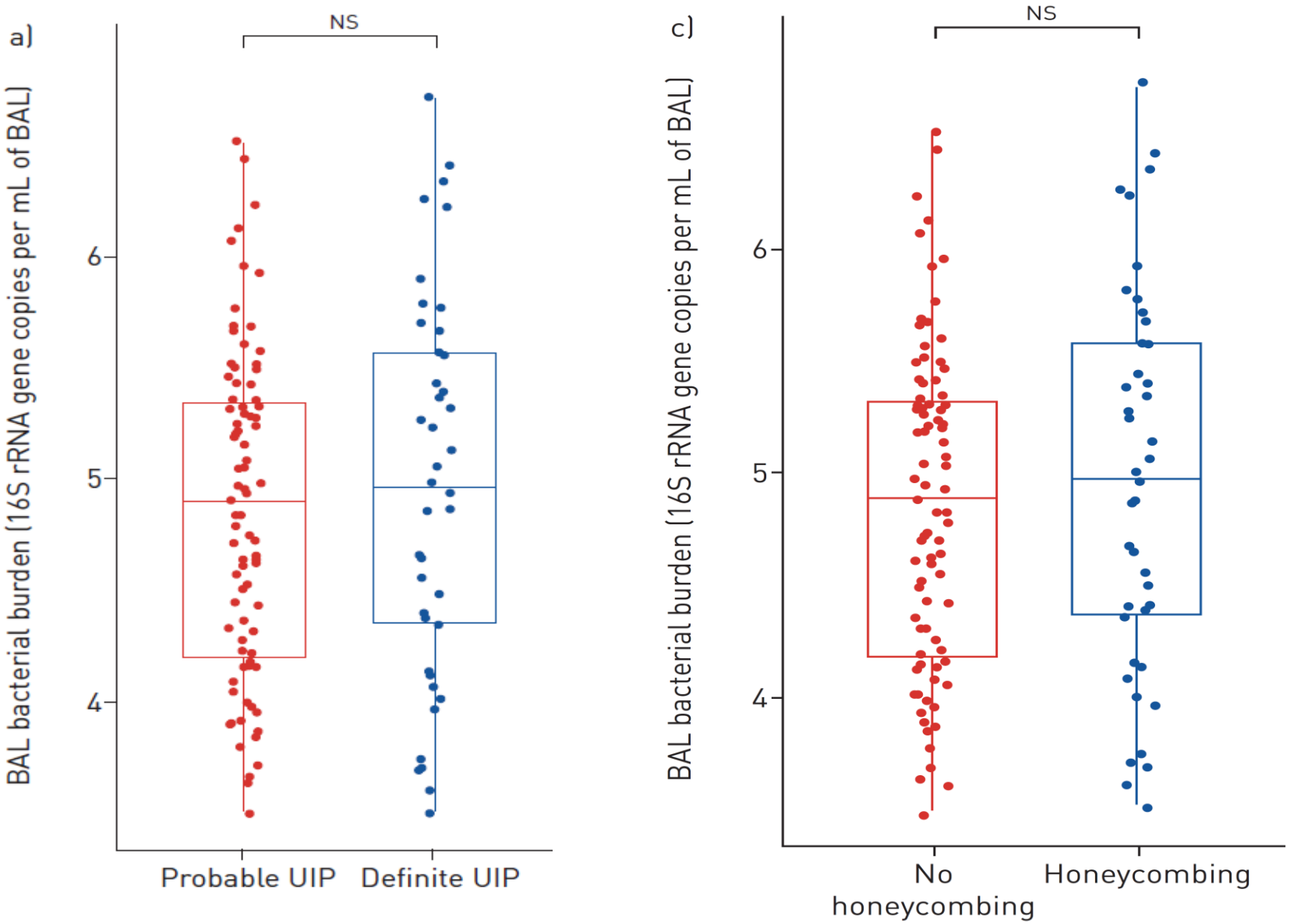
Bacterial burden in the lower airways predicts disease progression in IFP independent of radiological extent

- 193 IPF patients
- Bacterial DNA extraction in BAL

  → 16S rRNA gene quantitative PCR
- CT quantitative scores

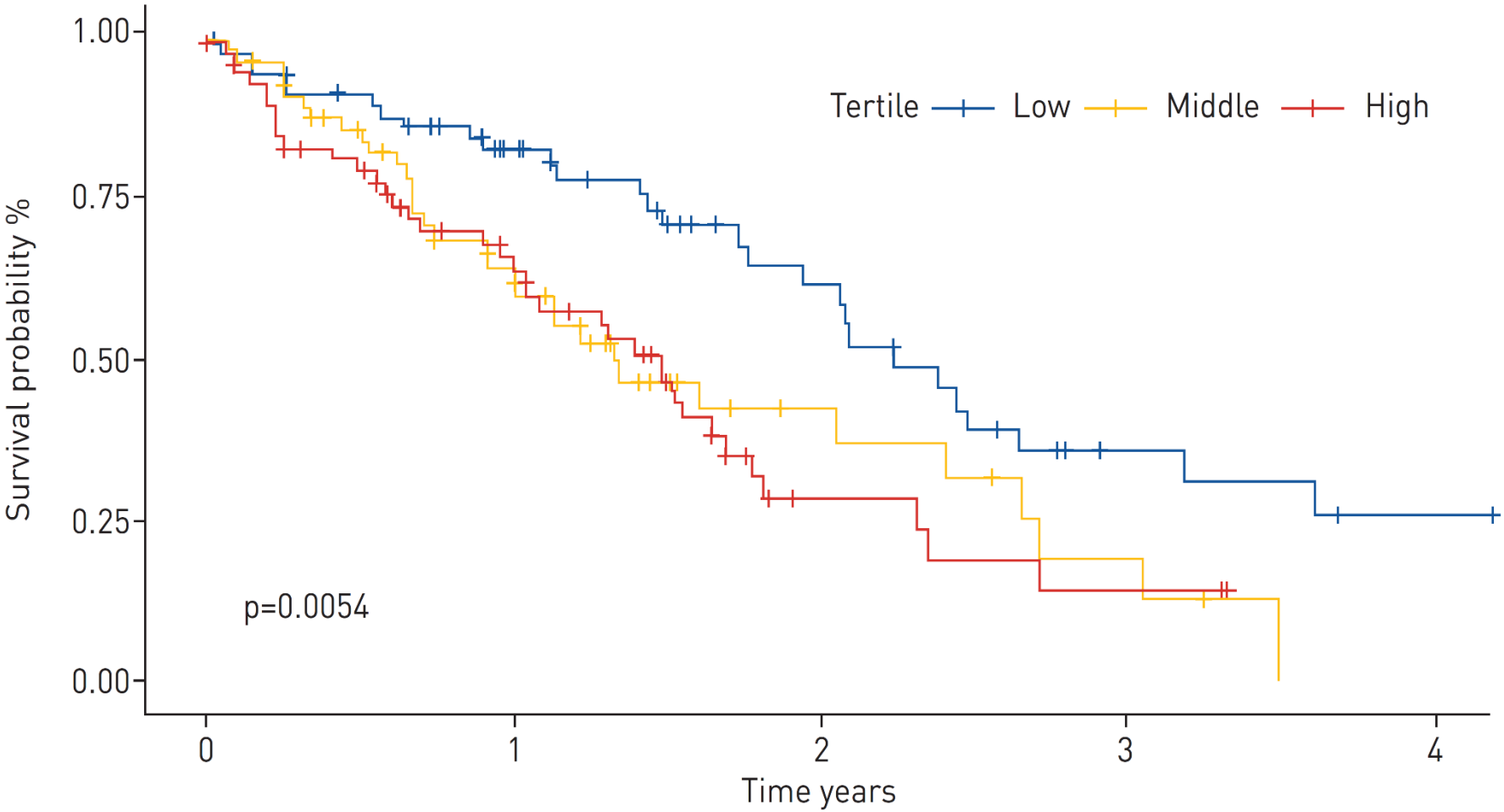
  → extent, severity and topography of radiographic changes
- Relationship of radiologic features with bacterial burden

Invernizzi R et al . ERJ 2020; 55: 1901519



Invernizzi R et al . ERJ 2020; 55: 1901519

Bacterial burden in the lower airways predicts disease progression in IFP independent of radiological extent



Invernizzi R et al . ERJ 2020; 55: 1901519

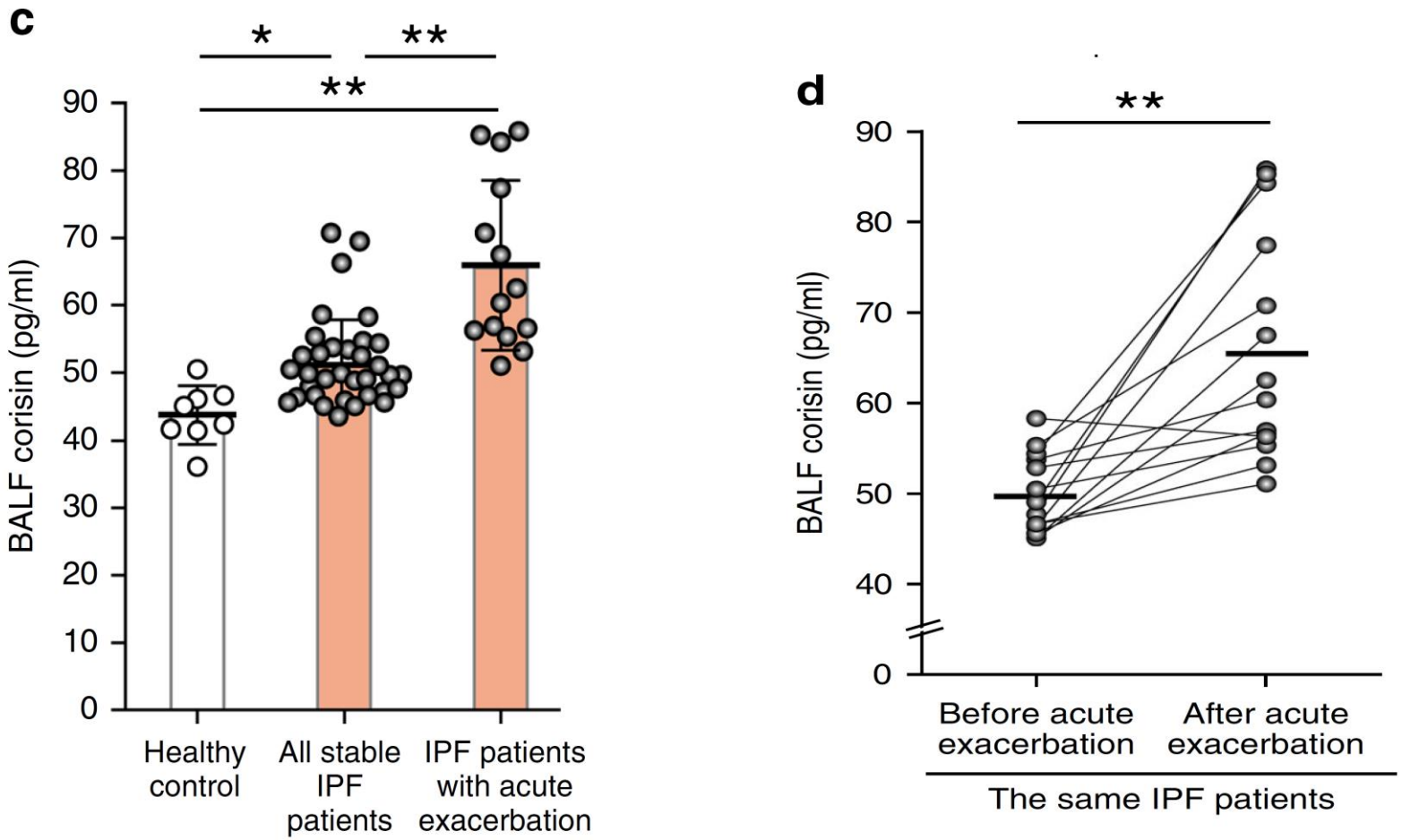
- Bacterial burden

→ independent predictor of survival even when incorporating radiographic features

→ Predictive of disease progression (HR 1.16; 95% CI 1.01–1.35; p=0.04)

Invernizzi R et al . ERJ 2020; 55: 1901519

A Staphylococcus pro-apoptotic peptide induces acute exacerbation of pulmonary fibrosis



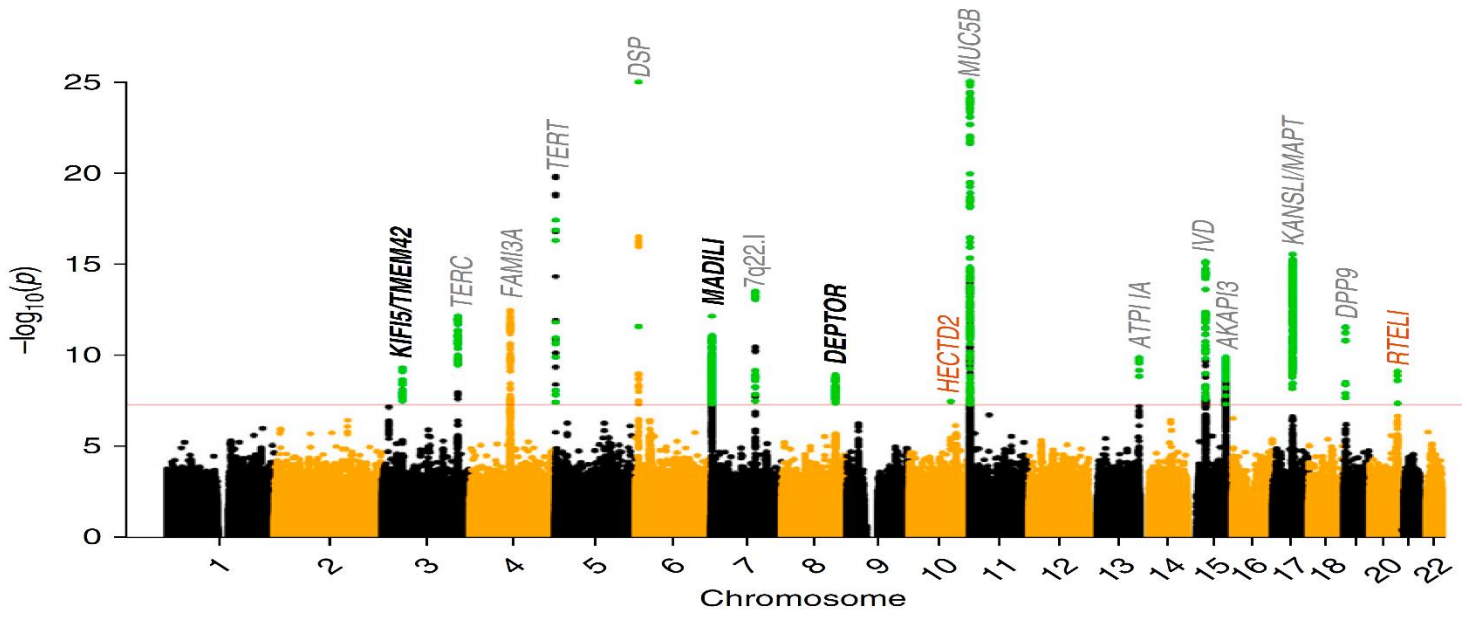
NATURE COMMUNICATIONS | (2020)11:1539

Genome-Wide Association Study of Susceptibility to IPF

- GWAS (2,668 IPF cases and 8,591 controls) across three independent studies and meta-analysis (Chicago, Colorado, and UK studies)
- Replication in two independent studies (1,456 IPF cases and 11,874 controls)

Allen R et al AJRCCM 2020; 55: 1901519

- KIF15, MAD1L1, and DEPTOR
- Decreased DEPTOR expression : increased susceptibility to mTOR signaling in lung fibrosis
- KIF15 and MAD1L1 : a possible role of mitotic spindle-assembly genes in IPF susceptibility



Allen R et al AJRCCM 2020; 55: 1901519

Occupational and environmental risk factors for IPF: a multicenter case-control study.

248 cases and 491 controls, aged 20-75 years, diagnosed at 16 referral centers between January 1989 and July 1993.

Occupational/ environmental exposure	OR*†	95% CI*	OR‡	95% CI
Cigarette smoking	1.6	1.1 - 2.4	1.8	1.2 - 2.7
Hairdressing§	4.4	1.2 - 16.3	4.8	1.2 - 19.0
Raising birds§	4.7	1.6 - 14.1`	4.1	1.3 - 13.4
Stone cutting/polishing§	3.9	1.2 - 12.7	3.2	1.0 - 10.8
Metal dust¶	2.0	1.0 - 4.0	2.0	1.0 - 4.0
Talc¶	2.8	0.7 - 11.2	3.3	0.8 - 13.3
Livestock#	2.7	1.3 - 5.5	2.2	1.0 - 4.7

†Adjusted for age (continuous) and cigarette smoking.
‡Adjusted for age and all other variables listed in table.

Baumgartner KB. Am J Epidemiol 2000 Aug 15;152(4):307-15.

Occupational risk factors for IPF in Southern Europe: a case-control study

- 69 cases with a UIP radiological pattern from a clinical database of the University Hospital of Perugia in Italy
- Controls (n = 277) among general population from the same catching area of cases
- January 2010 and December 2013

Paolocci et al BMC pulm med 2018; 18: 75

Occupational risk factors for IPF in Southern Europe: a case-control study

- Occupations associated with UIP.

→ Farmers, veterinarians and gardeners
(OR = 2.73, 95%CI = 1.47 – 5.10)

→ Metallurgical and steel industry workers
(OR = 4.80, 95%CI = 1.50 – 15.33)

- Increasing the length of occupational exposure in jobs at risk of pulmonary fibrosis, increased the risk of UIP.

Paolocci et al BMC pulm med 2018; 18: 75

Summary

Summary

- Anti-fibrotics are tried for progressive fibrosing ILD and systemic sclerosis associated ILD.
- Potential biomarkers for ILD

→ Imaging patterns (Interstitial Lung Abnormality)

→ Serum adipokines

→ Telomere length

- Etiologic studies

→ Bacterial burden in the lower airways

→ GWAS

→ Occupational risk factors